CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 040028

Name: Kionex Suspension (Sodium Polystyrene Sulfonate Suspension USP)
15 g/60 mL

Sponsor: Paddock Laboratories, Inc.

Approval Date: September 17, 2007

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 40-028

Paddock Laboratories, Inc.
Attention: Todd M. Delehant, Ph.D.
Regulatory Affairs Manager
3940 Quebec Avenue, North
Minneapolis, MN 55427

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated August 27, 1991, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Kionex Suspension (Sodium Polystyrene Sulfonate Suspension USP), 15 g/60 mL.

Reference is also made to your amendments dated September 20, 2004; and September 13, 2007.

We have completed the review of this ANDA and have concluded that adequate information has been presented to determine 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 Division of Bioequivalence has determined your Kionex Suspension (Sodium Polystyrene Sulfonate Suspension USP), 15 g/60 mL, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, SPS Suspension, 15 g/60 mL, of Carolina Medical Products Company.

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

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 directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
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
9/17/2007 11:09:14 AM
for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

LABELING

2124136

Kionex™

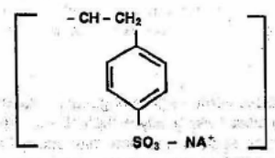
Sodium Polystyrene
Sulfonate Suspension, USP
Rx only

CATION-EXCHANGE RESIN

DESCRIPTION

Kionex™ (Sodium Polystyrene Sulfonate Suspension USP) can be administered orally or in an enema. It is a raspberry-flavored suspension containing 15 grams of cation-exchange resin (Sodium Polystyrene Sulfonate, USP); 21.5 mL of Sorbitol Solution USP (equivalent to approximately 19.3 grams of Sorbitol); 0.12 mL (0.2%) of Alcohol per 60 mL of suspension. Also contains Purified Water USP, Propylene Glycol USP, Magnesium Aluminum Silicate NF, Xanthan Gum NF, Sodium Saccharin USP, Sorbic Acid NF, Methylparaben NF, Propylparaben NF, and Flavor.

Sodium polystyrene sulfonate is a benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt and has the following structural formula:



The sodium content of the suspension is 1500 mg (65 mEq) per 60 mL. It is a brown, slightly viscous suspension with an *in vitro* exchange capacity of approximately 3.1 mEq (*in vivo* approximately 1 mEq) of potassium per 4 mL (1 gram) of suspension.

CLINICAL PHARMACOLOGY

As the resin passes along the intestine or is retained in the colon after administration by enema, the sodium ions are partially released and are replaced by potassium ions. For the most part, this action occurs in the large intestine, which excretes potassium ions to a greater degree than does the small intestine. The efficiency of this process is limited and unpredictably variable. It commonly approximates the order of 33%, but the range is so large that definitive indices of electrolyte balance must be clearly monitored.

Metabolic data are unavailable.

INDICATIONS AND USAGE

Kionex Suspension is indicated for the treatment of hyperkalemia.

CONTRAINDICATIONS

Kionex Suspension is contraindicated in patients with hypokalemia or those patients who are hypersensitive to it.

WARNINGS

Alternative Therapy in Severe Hyperkalemia: Since the effective lowering of serum potassium with sodium polystyrene sulfonate may take hours to days, treatment with this drug alone may be insufficient to rapidly correct severe hyperkalemia associated with states of rapid tissue breakdown (e.g., burns and renal failure) or hyperkalemia so marked as to constitute a medical emergency. Therefore, other definitive measures, including dialysis, should always be considered and may be imperative.

Hypokalemia: Serious potassium deficiency can occur from sodium polystyrene sulfonate therapy. The effect must be carefully controlled by frequent serum potassium determinations within each 24 hour period. Since intracellular potassium deficiency is not always reflected by serum potassium levels, the level at which treatment with sodium polystyrene sulfonate should be discontinued must be determined individually for each patient. Important aids in making this determination are the patient's clinical condition and electrocardiogram. Early clinical signs of severe hypokalemia include a pattern of irritable confusion and delayed thought processes. Electrocardiographically, severe hypokalemia is often associated with a lengthened Q-T interval, widening, flattening, or inversion of the T wave, and prominent U waves. Also, cardiac arrhythmias may occur, such as premature atrial, nodal, and ventricular contractions, and supraventricular and ventricular tachycardias. The toxic effects of digitalis are likely to be exaggerated. Marked hypokalemia can also be manifested by severe muscle weakness, at times extending into frank paralysis.

Electrolyte Disturbances: Like all cation-exchange resins, sodium polystyrene sulfonate is not totally selective (for potassium) in its actions, and small amounts of other cations such as magnesium and calcium can also be lost during treatment. Accordingly, patients receiving sodium polystyrene sulfonate should be monitored for all applicable electrolyte disturbances.

Systemic Alkalosis: Systemic alkalosis has been reported after cation-exchange resins were administered orally in combination with nonabsorbable cation-donating antacids and laxatives such as magnesium hydroxide and aluminum carbonate. Magnesium hydroxide should not be administered with sodium polystyrene sulfonate. One case of grand mal seizure has been reported in a patient with chronic hypocalcemia of renal failure who was given sodium polystyrene sulfonate with magnesium hydroxide as a laxative. (See PRECAUTIONS, Drug Interactions).

PRECAUTIONS

Caution is advised when sodium polystyrene sulfonate is administered to patients who cannot tolerate even a small increase in sodium loads (i.e., severe congestive heart failure, severe hypertension, or marked edema). In such instances, compensatory restriction of sodium intake from other sources may be indicated.

If constipation occurs, patients should be treated with sorbitol (from 10 to 20 mL of 70 percent syrup every 2 hours or as needed to produce 1 or 2 watery stools daily), a measure which also reduces any tendency to fecal impaction.

Drug Interactions

Antacids: The simultaneous oral administration of sodium polystyrene sulfonate with nonabsorbable cation-donating antacids and laxatives may reduce the resin's potassium exchange capability.

Systemic alkalosis has been reported after cation exchange resins were administered orally in combination with nonabsorbable cation-donating antacids and laxatives such as magnesium hydroxide and aluminum carbonate. Magnesium hydroxide should not be administered with sodium polystyrene sulfonate. One case of grand mal seizure has been reported in a patient with chronic hypocalcemia of renal failure who was given sodium polystyrene sulfonate with magnesium hydroxide as a laxative.

Intestinal obstruction due to concretions of aluminum hydroxide when used in combination with sodium polystyrene sulfonate has been reported.

Digitalis: The toxic effects of digitalis on the heart, especially various ventricular arrhythmias and A-V nodal dissociation, are likely to be exaggerated by hypokalemia, even in the face of serum digoxin concentrations in the "normal range" (See WARNINGS).

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Studies have not been performed.

Pregnancy Category C:

Animal reproduction studies have not been conducted with sodium polystyrene sulfonate. It is also not known whether sodium polystyrene sulfonate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Sodium polystyrene sulfonate should be given to a pregnant woman only if clearly needed.

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 polystyrene sulfonate is administered to a nursing woman.

ADVERSE REACTIONS

Kionex Suspension may cause some degree of gastric irritation. Anorexia, nausea, vomiting, and constipation may occur especially if high doses are given. Also, hypokalemia, hypocalcemia, and significant sodium retention may occur. Occasionally diarrhea develops. Large doses in elderly individuals may cause fecal impaction (See PRECAUTIONS). This effect may be obviated through usage of the resin in enemas as described under DOSAGE AND ADMINISTRATION. Rare instances of colonic necrosis have been reported. Intestinal obstruction due to concretions of aluminum hydroxide, when used in combination with sodium polystyrene sulfonate, has been reported.

DOSAGE AND ADMINISTRATION

The average daily adult dose is 15 g (60 mL) to 60 g (240 mL) of suspension. This is best provided by administering 15 g (60 mL) of Kionex Suspension one to four times daily. Each 60 mL of Kionex Suspension contains 1500 mg (65 mEq) of sodium. Since the *in vivo* efficiency of sodium-potassium exchange resins is approximately 33%, about one-third of the resin's actual sodium content is being delivered to the body.

In smaller children and infants, lower doses should be employed by using as a guide a rate of 1 mEq of potassium per gram of resin as the basis for calculation.

Kionex Suspension may be introduced into the stomach through a plastic tube and, if desired, given with a diet appropriate for a patient in renal failure.

Kionex Suspension may also be given, although with less effective results, as an enema consisting (for adults) of 30 g (120 mL) to 50 g (200 mL) every six hours. The enema should be retained as long as possible and followed by a cleansing enema.

After an initial cleansing enema, a soft, large size (French 28) rubber tube is inserted into the rectum for a distance of about 20 cm, with the tip well into the sigmoid colon, and taped into place. The suspension is introduced at body temperature by gravity. The suspension is flushed with 50 or 100 mL of fluid, following which the tube is clamped and left in place. If back leakage occurs, the hips are elevated on pillows or a knee-chest position is taken temporarily. The suspension is kept in the sigmoid colon for several hours, if possible. Then the colon is irrigated with nonsodium containing solution at body temperature in order to remove the resin. Two quarts of flushing solution may be necessary. The returns are drained constantly through a Y tube connection. Particular attention should be paid to this cleansing enema, because sorbitol is present in the vehicle.

The intensity and duration of therapy depend upon the severity and resistance of hyperkalemia.

HOW SUPPLIED

Kionex Suspension is a light brown, raspberry-flavored suspension supplied as follows:

Kionex™ Suspension (Sodium Polystyrene Sulfonate Suspension, USP)

480 mL (16 Fluid Ounce)	NDC	0574-2002-16
Unit-Dose 60 mL (2 Fluid Ounce)	NDC	0574-2002-02

SHAKE WELL BEFORE USING.

Store at Controlled Room temperature 15°- 30° C (59°- 86°F)

Kionex Suspension should not be heated for to do so may alter the exchange properties of the resin.

Dispense in a tight container, as defined in the USP.

If repackaging into other containers, store in refrigerator and use within 14 days of packaging.

Paddock Laboratories, Inc.

Manufactured by:
Paddock Laboratories, Inc.
Minneapolis, MN 55427

2124136 (12-02)

Kionex™

Sodium Polystyrene
Sulfonate Suspension, USP
Rx only

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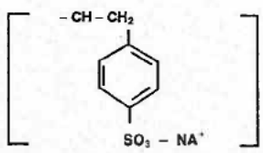

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HOW SUPPLIED

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Kionex™ Suspension (Sodium Polystyrene Sulfonate Suspension, USP)

480 mL (16 Fluid Ounce)	NDC	0574-2002-16
Unit-Dose 60 mL (2 Fluid Ounce)	NDC	0574-2002-02

SHAKE WELL BEFORE USING.
Store at Controlled Room temperature 15°- 30° C (59°- 86°F)

Kionex Suspension should not be heated for to do so may alter the exchange properties of the resin.

Dispense in a tight container, as defined in the USP.

If repackaging into other containers, store in refrigerator and use within 14 days of packaging.

Manufactured by:
Paddock Laboratories, Inc.
Minneapolis, MN 55427

Paddock Laboratories, Inc.

2122618 (01-03)

NDC 0574-2002-16

Kionex™
SODIUM POLYSTYRENE SULFONATE SUSPENSION USP
15 g/60 mL

FOR ORAL OR RECTAL USE

Rx only

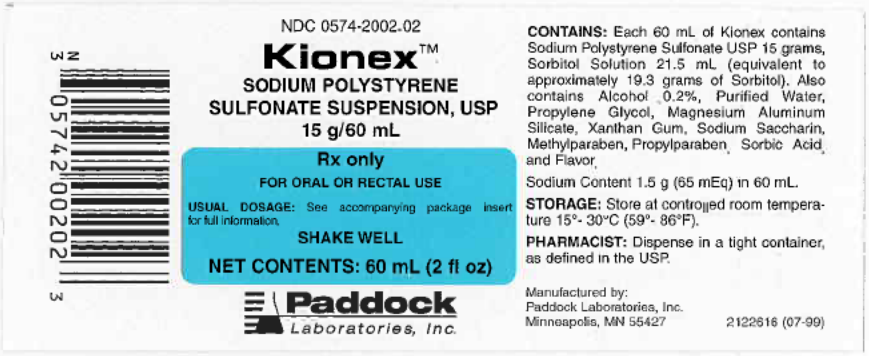
CONTAINS: Each 60 mL of Kionex contains Sodium Polystyrene Sulfonate USP 15 grams, Sorbitol Solution 21.5 mL (equivalent to approximately 19.3 grams of Sorbitol). Also contains Alcohol 0.2%, Purified Water, Propylene Glycol, Magnesium Aluminum Silicate, Xanthan Gum, Sodium Saccharin, Methylparaben, Propylparaben, Sorbic Acid and Flavor. Sodium Content 1.5 g (65 mEq) in 60 mL.

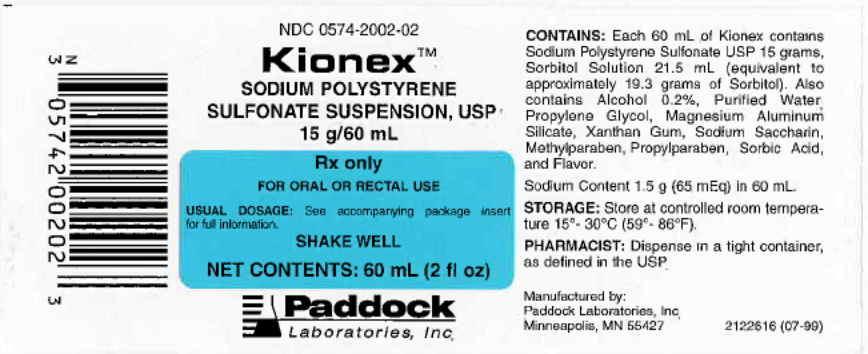
SHAKE WELL

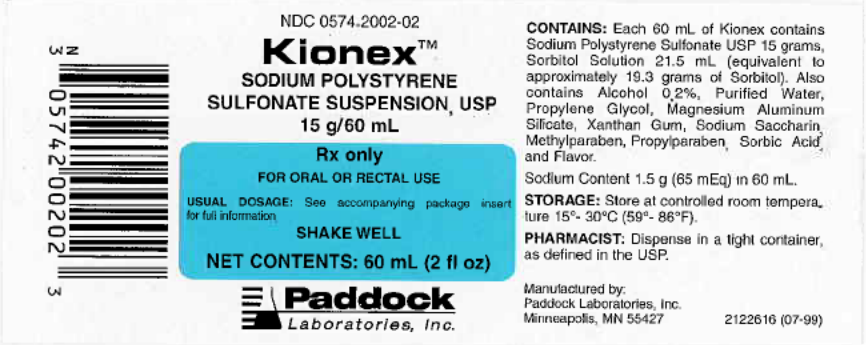
NET CONTENTS: 480 mL (One Pint)

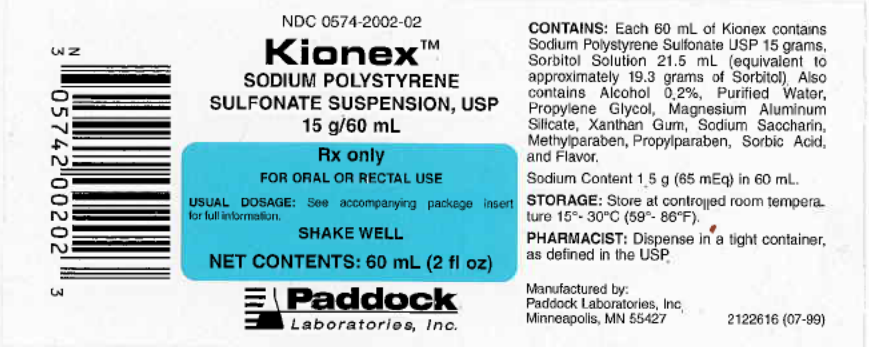
Paddock Laboratories, Inc.

Final printed Label for 60 mL (2 oz.) product:









CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING

ANDA

DRAFT

DATE OF REVIEW: March 6, 1992

ANDA #: 40-028

NAME OF FIRM: Paddock Laboratories

NAME OF DRUG: Trade: [redacted] (b)(4)
Generic: Sodium Polystyrene Sulfonate Suspension USP

DATE OF SUBMISSION: August 27, 1991

COMMENTS:

A. Container: Not Satisfactory

1. Delete the colon after "NDC".

2. We find your proposed proprietary name [redacted] (b)(4) unacceptable because it implies that the product [redacted] (b)(4). In accord with 21 CFR 201.10(c) we consider this misleading. Please delete or propose another proprietary name.

3. Revise the expression of net contents of the pint bottle in milliliters (i.e., 16 fl oz (____ mL)

4. Revise your "contains" statement to read:

   Each 60 mL contains:

   Sodium Polystyrene Sulfonate USP 15 grams, Sorbitol Solution USP 19.3 grams. Also contains.....

   NOTE TO FIRM: Please include the sodium content per 60 mL in grams and mEq.

5. The quantitative amount of active ingredient (15 g/60 mL) should be expressed beneath the established name. In addition, please note that the statement "FOR ORAL OR RECTAL USE" should appear beneath the quantitative amount on both package sizes.

6. You have failed to list alcohol as an ingredient on your 60 mL label. Please include.

B. Insert: Not Satisfactory

Please revise your insert labeling to be in accord with the approved labeling of SPS® Suspension (Carolina Medical Products Co; Approved December 12, 1991; Revised July 1991).

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Request the firm revise their container labels and package insert labeling, then prepare and submit a draft copy for our review and comment.

3. Note to Chemist:

   A. This firm has proposed [redacted] (b)(4) [redacted] (b)(4). Carolina Medical says that if repackaging into other containers, it should be stored in refrigerator and used within 14 days of packaging.

   B. Please verify the accuracy of the stated quantitative (19.3 grams) amount of sorbitol and the percent [redacted] (b)(4) of [redacted] (b)(4) alcohol in the preparation.

Terry Phillips 3/11/92
J.Phillips

cc;
HFD-638
JPhillips/TPoux
hab 3/9/92
40028REV
review
3/11/92

REVIEW OF PROFESSIONAL LABELING # 2

Original Amendment - MAJOR

DRAFT

DATE OF REVIEW: March 11, 1994

ANDA #: 40-028

NAME OF FIRM: Paddock

NAME OF DRUG: Sodium Polystyrene Sulfonate Suspension USP

DATE OF SUBMISSION: October 5, 1993

COMMENTS:

GENERAL COMMENTS

1. You list [redacted] (b)(4) and not sorbic acid as an inactive ingredient in your labels and labeling. This is inconsistent with your composition statement. Please revise your labels and labeling accordingly, and/or comment.

2. Throughout your insert labeling, please revise the "(tm)" to the appropriate trademark symbol: "™".

CONTAINER

1. USUAL DOSAGE [rather than "Usual Dose"]

2. Sodium content: Delete the "m" in "gm", as follows: "g"

3. Dispense in a tight container, as defined in the USP. [not "described"]

INSERT

1. TITLE

   See General Comment 2. above.

2. BOX

   Revise the following statement so that it appears in bold face print and is surrounded by a complete box, as follows:

Cation-Exchange Resin

3. DESCRIPTION

a. Line 2: ...administered orally or rectally in an enema. It...

b. Inactive ingredients, see General Comment 1. above.

c. We refer you to 21 CFR 201.10 (g)(1) which states that the established name shall be made clear by the use of a phrase such as "brand of" or by brackets surrounding the established name. In this case, you have the proprietary name in brackets. Please revise accordingly.

4. DOSAGE AND ADMINISTRATION

Paragraph 5, line 11: ...resin. Two quarts....
[correct spelling of "two"]

5. HOW SUPPLIED

a. Include the degree symbols "°" following the "15" and the "59", as follows:

... 15°-30°C (59°-86°F)

b. "Manufactured by" statement:

Please spell "Minneapolis" [rather than "Mpls"]

c. Include the following:

If repackaging into other containers, store in refrigerator and use within 14 days of packaging.

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Please revise your container labels and package insert labeling, and submit final printed (12) labels and labeling. Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

3. FOR THE RECORD

i) This review was based upon the labeling of SPS® (Carolina Medical Products Co; Revised: July 1991; Approved: December 12, 1991).

ii) *Storage*

NDA: CRT 15°-30°C (59°-86°F)
ANDA: CRT 15°-30°C (59°-86°F)

iii) *Container* Firm is using white HDPE containers with non-CRC for both package sizes.

iv) *Dispensing*

NDA: tight
ANDA: tight
USP: well-closed

v) *Note to the Chemist*:

Please see the General Comment 1. above. Please confirm inactive ingredients.

Cathy Shannon
3-14-94

cc:
ANDA 40-028
HFD-613/CShannon/JPhillips (no cc)
jp 3/12/94; 40028.mar
Review
Final

JPhillips 3/12/94

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

ANDA Number:	40-028
Date of Submission:	February 26, 2001
Applicant's Name:	Paddock Laboratories, Inc.
Established Name:	Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL
Proprietary Name:	Kionex™

Labeling Deficiencies:

1. **CONTAINER** – 60 mL, (b) (4) and 240 mL
   Satisfactory in **draft** as of the February 26, 2001 submission.

2. (b) (4)

3. **PACKAGE INSERT**
   See the attached mocked-up copy of package insert labeling for requested revisions.

Please revise your labels and labeling, as instructed above, and submit in final print or draft if you prefer.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Enclosed: A copy of mocked-up package insert labeling

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	X		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection. **Kionex®**	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? Note that this company already has a generic version of sodium polystyrene sulfonate being marketed as **Kionex® (powder form). Therefore, we did NOT submit this same name to OPDRA for the same drug product ONLY in a suspension form.**		X	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. (b) (4) [redacted]		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.

Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?			
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?			
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for the reference listed drug (SPS® – Sodium Polystyrene Sulfonate; Manufactured by Carolina Med; ANDA 87-859/SL 013 approved December 12, 1991). (b) (4)

2. **Patent/ Exclusivities:**

Patent Data – ANDA 87-859

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 87-859

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

3. Storage/Dispensing Conditions:
   NDA: Store at controlled room temperature 15 to 30°C (59 to 86°F).
   ANDA: Store at controlled room temperature 15 to 30°C (59 to 86°F)
   USP: None
   NDA: Dispense in a tight container, as defined in USP.
   ANDA: Dispense in a tight container, as defined in USP.
   USP: Preserve in well-closed containers, protected from freezing and excessive heat.

4. Product Line:
   The innovator markets their product in 60 mL, 120 mL and 473 mL bottles for **rectal and oral use.**
   The applicant proposes to market their product 60 mL and 480 mL bottles for **rectal and oral use** (b) (4)
   (b) (4)

5. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page** 183, Vol A. 3.1.

6. All manufacturing will be done by Paddock Laboratories, Inc. (See pg. 289 in vol. A. 3.1)

Date of Review: 6/6/01 Date of Submission: 4/25/01
Primary Reviewer: Jim Barlow Date: 9/13/01

Team Leader: John Grace Date: 9/14/2001

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cc:
ANDA: 40-028
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
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Review

4.1
CKO BARLOW,

APPROVAL SUMMARY

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

ANDA Number: 40-028
Date of Submission: July 14, 2003
Applicant's Name: Paddock Laboratories, Inc.
Established Name: Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL
Proprietary Name: Kionex™

APPROVAL SUMMARY

1. **Do you have 12 Final Printed Labels and Labeling? Yes**

2. **CONTAINER** – 60 mL and 240 mL
   Satisfactory in **final print** as of the July 14, 2003 submission.
   (See blue jacket volume 4.1)

3. **PACKAGE INSERT**
   Satisfactory in **final print** as of the July 14, 2003 submission.
   (See blue jacket volume 4.1)

4. Revisions needed post-approval; None

5. **Patent/ Exclusivities**
   Patent Data – ANDA 87-859

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 87-859

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: SPS® – Sodium Polystyrene Sulfonate
NDA Number: N 87-859
NDA Drug Name: SPS® – Sodium Polystyrene Sulfonate; Manufactured by Carolina Med; ANDA 87-859/SL 013 approved December 12, 1991
NDA Firm: Manufactured by Carolina Med
Date of Approval of NDA Insert and supplement: ANDA 87-859/SL 013 approved December 12, 1991
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 Labels: Most recently approved labeling of the reference listed drug, and SPS®.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	

Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	X		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection. Kionex®	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? Note that this company already has a generic version of sodium polystyrene sulfonate being marketed as Kionex® (powder form). Therefore, we did NOT submit this same name to DMETS for the same drug product ONLY in a suspension form.		X	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. (b) (4)		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X

Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?			
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?			
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for the reference listed drug (SPS® – Sodium Polystyrene Sulfonate; Manufactured by Carolina Med; ANDA 87-859/SL 013 approved December 12, 1991).

(b) (4)

2. Patent/ Exclusivities:
Patent Data – ANDA 87-859

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None	There are no unexpired patents for this	N/A	None

			product in the Orange Book Database.		

Exclusivity Data– NDA 87-859

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

3. Storage/Dispensing Conditions:
   NDA: Store at controlled room temperature 15 to 30°C (59 to 86°F).
   ANDA: Store at controlled room temperature 15 to 30°C (59 to 86°F)
   USP: None
   NDA: Dispense in a tight container, as defined in USP.
   ANDA: Dispense in a tight container, as defined in USP.
   USP: Preserve in well-closed containers, protected from freezing and excessive heat.

4. Product Line:
   The innovator markets their product in 60 mL, 120 mL and 473 mL bottles for **rectal and oral use.**
   The applicant proposes to market their product 60 mL and 480 mL bottles for **rectal and oral use**.

(b) (4)

5. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page** 183, Vol A. 3.1.

6. All manufacturing will be done by Paddock Laboratories, Inc. (See pg. 289 in vol. A. 3.1)

Date of Review: 9/4/03 Date of Submission: 7/14/03
Primary Reviewer: Jim Barlow Date: 9/4/03

Team Leader: John Grace Date:

John J Grace 9/4/2003

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cc:
ANDA: 40-028
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
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Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

CHEMISTRY REVIEWS

CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW FOR SODIUM POLYSTYRENE SULFONATE

1. CHEMIST'S REVIEW NO. #1

2. ANDA # 40-028

3. NAME AND ADDRESS OF APPLICANT
Paddock Laboratories
Attention: Mary Beth Erstad
P.O. Box 27286
3101 Louisiana Avenue North
Minneapolis, MN 55427

4. AF NUMBER	5. SUPPLEMENT(s)	6. PROPRIETARY NAME
N/A	N/A	N/A

7. NONPROPRIETARY NAME
Sodium Polystyrene Sulfonate Suspension

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
Orig. ANDA Submitted: August 27, 1991; Rec'd: Sept. 9, 1991
Refusal to file: Submitted: October 15, 1991: Paddock Laboratories did not provide Bioequivalence protocol or study for the proposed drug product.
Orig. Amend.: Submitted: Oct. 23, 1991: Rec'd: Oct. 30, 1991

10. PHARMACOLOGICAL CATEGORY
Treatment of hyperkalemia

11. Rx or OTC
Rx

13. DOSAGE FORM	14. POTENCY
Liquid Suspension	15 gm/60 mL

15. CHEMICAL NAME AND STRUCTURE
Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

19. REVIEWER: Elise Murphy *em 4/22/92* DATE COMPLETED: March 31, 1992

cc: ANDA 40-028
Division File
HFD-633/E. Murphy/3-31-92, revisions 4-22-92
R/D initialed by R. Kishore, Ph.D./4-28-92
dvw/5-1-92/B:\40028N01.REM
F/T by dvw/5-1-92

F/T recd. 5/5/92
R. Kishore 5-6-92

Following this page, 5 pages withheld in full (b)(4)

33. ESTABLISHMENT INSPECTION
Paddock has not been cited on the March, 1992 EER establishment inspection list.

34. BIOEQUIVALENCY STATUS
A Bioequivalence waiver has been requested on the basis of therapeutic equivalence code rating of AA for Sodium Polystyrene Sulfonate Suspension, and has been granted by the Division of Bioequivalence (Moo Park 1/14/92). Satisfactory.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Paddock Laboratories is petitioning for categorical exclusion under 21 CFR 25.24 there certification does not include how they comply with state, Federal and local regulations. Unsatisfactory.

36. ORDER OF REVIEW:
The application submission(s) covered by this review was taken in the date order of receipt Yes___X___
No_____

If no, explain reason(s) below:

DMF CHECKLIST FOR ANDA/AADA # 40-028
Sodium Polystyrene Sulfonate Suspension.

DMF #	DMF SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED	COMMENTS
[redacted] (b)(4)		7			pending review
		3	unsatisf	8/2/91	DMF previously reviewed by J. Pieschocki
		4			
		4			
		7			Review pending - working on.

ACTION CODES: (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").

PAGE ____ OF ____

Elsie Murphy
Reviewer

Elsie Murphy
Signature

3/31/92
Date

CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW FOR SODIUM POLYSTYRENE SULFONATE

1. CHEMIST'S REVIEW NO. #2

2. ANDA # 40-028

3. NAME AND ADDRESS OF APPLICANT
Paddock Laboratories
Attention: Mary Beth Erstad
P.O. Box 27286
3101 Louisiana Avenue North
Minneapolis, MN 55427

4. AF NUMBER	5. SUPPLEMENT(s)	6. PROPRIETARY NAME
NA	NA	NA

7. NONPROPRIETARY NAME
Sodium Polystyrene Sulfonate Suspension

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Orig. ANDA Submitted: August 27, 1991; Rec'd: Sept. 9, 1991
Refusal to file: Submitted: October 15, 1991: Paddock Laboratories did not provide Bioequivalence protocol or study for the proposed drug product.
Orig. Amend. 1: Submitted: Oct. 23, 1991:
Orig. Amend. 2: Submitted: Oct. 5, 1993

10. PHARMACOLOGICAL CATEGORY	11. Rx or OTC
Treatment of Hyperkalemia	Rx

13. DOSAGE FORM	14. POTENCY
Liquid Suspension	15 g/60 mL

17. COMMENTS
Because Paddocks first submission was grossly deficient they were asked to amend and re-evaluate their ANDA. They have amended their application, and changed the amount of ingredients in their components and composition. Therefore I have re-reviewed the entire ANDA, and have treated it as though it were an original.

18. CONCLUSIONS AND RECOMMENDATIONS: N/A Major

19. REVIEWER: Elise Murphy DATE COMPLETED: March 9, 1994

cc: ANDA 40-028
DUP Jacket
Division File
Field Copy

Endorsements:
HFD-623/EMurphy/3-2-94 Elise Murphy 4/12/94
HFD-623/JFan for RKishore/3-20-94 J Fan for R. Kishore 4/12/94
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F/T by dvw/4/12/94

Following this page, 12 pages withheld in full (b)(4)

31. SAMPLES AND RESULTS
Polystyrene Sulfonate suspension is a USP drug product, and does not require methods validation. Therefore sampling is not applicable.

32. LABELING
Finished product Labeling is pending.

33. ESTABLISHMENT INSPECTION
A follow-up EER was submitted for Paddock Laboratories

34. BIOEQUIVALENCY STATUS
A Bioequivalence waiver has been requested on the basis of therapeutic equivalence code rating of AA for Sodium Polystyrene Sulfonate Suspension, and has been granted by the Division of Bioequivalence (Moo Park 1/14/92).

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Paddock Laboratories is petitioning for categorical exclusion under 21 CFR 25.24; and certifies that they are in compliance with all Federal, National, State, and local environmental regulations.

36. ORDER OF REVIEW:
The application submission(s) covered by this review was taken in the date order of receipt Yes___X___
No_____

If no, explain reason(s) below:

37. **DMF CHECKLIST FOR ANDA# 40-028 REVIEW #2**

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
[redacted] (b)(4)		1	Def.	3/10/94

Comments: The DMF remains deficient.

[redacted] (b)(4)	3	Sat.	9/2/92

Comments: [redacted] (b)(4) was found satisfactory by R. Adams, Ph.D

[redacted] (b)(4)

Comments:

Comments:

Comments:

Comments:

Comments:

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no relevant revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Checklist
page 01 of 01.

Elise A. Murphy
Reviewer

Elise A. Murphy
Signature

4/12/94
Date

1. CHEMIST'S REVIEW NO. #3

2. ANDA # 40-028

3. NAME AND ADDRESS OF APPLICANT
Paddock Laboratories Inc.
Attention: Mary Beth Erstad
3940 Quebec Avenue North
Minneapolis, MN 55427

4. AF NUMBER	5. SUPPLEMENT(s)	6. PROPRIETARY NAME
NA	NA	NA

7. NONPROPRIETARY NAME
Sodium Polystyrene Sulfonate Suspension

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
FDA: 4/14/94 NA letter issued to firm.

Firm: 8/27/91 Original ANDA filed.
4/22/94 Correspondence
12/19/94 Response to NA letter dated 4/14/94 (This review).

10. PHARMACOLOGICAL CATEGORY	11. Rx or OTC
Treatment of Hyperkalemia	Rx

13. DOSAGE FORM	14. POTENCY
Liquid Suspension	15 g/60 mL

17. COMMENTS See comments in individual sections.

18. CONCLUSIONS AND RECOMMENDATIONS:
Not approvable.

19. REVIEWER:	DATE COMPLETED:
J.Fan	5/25/95

cc: ANDA 40-028
DUP Jacket
Division File
Field Copy

Endorsements:

HFD-623/J.Fan/5-26-95 6/1/95
HFD-623/R.Kishore, Ph.D./5-30-95 R. Kishore 6-8-95
X:\WPFILE\BRANCH1\FAN\40028N3.RJF
F/T by dvw/6-1-95

Following this page, 10 pages withheld in full (b)(4)

ii) Stability studies will be provided yearly in an annual report.

iii) If there is any evidence of deviation which is a single occurrence that does not affect the safety and efficacy of the drug product, then you will discuss with the Office of Generic Drugs and provide justification for the continued distribution of that batch.

Response: A revised stability protocol incorporating the requested information in (i), (ii) and (III) was provided in Section XVII, p.107. **Acceptable**

Note: Post approval commitments submitted in the 10/5/93 amendment (p.353) also stated that the first three commercial lots following approval will be placed on stability at 25°C and ambient humidity at 0, 3, 6, 9, 12, 24, 36 and 48 months until expiration is reached.

Comments:
The following comments pertain to your finished drug product stability program:

a. [redacted] (b) (4)

b. Please revise your stability data report format by adding the manufacturing date of the stability batch and the date at which the stability study starts.

c. Please revise your finished drug product stability protocol by adding stability test specifications for microbial limits, sodium content, potassium exchange capacity, sorbitol, pH, appearance, leak testing and preservative effectiveness testing.

30. CONTROL NUMBERS **Satisfactory per Review #2.**

31. SAMPLES AND RESULTS
Polystyrene Sulfonate suspension is a USP drug product, and does not require methods validation. Therefore sampling is not applicable.

32. LABELING **Satisfactory** per Labeling Review Worksheet dated 3/15/95 (C.Zimmermann/A.Payne).

33. ESTABLISHMENT INSPECTION
A follow-up EER was submitted on 3/3/94.

34. BIOEQUIVALENCY STATUS **Satisfactory**
A Bioequivalence waiver has been requested on the basis of therapeutic equivalence code rating of AA for Sodium Polystyrene Sulfonate Suspension, and has been granted by the Division of Bioequivalence (Moo Park 1/14/92).

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Satisfactory per Review #2.

36. ORDER OF REVIEW:
The application submission(s) covered by this review was taken in the date order of receipt Yes X
No_____

If no, explain reason(s) below:

37. **DMF CHECKLIST FOR ANDA # 40-028 REVIEW # 3**

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
[redacted] (b) (4)		3	Def.	3/10/94

Comments: Deficiency letter issued to holder on [redacted] (b) (4). Holder has not responded as of 5/24/95. Therefore, DMF [redacted] (b) (4) remains deficient.

[redacted] (b) (4)	3	Sat.	9/2/92

Comments: [redacted] (b) (4) was found satisfactory by R. Adams, Ph.D

[redacted] (b) (4)	4	-	-

Comments: Sufficient data in application.

[redacted] (b) (4)	4	-	-

Comments: Sufficient information application.

[redacted] (b) (4)	4	-	-

Comments: Sufficient information application.

[redacted] (b) (4)	4	-	-

Comments: Sufficient information in application.

[redacted] (b) (4)	4	-	-

Comments: Sufficient information in application.

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no relevant revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Checklist page 01 of 01.

J.Fan
Reviewer

Signature

5/25/95
Date

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

1. CHEMISTRY REVIEW NO. 4

2. ANDA # 40-028

3. NAME AND ADDRESS OF APPLICANT
Paddock Laboratories Inc.
Attention: Carol Subialka
3940 Quebec Avenue North
Minneapolis, MN 55427

Tel: 763-546-4676
FAX: 763-546-4842

4. LEGAL BASIS FOR SUBMISSION Based on Carolina Medical's Sodium Polystyrene Sulfonate Suspension

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME
Sodium Polystyrene Sulfonate Suspension USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
FDA: 6/14/95 NA letter issued to the firm.

Firm:
8/27/91 Original application submitted.
2/26/01 Amendment (Response to NA letter dated 6/14/95).

10. PHARMACOLOGICAL CATEGORY
Treatment of Hyperkalemia

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
See attached #37 DMF checklist.

13. DOSAGE FORM
Liquid suspension

14. POTENCIES
15 g/60 mL

15. CHEMICAL NAME AND STRUCTURE
Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

16. RECORDS AND REPORTS N/A

17. COMMENTS

This application was last reviewed on 5/2/95 (Review #3). In this amendment, the firm indicated that considering the length of time lapsed since their last submission in 12/94 and the number and nature of the proposed changes affecting their ANDA, they have updated the application to reflect their current manufacturing environment at their firm. This amendment has been organized to be more or less a complete presentation of the CMC portion of their ANDA. Therefore, this amendment will be reviewed as if it is an original ANDA submission.

18. CONCLUSIONS AND RECOMMENDATIONS

NA/Minor

19. REVIEWER: J. Fan

DATE COMPLETED: 7/24/01
8/3/01 (Revised)

Following this page, 17 pages withheld in full (b)(4)

37. **DMF CHECKLIST FOR ANDA #40-028 REVIEW # 4**

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
[redacted] (b) (4)		4		

Comments:

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

Comments:

[redacted] (b) (4)	4		

Comments:

[redacted] (b) (4)	4		

Comments:

[redacted] (b) (4)	4		

Comments:

[redacted] (b) (4)	4		

Comments:

ACTION CODES: (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").

[signature] 8/3/01

38. Chemistry Comments to be Provided to the Applicant

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please describe the pharmaceutical functions of the raw materials used in the manufacture of your drug product.

2. (b) (4)

3.

4.

5.

Following this page, 1 page withheld in full (b)(4)

[redacted] (b) (4)

12. Please revise your drug substance release specifications to include pH and impurity specifications. We recommend that you contact the drug substance manufacturer for their most current drug substance impurity specifications.

    In addition, please submit a revised a drug substance certificate of analysis (COA) to reflect these specifications revisions.

13. Please be advised that DMF [redacted] (b) (4) is currently deficient and the DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

14. Please provide sample calculations to demonstrate how you have derived the quantity of the active and the inactives for your Sodium Polstyrene Sulfonate Suspension USP production batches of [redacted] (b) (4) as provided on page 087 of your February 26, 2001 amendment.

15. Please establish release and stability impurity test specifications (both individual known, unknown and total) for your finished drug product. Specifications should be based on actual test data observed.

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

1. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

2. Bioequivalence information you have provided is under review by our Division of Bioequivalence. After the review is complete, any deficiencies found will be communicated to you under separate cover.

3. Labeling information you have provided is under review by our Division of Labeling. After the review is complete, any deficiencies found will be communicated to you under separate cover.

Sincerely yours,

Paul Schwartz for 8/6/01

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-028
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/J. Fan/7/24/01 8/3/01
HFD-623/A.Mueller/7/30/01 8/3/01
HFD-617/PBeersblock for T.Ames/PM/8/1/01
V:\firmsnz\paddock\ltrs&rev\40028n4.d.dot
F/T by: gp/8/2/01 8/6/01

CHEMISTRY REVIEW - NOT APPROVABLE LETTER - MINOR

#5

ANDA 40-028

Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Paddock Laboratories Inc.

Yusuf Amin
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 40-028

2. REVIEW #: 6 This review appears to be mis-numbered. It is review #5.

3. REVIEW DATE: 28 AUG 2003

4. REVIEWER: Yusuf Amin

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	27-AUG-1991
FDA NA letter	14-JUN-1995
Amendment (Response to NA letter)	26-FEB-2001
FDA NA letter	07-AUG-2001

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment (Response to FDA letter of 07-AUG-2001)	29-JUL-2003

7. NAME & ADDRESS OF APPLICANT:

Name:	Paddock Laboratories Inc.
Address:	3940 Quebec Avenue North Minneapolis, MN 55427
Representative:	Patrick Johnson
Telephone:	763-732-0393

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Sodium Polystyrene Sulfonate

9. LEGAL BASIS FOR SUBMISSION: Under section 505(j)(1) of FFD &CA.
SPS (RLD) Suspension USP 15 g/60 mL, Carolina Medical (NDA # 087859)
The firm certifies that to the best of its knowledge, no patents which claim Reference Listed Drug or that claims a use of such listed drug for which the firm is seeking approval will be infringed by the manufacture, use or sale of Sodium Polystyrene Sulfonate Suspension since there has never been a patent or filing for the listed drug.

10. PHARMACOL. CATEGORY: Treatment of Hyperkalemia

11. DOSAGE FORM: Suspension

12. STRENGTH/POTENCY: 15 g/60 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X_ Rx ___ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____ SPOTS product – Form Completed

_X_ Not a SPOTS product

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

Sodium Polystyrene Sulfonate
Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt.
Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Inadequate	10-SEP-2003	
	III			4			
	III			4			
	III			4			
	III			4			

Chemistry Review Data Sheet

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

[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
NDA for SPS (Carolina Medical)	87-859	Reference Listed Drug

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Acceptable	11-SEP-2003	J.Barlow
Bioequivalence	Pending		
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. _X__ Yes ____ No If no, explain reason(s) below:

V:\FIRMSAM\PADDOCK\LTRS&REV\40028.REV5.doc

The Chemistry Review for ANDA 40-028

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not recommended for approval at this time, DMF not adequate.

II. Summary of Chemistry Assessments

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

The reference listed drug is SPS 15 g/60 mL Suspension manufactured by Carolina Medical (NDA # 87-859). The active ingredient in SPS Suspension is Sodium Polystyrene Sulfonate which is used for Treatment of Hyperkalemia.

The chemical name for Sodium Polystyrene Sulfonate is:

Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt or Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

Each 60 mL of suspension contains 15 g of Sodium Polystyrene Sulfonate as the active ingredient and the inactive ingredients in the suspension are as follows: Sorbitol, Magnesium Aluminum Silicate, Methylparaben, Propylparaben, Propylene glycol, Purified Water, Saccharin Sodium, Sorbic Acid, Xanthan Gum and Raspberry (b) (4) Flavor.

The firm is seeking a bioequivalence waiver for this product.

(b) (4)

The stability studies were conducted under a stability protocol that is in conformance with the FDA stability guidance. Three months of accelerated and 24 months of CRT stability data are provided for the SPS Suspension USP exhibit batch, lot #9B6481 (2, and 16 oz fills) on pp. 150-161 (Vol.4.1, Attachment # 6). These data were generated the containers placed on the side. Data are within specs.

Both the drug product and the drug substance are compendial items. Method validation by the FDA District Laboratory may not be necessary.

The DMF is found deficient. The deficiencies noted have been communicated to the applicant.

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

Oral administration, used in the Treatment of Hyperkalemia. Hyperkalemia is an abnormally high concentration of potassium in the blood. The drug reduces amount of potassium by ion exchange.

C. Basis for Approvability or Not-Approval Recommendation

Firm needs to resolve issues related to drug substance (DMF).

III. Administrative

A. Reviewer's Signature

Yusuf Amin

B. Endorsement Block

Yusuf Amin/Chemist/9/12/03 11/3/03
Al Mueller, Ph.D./ChemistryTeamLeader/ 11-18-03
Craig Kiester/ProjectManager/ 11/5/03

C. CC Block: N/A

Following this page, 11 pages withheld in full (b)(4)

Deficiency # 9: Your stability protocols provided on pages 1067-1069 stated that "Shelf stability studies on the first three commercial lots of the drug product will include Anti-microbial Effectiveness Testing (AET) at 0, 12, 24 months." This is not adequate. We recommend that the AET testing be performed on all commercial lots of the drug product shelf stability studies and not just the first three commercial lots. You may file a supplemental application to request the deletion of this stability test requirement, when you have collected adequate data to support your request. Please provide Anti-Microbial Effectiveness Test data for your Sodium Polystyrene Sulfonate Suspension USP Demonstrated Batch for our evaluation.

Response to Deficiency # 9: The stability protocol was revised to include the Anti-Microbial Effectiveness Test for initial 12 and 24 months on all commercial lots subjected to shelf stability studies (Attachment 6). The test reports for the test on Demonstrated batch in 2 oz and 16 oz are provided (see Attachment 6 for stability and Attachment 10 for Initial). Satisfactory.

30. MICROBIOLOGY: N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: N/A

Both drug substance and drug products are USP monograph items

32. LABELING **Acceptable J. Barlow 11-SEP-2003**
The marketed trade name, Kionex, has been accepted by the Division of Drug Marketing, Advertising and Communication (DDMAC).

33. ESTABLISHMENT INSPECTION **Pending**
EES update is needed.

34. BIOEQUIVALENCY STATUS **Pending**

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Firm claimed a categorical exclusion for filing an EAS and certified that (p.1098). **Satisfactory.**

36. Chemistry Comments to be Provided to the Applicant

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

MAY 18 2011

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

The Drug Master File (DMF) (b) (4) which you have referenced for your supplier of the (b) (4) has been reviewed and found to be deficient. The deficiencies have been transmitted to the DMF holder. Please do not respond to this deficiency letter until you have received notification from the DMF holder that the deficiencies have been addressed. Please note that each of the deficiencies must be found to be satisfactory before the approval of this application.

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

1. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

2. Bioequivalence information you have provided is under review by our Division of Bioequivalence. After the review is complete, any deficiencies found will be communicated to you under separate cover.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-028
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/Y.Amin/11/3/03 11/18/03
HFD-623/A.Mueller/11/3/03
HFD-617/C.Kiester/PM/11/13/03 11/18/03

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F/T by: gp/11/17/03

CHEMISTRY REVIEW - NOT APPROVABLE LETTER - MINOR

#6

ANDA 40-028

Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Paddock Laboratories Inc.

Yusuf Amin
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 40-028

2. REVIEW #: 6

3. REVIEW DATE: 13 JAN 2004

4. REVIEWER: Yusuf Amin

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	27-AUG-1991
FDA NA letter	14-JUN-1995
Amendment (Response to NA letter)	26-FEB-2001
FDA NA letter	07-AUG-2001
Amendment (Response to FDA letter of 07-AUG-2001)	29-JUL-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment (Response to FDA letter of 18-NOV-2003)	29-DEC-2003

7. NAME & ADDRESS OF APPLICANT:

Name:	Paddock Laboratories Inc.
Address:	3940 Quebec Avenue North Minneapolis, MN 55427
Representative:	Daniel W. Rockcliffe
Telephone:	763-546-4676

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Sodium Polystyrene Sulfonate

9. LEGAL BASIS FOR SUBMISSION: Under section 505(j)(1) of FFD &CA.
SPS (RLD) Suspension USP 15 g/60 mL, Carolina Medical (NDA # 087859)
The firm certifies that to the best of its knowledge, no patents which claim Reference Listed Drug or that claims a use of such listed drug for which the firm is seeking approval will be

infringed by the manufacture, use or sale of Sodium Polystyrene Sulfonate Suspension since there has never been a patent or filing for the listed drug.

10. PHARMACOL. CATEGORY: Treatment of Hyperkalemia

11. DOSAGE FORM: Suspension

12. STRENGTH/POTENCY: 15 g/60 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

_X____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Sodium Polystyrene Sulfonate
Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt.
Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

17. RELATED/SUPPORTING DOCUMENTS:
A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Adequate	13-JAN-2004	
	III			4			
	III			4			
	III			4			
	III			4			

Chemistry Review Data Sheet

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

[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
NDA for SPS (Carolina Medical)	87-859	Reference Listed Drug

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Withhold	22-JAN-2002	B. Hartman
Methods Validation	N/A		
Labeling	Acceptable	11-SEP-2003	J.Barlow
Bioequivalence	Acceptable	7-MAY-2004	S.Gunther
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. _X__ Yes ____ No If no, explain reason(s) below:

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The Chemistry Review for ANDA 40-028

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The CMC is approvable, however EER is on **Withhold** status.

II. Summary of Chemistry Assessments

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

The reference listed drug is SPS 15 g/60 mL Suspension manufactured by Carolina Medical (NDA # 87-859). The active ingredient in SPS Suspension is Sodium Polystyrene Sulfonate which is used for Treatment of Hyperkalemia.

The chemical name for Sodium Polystyrene Sulfonate is:

Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt or Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

Each 60 mL of suspension contains 15 g of Sodium Polystyrene Sulfonate as the active ingredient and the inactive ingredients in the suspension are as follows: Sorbitol, Magnesium Aluminum Silicate, Methylparaben, Propylparaben, Propylene glycol, Purified Water, Saccharin Sodium, Sorbic Acid, Xanthan Gum and Raspberry (b) (4) Flavor.

The firm is seeking a bioequivalence waiver for this product.

(b) (4)

The stability studies were conducted under a stability protocol that is in conformance with the FDA stability guidance. Three months of accelerated and 24 months of CRT stability data are provided for the SPS Suspension USP exhibit batch, lot #9B6481 (2, and 16 oz fills) on pp. 150-161 (Vol.4.1, Attachment # 6). These data were generated from the containers placed on side (inverted position). Data are within specs.

Both the drug product and the drug substance are compendial items. Method validation by the FDA District Laboratory may not be necessary.

The DMF is found adequate on 13-JAN-2004.

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

Oral administration, used in the Treatment of Hyperkalemia. Hyperkalemia is an abnormally high concentration of potassium in the blood. The drug reduces amount of potassium by ion exchange.

C. Basis for Approvability or Not-Approval Recommendation

CMC approvable but EER is on Withhold status.

III. Administrative

A. Reviewer's Signature

Yusuf Amin

B. Endorsement Block

Yusuf Amin/Chemist/1/14/04 6/25/04
Al Mueller, Ph.D./ChemistryTeamLeader/ 6-25-04
Craig Kiester/ProjectManager/ 6/25/04

C. CC Block: N/A

Following this page, 7 pages withheld in full (b)(4)

Finished drug product stability specifications (pp.1067-1069, Vol.3.3):

(b) (4)

Expiry date: 24 months requested.

Reported results: Three months of accelerated and 24 months of CRT stability data are provided for the SPS Suspension USP exhibit batch, lot #9B6481 (2 and 16 oz fills) on pp. 150 - 161 (Attachment 6, Vol.4.1 These data were generated from the containers placed on side (inverted position). Data are within specs.

30. MICROBIOLOGY: N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: N/A

Both drug substance and drug products are USP monograph items

32. LABELING **Acceptable J. Barlow 11-SEP-2003**

The marketed trade name, Kionex, has been accepted by the Division of Drug Marketing, Advertising and Communication (DDMAC).

33. ESTABLISHMENT INSPECTION **Withhold (22-JAN-2002, B. Hartman)**

34. BIOEQUIVALENCY STATUS **Acceptable (07-MAY-2004, S.Gunther)**

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Firm claimed a categorical exclusion for filing an EAS and certified that (p.1098).
Satisfactory in review 5.

36. Chemistry Comments to be Provided to the Applicant

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

Deficiency:

The firms referenced in the application relative to the manufacture and testing of the product is on withhold status for cGMP(s) compliance. Please do not respond until the compliance issues have been resolved.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

JUL 07 2004

Needfax
Cover Sheet

cc: ANDA 40-028
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/Y.Amin/7/2/04 7/7/04
HFD-623/A.Mueller/
HFD-617/C. Kiester for S.Eng/PM/7/2/04

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F/T by: gp/7/6/04

CHEMISTRY REVIEW - NOT APPROVABLE LETTER - MINOR

ANDA 40-028

Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Paddock Laboratories, Inc.

Yusuf Amin
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 40-028

2. REVIEW #: 7

3. REVIEW DATE: 01-AUG-2007

4. REVIEWER: Yusuf Amin

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	27-AUG-1991
FDA NA letter	14-JUN-1995
Amendment (Response to NA letter)	26-FEB-2001
FDA NA letter	07-AUG-2001
Amendment (Response to FDA letter of 07-AUG-2001)	29-JUL-2003
Amendment (Response to FDA letter of 18-NOV-2003)	29-DEC-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	07-JUL-2007

7. NAME & ADDRESS OF APPLICANT:

Name:	Paddock Laboratories Inc.
Address:	3940 Quebec Avenue North Minneapolis, MN 55427
Representative:	David Rosenberg
Telephone: Fax:	763-546-4676 763-546-4842

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Sodium Polystyrene Sulfonate

9. LEGAL BASIS FOR SUBMISSION: Under section 505(j)(1) of FFD &CA.
SPS (RLD) Suspension USP 15 g/60 mL, Carolina Medical (NDA # 087859)

The firm certifies that to the best of its knowledge, no patents which claim Reference Listed Drug or that claims a use of such listed drug for which the firm is seeking approval will be infringed by the manufacture, use or sale of Sodium Polystyrene Sulfonate Suspension since there has never been a patent or filing for the listed drug.

10. PHARMACOL. CATEGORY: Treatment of Hyperkalemia

11. DOSAGE FORM: Suspension

12. STRENGTH/POTENCY: 15 g/60 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Sodium Polystyrene Sulfonate
Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt.
Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

17. RELATED/SUPPORTING DOCUMENTS:
A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Adequate	23-JUL-2007	By: Y. Amin
	III			4			
	III			4			
	III			4			

Chemistry Review Data Sheet

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

[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
NDA for SPS (Carolina Medical)	87-859	Reference Listed Drug

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	18-JUN-2007	S. Ferguson
Methods Validation	N/A		
Labeling	Acceptable	11-SEP-2003	J.Barlow
Bioequivalence	Acceptable	7-MAY-2004	S.Gunther
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW (OGD Only)

The application submission(s) covered by this review was taken in the date order of receipt. _X__ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 40-028

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The CMC is approvable.

II. Summary of Chemistry Assessments

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

The reference listed drug is SPS 15 g/60 mL Suspension manufactured by Carolina Medical (NDA # 87-859). The active ingredient in SPS Suspension is Sodium Polystyrene Sulfonate which is used for Treatment of Hyperkalemia.

The chemical name for Sodium Polystyrene Sulfonate is:

Benzene, diethenyl-, polymer with ethenylbenzene, sulfonated, sodium salt or Divinylbenzene copolymer with styrene, sulfonated, sodium salt.

Each 60 mL of suspension contains 15 g of Sodium Polystyrene Sulfonate as the active ingredient and the inactive ingredients in the suspension are as follows: Sorbitol, Magnesium Aluminum Silicate, Methylparaben, Propylparaben, Propylene glycol (b) (4) Purified Water, Saccharin Sodium, Sorbic Acid, Xanthan Gum and Raspberry Flavor.

The firm is seeking a bioequivalence waiver for this product.

(b) (4)

The stability studies were conducted under a stability protocol that is in conformance with the FDA stability guidance. Three months of accelerated and 24 months of CRT stability data are provided for the SPS Suspension USP exhibit batch, lot #9B6481 (2, and 16 oz fills) on pp. 150-161 (Vol.4.1, Attachment # 6). These data were generated from the containers placed on side (inverted position). Data are within specs.

Both the drug product and the drug substance are compendial items. Method validation by the FDA District Laboratory may not be necessary.

The DMF is found adequate on 13-JAN-2004.

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

Oral administration, used in the Treatment of Hyperkalemia. Hyperkalemia is an abnormally high concentration of potassium in the blood. The drug reduces amount of potassium by ion exchange.

C. Basis for Approvability or Not-Approval Recommendation

CMC approvable.

Following this page, 7 pages withheld in full (b)(4)

Finished drug product stability specifications (pp.1067-1069, Vol.3.3 and p. 163 Vol.4.1):

(b) (4)

Expiry date: 24 months requested.

Reported results: Three months of accelerated and 24 months of CRT stability data are provided for the SPS Suspension USP exhibit batch, lot #9B6481 (2 and 16 oz fills) on pp. 150 - 161 (Attachment 6, Vol.4.1 These data were generated from the containers placed on side (inverted position). Data are within specs.

30. MICROBIOLOGY: N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: N/A

Both drug substance and drug products are USP monograph items

32. LABELING **Acceptable J. Barlow 11-SEP-2003**
The marketed trade name, Kionex, has been accepted by the Division of Drug Marketing, Advertising and Communication (DDMAC).

33. ESTABLISHMENT INSPECTION **Acceptable (18-JUN-2007, S. Ferguson)**

34. BIOEQUIVALENCY STATUS **Acceptable (07-MAY-2004, S.Gunther)**

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
Firm claimed a categorical exclusion for filing an EAS and certified that (p.1098).
Satisfactory in review 5.

cc: ANDA 40-028
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/Y.Amin/8/01/2007
HFD-623/A.Mueller/
HFD-617/S.Eng/PM/

V:\firmsnz\paddock\ltrs&rev\40028.REV7.doc

F/T by:

CHEMISTRY REVIEW - APPROVABLE

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

/s/

Yusuf A. Amin
9/5/2007 04:29:09 PM
CHEMIST

Albert Mueller
9/10/2007 11:37:51 AM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

BIOEQUIVALENCE REVIEWS

1/14/92

Sodium Polystyrene Sulfonate
15 g/60 mL Suspension
ANDA #40-028
Reviewer: Moo Park
File name: 40028W.091

Paddock Laboratories
Minneapolis, MN
Submission Date:
October 23, 1991

Review of a Waiver Request

I. Objective

To review Paddock Laboratories' request for a waiver of in vivo bioequivalence study requirements for its Sodium Polystyrene Sulfonate Suspension, 15 g/60 mL strength.

Sodium polystyrene sulfonate is a cation-exchange resin used in the treatment of hyperkalemia. The drug aids in the removal of excess potassium from the body. Because of the relatively high concentration of potassium present in the large intestine, conversion of the resin to the potassium form occurs principally at this site. The cationically modified resin is excreted in the feces.

II. Comments

1. The test product and reference product (Carolina Medical's SPS^{R} Suspension) are in suspension dosage form for oral or rectal use and contain 15 g of sodium polystyrene sulfonate in 60 mL suspension. Both products specify approximately 3 mEq of in vitro potassium exchange capacity per 4 mL of suspension (equivalent to 1 g of resin).

2. The active ingredient, sodium polystyrene sulfonate, is not intended to be absorbed orally or rectally.

3. The formula of the test product is shown below. It does not contain inactive ingredients which are known to significantly affect the potassium exchange capacity of the resin.

1 mL suspension contains:

Ingredients	Amount (mg)
[redacted] (b)(4)	

III. Recommendation

The Division of Bioequivalence agrees that the information submitted by Paddock Laboratories demonstrates that Sodium Polystyrene Sulfonate Suspension, 15 g/60 mL strength, falls under 21 CFR 320.22 (b) of the Bioequivalence/Bioavailability Regulations. The waiver of in vivo bioequivalence study for the test product, Sodium Polystyrene Sulfonate Suspension, 15 g/60 mL strength, is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product to be bioequivalent to SPS[R] Suspension, 15 g/60 mL strength, manufactured by Carolina Medical.

The firm should be informed of the Recommendation.

Moo Park

Moo Park, Ph.D.
Review Branch III
The Division of Bioequivalence

RD INITIALED RMHATRE
FT INITIALED RMHATRE Ramakant M. Mhatre

cc: ANDA #40-028, HFD-630(OGD), HFD-604(Hare), HFD-658 (Mhatre, Park), HFD-22 (Hooton), HFC-130/JAllen, Drug File

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	40-028
Drug Product Name	Sodium Polystyrene Sulfonate Suspension
Strengths	15 g/60 mL
Applicant Name	Paddock Laboratories, Inc.
Address	3940 Quebec Avenue North, Minneapolis, MN 55427
Submission Date(s)	February 26, 2001 (original submission August 27, 1991)
Amendment Date(s)	October 23, 1991, October 5, 1993, December 19, 1994
Reviewer	Sheryl D. Gunther
First Generic	No
File Location	V:\firmsnz\paddock\ltrs&rev\40028A0201.doc

REVIEW OF AN AMENDMENT

I. Executive Summary

The firm is proposing a formula modification for its drug product in this submission. Sodium polystyrene sulfonate carries a therapeutic equivalence code of AA and is a DESI drug. The reference-listed drug is Carolina Medical's SPS® (Sodium Polystyrene Sulfonate) suspension, 15 g/60 mL (ANDA 87-859, approved December 8, 1982). The drug product is intended for rectal and oral administration. The active ingredient is not absorbed and acts as an ion exchange mediator of sodium ions for potassium ions in the intestinal tract. The Division of Bioequivalence (DBE) originally granted a waiver of *in vivo* testing for this product under the provisions of 21 CFR § 320.22(b) (See DBE review of ANDA #40-028 (submission date 10/23/91) under Bioequivalence Review Tracking Database). However, since the enactment of the final rules of the Waxman-Hatch Act as of 4/28/92, the regulations allowing for waivers of non-absorbed drug products under 21 CFR § 320.22(b) no longer exist. The previous formulation and the proposed formulation are provided in the Appendix. The DBE finds that the information submitted by the sponsor demonstrates that sodium polystyrene sulfonate suspension, 15 g/60 mL falls under the provisions of 21 CFR § 320.24(b)(6). The drug product is deemed bioequivalent to the RLD. (Note: There is a USP monograph for Sodium Polystyrene Sulfonate Suspension. The monograph does not identify an *in vitro* test for the drug product.)

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Sodium Polystyrene Sulfonate
Reference Product	SPS® (sodium polystyrene sulfonate) suspension, 15g/60mL
RLD Manufacturer	Carolina Medical
NDA No.	087859
RLD Approval Date	December 8, 1982
Background*	Sodium polystyrene sulfonate is a cation-exchange resin used in the treatment of hyperkalemia. The drug aids in the removal of excess potassium from the body when sodium ions are released from the resin and are replaced by potassium and small amounts of other cations. Because of the relatively high concentration of potassium present in the large intestine, conversion of the resin to the potassium form occurs principally at this site. The drug is not absorbed from the gastrointestinal tract. The cationically modified resin is excreted in the feces. * ***References***: *(1) AHFS Drug Information® (2004) Online by the American Society of Health-System Pharmacists, Inc., http://www.ahfsdruginformation.com* *(2) Martindale - The Complete Drug Reference - Monographs, copyright 1982-2004.; accessed via Micromedex online; http://csi.micromedex.com* *(3) USP DI® Drug Information for the Health Care Professional – 24th Ed. (2004) Online, accessed via STAT!Ref (http://online.statref.com)*
Relevant OGD/DBE History	There is one approved generic formulation for this drug product listed in the FDA *Approved Drug Products with Therapeutic Equivalents* (Orange Book, current through February, 2004): ANDA #89-049, (Roxane Laboratories, Inc., approved 11/17/86). The DBE granted a waiver of *in vivo* testing under 21 CFR § 320.22(b)(3) in November, 1986. Roxane submitted a formulation revision in a supplement (4/11/97). The revised formulation was deemed bioequivalent to the previous formulation by virtue of the minor formulation changes and the fact that the product is an AA listed drug and a DESI drug. The regulations allowing for the original biowaiver were no longer in place following the final rules of the Waxman-Hatch Act (4/28/92), however. The supplement was found acceptable under 21 CFR § 320.24(b)(6). **ANDA #40-028**: The DBE granted a waiver of *in vivo* testing for the original formulation for Sodium Polystyrene Sulfonate Suspension, 15g/60mL based on 21 CFR § 320.22(b). (See

DBE review of ANDA #40-028 (submission date 10/23/91) under Bioequivalence Review Tracking Database). There have been numerous CMC deficiencies for this application. The formula revision under review here is contained in the Amendment dated 2/26/01, which also contains a response to the CMC deficiencies of the FDA Not Approvable Letter of 6/14/95. The history of submissions for this application follows:

Submission/Letter:	**Date:**
Original Submission	August 27, 1991
FDA Not Approvable Letter	June 14, 1995
Amendment (Response to FDA letter of June 14, 1995)	February 26, 2001
FDA Not Approvable Letter	August 7, 2001
Amendment (Response to FDA letter of August 7, 2001)	July 29, 2003
FDA Not Approvable Letter	November 18, 2003
Amendment (Response to FDA letter of November 18, 2003)	December 29, 2003

Reviewer's Note: The drug product is also available in powder form for reconstitution. The RLD is Sanofi Synthelabo's Kayexalate® (sodium polystyrene sulfonate) powder for reconstitution, 454 g/bottle, approved June 5, 1958 (NDA #01-1287). The Orange Book lists two generic formulations of this drug product: ANDA #08-9910 (Carolina Medical, approved 1/19/89) and ANDA #40-029 (Paddock, approved 2/6/98). All products have an AA therapeutic equivalence rating. The DBE originally granted a waiver of *in vivo* testing for ANDA #40-029 on 12/31/91. Based on the regulation changes under the final rule of the Waxman-Hatch Act (4/28/92), Paddock submitted an addendum to the original review (10/23/91). The DBE granted a waiver for the product under 21 CFR § 320.22(c). (See DBE review of ANDA #40-029 (submission date 10/23/91) under Bioequivalence Review Tracking Database).

B. Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
In vitro dissolution	No	--
Waiver requests	No	--
Failed Studies	No	--
Amendments	Yes	1

C. Formulation

Location in Appendix	Section A, Page 6
Inactive ingredients within IIG Limits (yes or no)	Yes (See Reviewer Comment below).
If a tablet, is the product scored? (yes or no)	N/A
If yes, which strengths are scored?	--
Is scoring of RLD the same as test? (yes or no)	--
Formulation is acceptable (yes or no)	Yes

Reviewer Comment regarding IIG Limits: *The electronic version of the online IIG (accessed 4/2004) lists the maximum potency limit for sorbic acid in oral suspensions to be 0.01%. However, this entry appears to be incorrect; the apparent correct limit should be 0.1%-0.116%. The reviewer consulted the last published hardcopy of the Inactive Ingredient Guide (published January, 1996). In the entry for sorbic acid (oral route; suspension dosage form), the potency range is listed as 0.1%-0.116%, with the last NDA approved for this ingredient at the time of publication as NDA# (b) (4) (approved (b) (4). The reviewer verified that NDA # (b) (4) (b) (4) currently remains on the market, with a concentration of sorbic acid of (b) (4) (w/v). Additionally, the reviewer notes that the online IIG lists the maximum potency limit for sorbic acid in oral solutions and oral syrups to be 1.189% and 0.5%, respectively, greater than the concentration present in the sponsor's formulation. The electronic version of the online IIG does not report ANDAs associated with these limits, so a comparison of dosage regimens is not possible. The last published hardcopy of the IIG from 1996 listed the last approved ANDAs (at the time of publication) for oral solutions and oral syrups with sorbic acid concentrations much lower than the current maximum potencies given in the online version.*

Formulation Comments: The firm is proposing a revised formulation. The following are the formulation changes made by the firm. (Please see previous and revised formulations in Appendix.)

(b) (4)

(b) (4)

D. Reviewer Comments

(1) The test product (previous and revised formulations) and the reference product are suspensions for oral or rectal use and contain 15 g of sodium polystyrene sulfonate per 60 mL suspension. All products specify approximately 3 mEq of *in vitro* potassium exchange capacity per 4 mL of suspension (equivalent to 1 g of suspension).

(2) The active ingredient, sodium polystyrene sulfonate, is not intended to be absorbed orally or rectally.

(3) Sodium Polystyrene Sulfonate Suspension carries a therapeutic equivalence code of AA and is a DESI drug.

(4) The sorbitol content of both the test and reference products is similar ((b) (4) mg/mL sorbitol (test product); (b) (4) mg/mL sorbitol (reference product)).

E. Recommendations

The Division of Bioequivalence finds that the information submitted by Paddock Laboratories, Inc. demonstrates that its Sodium Polystyrene Sulfonate suspension, 15 g/ 60 mL (revised formulation) falls under the criteria set forth in 21 CFR § 320.24(b)(6). The test product is deemed bioequivalent to the reference-listed drug, Carolina Medical's SPS® (Sodium Polystyrene Sulfonate) suspension, 15 g/60 mL.

The firm should be informed of the above recommendation.

Sheryl D. Gunther 5/7/2004

Sheryl D. Gunther, Pharm.D., Reviewer, Branch I Date

5/7/2004

Shriniwas G. Nerurkar, Ph.D., Team Leader, Branch I Date

5/7/04

Dale P. Conner, Pharm. D., Director Date
Division of Bioequivalence
Office of Generic Drugs

CC: ANDA #40-028, original, HFD-652 (Gunther), Drug File, Division File

IV. Appendix

A. Formulation

Following is Paddock's proposed revised formulation for Sodium Polystyrene Sulfonate Suspension, 15 g/ 60 mL.

Ingredient	mg/mL	%w/w
Sodium Polystyrene Sulfonate	250.00	21.280%**
Sorbitol Solution (b) (4)		(b) (4)
Magnesium Aluminum Silicate (b) (4)		
Methylparaben		
Propylparaben		
Propylene Glycol		
Saccharin Sodium		
Sorbic Acid		
Xanthan Gum		
Flavor – Raspberry (b) (4)		
Purified Water		
(b) (4)		

Following is Paddock's previous formulation for Sodium Polystyrene Sulfonate Suspension, 15 g/ 60 mL.

Ingredient	mg/mL
(b) (4)	

[1] AHFS Drug Information® (2004) Online by the American Society of Health-System Pharmacists, Inc., http://www.ahfsdruginformation.com

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension, 15 g/ 60 mL

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

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews 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,

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

CC: ANDA #40-028
ANDA DUPLICATE
DIVISION FILE
HFD-651/ BIO Drug File
HFD-652/ Reviewer S.D. Gunther
HFD-617/ Project manager A.W. Sigler
HFD-652/ Team Leader S.G. Nerurkar

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Endorsements: (Final with Dates)
HFD-652/ S.D. Gunther S.D. Gunther 5/7/2004
HFD-652/ S.G. Nerurkar 5/7/04
HFD-650/ D.P. Conner 5/7/04

BIOEQUIVALENCE -ACCEPTABLE Submission Date: February 26, 2001

1. **STUDY AMENDMENT (STA)** Strength: 15 g/ 60 mL
✓ Outcome: AC

Outcome Decisions: **AC - Acceptable**

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 40-028/Amendment **SPONSOR:** Paddock Laboratories, Inc.

DRUG AND DOSAGE FORM: Sodium Polystyrene Sulfonate Suspension

STRENGTH(S): 15 g/ 60 mL

TYPES OF STUDIES: N/A

CLINICAL STUDY SITE(S): N/A

ANALYTICAL SITE(S): N/A

STUDY SUMMARY: The application is acceptable.

DISSOLUTION: N/A

DSI INSPECTION STATUS

Inspection needed: N.A.		Inspection status:	Inspection results:
First Generic	NO	Inspection requested: (date)	
New facility		Inspection completed: (date)	
For cause			
Other			

PRIMARY REVIEWER : Sheryl D. Gunther, Pharm.D. **BRANCH :** I

INITIAL : SDG **DATE :** 5/7/2004

TEAM LEADER : Shriniwas Nerurkar, Ph.D. **BRANCH :** I

INITIAL : [signature] **DATE :** 5/7/2004

DIRECTOR, DIVISION OF BIOEQUIVALENCE : Dale P. Conner, Pharm.D.

INITIAL : [signature] **DATE :** 5/7/04

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040028

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

PADDOCK LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

505(j)(2)(A) ok cpavia 9/12/91 10/7/91

August 27, 1991

Division of Generic Drugs
Attention: Document Control Room
MPN-2, HFD 600
CDER
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Division of Generic Drugs:

Enclosed please find an Abbreviated New Drug Application for Sodium Polystyrene Sulfonate Suspension for treatment of hyperkalemia.

We are proposing to manufacture the suspension product using the active material Sodium Polystyrene Sulfonate [redacted] (b) (4) (b) (4) This will be done prior to manufacture of the finished suspension by Paddock Laboratories. The finished dosage form will be packaged in 60 ml unit dose and 473 ml pint size containers for use by the medical community in the treatment of hyperkalemia.

The suspension detailed in this ANDA is consistent with the approved Sodium Polystyrene Sulfonate Suspension products in terms of packaging, and labeled use. The originator product is SPS by Carolina Medical. The tradename for our proposed product is [redacted] (b) (4) Suspension.

This Abbreviated Application is submitted under 21 CFR 314.55.

This application will follow the format suggested in the Federal Register Volume 54, Number 130 July 10, 1989. Accordingly, please find the following information:

- A complete Archival Copy of the abbreviated new drug application that contains :

    The information described under 314.50(a)(1), (3), (4), and (5), (the application)
    314.50(b) index
    314.50(d) (1) manufacturing and
    314.50(e) sampling and labeling
    314.50 (d)(3), bioavailability, is not applicable

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 · Telephone (612) 546-4676

- A review copy of the abbreviated new drug application containing a duplicate copy of the archival copy.

- An inspections copy of the abbreviated new drug application containing a duplicate copy of the archival copy. This copy is to be routed by you to our district office for the pre-approval inspection.

In the event that the submission of samples would, at this point, expedite the review process, please feel free to contact either myself or Mr. Bruce Paddock.

If you are in need of any further assistance, please contact myself or Bruce Paddock.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

ANDA CHECKLIST FOR COMPLETENESS AND ACCEPTABILITY OF THE APPLICATION

SUPERVISORY CHEMIST (Dr Rishore) Branch I 40-028

	YES	NO
·erapeutic Code (1020500 ✓)		
·omments EC1 ✓ On Cards ✓		
Methods Validation package (3 copies) (NO)	8/27/91	
Cover Letter	9/9/91	
356H Signed	✓	
Table of Contents	✓	
Information to show proposed product is the same as the listed product: (i)(a) indications (ii) active ingredients (iii) (a) route (b) dosage form (c) strength (iv) labeling Based on Carolina Medical	✓	
Patent Certification	(1) ✓	
Exclusivity Addresses (If Applicable)	NA	
Labeling Draft	✓	
Statement re Rx/OTC Status	on 356h	✓
Components & Composition (Unit Composition)	✓	
Manufacturing Controls	✓	
·ch Formulation	✓	
Certification of GMP	✓	
Description of Facilities	✓	
Manufacturing Procedures (Batch Records) R-4625	✓	
Specifications and Tests for Active Ingredient and Dosage Form	✓	
Stability Profile Including Stability Data (Use of Stability Indicating Method)	✓	
Samples Statement Plus Data	✓	
Bioavailability/Bioequivalence Protocol Study In Vivo Study/Waiver Request Dissolution Data		✓
Environmental Impact Analysis	✓	
Reviewing CSO (C Parise) 9/12/91		

R· ·sion 5-14-91 jmk/C:forms

ANDA Assignment Record

Appl Type/Number: N 040028 Status/Date: PN PENDING REVIEW 09-SEP-91
Firm: PADDOCK LABS
Trade Name: USP: Y
SC M POLYSTYRENE SULFONATE

Rx: ✓ OTC: ___ Dosage Form: SUS Strength: 15 G/60 ML

Therapeutic Class: 1020500

Doc Set Type: N 000 Amend/Type: ___ Letter Date: 27-AUG-91
Rec-d Date: 09-SEP-91 Acknl. Date: __-__-__
Bio Rev Type: To Bio: 11-15-91

		Assigned	Completed
Lbl:		__-__-__	__-__-__
Chm:	J. SMITH	10-10-91	__-__-__
Bio:		__-__-__	__-__-__
Ins:		__-__-__	__-__-__
Col:		__-__-__	__-__-__
Co2:		__-__-__	__-__-__

DESI Drug: ✓ Similar or Related: ___

Applicant Manufacturer: Yes ✓ No ___

If No: Name of Mfg: ___

ANDA # ___ Approved: ___ Pending: ___ Same Formulation: ___

.ication Complete: Yes ___ No ___

Application Acceptable: Yes ___ No ___

If No: Non-Acceptable Letter to Firm: __-__-__

CSO/CST: Cecelia Parisi Date: 9-12-91

505(j)(2)(A) OK

ANDA 40-028

OCT 15 1991

Paddock Laboratories, Inc.
Attention: Mary Beth G. Erstad
3101 Louisiana Ave. North
P.O. Box 27286
Minneapolis, MN 55427

Dear Madam:

Please refer to your Abbreviated New Drug Application (ANDA) submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

We have given your ANDA a preliminary review, and we find that it is not sufficiently complete to merit substantive review.

We are refusing to file this ANDA under CFR 314.101(d)(3) for the following reasons:

> You have not provided a bioequivalence protocol or study for the proposed drug product nor have you requested a waiver for the requirements of demonstrating in vivo bioavailability. Please refer to 21 CFR 320.22 regarding this requirement. Additionally, the Act [505 (j)(2)(A)(vii)] requires the applicant to provide a specific certification with respect to any patent applicable to the listed drug. This certification is required whether or not a patent is claimed.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505 (j) of the Act.

Within 30 days of the date of this letter, you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(c). If you do so, the application shall be filed over protest under 21 CFR 314.101(b). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Cecelia Parise, R.Ph.
Consumer Safety Officer
(301) 295-8315

Sincerely yours,

Kent Johnston for 10-11-91

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #40-028
DUP/Division File
HFD-82 (if w/d, AP, or R/F letter)
HFC-130/JAllen
HFD-632/RPollock/10-8-91
HFD-600/Reading File
R/D initialed by GJohnston
40028ref.fil(refuse)jkg/10-8-91
F/T by jkg/10-9-91
Refuse to File!
R. Kishore R. Kishore 10-10-91
GJohnston 10/10/91

PADDOCK LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

505(j)(2)(A) info acceptable for filing 11/15/91 Dup to Bio.

RECEIVED
OCT 30 1991
GENERIC DRUGS

October 23, 1991

Division of Generic Drugs
Attention: Document Control Room
MPN-2, HFD 600
CDER
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

NDA ORIG AMENDMENT
AC

re: ANDA 40-028

AVAILABILITY MATERIAL
WAI

Division of Generic Drugs:

We are in receipt of your letter dated October 15, 1991. In the letter you have stated our application is not sufficiently complete to merit substantive review.

Enclosed please find additional information relating to our Abbreviated New Drug Application for Sodium Polystyrene Sulfonate Suspension for treatment of hyperkalemia (ANDA 40-028). Included in the additional information are responses to your findings of insufficiencies:

- A request for waiver of bioequivalence under 21 CFR 320.22 based on the (AA) Therapeutic Equivalence Code assigned to the currently approved products in the 11th Edition Approved Drug Products with Therapeutic Equivalence Evaluations.

- Certification that Paddock Laboratories, Inc. will not be infringing upon any patent applicable to the listed drug, as required under 505 (j)(2)(A)(vii)(I).

If you are in need of any further assistance, please contact myself or Bruce Paddock.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676

PADDOCK
LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

November 7, 1991

ATTN: Robert West, FDA

We have a pending application ANDA 40-028, Sodium Polystyrene Sulfonate Suspension, currently filed with your agency. We have the following considerations regarding the application:

1)

2)

3)

4)

Thank you in advance for your consideration of these issues. Please respond at your earliest convenience by FAX or mail.

Sincerely,

Mary Beth Erstad

Mary Beth Erstad
New Product Development Manager

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676

ANDA 40-028

NOV 26 1991

Paddock Laboratories
Attention: Mary Beth Erstad
P.O. Box 27286
3101 Louisiana Avenue North
Minneapolis, MN 55427

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for the following:

NAME OF DRUG: Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

DATE OF APPLICATION: August 27, 1991

DATE OF RECEIPT: September 9, 1991

DATE ACCEPTABLE FOR FILING: October 30, 1991

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Sincerely yours,

Gerald L. Johnson for 11-26-91

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #40-028
DUP/Division File
HFC-130/JAllen
HFD-633/RKishore R. Kishore 11-25-91
HFD-632/RPollock/11-18-91
R/D initialed by GJohnston
bcw/11-18-91/40028ack.ltr
F/T by jkg/11-21-91
acknowledgment letter!

11/25/91

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE
12/18/91

NDA NUMBER
40-028

IND NUMBER

TELECON/MEETING

INITIATED BY
☐ APPLICANT/SPONSOR
☒ FDA

MADE
☒ BY TELEPHONE
☐ IN PERSON

PRODUCT NAME
Sodium Polystyrene Sulfonate Suspension

FIRM NAME
Paddock Labs Inc

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Mary Beth Erstad

TELEPHONE NO.
612 546 4676

Dr. Kishore + Dr. Smith on-line.

The firm requested information/advise regarding 4 items in a Fax sent to R. West. They proposed (b) (4) [redacted]

The firm was advised that the (b) (4) [redacted]

The firm said the changes were up for consideration at the moment, but the FDA would be informed of which one were eventually implemented.

P.S.: Firm was advised that we two were on phone, a speaker phone. They were also advised that our advice was not Agency opinion since it was based on limited knowledge of facts and had not read. higher management concurrence.

SIGNATURE
John L Smith 12/18/91

K. Laufer 12-19-91

DIVISION
CDER/OGD/ChemI

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1981-677-074/C

ANDA 40-028

MAY -7 1992

Paddock Laboratories
Attention: Mary Beth Erstad
3101 Louisiana Avenue North
P.O. Box 27286
Minneapolis, MN 55427

Dear Madam:

Please refer to your abbreviated new drug application dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL [redacted] (b)(4).

Reference is also made to your communication dated October 23, 1991 amending this application.

The application was globally reviewed and was found to be deficient and therefore not approvable under Section 505 of the Act. Some of the deficiencies are cited below. In addition to responding to these deficiencies, we recommend that you completely revise the content and format of the application concurrently with your response. You may wish to refer to the Center for Drug Evaluation and Research (CDER) guidelines for information pertaining to the content and format requirements for abbreviated new drug applications. We reserve the option to inform you of additional chemistry, manufacturing and control deficiencies in your application upon our review of your response to this letter.

1. We note that your proposed Master Manufacturing Procedure is different from your Test Procedure for both the mixing times and for the order of addition of various components. Please provide data to assure that these changes do not affect the quality and integrity of the product.

2. [redacted] (b)(4)

Following this page, 1 page withheld in full (b)(4)

15. We note that you did not provide a certificate of analysis (CoA) for the [redacted] (b)(4) test batches. Please provide a CoA for both batches.

16. Please provide the testing controls used for the finished product release testing.

17. It is indicated in your labeling for the product that your product is stable upon refrigeration for [redacted] (b)(4) after opening. Please provide data to validate this claim.

18. We recommend that you add the following specifications to your stability protocol:

    a. Appearance

    b. Dissolution and Redispersibility (particle size)

    c. Leak Integrity Testing

    d. USP Antimicrobial Preservative Effectiveness Testing at the lower limit.

19. The container/closure system of the caps, liners and resins should be reported as part of your stability report. Please incorporate this information in your stability data. In addition, the information provided for the packaging components is inadequate to provide the needed assurance of purity and integrity for the drug product.

20. In your stability report, we note that four months passed between the initial test date and the one-month test station. Please provide an explanation for the discrepancy. The dates of sampling should be on the stability protocol and the dates of testing should be clearly shown. In addition, please specify the storage parameters for the samples during the intervening period.

21. The following comments pertain to your labels and labeling.

    A. Container: Not Satisfactory

    1. Delete the colon after "NDC".

2. We find your proposed proprietary name [redacted] unacceptable [redacted]. In accord with 21 CFR 201.10(c), we consider this misleading. Please delete or propose another proprietary name.

3. Revise the expression of net contents of the pint bottle in milliliters (i.e., 16 fl oz (____ mL).

4. Revise your "contains" statement to read:

   Each 60 mL contains:

   Sodium Polystyrene Sulfonate USP 15 grams, Sorbitol Solution USP 19.3 grams. Also contains . . . .

   NOTE TO FIRM: Please include the sodium content per 60 mL in grams and mEq.

5. The quantitative amount of active ingredient (15 g/60 mL) should be expressed beneath the established name. In addition, please note that the statement "FOR ORAL OR RECTAL USE" should appear beneath the quantitative amount on both package sizes.

6. You have failed to list alcohol as an ingredient on your 60 mL label. Please include.

B. Insert: Not Satisfactory

Please revise your insert labeling to be in accord with the approved labeling of SPS(R) Suspension (Carolina Medical Products Co; Approved December 12, 1991; Revised July 1991.

Please revise your container labels and package insert labeling, then prepare and submit a draft copy for our review and comment.

The following comments are provided for your information:

22. Drug Master File (DMF) [redacted] has been reviewed and found to be deficient. The deficiencies have been provided to the DMF holder. A satisfactory resolution of the deficiencies is necessary prior to approval of the ANDA.

23. In addition, DMFs [redacted] (b) (4) are under review. Any deficiencies identified will be communicated to the holder of the DMF. Satisfactory resolution of the deficiencies found (if any) is necessary prior to approval of the ANDA.

24. Please be advised that all DMFs referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA. Some of the DMF holders may have to be inspected by our Division of Manufacturing and Product Quality. Any unsatisfactory review/evaluation will delay the approval of the ANDA. Thus, you are advised to withdraw any DMF references which are unnecessary to support the ANDA.

25. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMPs at the time of approval. We will request an evaluation from our Division of Manufacturing and Product Quality at the appropriate time.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a major amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

RKPatel 5/16/94

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:
ANDA # 40-028
DUP/Division File
HFC-130/JAllen
HFD-600/Reading File
HFD-638/J.Phillips
HFD-633/RWest/4.30.92
HFD-633/E.Murphy

Robert L. West 5/1/92

R/D Endorsed by:
J.Phillips 5.1.92
E.Murphy 3.31.92, 5.1.92
R.Kishore, Ph.D. 4.28.92

J. Phillips 5/4/92
EM 5/1/92
R. Kishore 5-6-92

Drafted:RLWest:4.30.92 A:\40-028N.LRW
FT by:rlw:5.1.92

NOT APPROVABLE LETTER

PADDOCK
LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

6/7/92
noted, NAI -
Robert Lest, CSO

May 14, 1992

Division of Generic Drugs
Attention: Document Control Room
MPN-2, HFD 600
CDER
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

NEW CORRESP

re: ANDA 40-028

Division of Generic Drugs:

We are in receipt of your letter dated May 7, 1992. In the letter you have stated our application is deficient and not approvable under Section 505 of the Act.

We propose to amend the application and will address each of the points covered in your letter. We will need some time to prepare and will provide a MAJOR AMENDMENT to our application on or about August 7, 1992.

If you are in need of any further assistance, please contact myself or Bruce Paddock.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

RECEIVED
MAY 21 1992
GENERIC DRUGS

6-25-92

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676 • FAX (612) 546-4842

PADDOCK
LABORATORIES, INC.
Pharmaceuticals for Medicine, Pharmacy and Science

July 6, 1992

Robert West
Division of Generic Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
FAX 301-295-8174

re: Questions on Deficiency letter of May 7, 1992 ANDA 40-028

Dear Robert:

We are in receipt of your letter dated May 7, 1992, and are preparing our MAJOR AMENDMENT to our ANDA 40-028. There is one comment from the letter on which we are in need of clarification.

Please specify what is required for the last segment of comment 19:

> "In addition, the information provided for the packaging components is inadequate to provide the needed assurance of purity and integrity for the drug product."

We have provided blueprints, [redacted] (b) (4) specifications and FDA status for the packaging components in the original application, Section C. Specifications and Analytical Methods for Inactive Components Pages 33 - 41J. Please advise on what else we need.

Thank you in advance for your time and consideration. If you are in need of further information, please contact myself or Bruce Paddock.

[redacted] (b) (4)

in-house testing
USP testing

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

PADDOCK LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

July 21, 1992

RECEIVED

JUL 29 1992

GENERIC DRUGS

Robert West
Division of Generic Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
FAX 301-295-8174

re: Proposed names for Sodium Polystyrene Sulfonate Powder and Suspension ANDA's 40-028, 40-029

Dear Robert:

We are in receipt of your letters dated May 7 and 13, 1992, and are preparing our MAJOR AMENDMENTS to our ANDA's 40-028 and 40-029.

We are considering the following names for our products and would appreciate a pre-review of them by the appropriate labeling staff.

Please run these by the labeling people and FAX their comments back to us at your earliest convenience. We wish our major amendments to be as complete and acceptable as possible and feel this pre-review is essential for us to be able to propose acceptable names in the actual amendments.

NAME CONSIDERATIONS:

(b) (4)
[redacted]

Kionex Suspension and Powder

Also, have you had a chance to get a response on my FAXes of July 6, 1992 asking for clarification on a few of the points in the May 7, and 13 deficiency letters? This is also needed for us to prepare our amendment.

Thank you in advance for your time and consideration. If you are in need of further information, please contact myself or Bruce Paddock.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

7/29/92
T-Con to Paddock Johnson (for M.B.G.E.)
Informed that we prefer "Kionex" as tradename (per J. Phillips & K.T. Johnson) and referred to last week's T-Con with Jeanne Taborsky in which questions in earlier FAXes were addressed.
Robert L. West CSO NAI

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676 • FAX (612) 546-4842

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 7-22-92

ANDA NUMBER: 40-029, 40-028

NDA NUMBER:

TELECON/MEETING

INITIATED BY: ☑ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: (b) (4) [redacted] Powder = 029

FIRM NAME: Paddock Labs

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Mary Beth Erstad

TELEPHONE NO.: 612-546-4676

Mark Anderson and I spoke with the applicant in response to FAX questions attached.

1. 40-029 -

#6 - We asked for these results to be written with units and specifically to list the name of the material as the USP name and state the grade.

#8 I did not understand what was confusing about this request. They seemed to want to know why we wanted it, not what we wanted. We stated that these tests would indicate if the (b) (4) [redacted] They agreed to provide data + add the tests.

2. 40-028 - I explained that we usually receive USP test results for containers and referred them to the appropriate sections of the USP.

SIGNATURE: Joanne Zabowsky

DIVISION: OGD Branch 1

FORM FD 2587 (11/77)

DIVISION FILE

U.S. GOVERNMENT PRINTING OFFICE

I N T E R O F F I C E M E M O R A N D U M

Public Health Service
Center for Drug Evaluation and Research
Office of Compliance

Date: July 23, 1992

From: Chief, Investigations and Compliance
Evaluation Branch (HFD-324)

Subject: Pre-approval Inspection Program, CP 7346.832
Submission of Inspection report

Applicant: Paddock Laboratories, Inc.
3101 Louisiana Ave.
Minneapolis, MN 55427

Firm: Paddock Laboratories, Inc.
3101 Louisiana Ave.
Minneapolia, MN 55427

To: Director,
Minneapolis District Office, HFR-MW300

Your recommendation to withhold approval of ANDAs 40-028 and 40-029 submitted by the referenced applicant has been forwarded to the Office of Generic Drugs (HFD-630) for their evaluation. To complete this evaluation, it will be necessary to forward the EIR, or that portion of the report, which substantiates the recommendation to withhold approval, to the reviewing office. We ask therefore, that the report be submitted to this office (HFD-324) within the thirty day time frame as provided for in the Compliance Program. Upon completion of their evaluation, the reviewing office will notify the applicant of the reason(s) if approval of the application is being withheld.

If the District becomes aware, through subsequent investigation or contacts with the applicant, that the problems which caused the original recommendation to withhold have been corrected, please advise this office promptly of the circumstances. We will in turn forward this notification to the reviewing unit.

Thank you for your cooperation in this matter.

Michael F. Karpers

C:
FD-633 DOLESKI
HFD-324 R/F
HFD-324 EER File
JULY 23, 1992:MLB
MICHELLE'S DISK I
B:\PADDOCK.MEM

PADDOCK LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

October 5, 1993

Division of Generic Drugs
Document Control Room
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Room 150
Rockville, Maryland 20855-2773

N/AC
NDA ORIG AMENDMENT
RECEIVED
OCT 0 8 1993
GENERIC DRUGS

Draft Labeling

re: MAJOR AMENDMENT TO ANDA 40-028

Division of Generic Drugs:

In response to your letter dated May 7, 1992, enclosed is a MAJOR AMENDMENT to our ANDA 40-028. This major amendment addresses all deficiencies listed in the May 7 letter and is a completely revised version of the original application. Each of the deficiencies is addressed by number in this cover letter as well as included in the body of the revised application.

1. Please see the new stability batch and corresponding data submitted in this major amendment. You will find the Master Manufacturing Procedure and the Test Procedure for this new stability batch are the same. The original procedures were, in fact, different. We propose to use the procedure included in this amendment, not that of the original application.

2. [redacted] (b) (4)

3.

Following this page, 2 pages withheld in full (b)(4)

ORIGINAL

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676 • FAX (612) 546-4842

17. In response to your comments of 21. B.

"Insert: Not Satisfactory... Please revise your insert labeling to be in accord with the approved labeling of SPS(R) Suspension (Carolina Medical Products Co; Approved December 12, Revised July 1991).";

We have revised our insert to state:

"If repackaging into other containers, store in refrigerator and use within 14 days of packaging."

18. We agree to add appearance, leak integrity testing and USP Antimicrobial Preservative Effectiveness Testing to our stability protocol.

USP Antimicrobial Preservative Effectiveness Testing is included for the test batch in this major amendment. This was performed at time 0 and 90 days accelerated storage (40°C/75% R.H.). We do not feel, however, that USP Antimicrobial Preservative Effectiveness Testing is necessary for the shelf stability studies on production batches.

(b) (4)

19. In this major amendment, we have provided new stability data which includes all requested container information. We have also provided container testing information for the 2 ounce (60 mL) and 16 ounce (480 mL) containers. Please see Section XIV. 4. for USP XXII Container - Permeation Testing.

20. Please see the attached letter from [redacted] (b) (4) it addresses all concerns listed in your comments.

21. Our new proposed proprietary name for the product is **Kionex™**, Sodium Polystyrene Sulfonate Suspension USP. Changes have been made to the labeling which addresses all comments listed. Please see the labeling section of this major amendment.

We thank you for the information in your comments 22. through 25. We have enclosed letters from [redacted] (b) (4) and [redacted] (b) (4) stating they have amended their DMF's as requested by FDA.

If you are in need of any further assistance, please contact myself or Bruce Paddock.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

REQUEST TYPE *(Check One)* ☐ Original ☒ Follow-Up ☐ FUR	DATE 3/3/11	PHONE NO. (301)594-0210	EER ID #
REQUESTOR'S NAME Elise Murphy		DIVISION OND Chem. I	MAIL CODE HFD- 622
APPLICATION AND SUPPLEMENT NUMBER ANDA 90-029			
BRAND NAME Kionex™		ESTABLISHED NAME Sodium Polystyrene Sulfonate	
DOSAGE AND STRENGTH 15 gram/60 mL			STERILE ☐ YES ☑ NO
PROFILE CLASS LIQ	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*		
APPLICANT'S NAME PadHark Laboratories			
ADDRESS 3101 Louisiana Ave. No. Minneapolis, Minnesota 55427			
COMMENTS			

FACILITIES TO BE EVALUATED

(Name and Complete Address)

	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	F KEY/ CIRTS ID	HFD-324 USE ONLY
1. PADHARK Laboratories 3101 Louisiana Ave. No. Minneapolis, Minnesota				
2. (b) (4)				
3.				
4.				
5.				

FOR HFD-324 USE ONLY:	CSO	DATE RECEIVED
	CGMP COMPLIANCE STATUS	DATE

FORM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324. Remaining Copies: Requesting Office

ANDA 40-028

Paddock Laboratories
Attn: Mary Beth Erstad
P.O. Box 27286
3101 Louisiana Avenue North
Minneapolis, MN 55427

APR 14 1994

Dear Madam:

This is in reference to your abbreviated new drug application dated, August 27, 1991 submitted pursuant to Section 505(j) of the Food, Drug, and Cosmetic Act, for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

Reference is also made to your amendment dated October 5, 1993.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies:

1. Please provide the calculations that you used to determine the specific gravity, and density for lot 3B6291.

2. Please re-calculate the amounts of ingredients you report in your components and composition section per 60 mL as they do not match the executed and production batch records.

3. These comments pertain to the drug substance Sodium Polystyrene Sulfonate USP:

a) (b) (4)

b)

Following this page, 2 page withheld in full (b)(4)

i) The first three commercial production lots of the product in each container/closure system will be placed on stability. Yearly thereafter, one production batch of the largest and smallest sizes of each marketed container/closure system will be added to the stability program.

ii) Stability studies will be provided yearly in an annual report.

iii) If there is any evidence of deviation which is a single occurrence that does not affect the safety and efficacy of the drug product, then you will discuss with the Office of Generic Drugs and provide justification for the continued distribution of that batch.

B. Labeling Deficiencies

GENERAL COMMENTS

1. You list [redacted] (b) (4) and not sorbic acid as an inactive ingredient in your labels and labeling. This is inconsistent with your composition statement. Please revise your labels and labeling accordingly, and/or comment.

2. Throughout your insert labeling, please revise the "(tm)" to the appropriate trademark symbol: "™".

CONTAINER

1. USUAL DOSAGE [rather than "Usual Dose"]

2. Sodium content: Delete the "m" in "gm", as follows: "g"

3. Dispense in a tight container, as defined in the USP. [not "described"]

INSERT

1. TITLE

See General Comment 2. above.

2. BOX

Revise the following statement so that it appears in bold face print and is surrounded by a complete box, as follows:

Cation-Exchange Resin

3. DESCRIPTION

a. Line 2: ...administered orally or rectally in an enema. It...

b. Inactive ingredients, see General Comment 1. above.

c. We refer you to 21 CFR 201.10 (g)(1) which states that the established name shall be made clear by the use of a phrase such as "brand of" or by brackets surrounding the established name. In this case, you have the proprietary name in brackets. Please revise accordingly.

4. DOSAGE AND ADMINISTRATION

Paragraph 5, line 11: ...resin. Two quarts....
[correct spelling of "two"]

5. HOW SUPPLIED

a. Include the degree symbols following the "15" and the "59", as follows:

... 15°-30°C (59°-86°F)

b. "Manufactured by" statement:

Please spell "Minneapolis" [rather than "Mpls"]

c. Include the following:

If repackaging into other containers, store in refrigerator and use within 14 days of packaging.

Please revise your container labels and package insert labeling, and submit final printed (12) labels and labeling. Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

In addition to responding to these deficiencies, please note and acknowledge the following in your response:

The following comments are provided for your information:

Please be advised that DMF (b)(4) is currently deficient. The DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Recited 4/14/94

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-028
DUP Jacket
Division File
Field Copy
HFD-600/Reading File

Endorsements:

HFD-623/EMurphy/3-10-94 Elise Murphy 4/12/94
HFD-613/JPhillips for CShannon/4-7-94 4-13-94
HFD-623/JFan for RKishore/3-20-94 4/14/94 for Dr. Kishore
HFD-617/JWilson/CSO/3-21-94 4/13/94
HFD-611/YMille/4-7-94 4/13/94
X:\WPFILE\BRANCH1\MURPHY\40028N02.LEM
F/T by dvw/4-12-94

NOT APPROVABLE: MAJOR AMENDMENT

PADDOCK LABORATORIES, INC.

Pharmaceuticals for Medicine, Pharmacy and Science

NOTED 4/28/94

April 22, 1994

NEW CORRESP

Office of Generic Drugs
Document Control Room
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Room 150
Rockville, Maryland 20855-2773

re: MAJOR AMENDMENT TO ANDA 40-028

Please accept this letter as acknowledgement of our receipt of the agency's letter dated April 14, 1994, requiring a MAJOR AMENDMENT to our pending ANDA 40-028.

We plan to amend the application as soon as possible, we are awaiting response from the sponsor of DMF [redacted] (b)(4).

We have contacted [redacted] (b)(4) regarding their DMF [redacted] (b)(4) and expressed our concern regarding unresolved deficiencies. We are anxious to gain approval of our application and will keep in communication with them regarding resolution of the deficiencies.

If you are in need of any further assistance, please contact myself or Patrick Johnson, Regulatory Affairs Manager.

ORIGINAL

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

RECEIVED
APR 25 1994
GENERIC DRUGS

cc: Sharon Thoma, Minneapolis District FDA

3101 Louisiana Ave. No., P.O. Box 27286, Minneapolis, Minnesota 55427 • Telephone (612) 546-4676 • FAX (612) 546-4842

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

December 19, 1994

Labeling review completed C Zimmerman 3/2/95

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CONFIDENTIAL
REVIEW, DUPLICATION, OR USE PROHIBITED
WITHOUT PRIOR WRITTEN CONSENT

Office of Generic Drugs
Document Control Room
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Room 150
Rockville, Maryland 20855-2773

AMENDMENT FPL N/AC

re: MAJOR AMENDMENT TO ANDA 40-028

In response to the Agency's letter dated April 14, 1994, enclosed is a MAJOR AMENDMENT to our pending ANDA 40-028. This amendment addresses all deficiencies listed in the April 14 letter. A duplicate copy is included for the archive volume of ANDA 40-028.

A third copy has been submitted to the Minneapolis District Office. Paddock Laboratories does hereby certify that the district copy is a true and complete copy of this MAJOR AMENDMENT.

Mary Beth Erstad 12/19/94
Signature/date

In response to each of the deficiencies listed in the Agency's letter of April 14, 1994 we submit the following:

A. Chemistry Deficiencies:

1. Enclosed is a copy of the worksheet and calculations used for determining the specific gravity and density for lot 3B6291. This is included in Section XXI. Other.

2. The amounts of ingredients have been re-calculated and are included in this major amendment, as Section VII. Revised Components and Composition Statement.

RECEIVED
DEC 27 1994
GENERIC DRUGS

ORIGINAL

Following this page, 3 pages withheld in full (b)(4)

3940 Quebec Avenue North, Minneapolis, MN 55427 • 612.546.4676 • FAX: 612.546.4842 • 800.328.5113

[redacted] (b) (4)

10. Pertaining to the stability of the finished product:

a) We have updated our specifications and CoA for Sodium Content, a copy is provided. Please see the revised Master Control Records in Section XI. Manufacturing and Processing Instructions, 1. Blank Batch Records for Intended Production Runs with Equipment Specified (Master Control Records).

b) We have submitted a revised stability protocol. Please see Section XVII. Stability of Finished Dosage Form, 1. Revised Protocol and Commitment.

c) Please reference revised stability protocol mentioned in b), above.

B. Labeling Deficiencies:

All noted labeling revisions have been made and 12 copies of final printed labeling are included in Section V. Final Printed Labeling.

We have contacted [redacted] (b) (4) regarding their DMF [redacted] (b) (4) and expressed our concern regarding unresolved deficiencies. We are anxious to gain approval of our application and will keep in communication with them regarding resolution of the deficiencies.

We will submit to this application, a letter from the DMF holder [redacted] (b) (4) verifying their resolution of the DMF issues, as soon as it is available.

If you are in need of any further assistance, please contact myself or Carol Anding, Regulatory Affairs Manager.

Sincerely,

Mary Beth G. Erstad

Mary Beth G. Erstad
New Product Development Manager

cc: Minneapolis District FDA - District Copy

LABELING REVIEW WORKSHEET

FIRM: Paddock Lab Inc. ANDA(s) 40-028
DRUG: Sodium Polystyrene Sulfonate Suspension

LABELING OF THE LISTED DRUG

FIRM: Winthrop Pharmaceuticals NDA#: 11-287
APPROVAL DATE: October 21, 1991 REV.DATE: September 1991

CONTAINER LABELS

APPROVED COPY ON FILE? ✓ Y ___ N ___ DATE
USP CONTAINER/CLOSURE REQUIREMENTS: Preserve in well-closed containers, protected from freezing, and from excessive heat
RECOMMENDED STORAGE STATEMENT:
ANDA: Store at CRT 15°-30°C (59°-86°F) Dispense in a tight container, as defined in the USP
NDA: Store at room temperature
OTHER KEY ISSUES: * USP requires the label to state the quantity of sorbitol in a given volume of suspension.

INSERT LABELING

PATENT & EXCLUSIVITY ISSUES: None

BIO ISSUES: Bio waiver granted 1/14/92 per chem rev. #2

ALL INACTIVE INGREDIENTS CITED? ✓ Y ___ N ___
OTHER KEY ISSUES:

APPROVAL SUMMARY

CONTAINER LABELS (SUBMISSION DATE): 60 mL and 480 mL - December 19, 1994

CARTON LABELING (SUBMISSION DATE): none

INSERT LABELING (SUBMISSION DATE): December 19, 1994 (Rev. April 1994).

FORMULATION/SCORING SUMMARY: NONE - suspension

COMMENTS OR FUTURE REVISIONS NEEDED: DESCRIPTION - Identify flavor; WARNINGS - Delete the extra spaces between words in paragraphs 4
Mfg statement - Please spell "Minneapolis" [rather than "Mpls"]

DATE: 3/2/95 REVIEWER: Carol A. Zimmerman /[illegible] 3/10/
SUPERVISOR: [signature] 3/17/95

REV. 2/93; WP: WORK.293;JP

ANDA 40-028

Paddock Laboratories, Inc.
Attention: Mary Beth Erstad
3940 Quebec Avenue North
Minneapolis, MN 55427

JUN 14 1995

Dear Madam:

This is in reference to your abbreviated new drug application dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

Reference is also made to your correspondence dated April 22, 1994, and your amendment dated December 19, 1994.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Chemistry Deficiencies

1. (b) (4)

2.

3.

4.

5.

6. The following comments pertain to your finished drug product stability program:

   a. Please revise your stability data report format by adding the manufacturing date of the stability batch and the date at which the stability study starts.

   b. Please revise your finished drug product stability protocol by adding stability test specifications for microbial limits, sodium content, potassium exchange capacity, sorbitol, pH, appearance, leak testing and preservative effectiveness testing.

7. [redacted] (b) (4)

8. Please be advised that, as of this date, the DMF (b) (4) holder, [redacted] (b) (4), still has not responded to the deficiency letter issued by the FDA on [redacted] (b) (4). Therefore, DMF (b) (4) remains deficient. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

   Please do not respond to this letter until you have obtained evidence from the DMF holder stating that they have taken action on the DMF issues.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Frank O. Holcombe Jr 6/14/05

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-028
DUP File
Division File
Field Copy
HFD-600/Reading File

Endorsements:

HFD-623/J.Fan/5-26-95 6/7/95
HFD-623/R.Kishore, Ph.D/5-30-95 R. Kishore 6-8-95.
HFD-613/C.Zimmermann/A.Payne/6- -95 C Zimmermann 6/7/95
HFD-617/J.Wilson/CSO/5-31-95, 6-7-95 Concur for J. Wilson 6-8-95
X:\WPFILE\BRANCH1\FAN\40028N3.LJF
F/T by dvw/6-1-95.

NOT APPROVABLE: MAJOR AMENDMENT

Larry Phillips 6/8/95

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

ANDA 40-028

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Paddock Laboratories, Inc.
Attention: Mary Beth Erstad
3940 Quebec Avenue North
Minneapolis, MN 55427

MAY 16 2000

Dear Madam:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

We refer you to our "Not Approvable" letter dated June 14, 1995, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

Wm Peter Rickmam
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA # 40-028
DUP/Division File
HFD-610/PRickman

Endorsement:
HFD-617/NMahmud, Chief, RSB, H Spaeth date 5/16/00
HFD-617/SMiddleton, CSO, S. Middleton date 5/11/00
Word File
V:\FIRMSNZ\PADDOCK\LTRS&REV\40028.OTH
F/T by mjl/5/11/00
10 DAY LETTER!

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

May 24, 2000

NEW CORRESP
NC

Office of Generic Drugs
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: **Request NOT to Withdraw ANDA 40-028 for**
Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL
(reference your letter dated May 16, 2000)

Dear Staff:

In a letter dated May 16, 2000 (copy attached), the Agency requested that we take action on Paddock Laboratories' Abbreviated New Drug Application dated August 27, 1991, for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, ANDA 40-028. We were requested to either amend the application or submit a request to withdraw the application within ten days of receipt of the letter.

We are currently preparing a Major Amendment to our application and expect to submit it shortly. However, we will not be able to amend the application within the time period specified in your May 16th notice.

We respectfully request that you NOT initiate an action to withdraw the application at this time.

Archival and review copies are provided. Please let me know if you have any questions or need further information. I can be reached at 763-546-4676 (direct dial) and 763-546-4842 (fax).

Sincerely,
Paddock Laboratories, Inc.

Carol Anding for

Carol Anding
Regulatory Affairs Manager

attachment

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 25 2000
OGD

3940 Quebec Avenue North, Minneapolis, MN 55427 • 612.546.4676 • FAX: 612.546.4842 • 800.328.5113

Paddock Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

NEW CORRESP
NC

June 9, 2000

Office of Generic Drugs
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: **Additional Information regarding our May 24, 2000 Request NOT to Withdraw ANDA 40-028 for Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL (reference your letter dated May 16, 2000)**

Dear Staff:

In a letter dated May 16, 2000, the Agency requested that we take action on Paddock Laboratories' Abbreviated New Drug Application dated August 27, 1991, for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, ANDA 40-028. We were requested to either amend the application or submit a request to withdraw the application. In a letter dated May 24, 2000, we responded by requesting that you NOT initiate an action to withdraw the application. We also stated in the letter that we are preparing a Major Amendment to our application and expected to submit the amendment shortly.

In a telephone communication on June 7, 2000, Saundra Middleton, Project Manager, Regulatory Support Branch, asked that we specify the date we expect to submit the amendment.

We anticipate submitting a Major Amendment to ANDA 40-028 for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL by August 15, 2000. Therefore, we respectfully request that you NOT initiate an action to withdraw the application at this time.

Archival and review copies are provided. Please let me know if you have any questions or need further information. I can be reached at 763-546-4676 (direct dial) and 763-546-4842 (fax).

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUN 12 2000
OGD

Sincerely,
Paddock Laboratories, Inc.

Carol Anding

Carol Anding
Regulatory Affairs Manager

3940 Quebec Avenue North, Minneapolis, MN 55427 • 612.546.4676 • FAX: 612.546.4842 • 800.328.5113

Paddock Laboratories, Inc.

Will amend by 12/1/00 check w/ Saundra Middleton 9/25/00

Pharmaceuticals for Medicine, Pharmacy and Science

September 14, 2000

Office of Generic Drugs
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP
N c

Re: **Update to Request NOT to Withdraw ANDA 40-028**
for Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Staff:

In a letter dated May 16, 2000, the Agency requested that we take action on Paddock Laboratories' Abbreviated New Drug Application dated August 27, 1991, for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, ANDA 40-028. We were requested to either amend the application or submit a request to withdraw the application. We responded in letters dated May 24, 2000 and June 9, 2000, by requesting that you NOT initiate an action to withdraw the application as we were preparing a Major Amendment to our application and expected to submit it by August 15, 2000.

In a telephone communication on September 13, 2000, Saundra Middleton, Project Manager, Regulatory Support Branch, asked that we provide an update since we have not as yet submitted the amendment.

We anticipate submitting the Major Amendment to ANDA 40-028 for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL by December 1, 2000. Therefore, we respectfully request that you NOT initiate an action to withdraw the application at this time.

We have experienced some delays in preparing the amendment and appreciate your patience in this matter. Archival and review copies of this letter are provided. Please let me know if you have any questions or need further information. I can be reached at 763-546-4676 (direct dial) and 763-546-4842 (fax).

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
SEP 15 2000
OGD

Sincerely,
Paddock Laboratories, Inc.

Carol Anding

Carol Anding
Regulatory Affairs Manager

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.4842 • 800.328.5113

MEMO TO FILE

To: 40-028 Paddock's
Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

From: Saundra T. Middleton

Date: February 22, 2001

Subject: Withdrawal letter dated February 15, 2001

Background:

On May 16, 2000 a dunner letter was sent to Paddock Labs., giving them the opportunity to respond to the NA letters of June 14, 1995. On May 24 and September 14, 2000 Paddock responded saying they will amend their application by a particular date.

Since we did not receive a response from them as promised, we initiated an unofficial WD letter. **Only** the original letter was sent to Paddock February 15, 2001 (the other copies were not officially processed). This letter was sent to Paddock expecting them to call and say that they did not want the above ANDA withdrawn.

February 22, 2001, Ms. Carol Sublalka called and stated that she did not want the above ANDA WD and will respond to the NAs by February 27, 2001.

I informed Ms. Sublalka that if we did not receive responses to the NA by February 27, 2001 2001 the above ANDA will be officially withdrawn.

FROM THE DESK OF...

SAUNDRA T. MIDDLETON
CONSUMER SAFETY OFFICER
CDER\FDA\OGD\DLPS
7500 STANDISH PLACE
ROCKVILLE MD 20855

301-827-5862
Fax: 301-594-1174

FROM THE DESK OF...

SAUNDRA T. MIDDLETON
CONSUMER SAFETY OFFICER
CDER\FDA\OGD\DLPS
7500 STANDISH PLACE
ROCKVILLE MD 20855

301-827-5862
Fax: 301-594-1174

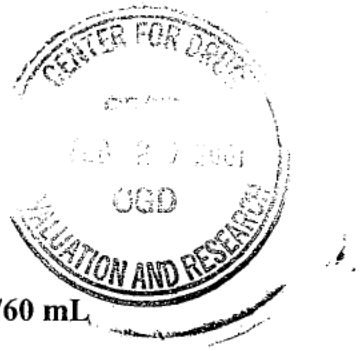
Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

February 26, 2001

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT
N/AC



Re: **MAJOR AMENDMENT to ANDA 40-028 and**
Response to Deficiency Letter dated June 14, 1995, for
Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Staff:

Please accept this Major Amendment to Paddock Laboratories' pending abbreviated new drug application dated August 27, 1991, and amendments dated October 23, 1991, October 5, 1993, and December 19, 1994, for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, ANDA 40-028. This amendment encompasses proposed changes to our ANDA, as well as a response to the June 14, 1995 deficiency letter.

In addition to providing a response to the June 14, 1995 deficiency letter, we propose to amend our application with the following changes and updated information.

1. Paddock Laboratories built a new manufacturing facility and transferred operations to this facility in September 1994. Upon approval of this application, we plan to manufacture Kionex Suspension in the new facility. Supporting information regarding this change is provided in **Section IX.** of this amendment.

2. (b) (4)

3940 Quebec Avenue North, Minneapolis, MN 55427 • 612.546.4676 • FAX: 612.546.4842 • 800.328.5113

Following this page, 3 pages withheld in full (b)(4)

7. (b) (4)

8. **Please be advised that, as of this date, the DMF (b) (4) holder, (b) (4), still has not responded to the deficiency letter issued by the FDA on (b) (4). Therefore, DMF (b) (4) remains deficient. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.**

   Please do not respond to this letter until you have obtained evidence from the DMF holder stating that they have taken action on the DMF issues.

(b) (4)

Finally, we would like to comment on the format and organization of the enclosed amendment. Considering the length of time that has passed since our last submission in December 1994, and the

number and nature of the proposed changes affecting our ANDA, we thought it was important to update our application so that it reflects the current manufacturing environment at Paddock Laboratories. Therefore, this amendment has been organized to be a more or less complete presentation of the Chemistry and Manufacturing Controls portion of our ANDA. We hope this method of organizing the material will facilitate the reviewer's task by limiting the necessity of going "back and forth" between the present amendment and previously submitted material.

The amendment is divided into sections designated by roman numerals. A Table of Contents is provided that cross-references each section, as well as significant subparts of the individual sections, to the actual page number where the section or subpart begins. (A photocopy of the Table of Contents is provided at the beginning of each binder.) Each section of the amendment is marked with a color tabbed divider sheet bearing the number and identity of that section, e.g., "Section V., Labeling". For larger sections, plain white tabbed divider sheets mark the beginning of subparts. Occasionally, untabbed blue divider sheets have been used to mark transitions, for example, the end of a lengthy set of raw data. Whenever the text of a section references either text or an attachment, a cross-reference has been provided to the section where the text or attachment is located. If an attachment is referred to more than once, it usually will only be physically included once in the submission and will be cross-referenced to the section where it is provided. In some instances, a test method provided in one section will be provided in another applicable section for ease of reviewing. Page numbering begins with Section V. "Labeling". The page numbering of the amendment consists of three-digit or four-digit chronological numbers ranging from 001 to 1134. The page number is located in the bottom center of each page.

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please direct any written, telephone or fax communication regarding this amendment to:

Carol Subialka, Regulatory Affairs Analyst
Paddock Laboratories, Inc.
3940 Quebec Avenue North
Minneapolis, Minnesota 55427
Phone: 763-546-4676 Fax: 763-546-4842

Thank you.

Sincerely,
Paddock Laboratories, Inc.

Prepared by: Carol Subialka
Carol Subialka
Regulatory Affairs Analyst

Approved by: Mary Beth Erstad
Mary Beth Erstad
Directory of Product Development

enclosures

MINOR AMENDMENT

ANDA 40-028

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

AUG -7 2001

TO: APPLICANT: Paddock Laboratories, Inc. TEL: 763-546-4676

ATTN: Carol Sublaika FAX: 763-546-4842

FROM: Tim Ames PROJECT MANAGER: 301-827-5848

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

Reference is also made to your amendment(s) dated: February 26, 2001.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (4 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

CMC comments are attached.

Barlow 2-2601 3-1

AUG -7 2001 #4

38. Chemistry Comments to be Provided to the Applicant

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please describe the pharmaceutical functions of the raw materials used in the manufacture of your drug product.

2. (b) (4)

3.

4.

5.

Following this page, 1 page withheld in full (b)(4)

[redacted] (b) (4)

12. Please revise your drug substance release specifications to include pH and impurity specifications. We recommend that you contact the drug substance manufacturer for their most current drug substance impurity specifications.

    In addition, please submit a revised a drug substance certificate of analysis (COA) to reflect these specifications revisions.

13. Please be advised that DMF [redacted] (b) (4) is currently deficient and the DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required prior to the approval of this ANDA.

14. Please provide sample calculations to demonstrate how you have derived the quantity of the active and the inactives for your Sodium Polstyrene Sulfonate Suspension USP production batches of [redacted] (b) (4) as provided on page 087 of your February 26, 2001 amendment.

15. Please establish release and stability impurity test specifications (both individual known, unknown and total) for your finished drug product. Specifications should be based on actual test data observed.

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

1. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

2. Bioequivalence information you have provided is under review by our Division of Bioequivalence. After the review is complete, any deficiencies found will be communicated to you under separate cover.

3. Labeling information you have provided is under review by our Division of Labeling. After the review is complete, any deficiencies found will be communicated to you under separate cover.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date SEP 25 2001

From Consumer Safety Officer, Investigations & Pre-approval Compliance Branch/DMPQ (HFD-324)

Subject Concurrence with District Withhold Recommendation
See below ANDA

To Patricia Beers- Block - Branch Chief, Review Support Branch
Office of Generics Drugs

Firm: Paddock Laboratories, Inc
3940 Quebec Avenue North
New Hope, MN 55427
CFN: 2127022

The purpose of this memo is to provide the Office of Compliance's concurrence to withhold approval of the below-mentioned ANDA.

On March 6, 2001, this firm received a Warning Letter from Minneapolis District. Paddock Laboratories, Inc is considered unacceptable manufacturer for profile classes LIQ, CTL, POW and SUP until a reinspection confirms the firm's corrective actions.

A copy of the Warning Letter is enclosed for your information.

Should you have any questions, please contact me at (301) 827-0062.

ANDA# 40028/000 Sodium Polystyrene Sulfonate 15g/ 60mL
ANDA# 75600/000 Podofilox Solution 0.5%

Wilma Labrador
Compliance Officer

Distribution (with a copy of the March 6, 2001 Warning Letter) as indicated

Cc:
HFD-324 R/F
HFD-324 W. Labrador
HFR-CE800
Concur: BHartman 9/24/01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

file in jacket

ANDA 40-028

Memorandum

Date • JAN 22 2002

From CSO, Investigations and Preapproval
Compliance Branch, HFD-324

Subject Recommendation to withhold Approval
ANDA 40-028

Firm: [redacted] (b) (4)

To Patricia Beers Block, HFD-617
Office of Generic Drugs

We have completed our review of the inspection reports that covered the subject ANDAs and firm. The inspection was performed from [redacted] (b) (4) through [redacted] (b) (4) and resulted in a district recommendation to withhold approval. The Division of Manufacturing and Product Quality concurs with the recommendation to withhold approval of the subject ANDA. An [redacted] (b) (4) recommendation is currently under review by the Case Management Branch.

1. [redacted] (b) (4)
2.
3.
4.
5.

We are including a copy of the inspection report for your review. If you have questions, please contact the undersigned at 301-827-0062.

Bruce W. Hartman

attachment

October 31, 2002

NAI CK
11/19/02

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, Room 150
Rockville, MD 20855

NEW CORRESP
NC

Re: **ANDA 40-028**
FDA Deficiency Facsimile dated August 7, 2001 for
Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Paddock Laboratories is in the process of completing our response to the Minor Deficiency Letter referenced above. We plan to respond to all deficiencies cited in this facsimile early next year.

Please also note that we await your decision on the bioequivalency waiver request for this product. Thank you.

Sincerely,

Frank B. Freedman

Frank B. Freedman, Ph.D.
Regulatory Affairs Analyst

RECEIVED
NOV 0 1 2002
OGD / CDER

11/1/02

ANDA 40-028

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

DEC 30 2002

Paddock Laboratories, Inc.
Attention: Carol Subialka
3940 Quebec Avenue North
Minneapolis, MN 55427

Dear Madam:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60mL.

We refer you to our "Not Approvable" letter dated August 7, 2001, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

If you have further questions you may contact Martin H. Shimer, Project Manager, Regulatory Support Branch, at (301) 827-5862.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

Wm Peter Rickmam
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA # 40-028
DUP/Division File
HFD-610/PRickman
Endorsement:
HFD-617/Gregg Davis, Chief, RSB
HFD-617/MShimer, CSO, 31 December 2002

V:\FIRMSNZ\PADDOCK\LTRS&REV\40028.OTH

F/T by cll/12/6/02

10 DAY LETTER!

PADDOCK LABORATORIES 1978–2003 25 years

4/28/03 Spoke with Dr. Stan Freedman. He states they hope to have a response by 6/03. I told him if we did not receive full amend by 7/31/03 we will WD ANDA – S. Middleton

NAI NAS 1-30-03

NEW CORRESP NC

January 27, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attention: Mr. Martin H. Shimer

Re: **FDA Letter Dated January 17, 2003 About ANDA 40-028**
Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Mr. Shimer:

Paddock Laboratories is working on the above referenced product, so we can provide a Minor Amendment to respond to deficiencies cited: (1) in your letter of August 7, 2001 and (2) facsimile from Craig Kiester dated December 16, 2002. We plan to submit the Minor Amendment late summer, assuming that we have sufficient time to complete our chemistry development activities. Therefore, kindly keep the ANDA file open for this product.

Please direct any questions to my attention at the address below or by telephone (763.546.4676). Thank you.

Sincerely,

Frank B. Freedman

Frank B. Freedman, Ph.D.
Regulatory Affairs Analyst

RECEIVED
JAN 28 2003
OGD / CDER

SMART ALTERNATIVES

Paddock Laboratories, Inc.

3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

July 14, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AF

Re: Minor Amendment to ANDA 40-028
Kionex™ Polystyrene Sodium Sulfonate Suspension, USP, 15 g/60 mL
Deficiency Response and Final Printed Labeling

Dear Staff:

Please accept this Minor Amendment Paddock Laboratories' ANDA 40-028 for Kionex Polystyrene Sodium Sulfonate Suspension, USP, 15 g/60 mL. This Minor Amendment:

- provides our response to labeling deficiencies cited in the FDA facsimile dated December 16, 2002 and
- provides proposed final printed labeling.

Attachment 1 contains a copy of the FDA facsimile of December 16, 2002 with the stated labeling deficiencies and our response to them. Attachment 2 provides a side-by-side comparison of the proposed labeling changes. Attachment 3 contains the final printed labeling, using the generic name "Kionex™ Polystyrene Sodium Sulfonate Suspension, USP" (sodium polystyrene sulfonate suspension, USP).

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., certifies that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)]. Please contact Pat Johnson at 763-732-0393 or 763-546-4842 (facsimile) if you have any questions or need additional information. Thank you.

Sincerely,

Frank B. Freedman, Ph.D.
Regulatory Affairs Analyst

Attachments

RECEIVED
JUL 15 2003
OGD/DDER

Paddock Laboratories, Inc.
3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

ORIG AMENDMENT
N/AM

July 29, 2003

BIOAVAILABILITY

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: **MINOR AMENDMENT to ANDA 40-028**
Kionex ™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL
Response to FDA Deficiency Letter dated August 7, 2001

Dear Staff:

Please accept this Minor Amendment for the above-referenced FDA Deficiency Letter about deficiencies in our Major Amendment of February 26, 2001 (herein referred to as the "Major Amendment" in this submission). A copy of this Deficiency Letter is enclosed in Attachment 1. Attachment 2 provides our response to each deficiency. Attachments 3-10 contain supporting documents for our deficiency responses.

Paddock Laboratories seeks a bioequivalence waiver for this product. This request was part of our ANDA in 1991. The Company has inquired several times in the last year about this waiver.

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., certifies that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact Patrick Johnson, Director of Regulatory Affairs, at 763-732-0393 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,

Frank B. Freedman, Ph.D.
Regulatory Affairs Analyst

RECEIVED
JUL 30 2003
OGD/CDER

Attachments
FBF:sw

8/5/03

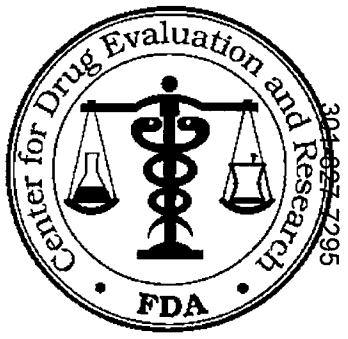
3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

MINOR AMENDMENT

ANDA 40-028

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

NOV 18 2003



APPLICANT: Paddock Laboratories, Inc. TEL: 763.732.0393

ATTN: Patrick Johnson FAX: 763.546.4842

FROM: Craig Kiester PROJECT MANAGER: (301) 827-5765

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL.

Reference is also made to your amendment(s) dated: July ~~28~~ 29, 2003. 11/19/03

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__1__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

11/18/03

pt

36. Chemistry Comments to be Provided to the Applicant

NOV 18 2005

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

The Drug Master File (DMF) (b) (4) which you have referenced for your supplier of the (b) (4) has been reviewed and found to be deficient. The deficiencies have been transmitted to the DMF holder. Please do not respond to this deficiency letter until you have received notification from the DMF holder that the deficiencies have been addressed. Please note that each of the deficiencies must be found to be satisfactory before the approval of this application.

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

1. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with cGMP(s) at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

2. Bioequivalence information you have provided is under review by our Division of Bioequivalence. After the review is complete, any deficiencies found will be communicated to you under separate cover.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

ORIG AMENDMENT

December 29, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: MINOR AMENDMENT to ANDA 40-028 in Response to the Deficiency Letter dated November 18, 2003 for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Staff:

Please accept this Minor Amendment to Paddock Laboratories' pending abbreviated new drug application for Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, ANDA 40-028, dated October 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment provides our responses to the November 18, 2003 deficiency letter.

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact me at 763-732-0364 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,

Daniel W. Rockcliffe
Regulatory Affairs Analyst

RECEIVED
DEC 30 2003
OGD/CDER

Paddock Laboratories, Inc.
3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

Nerurkar, Shriniwas G

From: Conner, Dale P
Sent: Wednesday, April 28, 2004 5:54 PM
To: Nerurkar, Shriniwas G; Davit, Barbara M
Cc: Gunther, Sheryl
Subject: RE: REVIEW 40028 Paddock Sodium Polystyrene Sulfonate Suspension, 15 g/60 mL 2-26-01 Sheryl AC

Vijay:

I have put this comment in the review but you may have trouble finding it. The comment about IIG and sorbic acid doesn't make sense to me. I think that you are mixing up the concept of a non-absorbable drug substance with the inactive ingredients that actually may be absorbable. YOU MADE THIS COMMENT BECAUSE ON PAGE 4 WE WROTE THAT [redacted] (b) (4). THAT SENTENCE IS REMOVED.
Also if your reviewers want to use their old reviews as templates to do their newer reviews (not recommended) please tell them to turn track changes off when they are deleting the old information. In this case it was clotrimazole troche, ANDA 76387. Although this might seem to save time, it runs the risk of leaving information pertaining to another review in your new review. People should be encouraged to use a blank template.

Dale

5/7/2004

D.

WE DISCUSSED ABOUT, IIG LIST, DOSAGE FORMS, AND DRUG REGIMENS AND INACTIVE INGREDIENT INGESTED/DAY. PLEASE, SEE P4 (REVIEWER COMMENT REGARDING IIG LIMITS), WE TRIED TO DETERMINE IIG LEVELS AS PER OUR DISCUSSION. WE SIMPLY COULD NOT DO IT.

THANKS
V.

40028A0201.doc (1 MB)

-----Original Message-----
From: Nerurkar, Shriniwas G
Sent: Monday, April 26, 2004 7:04 PM
To: Conner, Dale P; Davit, Barbara M
Cc: Gunther, Sheryl
Subject: REVIEW 40028 Paddock Sodium Polystyrene Sulfonate Suspension, 15 g/60 mL 2-26-01 Sheryl AC

Dale and Barbara:

Please find Sheryl's document for a tertiary review.

Thanks.

Vijay

<< File: 40028A0201.doc >>

MINOR AMENDMENT

ANDA 40-028

JUL 09 2004

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

APPLICANT: Paddock Laboratories, Inc. TEL: 763.732.0364

ATTN: Daniel W. Rockcliffe FAX: 763.546.4842

FROM: Simon Eng PROJECT MANAGER: (301) 827-5765

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated August 27, 1991, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Polystyrene Sulfonate Suspension USP, 15g/50mL.

Reference is also made to your amendment(s) dated: July 14 and December 29, 2003.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachment (__1__ page). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

7/9/04

36. Chemistry Comments to be Provided to the Applicant

ANDA: 40-028 APPLICANT: Paddock Laboratories, Inc.

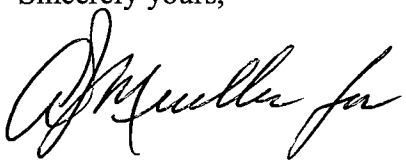
DRUG PRODUCT: Sodium Polystyrene Sulfonate Suspension USP, 15 mg/60 mL

The deficiencies presented below represent MINOR deficiencies.

Deficiency:

The firms referenced in the application relative to the manufacture and testing of the product is on withhold status for cGMP(s) compliance. Please do not respond until the compliance issues have been resolved.

Sincerely yours,



Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

September 20, 2004

Mr. Gary Buehler
Director, Office of Generic Drugs
CDER/FDA
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

ORIGINAL

ORIG AMENDMENT
N/AM

Re: **Minor Amendment to ANDA 40-028**
For Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Mr. Buehler:

In a letter dated JUL 09, 2004, (copy attached) the Agency informed us that our application, Paddock Laboratories' ANDA 40-028, for Kionex™ Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL, submitted August 27, 1991, is deficient. We were requested to either amend the application or submit a request to withdraw the application. The deficiency is stated in bold on the following page, followed by our response.

Archival and review copies of this letter are provided. A third copy has been sent to the Minneapolis District Office (field copy). Paddock does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please let me know if you have any questions or need further information. I can be reached at 763-732-0297 (direct dial) and 763-546-4842 (fax).

Sincerely,
Paddock Laboratories, Inc.

David Rosenberg

David Rosenberg
Regulatory Affairs Analyst

RECEIVED
SEP 2 2 2004
OGD/OLRR

Paddock Laboratories, Inc.
3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

ANDA 40-028 Paddock Laboratories, Inc.
Sodium Polystyrene Sulfonate Suspension USP, 15 mg /60 mL
September 20, 2004; Minor Amendment response to Deficiency Letter, July 9, 2004

Deficiency:

The firm referenced in the application relative to the manufacture and testing of the product is on withhold status for cGMP(s) compliance. Please do not respond until the compliance issues have been resolved.

We are updating the application to state that the firm, (b) (4), designated for testing of the drug product, is being removed. We are in the process of qualifying a new testing laboratory.

Paddock Laboratories, Inc.

06 July 2007

Pharmaceuticals for Medicine, Pharmacy and Science

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North 4 (MPN4) HFD-600
7519 Standish Place
Rockville, MD 20855

FW CORRESP

Re: TELEPHONE AMENDMENT to ANDA 40-028; Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL

Dear Mr. Buehler:

Please accept this Telephone Amendment to Paddock Laboratories' (Paddock) pending abbreviated new drug application for the above referenced drug product. This amendment provides our response to a Telephone Communication with Project Manager Dr. Simon Eng, dated June 19, 2007, in which Dr. Eng stated that the drug substance manufacturing site listed in the original application needs to be withdrawn prior to the Agency granting approval of our application.

Please be advised Paddock officially requests that you withdraw [redacted] (b) (4) [redacted] (b) (4) (as was listed in our original ANDA application.) Please note that this change is the same change as was requested in Paddocks' *"Response to Deficiency Letter dated June 14, 1995"* which was sent to FDA on February 26, 2001. Specifically, reference is made to page 5 of 6, section 8 in which Paddock states "…we ask that you withdraw DMF [redacted] (b) (4) from our ANDA and replace it with DMF [redacted] (b) (4)".

Paddock is also requesting to withdraw [redacted] (b) (4) testing facility, and [redacted] (b) (4) facility, both of which were listed in our original ANDA application.

Please be advised, however, that Paddock does intend to use [redacted] (b) (4) [redacted] (b) (4) testing facility as was listed in our original ANDA application.

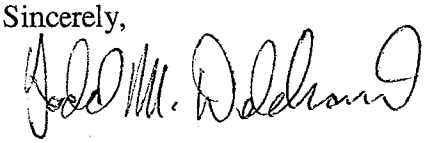
Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc. does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

RECEIVED
JUL 10 2007
OGD

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.1342 • 800.328.5113

Please contact me at 763-732-0364 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,



Todd M. Delehant, Ph.D.
Regulatory Affairs Manager

N000/MC F

ORIG AMENDME

Paddock Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

September 13, 2007

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North 4 (MPN4) HFD-600
7519 Standish Place
Rockville, MD 20855

RECEIVED
SEP 14 2007
OGD / CDER

Re: ANDA 40-028; Sodium Polystyrene Sulfonate Suspension USP, 15 g/60 mL
TELEPHONE AMENDMENT

Dear Mr. Buehler:

Please accept this Telephone Amendment to Paddock Laboratories' (Paddock) pending Abbreviated New Drug Application for the above referenced drug product. This amendment provides our response to a Telephone Communication with Bob West dated September 13, 2007, in which Mr. West stated that the above named drug product may require (b) (4) (b) (4) contained in the product should the Agency request such action from Carolina Medical for the reference listed drug product (RLD).

Please be advised that Paddock acknowledges that the RLD may be (b) (4) (b) (4). Should this occur Paddock commits to cooperating with the Agency to (b) (4) as appropriate.

This response is initially being sent via facsimile. Review and archival copies will be sent via next day air today. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact me at 763-732-0364 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,
Paddock Laboratories, Inc.

Todd M. Delehant, Ph.D.
Regulatory Affairs Manager

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.4842 • 800.328.5113

From: West, Robert L
Sent: Thursday, September 13, 2007 8:34 AM
To: Eng, Simon
Cc: Doan, Dat
Subject: FW: (b) (4) OF SODIUM POLYSTYRENE SULFONATE SUSPENSION USP,

Simon/Dat:

Please file this series of emails in DFS for ANDA 40-028.

Thank you,

Bob

From: Buehler, Gary J
Sent: Thursday, September 13, 2007 7:24 AM
To: West, Robert L
Subject: FW: (b) (4) OF SODIUM POLYSTYRENE SULFONATE SUSPENSION USP,

Hey Bob

Looks like Norman is OK with our moving ahead. They do have to be aware that they may have (b) (4) We can go ahead and approve.

Gary

From: Stockbridge, Norman L
Sent: Thursday, September 13, 2007 7:20 AM
To: West, Robert L
Cc: Buehler, Gary J; Eng, Simon; Patel, Rashmikant M
Subject: RE: (b) (4) OF SODIUM POLYSTYRENE SULFONATE SUSPENSION USP,

Sounds like they are already familiar with the issue. I think it is reasonable to approve them with the clear understanding that we may require them (b) (4).
Regards,
Norman

From: West, Robert L
Sent: Wednesday, September 12, 2007 4:31 PM
To: Stockbridge, Norman L
Cc: Buehler, Gary J; Eng, Simon; Patel, Rashmikant M
Subject: (b) (4) OF SODIUM POLYSTYRENE SULFONATE SUSPENSION USP,

Dr. Stockbridge:

Please recall the agency's (b) (4) of Sodium Polystyrene Sulfonate Suspension USP, (Kayexalate). Dr. Elizabeth Hausner's review of Carolina Medical's proposed protocol can be accessed in DFS under ANDA 87-859.

We believe that the sponsor of the reference listed product, Carolina Medical, is currently conducting a rat study to assess the G.I. obstruction potential of sorbitol. (b) (4)
(b) (4)

We currently have an ANDA from Paddock Laboratories for this drug product that also

contains sorbitol and is otherwise ready for approval. Paddock is requesting approval based upon the continued marketing of the Carolina product containing an equivalent concentration of sorbitol.

Would it be advisable to delay the approval of Paddock's ANDA until the Carolina Medical study is completed (timeframe unknown) and analyzed? Alternatively, would it be reasonable to proceed to approve the Paddock at this point with a commitment from Paddock that they will (b) (4) if the agency concludes that the Carolina Medical product (b) (4) (b) (4)?

Thank you,

Bob West
Deputy Director
OGD

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

/s/

Dat Doan
9/13/2007 09:44:24 AM
CSO

Dat Doan
9/13/2007 09:44:44 AM
CSO

OGD APPROVAL ROUTING SUMMARY

ANDA # 40-028 Applicant Paddock Laboratories, Inc.
Drug Sodium Polystyrene Sulfonate Suspension USP Strength(s)15 g/60 mL

APPROVAL ☒ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

REVIEWER: **DRAFT Package** **FINAL Package**

1. **Martin Shimer**
Chief, Reg. Support Branch
Date31 Aug 2007 Date9/12/07
InitialsMHS Initials rlw

Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92) Pediatric Exclusivity System
RLD = _____ NDA#87-859
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked N/A
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days:Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
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:Full Approval
Comments:This ANDA was submitted in 1992 based upon the RLD SPS, ANDA 87-859. There are no patents or exclusivities which remain protecting this drug product. This ANDA is eligible for Full Approval.

2. Project Manager, Simon Eng Team1
Review Support Branch
Date8/30/07 Date_____
Initialsdd Initials_____

Original Rec'd date8/27/91
Date Acceptable for Filing
Patent Certification (type)I
Date Patent/Exclus.expires
Citizens' Petition/Legal Case Yes☐ No ☐
(If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒
Priority Approval Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise)

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 6/18/07
Date of Office Bio Review 5/7/04
Date of Labeling Approv. Sum.
Date of Sterility Assur. App.
Methods Val. Samples Pending Yes ☐ No ☒
MV Commitment Rcd. from Firm Yes ☐ No ☒
Modified-release dosage form: Yes ☐ No ☒
Interim Dissol. Specs in AP Ltr: Yes ☐

Acceptable Bio review tabbed Yes ☒ No ☐
Bio Review Filed in DFS: Yes ☐ No ☒
Suitability Petition/Pediatric Waiver
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____
Comments:

3. Labeling Endorsement
Reviewer:
Date_____
Name/Initials_____

Labeling Team Leader:
Date9/12/07
Name/Initialsrlw/for

Comments:
From: Grace, John F
Sent: Thursday, August 30, 2007 10:48 AM
To: Barlow, James T; Doan, Dat
Subject: RE: 40-028 endorsement

concur

From: Barlow, James T
Sent: Thursday, August 30, 2007 10:45 AM

To: Doan, Dat
Cc: Grace, John F
Subject: RE: 40-028 endorsement

I checked Drugs@FDA,OB and USP.
The labeling AP summary signed by John Grace on 9/4/03 remains acceptable.

From: Doan, Dat
Sent: Thursday, August 30, 2007 10:39 AM
To: Barlow, James T
Cc: Grace, John F
Subject: 40-028 endorsement

Hi John, Jim:

Can I please get an endorsement for the following ANDA 40-028/Paddock Labs?

<< File: 40028.ap.letter.DOC >>
<< File: 40028.ap.labeling.summary.pdf >>
Thanks,

Dat Doan, R.Ph.

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 9/12/07
OGD Regulatory Counsel, Post-MMA Language Included ☐ Initials rlw/for
Comments:N/A. No patents listed in the current "Orange Book".

5. Div. Dir./Deputy Dir. Date 9/10/07
Chemistry Div. I II OR III Initials RMP
Comments:The CMC section is satisfactory for AP. The EER is now satisfactory too. The AP draft letter however needs a correction because there is no in-vitro dissolution specification for this DP in USP since sodium polystyrene sulfonate resin is not absorbed in-vivo.

6. Frank Holcombe **First Generics Only** Date 9/12/07
Assoc. Dir. For Chemistry Initials rlw/for
Comments: (First generic drug review)
N/A. Both Roxane and Carolina Medical currently have approved ANDas for this drug product.

7. Vacant Date _____
Deputy Dir., DLPS Initials _____
RLD = SPS Suspension 15 g/60 mL
Carolina Medical ANDA 87-859

8. Peter Rickman Date 9/12/07
Director, DLPS Initials rlw/for
Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐No ☐;Petition: Yes☐ No☐
Comments:Bioequivalence waiver granted under 21 CFR 320.24 (b)(6). Office-level bio endorsed 5/7/04.

FPL found acceptable for approval 9/4/03 (as endorsed 8/30/07, above).

CMC found acceptable for approval

OR

8. Robert L. West — Date 9/14/07
Deputy Director, OGD — Initials RLWest
Para.IV Patent Cert: Yes☐ No☒; Pending Legal Action: Yes☐ No☒; Petition: Yes☐ No☒
Press Release Acceptable ☐
Comments:Acceptable EES dated 6/18/07 (Verified 9/12/07). No "OAI" Alerts noted.

We are aware of the agency's concern over the potential of high concentrations of sorbitol in an oral formulation to cause bowel necrosis. The agency has been in communication with the NDA and ANDA holders on this issue. In response, Carolina Medical is currently conducting a rat study. Paddock submitted an amendment dated September 13, 2007, agreed to a [redacted (b)(4)] of this drug product if the agency were to conclude that the RLD, Carolina Medical's SPS Suspension, [redacted (b)(4)] to address the sorbitol/bowel necrosis issue. I have contacted Dr. Norman Stockbridge of CDER's gastrointestinal drugs division who agreed that this was a reasonable approach to take with regard to Paddock's ANDA (memo in DFS).

There are no patents or exclusivity listed in the current "Orange Book" for this drug product.

This ANDa is recommended for approval.

9. Gary Buehler — Date 9/14/07
Director, OGD — Initials rlw/for
Comments:
First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Team Simon Eng — Date9/17/07
Review Support Branch — Initials se

_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
11:15amTime notified of approval by phone
11:17amTime approval letter faxed

FDA Notification:
9/17Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
9/17Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

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

/s/

Simon Eng
9/17/2007 11:20:15 AM