Date: January 6, 2015

To: Petar Mamula
CC: Jennifer Swope
From: The Committees for the Protection of Human Subjects (IRB)

Re: IRB 13-010687, **Protocol Title:** A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and
Efficacy of Prepopik™ versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years
Sponsor or Funder: Ferring Pharmaceuticals, Inc.

IRB SUBMISSION: NOTICE OF IRB APPROVAL

Dear Dr. Mamula,

The study referenced above was reviewed and approved by the convened CHOP IRB on June 4, 2014. Any remaining stipulations have since been addressed and required ancillary committee approvals have been received.

Approval is effective as of January 6, 2015. IRB approval for the study will expire on June 3, 2015.

The approved enrollment limit for this study at CHOP is 15 subjects, with a total enrollment study wide of 75 subjects.

Please note that an amendment must be submitted to upload a study summary document for IRB review and approval prior to the enrollment of any non-English speaking individuals.

Main Study Document(s):

- Protocol, version 5 (dated July 28, 2014; uploaded August 20, 2014)
- Protocol Note to File (dated February 12, 2014; uploaded April 16, 2014)
- Consent Form (dated December 19, 2014; uploaded January 5, 2015)
- PREPOPIK Package insert (dated November 2013; uploaded April 16, 2014)

Submitted Document(s):

- Tolerability & Satisfaction Questionnaire, version 10 (dated January 31, 2014; uploaded April 16, 2014)
- PREPOPIK Dosing Instructions, version 1.1 (dated February 10, 2014; uploaded April 16, 2014)

Please refer to the eIRB application for a complete list of all documents submitted to the IRB.

Subpart Determination(s):

- **Subpart B Determination:** §46.204 for subjects who become pregnant while on the study
- **Subpart D Determinations:** §46.405 or §50.52 for the main clinical trial, §46.404 or §50.51 for infants born to subjects who become pregnant while on the study

Consent/Assent/HIPAA:

- **Consent Form:** Written consent/assent/HIPAA authorization are required for the main clinical trial. The approved, date-stamped informed consent document is available in the main study workspace under the IRB Correspondence tab.
- **Waiver of Assent:** A waiver of assent has been approved per 45 CFR 46.408(a) / 21 CFR 50.55(c) for infants born to subjects who become pregnant while on the study, due to their age.

Please note the following conditions for conducting this study:

INVESTIGATOR RESPONSIBILITIES: Please refer to the following page on the IRB's website for information and guidance on the responsibilities of investigators who conduct human subjects research at CHOP: https://intranet.research.chop.edu/display/cmtirb/Investigator+Responsibilities.

REPORTABLE EVENTS: On-site reportable events, such as serious adverse events, protocol deviations/violations, unanticipated problems involving risk to subjects or others, and non-compliance that occurs in relation to this study, must be reported to the IRB in a timely manner, as outlined in IRB SOP 408. Please refer to the following page on the IRB's website for information about reportable events: https://intranet.research.chop.edu/display/cmtirb/Reportable+Events.

RENEWAL (Continuing Review/Progress Reports): Approval is valid until the expiration date for your protocol shown above. The IRB must review and approve all human subject research studies at intervals appropriate to the degree of risk. To avoid lapses in study approval and suspension of study procedures, please submit the application for continuing review at least 45 days before the expiration date for your protocol. This will provide the IRB will sufficient time to review your study. As a courtesy, the IRB will send you a reminder; however, it is your responsibility to ensure that you submit the continuing review application on time.

CHANGES/AMENDMENTS/MODIFICATIONS/REVISIONS: You must obtain IRB review and approval under 45 CFR 46 / 21 CFR 50, 56 if you change any aspect of this study, including but not limited to study procedures, consent form(s), co-investigator, study staff, advertisements, protocol document or procedures, investigator drug brochure or accrual goals. Implementation of these changes cannot occur until you receive the IRB Approval notice.

COMPLETION OF STUDY: Notify the IRB when your study is completed. Neither study closure by the sponsor nor the investigator removes your obligation for submitting a timely continuing review or a final report.

If you have any questions, please click on the IRB# (above) and contact the IRB analyst listed in the study work space.

DHHS Federal Wide Assurance Identifier: FWA0000459

IS_034

**** *This memorandum constitutes official CHOP IRB correspondence.* ****

3535 Market Street, Suite 1200, Philadelphia, PA, 19104
Tel: 215-590-2830
Email: IRBOffice@email.chop.edu
Website: https://irb.research.chop.edu/

INDIANA UNIVERSITY

OFFICE OF THE VICE PRESIDENT FOR RESEARCH

Office of Research Compliance

To: Joseph Croffie
PED-GASTROINTESTINAL DISEASES

From: Human Subjects Office
Office of Research Administration – Indiana University

Date: February 06, 2014

RE: **NOTICE OF APPROVAL - NEW PROTOCOL**

Protocol Title:	A Randomized, Assessor-Blind, Multicenter, Dose-Randing Study Comparing the Safety and Efficacy of Prepopik versus Polyethylene Glycol Preparation (local standard of care) in Children Aged 9 Years to 16 years
Protocol #:	1312998338 | no
Funding Agency/Sponsor:	FERRING INTERNATIONAL PHARMASCIENCE CENTER U.S. 00349228
Review Level:	Full

Study Expiration Date: January 28, 2015

The Indiana University Institutional Review Board (IRB-05) recently reviewed the above-referenced protocol. In compliance with (as applicable) 21 C.F.R. § 56.109 (e) and 46 C.F.R. § 46.109 (d), this letter serves as written notification of the IRB's determination.

The study is approved. The approval period is valid from January 29, 2014 to January 28, 2015

Approval of this study is based on your agreement to abide by the policies and procedures of the Indiana University Human Research Protection Program and does not replace any other approvals that may be required. Relevant policies and procedures governing Human Subject Research can be found at: http://researchadmin.iu.edu/HumanSubjects/hs_policies.html.

IRB approval is required prior to implementing any changes or amendments in the protocol, regardless of how minor, except to eliminate immediate hazards to subjects. No changes to the informed consent document may be made without prior IRB approval.

If you submitted and/or are required to provide participants with an informed consent document, **a copy of the most recently approved stamped document is enclosed and must be used to enroll participants.**

The initial approval period is noted above. Continued approval is contingent upon the submission of a renewal application to the Human Subjects Office in a timely fashion. Failure to submit the renewal notice in a timely fashion may result in the expiration and subsequent suspension of all protocol activities. **Failure to receive notification from the Human Subjects Office will not relieve you of your responsibility to ensure compliance with Federal Regulations regarding annual review [as applicable, 21 C.F.R. § 56.109(f) and 45 C.F.R. § 46.109(e)]**

You should retain a copy of this letter and all associated approved study documents for your records. Please refer to the assigned study number and exact study title in future correspondence with our office. Additional information is available on our website at http://researchadmin.iu.edu/HumanSubjects/.

If your source of funding changes, you must submit an amendment to update your study documents immediately.

If you have any questions or require further information, please contact the Human Subjects Office via email at irb@iu.edu or via phone at (317)274-8289 (Indianapolis) or (812) 856-4242 (Bloomington).

/enclosures

Western Institutional Review Board®
1019 39th Avenue SE | Puyallup, WA 98374
Office: (360) 252-2500 | Toll Free: (800) 562-4789
www.wirb.com

Certificate of Approval

THE FOLLOWING WERE APPROVED

INVESTIGATOR: Reed A. Dimmitt MD, MSPH
Department of Pediatric Gastroenterology and Nutrition
Suite 618, Jarman F. Lowder Building
1600 7th Avenue South
Birmingham, Alabama 35233

BOARD ACTION DATE: 02/04/2014
PANEL: 2
STUDY APPROVAL EXPIRES: 11/22/2014
STUDY NUM: 1144377
WIRB PRO NUM: 20132048
INVEST NUM: 118097
WO NUM: 1-821573-1
CONTINUING REVIEW: Annually
SITE STATUS REPORTING: Annually
INST. NUM: W140115001

SPONSOR: Ferring International Center U.S., Inc. (FIPCUS)
PROTOCOL NUM: 000103
AMD. PRO. NUM:
TITLE:
A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and Efficacy of Prepopik™ versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years

APPROVAL INCLUDES:
Investigator
Administrative Letter – Confirmation that Pregnant Females will not be enrolled (12-18-2013)
Administrative Letter (12-11-2013)
Protocol (08-21-2013) Version 4
Assent Information Sheet [IN0]
Consent Form [IN0]

WIRB APPROVAL IS GRANTED SUBJECT TO:

WIRB HAS APPROVED THE FOLLOWING LOCATIONS TO BE USED IN THE RESEARCH:
University of Alabama at Birmingham/Children's of Alabama, 1600 7th Avenue South, Birmingham, Alabama 35233

If the PI has an obligation to use another IRB for any site listed above and has not submitted a written statement from the other IRB acknowledging WIRB's review of this research, please contact WIRB's Client Services department.

ALL WIRB APPROVED INVESTIGATORS MUST COMPLY WITH THE FOLLOWING:

1. Conduct the research in accordance with the protocol, applicable laws and regulations, and the principles of research ethics as set forth in the Belmont Report.

2. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the participant's rights.

3. Unless consent has been waived, conduct the informed consent process without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate. (Due to the unique circumstances of research conducted at international sites outside the United States and Canada where WIRB approved materials are translated into the local language, the following requirements regarding consent forms bearing the WIRB approval stamp and regarding certification of translations are not applicable.)
    a. Use only the most current consent form bearing the WIRB "APPROVED" stamp.
    b. Provide non-English speaking subjects with a certified translation of the approved consent form in the subject's first language. The translation must be approved by WIRB unless other arrangements have been made and approved by WIRB.
    c. Obtain pre-approval from WIRB for use of recruitment materials and other materials provided to subjects.

4. Enrollment of limited readers and non-readers: unless consent has been waived or the protocol excludes enrollment of limited readers or non-readers, involve an impartial witness in the consent process when enrolling limited or non-readers and document the participation of the impartial witness using the designated signature lines on the WIRB-approved consent form. In the absence of designated signature lines, download the WIRB standard impartial witness form from www.wirb.com.

5. Obtain pre-approval from WIRB for changes in research.

6. Obtain pre-approval from WIRB for planned deviations and changes in research activity as follows:
    - If the research is federally funded, conducted under an FWA, or is a clinical investigation of a drug or biologic, then all planned protocol deviations must be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].
    - However, if the research is a clinical investigation of a device and the research is not federally funded and not conducted under an FWA, then only planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].

    The reason for these different requirements regarding planned protocol deviations is that the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) drug and biologic divisions have adopted the regulatory interpretation that every planned protocol deviation is a change in research that needs prior IRB review and approval before implementation; however, the FDA device division operates under a distinct regulation (See 21 CFR 812.150(a)(4).

    Deviations necessary to eliminate apparent immediate hazards to the human subjects should be reported within 10 days.

7. Report the following information items to the IRB within 5 days:
    a. New or increased risk
    b. Protocol deviation that harmed a subject or placed subject at risk of harm
    c. Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject
    d. Audit, inspection, or inquiry by a federal agency
    e. Written reports of federal agencies (e.g., FDA Form 483)
    f. Allegation of Noncompliance or Finding of Noncompliance
    g. Breach of confidentiality
    h. Unresolved subject complaint
    i. Suspension or premature termination by the sponsor, investigator, or institution
    j. Incarceration of a subject in a research study not approved to involve prisoners
    k. Adverse events or IND safety reports that require a change to the protocol or consent
    l. State medical board actions
    m. Unanticipated adverse device effect
    n. Information where the sponsor requires prompt reporting to the IRB

    Information not listed above does not require prompt reporting to WIRB.

    Please go to www.wirb.com for complete definitions and forms for reporting.

8. Provide reports to WIRB concerning the progress of the research, when requested.

9. Ensure that prior to performing study-related duties, each member of the research study team has had training in the protection of human subjects appropriate to the processes required in the approved protocol.

Federal regulations require that WIRB conduct continuing review of approved research. You will receive Continuing Review Report forms from WIRB. These reports must be returned even though your study may not have started.

DISTRIBUTION OF COPIES:

Contact, Company

Reed A. Dimmitt MD, MSPH, University of Alabama at Birmingham
Margie M. Lawson BS, University of Alabama at Birmingham
Chris Bartony, Novella Clinical, Inc.
Sally Headley, University of Alabama at Birmingham
Quantes Randle, Novella Clinical
Meg Mosteller-Barnum, University of Alabama at Birmingham

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Office: (360) 252-2500 | **Toll Free**: (800) 562-4789
www.wirb.com

Certificate of Approval

THE FOLLOWING WERE APPROVED

INVESTIGATOR: Alka Goyal MD
Children's Hospital of Pittsburgh of the
University of Pittsburgh Medical Center
Office 6119, 6th Floor, Faculty Pavilion
4401 Penn Avenue
Pittsburgh, Pennsylvania 15224

BOARD ACTION DATE:	04/01/2014
PANEL:	2
STUDY APPROVAL EXPIRES:	11/22/2014
STUDY NUM:	1144701
WIRB PRO NUM:	20132048
INVEST NUM:	188778
WO NUM:	1-823650-1
CONTINUING REVIEW:	Annually
SITE STATUS REPORTING:	Annually

SPONSOR: Ferring International Center U.S., Inc. (FIPCUS)
PROTOCOL NUM: 000103
AMD. PRO. NUM:
TITLE:
A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and Efficacy of Prepopik™ versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years

APPROVAL INCLUDES:
Investigator
Administrative Letter – Confirmation that Pregnant Females will not be enrolled (12-18-2013)
Administrative Letter (12-11-2013)
Prepopik 2.5oz Cup #11659825.0 - As Submitted
Prepopik Subject Bags #11659826.0 - As Submitted
Protocol (08-21-2013) Version 4
Study Drug Dosing Instructions #11659830.1 -As Submitted
Subject Confidential Non-Disclosure Affidavit #11659829.0 - As Submitted
Subject's Tolerability and Satisfaction Questionnaire #11659832.0 - As Submitted
Assent Information Sheet [IN0]
Consent Form [IN0]
Preliminary Screening Form #11842680.0 - As Submitted

WIRB APPROVAL IS GRANTED SUBJECT TO:

WIRB HAS APPROVED THE FOLLOWING LOCATIONS TO BE USED IN THE RESEARCH:
Children's Hospital of Pittsburgh of the University of Pittsburgh Medical Center, 4401 Penn Avenue, Pittsburgh, Pennsylvania 15224

If the PI has an obligation to use another IRB for any site listed above and has not submitted a written statement from the other IRB acknowledging WIRB's review of this research, please contact WIRB's Client Services department.

ALL WIRB APPROVED INVESTIGATORS MUST COMPLY WITH THE FOLLOWING:

1. Conduct the research in accordance with the protocol, applicable laws and regulations, and the principles of research ethics as set forth in the Belmont Report.

IF YOU HAVE ANY QUESTIONS, CONTACT WIRB AT 1-800-562-4789
This is to certify that the information contained herein is true and correct as reflected in the records of the Western Institutional Review Board (WIRB), OHRP/FDA parent organization number IORG 0000432, IRB registration number IRB00000533. WE CERTIFY THAT WIRB IS IN FULL COMPLIANCE WITH GOOD CLINICAL PRACTICES AS DEFINED UNDER THE U.S. FOOD AND DRUG ADMINISTRATION (FDA) REGULATIONS, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) REGULATIONS, AND THE INTERNATIONAL CONFERENCE ON HARMONISATION (ICH) GUIDELINES.

2. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the participant's rights.

3. Unless consent has been waived, conduct the informed consent process without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate. (Due to the unique circumstances of research conducted at international sites outside the United States and Canada where WIRB approved materials are translated into the local language, the following requirements regarding consent forms bearing the WIRB approval stamp and regarding certification of translations are not applicable.)
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6. Obtain pre-approval from WIRB for planned deviations and changes in research activity as follows:
    - If the research is federally funded, conducted under an FWA, or is a clinical investigation of a drug or biologic, then all planned protocol deviations must be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].
    - However, if the research is a clinical investigation of a device and the research is not federally funded and not conducted under an FWA, then only planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].

    The reason for these different requirements regarding planned protocol deviations is that the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) drug and biologic divisions have adopted the regulatory interpretation that every planned protocol deviation is a change in research that needs prior IRB review and approval before implementation; however, the FDA device division operates under a distinct regulation (See 21 CFR 812.150(a)(4).

    Deviations necessary to eliminate apparent immediate hazards to the human subjects should be reported within 10 days.

7. Report the following information items to the IRB within 5 days:
    a. New or increased risk
    b. Protocol deviation that harmed a subject or placed subject at risk of harm
    c. Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject
    d. Audit, inspection, or inquiry by a federal agency
    e. Written reports of federal agencies (e.g., FDA Form 483)
    f. Allegation of Noncompliance or Finding of Noncompliance
    g. Breach of confidentiality
    h. Unresolved subject complaint
    i. Suspension or premature termination by the sponsor, investigator, or institution
    j. Incarceration of a subject in a research study not approved to involve prisoners
    k. Adverse events or IND safety reports that require a change to the protocol or consent
    l. State medical board actions
    m. Unanticipated adverse device effect
    n. Information where the sponsor requires prompt reporting to the IRB

    Information not listed above does not require prompt reporting to WIRB.

    Please go to www.wirb.com for complete definitions and forms for reporting.

8. Provide reports to WIRB concerning the progress of the research, when requested.

9. Ensure that prior to performing study-related duties, each member of the research study team has had training in the protection of human subjects appropriate to the processes required in the approved protocol.

Federal regulations require that WIRB conduct continuing review of approved research. You will receive Continuing Review Report forms from WIRB. These reports must be returned even though your study may not have started.

DISTRIBUTION OF COPIES:

Contact, Company

Chris Bartony, Novella Clinical, Inc.
Sharon Ralph PhD, UPMC
Quantes Randle, Novella Clinical
Alka Goyal MD, University of Pittsburgh
Donna D. Smith MS, University of Pittsburgh

Vanderbilt University
Institutional Review Board
504 Oxford House Nashville, Tennessee 37232-4315
(615) 322-2918 Fax: (615) 343-2648
www.mc.vanderbilt.edu/irb

February 24, 2014

Julia Anderson, M.D.
Pediatric GI
10229 DOT 37232

Cynthia Womack-Ramirez
Pediatrics - Gastroenterology
10238 DOT 37232

RE: IRB# 140100 "A RANDOMIZED, ASSESSOR-BLIND, MULTICENTER, DOSE-RANGING STUDY COMPARING THE SAFETY AND EFFICACY OF PREPOPIK VERSUS POLYETHYLENE GLYCOL PREPARATION (LOCAL STANDARD OF CARE) IN CHILDREN AGED 9 YEARS TO 16 YEARS. STUDY NUMBER: 00103 (IND 101738)
" (Ferring Pharmaceuticals)

Edited to correct approval date 7/21/2014 rw

Dear Julia Anderson, M.D.:

At the meeting on 2/19/2014, the Institutional Review Board reviewed the research application identified above. The Committee determined the study poses Greater than Minimal Risk to participants. Approval is extended for the Protocol Version 4 dated 8/21/2013.

The research protocol has been reviewed and meets the criteria for a Qualifying Clinical Trial in accordance with the Centers for Medicare and Medicaid Services Clinical Trial Policy National Coverage Decision.

The Consent Form(s) have been stamped with the approval and expiration date and this copy should be used when obtaining the participant's signature. Federal regulations require that the original copy of the participant's consent be maintained in the principal investigator's files and that a copy be given to the subject at the time of consent. An additional record (i.e., case report form, medical record, database, etc.) of the consent process should also be maintained in a separate location for documentation purposes.

As the Principal Investigator, you are responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events and unanticipated problems involving risks to participants or others. The IRB Adverse Event reporting policy III.L is located on the IRB website at http://www.mc.vanderbilt.edu/irb/.

Please note that approval is for a 12-month period. According to federal regulations, this period is calculated from the date of the convened meeting as noted above. Any changes to the research study must be presented to the IRB for approval prior to implementation.

If this trial requires registration as a clinical trial, accrual cannot begin until this study has been registered at clinicaltrials.gov and a National Clinical Trial Number (NCT) provided. Please provide the NCT# to the IRB as soon as it is obtained. If an approval is required from an additional source other than the Vanderbilt IRB, this must be obtained prior to study initiation. These approvals may include, but

are not limited to CRC, SRC, , IND, IDE.

DATE OF IRB APPROVAL: 2/24/2014 **DATE OF IRB EXPIRATION: 2/18/2015**

Sincerely,

Steven L. Goudy, M.D., Chair
Institutional Review Board
Health Sciences Committee #2

SLG/rw
Electronic Signature: Steven L Goudy/VUMC/Vanderbilt : (70849760B48E5F75C51A73340E68EEEC)
Signed On: 02/24/2014 05:41:45 PM CST

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

March 25, 2014

Steven Ciciora
Gastroenterology/Nutrition

Study ID: IRB14-00011

Study Name: A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and Efficacy of Prepopik™ versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years

Dear Dr. Ciciora,

The response to modifications requested, submitted on 3/21/2014, for the above study has been reviewed by the Institutional Review Board on 3/25/2014- **STUDY APPROVED.**

Date of Approval: 2/4/2014
Date of Expiration: 2/3/2015

This approval is for one year only. A Continuing Review Report must be approved before this study can proceed beyond the date of expiration. Please be aware that all changes to the research protocol consent form, or any other aspect of this study must receive prospective IRB approval. IRB policy requires that provisions are made for assent of subjects age nine and older.

The Federalwide Assurance number assigned to the IRB at Nationwide Children's Hospital, Inc. is FWA00002860.

If we can provide additional assistance, please do not hesitate to call this office at ext. 22708.

Sincerely,

Grant Morrow III, MD, Vice-Chair
Institutional Review Board

UNIVERSITY OF MINNESOTA

Twin Cities Campus

Human Research Protection Program
Office of the Vice President for Research

D528 Mayo Memorial Building
420 Delaware Street S.E.
MMC 820
Minneapolis, MN 55455

Office: 612-626-5654
Fax: 612-626-6061
E-mail: irb@umn.edu or ibc@umn.edu
Website: http://research.umn.edu/subjects/

September 9, 2014

Boris Sudel
Div. of Ped Gastroenterology
6th Floor East Building, 8952C
2450 Riverside Ave
Minneapolis, MN 55454

RE: "A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and Efficacy of Prepopik versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years"
IRB Code Number: 1401M46841

Dear Dr. Sudel,

The Institutional Review Board (IRB) received your response to its stipulations. Since this information satisfies the federal criteria for approval at 45CFR46.111 and the requirements set by the IRB, final approval for the project (version number 4.0, protocol date August 21, 2013) is noted in our files. Upon receipt of this letter, you may begin your research.

IRB approval of this study also includes:

- Parent/guardian consent form version dated September 3, 2014
- Assent form version dated November 25, 2013
- Addendum to assent for female minors form version dated September 3, 2014
- Confidential non-disclosure affidavit version 1.0, dated January 31, 2014
- HIPAA Authorization version dated September 3, 2014
- Protocol administrative change (note to file), version dated February 12, 2014
- Subject's tolerability and satisfaction questionnaire version number 4.0, dated August 21, 2013
- Ferring Pharmaceuticals, Inc. study dosing instructions version 1.1, dated February 10, 2014
- Ferring Pharmaceuticals, Inc. prescribing information, received on January 2, 2014
- Ferring Pharmaceuticals, Inc. medication guide, received on January 2, 2014

NOTE: The IRB committee has been made aware of the address change of Ferring Pharmaceuticals, Inc.

The IRB notes that the use of drugs/biologics/devices in this study is carried out under IND #101,738.

The IRB determined that children could be included in this research under 45CFR46.405; research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

The IRB would like to stress that subjects who go through the consent process are considered enrolled participants and are counted toward the total number of subjects, even if they have no further participation in the study. Please keep this in mind when calculating the number of subjects you request. This study is currently approved for 30 subjects. If you desire an increase in the number of approved subjects, you will need to make a formal request to the IRB.

For your records and for grant certification purposes, the approval date for the referenced project is August 21, 2014 and the Assurance of Compliance number is FWA00000312 (Fairview Health Systems Research FWA00000325, Gillette Children's Specialty Healthcare FWA00004003). Research projects are subject to continuing review and renewal; approval will expire one year from that date. You will receive a report form two months before the expiration date. If you would like us to send certification of approval to a funding agency, please tell us the name and address of your contact person at the agency.

As Principal Investigator of this project, you are required by federal regulations to:

*Inform the IRB of any proposed changes in your research that will affect human subjects, changes should not be initiated until written IRB approval is received.

*Report to the IRB subject complaints and unanticipated problems involving risks to subjects or others as they occur.

*Inform the IRB immediately of results of inspections by any external regulatory agency (i.e. FDA).

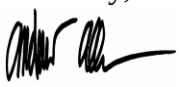
*Respond to notices for continuing review prior to the study's expiration date.

*Cooperate with post-approval monitoring activities.

Information on the IRB process is available in the form of a guide for researchers entitled, What Every Researcher Needs to Know, found at http://www.research.umn.edu/irb/WERNK/index.cfm.

The IRB wishes you success with this research. If you have questions, please call the IRB office at 612-626-5654.

Sincerely,



Andrew Allen, CIP
Research Compliance Supervisor
AA/do

CC: Shannon Riggs

CHESAPEAKE IRB

Human Research Protection Experts
IRB Services • Consultation • Education
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
410-884-2900

PROTOCOL APPROVAL WITH MODIFICATION

DATE: 27 May 2014

TO: Anupama Chawla, M.D.
Stony Brook University Medical Center

PROTOCOL: Ferring International Center U.S., Inc. (FIPCUS) - 000103, A Randomized, Assessor-Blind, Multicenter, Dose-Ranging Study Comparing the Safety and Efficacy of Prepopik™ versus Polyethylene Glycol Preparation (Local Standard of Care) in Children Aged 9 Years to 16 Years (Pro00009776)

APPROVAL DATE: 21 May 2014

EXPIRATION DATE: 21 May 2015

IRB APPROVED DOCUMENTATION:

Protocol Version:
- Protocol (Version 4; Date: 21 Aug 2013)

Consent Forms:
- DRAFT Parent Informed Consent and Authorization Form (Chesapeake IRB Approved Version 23 May 2014)
- DRAFT Assent Form (Chesapeake IRB Approved Version 23 May 2014)
- DRAFT Confidential Non-Disclosure Form (Chesapeake IRB Approved Version 23 May 2014)

Product Information:
- Prescribing Information for PREPOPIK (Revised: 11/2013)

Other Materials:
- Note to File - Administrative Change (Dated 12 February 2014)
- "Cup Bag Photo" to be given to subjects
- "Dosing Cup Photo" to be used by subjects
- Study Drug Dosing Instructions (Version 1.1_ 10Feb2014)

The IRB approved the above referenced protocol with the modification listed below:

- Revisions to the Informed Consent and Authorization Forms

The IRB approved additional revisions to the Consent Forms on 23 May 2014.

Please note: The Informed Consent and Authorization Forms available under the "IRB Issued Documents" tab are DRAFT documents and not for use.

Please forward the IRB Approved DRAFT Consent Forms, with the approved modifications incorporated, to the Sponsor and confirm that both the Institution and the Sponsor accept the documents as written.

If the modifications to the Consent Forms as approved by the IRB are acceptable and no further edits are needed, please submit via the Modification submission pathway in CIRBI. If the Consent Forms require additional changes, please track the changes and submit via the Modification submission pathway in CIRBI.

The IRB reviewed the project in accordance with the 21 CFR Part 50, Subpart D Federal Regulations which provide for additional protections for children as research subjects.

The IRB determined that the research study meets the criteria found in the risk category described as follows:

- 21 CFR 50.52: "*Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects*." *Permission of one parent is required.*

Please review the Investigator Handbook by accessing CIRBI™ (www.cirbi.net). Log on to your CIRBI homepage ("My Home") and select the "Reference Materials" tab for IRB requirements and guidance. A copy of the most recent IRB roster is also available under "Reference Materials".

Thank you for selecting Chesapeake IRB to provide oversight for your research project.