DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021551/S-013 **SUPPLEMENT APPROVAL**

Braintree Laboratories, Inc.
Attention: Mark Cleveland, Ph.D.
Vice President, New Product Development
60 Columbian Street West
P.O. Box 850929
Braintree, MA 02185

Dear Dr. Cleveland:

Please refer to your Supplemental New Drug Application (sNDA) dated September 11, 2009, received September 17, 2009 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for HalfLytely® and Bisacodyl Tablet Bowel Prep Kit (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed-release tablet).

We acknowledge receipt of your submissions dated November 4, 11, 2009; December 17, 18, 2009; January 26, 29, 2010; February 26, 2010; March 25, 2010; April 30, 2010; June 2, 3, 30, 2010; July 6, 8, 12, 13, 14, 15, 2010.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your July 6, 2010 submission containing final printed carton and container labels.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages birth to 11 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1666-1 A Retrospective Survey of Colonoscopy Rates in the Pediatric Population.

This data review will determine the number of colonoscopies being performed in the pediatric age groups under consideration (0 - 5 years and 6 - 11 years). The need to develop an age appropriate formulation will be based on the colonoscopy utilization data obtained in this study.

Protocol Submission: October 31, 2010
Study Completion: April 30, 2011
Final Report Submission: July 31, 2011

1666-2

A randomized, single-blind, multicenter dose-ranging study to obtain pharmacokinetic data and to compare the safety and efficacy of HalfLytely and Bisacodyl Tablet versus NuLYTELY in children (6 - 11 years of age).

Protocol Submission: August 31, 2011
Study Completion: August 31, 2013
Final Report Submission: February 28, 2014

Study 3 will be conducted if data from Study 1 and 2 support evaluation of HalfLytely and Bisacodyl Tablet in younger pediatric subgroups.

1666-3

A randomized, single-blind, multicenter dose-ranging study to obtain pharmacokinetic data and to compare the safety and efficacy of HalfLytely and Bisacodyl Tablet versus NuLYTELY in children (birth - 5 years of age).

Protocol Submission: February 28, 2014
Study Completion: February 28, 2016
Final Report Submission: August 31, 2016

Submit all clinical protocols to your IND for this product. Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments".**

We note that you have fulfilled the pediatric study requirement for ages 11 to 17 years for this application.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment in your submission dated June 30, 2010. This commitment is listed below.

1666-4

Conduct a prospective, 3-arm trial evaluating HalfLytely with 5 mg bisacodyl, 2L polyethylene glycol solution plus electrolytes without bisacodyl, and 4L polyethylene glycol solution plus electrolytes without bisacodyl. The trial should evaluate the pharmacokinetics, efficacy and safety of each regimen in cleansing the colon as a preparation for colonoscopy in adults. Collect pharmacokinetic data in a subset of patients.

Protocol Submission: January 31, 2011
Study Completion: January 31, 2014
Final Report Submission: July 31, 2014

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). The details of the REMS requirements were outlined in our REMS notification letter dated July 7, 2010.

Since HalfLytely® and Bisacodyl Tablets Bowel Prep Kit (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed-release tablet) was approved on September 24, 2007, we have become aware of new safety information derived from clinical trial data related to a class effect regarding fluid and electrolyte disturbances that can lead to serious adverse events, including cardiac arrhythmias, seizures and renal impairment. We consider this information to be "new safety information" as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on July 15, 2010 and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to an evaluation of patients' understanding of the serious risks of HalfLytely® and Bisacodyl Tablets Bowel Prep Kit (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed-release tablet).

Assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 021551 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021551
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT FOR (NEW INDICATION FOR USE)
FOR NDA 021551
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter,

submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

As required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Diane Munro, Regulatory Project Manager, at (301) 796-4257.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21551	SUPPL-13	BRAINTREE LABORATORIES INC	HALF LYTELY BISACODYL BOWEL PREP KIT

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

/s/

DONNA J GRIEBEL
07/16/2010