BENAROYA RESEARCH INSTITUTE
Virginia Mason

BRI IRB REC'D
JUL 6 2016

CONTINUING REVIEW REPORT

Return submissions to the Research Protections Office (Mailstop: IN-RC). NOTE: a) **each question must be answered** or marked "N/A"; b) forms will be returned if responses are handwritten. See the Clinical_Research_Glossary for definitions. **Password to unlock form is "benaroya".** *Contact the Research Protections Department with questions: IRB@benaroyaresearch.org [IRB Staff]*

IRB Number: IRB10090	**VM/BRI funding #(s):** 0591516, 0545016	**Date:** 5/31/2016

TITLE OF RESEARCH PROPOSAL (PROTOCOL TITLE): Inflammatory Bowel Disease Registry and Repository

Principal Investigator (PI): James Lord, MD, PhD	Study Coordinator: Kassidy Benoscek
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Address *(if not VM/BRI)*:	Address *(if not VM/BRI)*: 2
GCP ☐ Ethics ☐ FDS ☐ *(IRB use only)*	GCP ☐ Ethics ☐ FDS ☐ *(IRB use only)*

IRB Regulatory Contact *(optional)* *(if designating someone other than the study coordinator)*	**GCP/Ethics/FDS** *(IRB use)*	Phone:	Email:
	☐/☐/☐		
Dept. & Mailstop:		Address *(if not VM/BRI)*:	

I. CURRENT STATUS OF RESEARCH PROJECT: *(For all sites engaged with VM/BRI. Check the appropriate box[es]):*

☒	Continue accrual.
☐	Accrual complete, but research-related intervention(s) continues.

OR:

If your study did not initially qualify for Expedited Review, it may qualify now if ***one or more*** *of the following 3 items are true*

☐	Research is permanently closed to enrollment of new subjects, **AND** all subjects have completed all research-related interventions at all sites, **AND** the research remains active only for long-term follow-up of subjects.
☐	No subjects have been enrolled, and no additional risks have been identified at any site.
☐	All remaining research activities are limited to data collection/analysis.

OR:

☐	Permanent Closure (research is permanently closed to enrollment of new subjects, **AND** all subjects have completed all research-related interventions at all sites, **AND** data collection/analysis is complete). ***If this box is applicable, STOP. Do not fill out this form. Submit instead the BRI IRB "Closure_Report" Form.***
☐	Withdrawal Closure (study closed prior to any local accrual). ***If this box is applicable, STOP. Do not fill out this form. Submit instead the BRI IRB "Closure_Report" Form.***
☐	Other *(Describe)*:

II. BASIC INFORMATION:

A. List **all VM/BRI "Key Personnel"** for this study *(excluding PI & study coordinator). Key_Personnel_defined*
(NOTE: Documentation of GCP & Ethics Training is required for all "Key Personnel" prior to granting final IRB approval. Training link is located at CITI Ethics/GCP Training)

Name	GCP/Ethics/FDS *(IRB use)*	Title/Role *(e.g. Sub-I, coordinator)*	Dept.	Institution Affiliation
Richard Thirlby, MD	☐/☐/☐	Co-Investigator	General Surgery	VM
Jane Buckner, MD	☐/☐/☐	Co-Investigator	Translational	BRI/VM
Elisa Boden, MD	☐/☐/☐	Co-Investigator	Translational	BRI/VM
Sylvia Posso	☐/☐/☐	Clinical Research Coordinator	Translational	BRI
Gina Marchesini	☐/☐/☐	Translational Research Mgr	Translational	BRI
Kavitha Gilroy	☐/☐/☐	Research Assistant	Translational	BRI
Michael Chiorean	☐/☐/☐	MD	Gastro	VM

Mohammad Pourmandi	☐ / ☐ / ☐	Research Assistant	Translational	BRI
Patrick O'Reilly	☐ / ☐ / ☐	Research Assistant	Translational	BRI
Daniel Lim	☐ / ☐ / ☐	Research Assistant	Translational	BRI
Lisa Koch	☐ / ☐ / ☐	Abstract Historical Information	BRI Lab	BRI

B. Are any "Key Personnel" **non-VM/BRI** employees? ☒ Yes ☐ No *If yes, define the role of each individual in the study below:*

Name	GCP/Ethics/FDS *(IRB use)*	Role in study *(e.g. pulling files, consenting, etc.)*	Institution Affiliation
Bernadette McLaughlin	☐ / ☐ / ☐	Research Nurse	FHCRC
Christine Kane	☐ / ☐ / ☐	Protocol Coordinator	FHCRC
George McDonald	☐ / ☐ / ☐	Co-Investigator	FHCRC
Chris Damman	☐ / ☐ / ☐	Co-Investigator	UW
Tim Zisman	☐ / ☐ / ☐	Co-Investigator	UW
Greg Cruikshank	☐ / ☐ / ☐	Research Manager	UW

C. In less than 100 words, provide in **"lay terms"** a summary of the **Purpose & Objectives**, which may include major Inclusion & Exclusion Criteria of this study: *(Please do not cut and paste from the protocol)*

The purpose of the registry and repository is to increase knowledge of the causes, progression, and treatment of inflammatory gastrointestinal diseases, including disease mechanisms and responses to therapy, and the development of diagnostic and prognostic assays. People who are eligible for the study include those with well-defined gastrointestinal diseases (Crohn's disease, Ulcerative Colitis, Indeterminate Colitis, Microscopic Colitis, Celiac Sprue, Eosinophilic Esophagitis), non-IBD patients undergoing endoscopy or surgery, suspected IBD patients undergoing endoscopy to confirm diagnosis. First-degree relatives who do not have a gastrointestinal inflammatory condition may be recruited, as well as to act as a "control" for comparison purposes.

D. In 150 words or less, provide in **"lay terms"** a description of **Research Study Procedures:** *(Please do not cut and paste from the protocol)*

Participants are asked to complete a consent form, which is administered by the coordinator, research assistant or investigator either in person or over the phone, as well as a questionnaire. The questionnaire covers information including demographics, ethnicity, disease history, medications, current disease activity, and family history. We also collect up to 106cc of blood for initial draws, with the possibility of collecting up to 253cc for subsequent draws (obtaining no more than 500ml in an 8 week period). If participating subjects are undergoing lower Gi endoscopy or colonoscopy, eight biopsies will be collected. In some cases, such as Celiac Sprue, eight biopsies will be collected from participating subjects undergoing upper endoscopy. If participating subjects are undergoing surgery to remove a portion of intestines as part of their direct medical care, some removed intestine or tissue may be obtained that is not needed for clinical diagnostic purposes.

E. Will institutions (or collaborators) **other than** VM/BRI be "**engaged**" in this research? ☒ Yes ☐ No

*(**If yes,** answer question #1 below. **If no,** skip to "Section III".) [In general, an institution is considered engaged in a research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.] Refer to the following website for clarification & examples: OHRP_Guidance_for_"Engagement"_in_Research*

1. Check the appropriate box:
   - (a) ☐ VM/BRI is one of several investigative sites but is not the coordinating center.
   - (b) ☐ This is a multi-site collaborative research for which VM/BRI is the coordinating center.
   - (c) ☒ Neither (a) nor (b), but at least one other institution or collaborator will be "engaged" in this research *(e.g. CCOP studies at VM)*

   ***If (b) or (c) checked** above, answer question #2 below. **If (a) checked**, skip to question #3:*
2. (a) List all institutions and collaborators "engaged" in this research: ☐ Pacific Medical Center ☐ Fairbanks Memorial ☐ Peace Health ☐ Cascade Cancer Center/Evergreen Hospital ☐ Other(s):
   (b) Specify the types of IRB_authorization_agreements/contracts/assurances used with each institution/collaborator:
   ☒ VM/BRI has an IRB authorization agreement to be the IRB of record for all CCOP affiliate sites listed (a) and all Federalwide Assurances (FWAs) are current (*search here*).
   ☐ Other:
3. Will study procedures be conducted outside of VM/BRI campus? ☒ Yes ☐ No
   If yes, list procedures and locations: Blood draw and biopsy collection at and by UW.

III. RESEARCH PARTICIPANTS:

A. Complete the subject accrual* information below *(*Note: IRB defines "accrual" as subjects consented, if a consent form is present.)*:

Subject Group *(Same as initial submission: cases/controls/records/specimens etc.)*	LOCAL Numbers:					TOTAL Numbers: *(For multi-site trials)*			
	Accrual since last IRB review	Accrual to date	Still on treatment or intervention *(if applicable)*	Expected Numbers next 12 months	Expected Number at End of Study	Accrual since last IRB review	Accrual to date	Expected Numbers next 12 months	Expected Number at End of Study
IBD	49	640	n/a	50	Ongoing				
Non-IBD	17	205	n/a	20	Ongoing				

B. Is your accrual to date on track to complete this project by your initial estimated timeframe? *(see initial study submission)* ***If no***, explain why and your new estimated completion date:	☒ Yes ☐ No ☐ N/A
C. Have any subjects (locally) withdrawn since submission of your last Continuing Review or New Application? ***If yes***, how many and why *(e.g., voluntary withdrawal/reason, withdrawal by investigator/reason, lost to follow-up, etc.)*?	☐ Yes ☒ No ☐ N/A
D. Does subject population include equitable gender representation? ***If no or N/A***, explain why and what measures are being taken:	☒ Yes ☐ No ☐ N/A
E. Does subject population include equitable ethnic/racial representation? ***If no or N/A***, explain why and what measures are being taken:	☒ Yes ☐ No ☐ N/A
F. Have there been any unexpected/unusual or negative responses as a result of recruitment or study participation *(e.g. angry letters, phone calls, etc)*? ***If yes***, explain:	☐ Yes ☒ No
G. Is accrual since your last IRB approval "low" *(25% ≤ projected number)* or "zero"? *(N/A if accrual is complete.)* ***If no, skip to section IV.*** ***If yes***, answer the following: 1. Explain why accrual is "low" or "zero" *(e.g., rare disease, sponsor suspended etc.)*? 2. What measures **specifically** are being taken to increase accrual? 3. Provide compelling rationale why this study should remain open: *NOTE: If study was reviewed Full initially, and this is the second year with zero accrual, an investigator is requested to attend the IRB meeting to explain rationale for continuation of the study.*	☐ Yes ☒ No ☐ N/A

IV. MODIFICATIONS/REVISIONS/AMENDMENTS:

A. Are there new changes to this study *(e.g. modifications to the protocol/consent form, new questionnaires, change in "key personnel" etc.)* included with this report not previously approved by the BRI IRB? ***If yes,*** describe ALL changes briefly below and attach tracked copies *(underlined or balloons)* of all modified document(s): *(do not cite "see attached")* Added Lisa Koch ~~and Andrea Martin~~ as Key Personnel. Removed Yen Truong from Key Personnel. per K. Benoscek, 7.13.16	☒ Yes ☐ No ***If no,*** *skip to section V*
1. Will requested modifications change the scope or research objectives of the protocol? *(e.g. change in the specific aims, change from the previously approved use of human subject, etc.)* ***If yes***, describe:	☐ Yes ☒ No
2. Are any NEW potentially vulnerable subjects *(e.g. children, pregnant women, illiterate etc.)* being added as targeted or possibly included in this study? ***If yes,*** define your NEW study population and provide steps to protect the population: Complete checklist if "**children**" are being added.	☐ Yes ☒ No
3. Were changes made to the Consent Form/study that could affect a subject's willingness to consent to research? ***If yes***, describe:	☐ Yes ☒ No ☐ N/A

B. If this study was originally reviewed Expedited, do you attest this project continues to presents no more than minimal risk of harm to subjects? *("Minimal Risk" means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life, or during the performance of routine physical/psychological examinations/tests.)* ***If no,*** your study must be reviewed by the Full Board IRB.	☐ Yes ☐ No ☒ N/A

V. ADVERSE EVENTS (AE's):

The following guidance defines what constitutes a reportable Adverse Event to the IRB (e.g. unexpected, related/possibly related, and places subjects at greater risk): OHRP guidance, FDA guidance (drug/device studies).

A. Are any **NEW adverse events** fitting the above referenced criteria **being submitted at this time** *(i.e., **not** previously submitted to the IRB Office)*? ***If yes,*** attach a BRI IRB Adverse Event Reporting Form for each event not reported.	☐ Yes ☒ No
B. Have **ANY adverse event reports** fitting the above criteria been submitted to the IRB **since the study's last review**? ***If yes,*** briefly summarize and/or attach a summary of AE reports *(by type/ # of occurrences/relation to study etc.)*:	☐ Yes ☒ No
C. ***If yes to "A" or "B",*** are any of these reports comparable to events reported since the study began? ***If yes,*** explain:	☐ Yes ☐ No ☒ N/A

VI. RISKS vs. BENEFITS:

A. Check all **potential risks/side effects to subjects**. Check only **added** potential risks/side effects that may occur to subjects from the research and **not** those that would occur if subject were to receive standard treatment/procedures only. *[NOTE: Virtually all research studies involve "breach of confidentiality" and "invasion of privacy" as potential risks since several entities may have access to research records (e.g., FDA, NIH, IRB, etc.) Risks must be consistent with the consent form and protocol.]* **At least one box must be checked in each column.**

Physical Harms	Psychological	Social Economic
☒ Minor pain	☐ Depression	☒ Breach of Confidentiality, resulting in:
☒ Discomfort	☐ Confusion	☒ Invasion of privacy
☐ Serious injury	☐ Hallucination	☐ Potential loss of employment / insurability
☐ Death	☒ Stress	☐ Potential criminal prosecution
☒ Injury from invasive medical procedure	☐ Guilt	☐ Other *(specify):*
☐ Harm from possible side effects from drugs	☒ Loss of self-esteem	☐ None *(applicable if all data is anonymous)*
☒ Other *(specify):* Blood transfusion or surgery from colonoscopy. Fainting.	☐ Embarrassment	
☐ None	☐ Other *(specify):*	
	☐ None	

B. Based on this past year's experience, do you think the study's potential benefits to subjects (and/or to society) still outweigh the actual and potential risks? ***If no,*** explain:	☒ Yes ☐ No

VII. FINDINGS TO DATE:

Briefly summarize the findings to date and attach any recent literature or other relevant information (including data, manuscripts, publications,abstracts, etc.) especially about risks associated with the research: The samples archived under this protocol have been used for a variety of related experiments this past year. First, information on the effect of thiopurine drugs of lymphocyte subsets was written up as a manuscript (enclosed) although it has, to date, been rejected for publication by two journals. Second, immunophenotypic comparison of regulatory T cell (Treg) subsets in patients with or without IBD was published in PLoS One (enclosed). Third, a study characterizing circulating T cells specific for a gut bacterial antigen was presented in poster form (enclosed) at the American Association of Immunology's annual meeting. Fourth, analyses of mucosal Tregs revealed a novel CD177+ subset, preliminary characterization of which led to the successful funding of a pilot proposal (enclosed). Additional studies involving the characterization of cells which express the vedolizumab drug target intergrin alph4/beta7, and the effect of this drug in recipients, are ongoing. Additional studies to characterize a novel T cell subset, called MAIT cells, in IBD is also ongoing, and has been funded by an NIH consortium. In none of this research were any findings revealed that would represent risk to research participants.

VIII. PLANS FOR THE NEXT TWELVE MONTHS:

Summarize in 50 words or less your plans for this project in the next 12 months: Continue to enroll subjects with IBD, Celiac and controls in to the Registry and Repository, as well as obtain samples from certain subjects who are already enrolled in to the Registry and Repository, to continue ongoing research.

IX. OTHER INFORMATION:

A. Has this study ever undergone scientific review previously *(e.g. During Feasibility Review etc.)*? *If yes,* on what date: *(submit if available)*	☐ Yes ☒ No
B. Has any "key personnel" reported a Conflict of Interest (COI) for this study? *If yes,* is COI management plan in place and being followed? ☐ Yes ☐ No *If no,* (explain):	☐ Yes ☒ No ☐ N/A

X. SUBMISSION CHECKLIST (ORDER OF ATTACHMENTS): *Check each item. See IRB_Forms for reference.*

☒ Yes	**1. Continuing Review Report** *(this form and all attachments)*		
☒ Yes	**2. Protocol** *(If Retrospective Chart Review, Application serves as protocol. Please submit 2 copies of approved application.)*	**Version #:** 9	**Dated:** 6/19/2015
☒ Yes ☐ No ☐ N/A	**3. BRI/VM Consent Document(s)** ***If yes,*** list all forms: *(e.g. assents, short forms)* *Attach clean and tracked versions [if consents have been modified (question IV. A)].* ***If no or N/A,*** *boxes (a), (b), or (c) below must be checked. Check all boxes that apply.* 1. ☐ Permanently closed AND all research activity limited to data collection/analysis only. 2. ☐ Consent and HIPAA waiver granted at initial IRB approval. *(skip HIPAA section below if checked)* 3. ☐ Other (state reason):		

Title of Consent Form(s):	Version #:	Date of current version:
Immune-Mediated Diseases Registry and Repository: Inflammatory Bowel Diseases Translational Research	~~13~~ 14	~~6/17/2015~~ 7-5-16

☐ Yes ☐ No ☒ N/A	**4. HIPAA Authorization Form**	**Version #:**	**Dated:**
	If no or N/A, *at least one box below must apply.* (a) ☐ Permanently closed **AND** all research activity limited to data collection/analysis only. (b) ☐ HIPAA waiver granted at initial IRB approval. (c) ☐ HIPAA language incorporated in main consent form at initial approval. (d) ☐ Study approved prior to 04/14/03 **AND** HIPAA requirements waived at that time. (e) ☐ Other (State reason):		
☐ Yes ☐ No ☒ N/A *(N/A if no drugs used)*	**5. Investigator's Brochure** *(required if existing. If not, other drug safety information; e.g. package insert.)*	**Version #:**	**Dated:**
☒ Yes ☐ No	**6. Questionnaires/Surveys/Study Diaries** *(i.e. any study specific items seen by subjects.) NOTE: Documents previously approved by the IRB (with the exception of questionnaires) do NOT need to be submitted, unless revisions are being made to those items.)*		

Title(s) of Questionnaires/Surveys/Study Diaries:	Version #:	Date of current version:
IBD Questionnaire	7	6/17/2015
Celiac Questionnaire	3	6/17/2015
Off-Site Participation Information	3	6/17/2015

☐ Yes ☒ No ☐ N/A	**7. NEW Advertising/Recruiting materials** not previously approved during Initial or previous Continuing Review *(print ads, radio scripts, brochures, etc.)* FDA_guidance		

Title(s) of Recruitment/Advertising material(s):	Version #:	Date of current version:

*pr [illegible] Kassidy, 7-6-16, VA

☐ Yes ☐ No ☒ N/A	**8. Financial Disclosure Statement** (*click here*) *Required* of all Investigators, clinical research coordinators, and other research personnel *(All "Key Personnel" listed in this application , more info)* ***If yes***, name of all entities providing funding/support: ***If N/A****, at least one exception below must apply.* (a) ☐ Solely internally funded through restricted or unrestricted BRI funds, **OR** (b) ☐ Solely funded by federal or not-for profit foundation monies; *no underlying drug/device funding*; **OR** (c) ☐ Funded by a combination of (a) and (b) above **OR** (d) ☐ No budget required. Absolutely no internal or external funds, services, skills, or products, (e.g., statistical services, database warehousing, free test article, are provided by a non-VMMC/BRI entity.)
☐ Yes ☐ No ☒ N/A	**9. Conflict of Interest Management Plan** ***(if yes,*** *on question IX, B)* ***If no***, explain:
☐ Yes ☒ No	**10. Additional attachments submitted?** *(e.g. any relevant multi-center trial or grant summary reports)*

Title(s) of Additional Attachments:	Version #:	Date of current version:

☐ Yes ☒ No	**11. Unaffiliated Investigator Agreement** *(if ANY investigator(s) is a NON-VM/BRI employee. Submit only if not previously submitted. See criteria listed at Unaffiliated_Investigator_Agreement or Guidance_on_Extension_of_an_FWA_to_Cover_Collaborating_Individual_Investigators*
☐ Yes ☐ No ☒ N/A	**12. Regulatory Compliance Checklist**: *(When **"children"** are listed as subjects per 45CFR46_Subpart_D or 21CFR50_Subpart_D. See guidance for more details.)*
☐ Yes ☐ No ☒ N/A	**13. Patient Card**

XI. IRB Submission Requirements:

☒ Yes ☐ No	Do you want to receive a Confirmation of Receipt email notification for this submission?
☒ Yes	2 copies of all documents typed/word-processed *(plus one tracked copy of any revised documents).*
☒ Yes	Documents single-sided *(unless Expedited Review)*, secured by binder clips or paper clips **(no staples).**
☒ Yes	The Principal Investigator has signed the application.

Person completing this application:	☐ PI ☐ Study Coordinator ☐ IRB Regulatory Contact ☐ Other: *Cite below.*	
Printed Name: Kassidy Benoscek	Role in Study: Study Coordinator	Phone: 206-342-6537

INVESTIGATOR'S STATEMENT: *(Only the Principal Investigator's original signature will be accepted):*

As PRINCIPAL INVESTIGATOR, I acknowledge that I am responsible for reporting any emergent problems, adverse effects or reactions, or proposed procedural modifications. No modifications will be put into effect without prior Institutional Review Board (IRB) approval except where necessary to eliminate apparent immediate hazards; that unless otherwise directed by the IRB Chairperson, I will renew this application with the IRB every 11 months *(or at more frequent intervals if requested by the IRB)***; that the research project is being conducted in compliance with the IRB's understanding and recommendations; that the IRB is provided all the information on the research project necessary for its complete review; and that this research project will not be put into effect until final IRB approval is received. If I am a physician** *[or other licensed health care professional]***, I certify that my medical** *[or other]* **license is current.**

Principal Investigator Signature

Date of Signature 7-6-16

FINAL INSTITUTIONAL REVIEW BOARD SIGN-OFF *(IRB use only)*
(Including consent form(s) and previously approved materials as applicable)

Minimum Informed Consent Recommendations: ☐ N/A
☐ Re-consent not required ☑ Consent all new subjects with modified consent form(s)
☐ Re-consent active participants receiving test article
☐ Re-consent all subjects including those who have completed the study ☐ Other: _____

James Bredfeldt, MD, BRI IRB Chair _____ 7/08/2016
Name and Title **Signature** **Date of Signature**

Dates of approval: 6-27-16 to 6-26-17 **Agenda Date (Full Rvw.):** 6-27-16 **Minutes Date (Exp. Rvw.):** NA

Type of Review: ☒ Full ☐ Expedited *(minimal risk)* **Date of Initial IRB Approval:** 12-20-10 Review Date: 6-27-16

VALID ONLY AS LONG AS APPROVED PROCEDURES ARE FOLLOWED
FWA00001994 (VMMC) / FWA00001995 (BRI) / IRB00000057