IBD Plexus
Overview for SRA RFP

February 2020

Contents

1. Overview

The Crohn's & Colitis Foundation (Foundation) is excited to make IBD Plexus data and biosamples available to Senior Research Award Investigators.

IBD Plexus™ was founded by the Foundation with a mission to advance science, accelerate progress towards precision medicine and improve the care of patients living with IBD. The first-of-its kind, national-scale, cloud-based platform integrates clinical, patient-reported, genetic and other molecular data from diverse research study cohorts, real world clinical care settings and patients' experiences. IBD Plexus provides academic and industry researchers with access to research-ready datasets to more rapidly perform activities that promise to speed treatment development, optimize existing therapies through development of biomarkers and diagnostics, and improve health outcomes. IBD Plexus unites clinicians, scientists, educators, industry partners, and patients to answer questions that are critically important to advance the field of IBD research.

The multi-component IBD Plexus includes a biobank, pediatric and adult patient clinical data, patient-reported data, and biosamples, central reference labs to generate molecular data (genetic, transcriptomic, microbiomic, etc.), as well as a data and analytical platform to house, organize, aggregate, and provide data for research.

IBD Plexus provides access to data across four patient cohorts, by using a novel technological platform that captures, organizes, and shares large amounts of data on individuals with IBD, and that also supports the mining and integration of this data for insights into IBD causes, mechanisms, biomarkers and potential new treatments. The "exchange" model functions under the guiding principle that researchers who take advantage of the resources will also contribute back the raw data (not the analyses) they derive from patient biosamples. As more stakeholders, including patients, clinicians, and researchers, contribute data, the IBD Plexus platform will evolve into an even more powerful database for future scientific research benefitting the entire IBD community.

2. IBD Plexus Cohorts

IBD Plexus centralizes and links data across diverse IBD research cohorts to facilitate sharing across the research community. The cohorts are all independent programs that have unique goals but also encourage clinicians and patients to participate in multiple cohorts, when applicable. IBD Plexus links the data and biosamples across these cohorts to create a robust individual patient dataset, enabling Plexus to achieve a comprehensive collection of holistic information to facilitate research and advance the scientific understanding of IBD.

This RFP provides the opportunity to gain access to biosamples and / or data from these study cohorts. Please click on the cohort hyperlink to learn more.

- RISK – A pediatric research study of newly diagnosed Crohn's disease patients, designed to identify risk factors associated with developing penetrating and/or stricturing complications within 3 to 5 years of diagnosis *(Data sets and biosamples available – Table 1)*
- SPARC IBD – A research program that enrolls adult patients with Crohn's disease and ulcerative colitis and follows them longitudinally to support the advancement of precision medicine *(Data sets and biosamples available – Table 1)*
- IBD Qorus – A longitudinally-followed adult quality of care program designed to drive progress towards improved care and health outcomes for patients living with IBD *(Data sets available – Table 1)*
- IBD Partners – An internet-based registry, open directly to patients, designed to better understand the patient view of the course of IBD and how patient experiences and unique IBD journeys impact their disease course *(Data sets available – Table 1*)

Patient-level data and biosamples collected from various cohorts include:

- Longitudinal, clinical patient-level data collected through electronic clinical case report forms and electronic health records
- Patient-reported data collected through patient surveys
- Genetic and molecular raw data generated from RISK and SPARC patients' biosamples
- Biosamples from the RISK and SPARC IBD cohorts

Table 1: Cohorts Data and Biosamples Collection Details

Cohort	Clinical Data	Patient Reported Data	Molecular Data	DNA	RNA	Plasma	PMBCs	Stool	Tissue Biopsies
SPARC IBD	✓	✓	✓	✓	✓	✓	✓	✓	✓
RISK	✓	✓	✓	✓	✓	✓		✓	✓
IBD Qorus	✓	✓							
IBD Partners		✓							

Further details about the data collected in these cohorts can be found in the IBD Plexus Patient Data Specification document. This document is located in proposalCENTRAL within the Download Templates & Instructions section.

Table 2: Select clinical and demographic characteristics of IBD Plexus patients

Characteristics	RISK	SPARC IBD	IBD Qorus	IBD Partners
Gender				
Female	42%	55%	57%	72%
Male	58%	45%	43%	28%
Age at enrollment				
<21	100%	2%	3%	4%
21-40	n/a	55%	48%	45%
41-60	n/a	31%	33%	38%
>60	n/a	13%	16%	13%
Diagnosis at enrollment				
Crohn's Disease	63%	67%	60%	62%
Ulcerative Colitis	8%	31%	38%	35%
IBD-U	10%	2%	2%	2%
Not IBD	20%	n/a	n/a	n/a
Medications (at any encounter)				
5-ASAs	43%	26%	39%	48%
Antibiotics	35%	9%	6%	12%
Biologics	44%	68%	68%	44%
Immunomodulators	51%	36%	42%	33%
Steroid therapies	61%	16%	12%	30%
Adalimumab	13%	20%	19%	20%
Certolizumab	1%	3%	3%	5%
Golimumab	n/a	0.7%	1%	0.6%
Infliximab	40%	26%	37%	21%
Natalizumab	0.2%	0.1%	0.5%	0.9%
Ustekinumab	n/a	9%	5%	2%
Vedolizumab	n/a	13%	19%	5%

Table 3: IBD Plexus Molecular data

Service	RISK		SPARC IBD	
	Samples	Patients	Samples	Patients
Immunochip *(genotyping)*	1,456 blood DNA	**1,456**		
Global screening array *(genotyping)*	1,000 blood DNA	**982**	2,000 blood DNA	**2,000 CD & UC**
Whole exome sequencing) *(genomics)*			2,000 blood DNA	**2,000 CD & UC**
RNAseq - 10 M reads *(transcriptomics)*	778 baseline tissue 10 follow-up tissue	**565**		
RNAseq – 30 M reads *(transcriptomics)*	850 baseline tissue 44 follow-up tissue	**540** **63**	1,089 baseline tissue 116 follow-up tissue	**350 CD**
16S *(rDNA sequencing)*	888 (tissue and stool)	**625**		
WGS - bacteria and fungi *(metagenomics)*	295 baseline stool	**295**	400 baseline stool CD	**400 CD**
WGS viruses *(metagenomics)*	100 baseline stool	**100**	100 baseline stool CD	**100 CD**
Methylation *(epigenetics)*	402 baseline and follow-up blood DNA	**238**		

Table 4: IBD Plexus RISK Biosamples

RISK Biosamples			
Source	**Sample Type**	**Time Point**	**Samples available details**
Peripheral Blood	DNA	Enrollment, 1 year, 2 years and 3 years	DNA extracted
Peripheral Blood	Tempus™ RNA	Enrollment, 1 year, 2 years and 3 years	RNA extracted
Peripheral Blood	Plasma	Enrollement, 1 year, 2 years and 3 years	Stored -80C
Stool	Unprocessed	Enrollment	Aliquots stored -80C
Intestinal Tissue	RNAlater	Scope	RNA/DNA extracted

Periodicity of RISK Biosample Collection

Baseline blood and stool samples were collected at / or around the time of enrollment. Follow-up blood samples were collected at year 1 and years 2 and 3. Mucosal biopsies are collected during routine colonoscopy as part of patient's clinical care.

Peripheral Blood
Collected at the time of baseline, year-1, year-2, and year-3. Blood samples were used to isolate plasma, DNA and RNA, and thus whole blood samples or PBMCs are not available.

Stool
Fresh fecal samples were collected within 2 weeks of enrollment and flash frozen.

Intestinal tissue biopsies
Pinch biopsies were collected from Crohn's disease patients during routine scheduled colonoscopies. 4 ileal and 4 rectal biopsy samples were collected in triplicate and stored in RNAlater.

Table 5: IBD Plexus SPARC IBD Biosamples

SPARC Biosamples			
Source	**Sample Type**	**Time Point**	**Samples available details**
Peripheral Blood	DNA	Baseline	DNA extracted
Peripheral Blood	Paxgene RNA	Baseline, Scope and 3 months after scope if change in therapies	Stored -80C
Peripheral Blood	PBMC's	Baseline, Scope and 3 months after scope if change in therapies	Aliquots of 5 million cells stored -80C
Peripheral Blood	Plasma	Baseline, Scope and 3 months after scope if change in therapies	Stored -80C
Stool	Nucleic Acid Archiving	Baseline, Scope and 3 months after scope if change in therapies	Stool in ethanol stored frozen
Stool	Unprocessed	Baseline, Scope, and 3 months after scope if change in therapies	faecal calprotectin generated + 6 aliquots unprocessed stored -80C
Intestinal Tissue (CD or UC or IBDU)	RNAlater	Scope	Stored -80C
Intestinal Tissue (CD or UC or IBDU)	Formalin	Scope	Paraffin embedded block
Intestinal Tissue (CD or UC or IBDU)	Flash Freeze (LN2)	Scope	Stored -80C

Periodicity of SPARC IBD Biosample Collection

Biosamples are collected around the time of consent (blood and stool) and when the patient undergoes a sigmoidoscopy or colonoscopy as part of his or her clinical care. Blood and stool samples are also obtained approximately 3 months after a change in therapy that follows a colonoscopy or sigmoidoscopy if the patient has a follow-up office visit during that time.

Peripheral Blood
Collected at the time of enrollment, and used to isolate plasma, RNA and DNA. Additional samples are collected at the time of colonoscopy and 3 months after a colonoscopy if change in therapy; and plasma, RNA, and PBMCs are isolated. These samples can be used for a variety of purposes including genotyping, transcriptomics, proteomics and metabolomics.

Stool
For baseline stool sample collection participants are provided with a stool kit at their first visit with instructions to collect the stool sample immediately after their visit. Participants collect the sample at home and ship two aliquots to the biobank; one aliquot of preservative-free stool and a second aliquot of stool stored in 95% alcohol to preserve

the sample for metabolomics. For the collection of stool at the time of colonoscopy, participants receive the stool kit 2 weeks prior the colonoscopy with instructions to collect samples preceding their bowel preparation. Preservative-free samples are subaliqouted upon arrival to the biobank and stored at -80˚C. Stool samples are suitable for microbiomics, proteomics and metabolomics studies as well as for measurement of routine inflammatory markers such as fecal calprotectin.

Intestinal tissue biopsy
For patients with Crohn's disease undergoing colonoscopy up to 5 pinch biopsies are obtained using forceps from the ileum or the most proximal extent of the exam and the rectum (at 20 cm from the anal verge). If both the rectum and the ileum (or cecum) appear normal on insertion of the colonoscope, an additional 5 pinch biopsies are obtained from an area with macroscopically active disease, if present.
For those with ulcerative colitis or IBDU, up to 5 pinch biopsies are obtained from the cecum (or most proximal extent of the exam) and the rectum (at 20 cm). When there is not pancolitis, if feasible and safe, biopsies from the normal area just adjacent to the transition area from abnormal to normal appearing mucosa are obtained. If the only evidence of inflamed tissue on colonoscopy is located distal to 20 cm, the biopsies from the rectum are obtained more distally in the area of active inflammation.
For each anatomical region, biopsies are collected in RNAlater, snapped frozen at sites equipped with LN2, or collected in formalin and embedded into paraffin blocks at the biobank within 24hrs of collection.

3. Data and Bisosample Use

Investigators accessing IBD Plexus data and biosample need to abide by data use and material transfer agreement terms. Please reference Appendix 1 – IBD Plexus Data Use Agreement and Appendix 2 - Material Transfer Agreement for more details. Please note, in particular, Section 5 of both appendices (Intellectual Property Rights; New Resources), which explains terms relevant to the role of IBD Plexus as a data exchange platform.

Appendix 1 – IBD Plexus Data Use Agreement

IBD Plexus

This Data Use Agreement ("Agreement") is by and between the Crohn's & Colitis Foundation ("Foundation"), a non-profit tax exempt organization pursuant to Section 501(c)(3) of the Internal Revenue Code, with an address at 733 Third Avenue, Suite 510, New York, NY 10017 and XXX ("Institution"), with offices at XXX. Foundation and Institution each may be referred to herein as a "Party" or collectively as the "Parties" to this Agreement.

Recitals

A. Foundation administers IBD Plexus, a resource for scientific researchers which includes patient data and information, that was created to accelerate research, drive progress toward precision medicine, and transform the care of patients living with Inflammatory Bowel Diseases ("IBD").

B. Institution employs XXX (the "Principal Investigator" or "PI"), an IBD researcher approved by the IBD Plexus Project Selection Committee ("PSC") to receive IBD Plexus data.

C. Foundation and Institution agree that PI shall receive access to certain IBD Plexus data on the terms and conditions of this Agreement.

Agreements

For good and valuable consideration, the sufficiency of which is acknowledged, the Parties agree as follows:

1. Data. PI shall receive the data identified at Exhibit A ("Data") for the purpose of conducting the project set forth in the PSC approved research proposal attached as Exhibit B (the "Approved Project"). PI may request additional use of the Data but no such additional use shall occur without prior written permission of Foundation and, upon such written permission such additional use shall be an Approved Project.

(a) Transfer/Disclosure of Data. The Data shall not be transferred to anyone not working on the Project without the prior written permission of Foundation, provided that nothing herein shall prevent Institution from meeting its obligations pursuant to any applicable law, or PI from meeting any obligation requiring the Data to be made available in connection with publication of the results of the Approved Project.

(b) Subject PHI. PI shall receive a deidentified data set. Neither Institution nor PI shall be permitted to use such information to re-identify the individuals nor to contact them

under any circumstances. In the event PI receives protected health information or information that is otherwise protected by any applicable law (any of the foregoing, "Subject PHI"), then PI shall not use such information to identify any individual nor contact them under any circumstances, shall only use such Subject PHI in accordance with applicable law, and PI shall return or destroy upon Foundation's written request and option, or, if PI requests in writing and Foundation agrees that return or destruction is not feasible under the circumstances, then Institution shall retain such information under these terms and conditions.

2. **Storage and Access to/Use of Data**. Institution shall safeguard storage of the Data and prevent its use or disclosure in violation of this Agreement. Only the PI, and individuals under the PI's supervision, will have access to and use the Data.

3. **Compliance; Notice of Withdrawal**. PI shall use the Data in compliance with all applicable laws. Institution and PI are responsible for obtaining and adhering to any Institutional Review Board ("IRB") approvals necessary to perform the Approved Project. If Institution receives written notice from Foundation that a patient, as identified using the unique coded identifier, whose Data has been provided, wishes to withdraw permission for use of such Data (a "Notice of Withdrawal"), then PI only shall use such Data to the extent necessary to protect the integrity of the Project.

4. **Notifications of Breaches and Security Incidents**. Institution shall notify Foundation in writing as soon as possible, but in no event more than three (3) calendar days, after becoming aware of any breach or, or security incident involving, Subject PHI. Institution shall be deemed to be aware of any breach or security incident as of the first day on which such breach or security incident is known to any of its officers or employees. Institution shall identify as soon as practicable each individual whose Subject PHI has been, or is reasonably believed to have been accessed, acquired, or disclosed during such breach or security incident. Institution shall cooperate in good faith, at its own cost and expense, in the investigation by Foundation of any breach or security incident.

(a) Prompt Corrective Actions. Institution shall: (i) take prompt corrective action to remedy any breach or security incident, and (ii) mitigate, to the extent practicable, any harmful effect of a use or disclosure of Subject PHI in violation of this Agreement.

(b) Notification of Corrective Action and Provision of Policies. Institution will provide written notice as soon as possible but no later than ten (10) calendar days from the date that Institution provided notice to Foundation, of: (i) the actions taken by Institution to mitigate any harmful effect of such breach or security incident; and (ii) the corrective action Institution has taken or shall take to prevent future similar breaches or security incidents. Upon Foundation's request, Institution will also provide to Foundation a copy of Institution's policies and procedures for handling patient information or information security.

5. **Intellectual Property Rights ("IPRs"); New data/information; New Resources**.

(a) Claim of IPRs. Institution and/or PI may claim IPRs on inventions or discoveries involving use of the Data provided that Institution and PI shall not claim any IPRs or

any ownership rights, or permit any claim or assertion of IPRs or ownership rights, in any of or any part of, the Data.

(b) Non-Targeted Data. If the Approved Project generates analyzed or interpreted Approved Project data ("Project Results") not directed at a particular hypothesis, but rather is a preliminary exploration of the data ("Non Targeted Data"), then, with respect to such Non-Targeted Data, upon the earlier of: (a) one hundred eighty (180) days after the last grant of Data to PI; (b) acceptance of an Approved Project manuscript for publication; or, (c) filing of a patent application, Institution shall provide to Foundation in writing: (i) information about the status of the Approved Project, including identification of any New Resource (defined in Subsection (d)); and (ii) new raw Approved Project data in a manner that retains linkage of such data to the Data, which new raw Approved Project data may be released to third party researchers in connection with new research projects.

(c) Targeted Data. If the Approved Project generates Project Results directed at one or more particular hypotheses ("Targeted Data"), then, with respect to such Targeted Data, upon the earlier of: (a) five hundred forty (540) days after the last grant of Data to PI; (b) acceptance of an Approved Project manuscript for publication; or, (c) filing of a patent application, Institution shall provide to Foundation in writing: (i) information about the status of the Approved Project, including any New Resource; and, (ii) new raw Approved Project data in a manner that retains linkage of such data to the Data, which new raw Approved Project data may be released in connection with new research projects.

(d) New Resources. If PI and/or Institution creates any novel resources (which shall include new data, information and results) useful to scientific researchers that arise from use of the Data, including without limitation that may be protectible as an IPR ("New Resources"), then Institution shall notify Foundation and, if requested by Foundation, provide a copy of all such New Resources to Foundation at cost and without markup, for at cost distribution to scientists performing research into the causes of and cures for IBD, and provided that (i) any New Resource that is not new raw Approved Project data that may be commercializable by Institution only shall be made available by Foundation to non-commercial organizations, (ii) this sublicensable license shall be subject to Sections 5(b) and (c), (iii) such distribution will not grant to any third party any other right to such New Resources; and (iv) any recipient of such New Resources shall agree to substantially similar terms and conditions as the ones set forth in this Agreement, including without limitation release and indemnification of Institution and PI as contributor for receipt, storage and use of any New Resource.

6. **Notice**. Any notice required or permitted by this Agreement shall be made by one Party to the other Party as follows:

to Foundation: to Institution:

Orlando Green
Senior Manager, Grants & Contracts
Crohn's & Colitis Foundation
733 Third Avenue, Suite 510
New York, NY 10017
E: ogreen@crohnscolitisfoundation.org
T: (646) 943-7505

7. Publication.

(a) Within thirty (30) days after creation of the final draft of any paper analyzing or otherwise utilizing Data and prior to its submission for publication (each manuscript, a "Project Paper"), PI shall provide the IBD Plexus Publication Review Committee with a copy. PI shall use best efforts to seek publication of any Project Paper in accordance with generally accepted scientific standards.

(b) Project Papers will be reviewed by a subset of the Publication Review Committee on an ad hoc basis, provided that such review shall not exceed thirty (30) days from receipt of the Project Paper by such Committee. If there are no concerns with publication, then PI may move forward with publication efforts; however, if review of the manuscript indicates that issues need to be addressed, then the Project Paper will be reviewed by the entire Publication Review Committee, provided that such review shall not exceed sixty (60) days from receipt of the Project Paper by such Committee. Reasons for additional review include, but are not limited to, the following:

1. Manuscript contains one or more egregious methodological errors
2. Manuscript generates major reviewer concerns regarding methodology, findings and/or conclusions that are found to misinterpret the data and/or cohorts
3. Manuscript is market research analysis
4. Manuscript falls outside the scope of the approved Project

(c) In the event that the Committee provides comments to the PI, PI shall consider such comments.

(d) Foundation may make any Project Paper available through IBD Plexus after its publication, provided that it is permissible by the publishing journal and doing so does not compromise the publishability of any Project Paper.

(e) Any Project Paper shall include written acknowledgement of the Foundation: e.g., "The results published here are in whole or part based on data obtained from the IBD Plexus program of the Crohn's & Colitis Foundation."

The Foundation acknowledges that researchers with access to IBD Plexus resources may be required by third parties to provide copies of data they use in research projects for the purposes of validating or reproducing research results, for example, in order to publish their results in a journal, or because they are subject to other data sharing requirements, for example, because they receive funding from the U.S. government.

This Policy sets forth the Foundation's commitment to support these researchers in fulfilling their commitments to third parties by allowing for the use of IBD Plexus data resources for validation, reproducibility, data sharing or other legitimate purposes.

The Foundation will use the following procedures to allow for access to IBD Plexus data as discussed in this Policy:

1. A researcher with access to IBD Plexus resources will notify the Foundation in writing promptly upon becoming aware that the researcher is subject to a requirement described in this Policy, including identification of the IBD Plexus data that is subject to this requirement, a description of the requirement, and the third party that imposes this requirement, as follows: [name and email address]. If the circumstances are such that the researcher cannot provide this notice, then the entity requiring access to the IBD Plexus data may provide this information to the Foundation.

2. The Foundation will cooperate in good faith to make available the IBD Plexus data that must be accessed for a purpose set forth in this Policy. Ordinarily, this will mean that a particular third party researcher or research team will be given access to IBD Plexus data through execution of a data use agreement with a researcher or research team for access to the IBD Plexus data only for the purpose of validating or reproducing the results as required by a journal policy, data sharing requirement, or other legitimate purpose. The Foundation may require other reasonable terms and conditions in return for providing access to IBD Plexus data, such as: that the third party researcher or research team not use the data for any purpose other than validation or reproduction of the research results, and that the data and all copies be securely stored so that the data is not used for any other purpose, and/or returned or destroyed.

3. In the event that a researcher with access to IBD Plexus data is subject to a requirement by a third party for which a data use agreement and provision of the data by the Foundation directly to a researcher or research team as set forth above is not sufficient, for example, if a U.S. government data sharing policy to which the researcher is subject requires deposit of a data set into a non IBD Plexus repository, then the Foundation will cooperate in good faith to allow that researcher to discharge his or her obligations with respect to that requirement.

4. Ordinarily, the Foundation will agree to allow a researcher who is subject to a requirement to deposit IBD Plexus data into a non IBD Plexus repository on the following conditions: (a) the researcher informs the Foundation in writing promptly upon learning that he or she is subject to such a requirement (and ideally at the time that the researcher submits a request to IBD Plexus for IBD Plexus data) and allows the

Foundation the opportunity to ensure that such deposition requirement will include the license features set forth in Section 4(b) of this Policy and will not violate Section 5 of this Policy; and (b) the Foundation will approve deposition of IBD Plexus data provided that the researcher deposits such data subject to a Creative Commons license with all of the Attribution (including identification of IBD Plexus as a source of the IBD Plexus data), Non Commercial and Share Alike features or their equivalent.

5. With respect to all of the foregoing in this Policy, the Foundation reserves its rights to, at its discretion, manage IBD Plexus so that the Foundation's obligations to third parties are not violated or otherwise compromised in its efforts to support researchers in fulfilling their responsibilities with respect to journal publication requirements, receipt of U.S. government funding and other requirements.

8. No Representations or Warranties. EACH PARTY MAKES NO REPRESENTATIONS OR WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, WITH RESPECT TO THE DATA OR OTHER SUPPLIED MATERIALS, INCLUDING WITHOUT LIMITATION ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE, OR THAT THE DATA OR OTHER SUPPLIED MATERIALS WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK OR OTHER PROPRIETARY RIGHTS. ALL DATA AND OTHER SUPPLIED MATERIALS ARE PROVIDED ON AN "AS IS" BASIS.

9. Risk of Liability/Indemnification. Each Party shall assume all risk of and hereby does release the other Party, including without limitation, Foundation, IBD Plexus, its members, contributors, and their directors, officers, employees and agents (collectively, the "Releasees"), from all liability related to access to, storage and use of any data and other materials supplied to it by the other Party (the "Activities") and, only if Institution is permitted by law to do so, each Party shall and hereby does indemnify, defend and hold Releasees harmless from and against all liability relating to the Activities, except to the extent that any such liability is caused by the gross negligence or willful misconduct of any of the Releasees.

10. Remedies for Violation. Any material violation of these terms and conditions shall constitute good cause for Foundation to immediately revoke permission granted for use of the Data and, upon such written notice from Foundation, Institution and PI shall promptly cease all such use and at the election of Foundation return or destroy all such Data. Institution agrees that any material violation of these terms and conditions may cause Foundation to pursue any and all available legal remedies.

The Parties, by their duly authorized representatives, agree to the foregoing:

Crohn's Colitis Foundation	**Institution**
_____	_____
Name	
Title	
Date	

Principal Investigator

_____

Name:
Title:
Date:

Exhibit A – Data
Exhibit B – Approved Proposal

Appendix 2 – Material & Data Transfer Agreement

This Materials Use Agreement ("Agreement") is by and between the Crohn's & Colitis Foundation ("Foundation"), a non-profit tax-exempt organization pursuant to Section 501(c)(3) of the Internal Revenue Code, with an address at 733 Third Avenue, Suite 510, New York, NY 10017 and XXX ("Company"), with offices at [XXX]. Foundation and Company each may be referred to herein as a "Party" or collectively as the "Parties" to this Agreement.

Recitals

Foundation administers IBD Plexus, a resource for scientific researchers which includes patient Materials and information, that was created to accelerate research, drive progress toward precision medicine, and transform the care of patients living with Inflammatory Bowel Diseases ("IBD").

Company employs [XXX] (the "Principal Investigator" or "PI"), an IBD researcher approved by the IBD Plexus Project Selection Committee ("PSC") to receive IBD Plexus biosamples ("Materials") pursuant to an approved research proposal.

Foundation and Company agree that Company shall receive access to certain Materials on the terms and conditions of this Agreement.

Agreements

For good and valuable consideration, the sufficiency of which is acknowledged, the Parties agree as follows:

1. **Materials**. Company shall receive the Materials identified at Exhibit A ("Provided Items") for the purpose of conducting the project set forth in the PSC approved research proposal attached as Exhibit B (the "Approved Project"). Foundation agrees that the Provided Items shall not include any Protected Health Information, as that term is defined in the Health Insurance Portability and Accountability Act of 1996, as well as the implementing privacy and security regulations (collectively, "HIPAA"). Any data or information related to human tissue or sera samples shall be de-identified in accordance with the requirements set forth in 45 C.F.R. § 164.514(a) and (b) prior to disclosure to Company. Company shall maintain the Materials and other Provided Items in a secure environment and prevent their unauthorized use or disclosure and shall be solely responsible to remediate any breach or any unauthorized use or disclosure of Materials or Provided Items in its possession in accordance with all applicable laws and to the extent practicable. Company, upon knowledge, shall promptly report to Foundation any use or disclosure of Materials or Provided Items that are in material violation of any applicable law or this Agreement.

   (a) Transfer/Disclosure of Materials. The Provided Items shall not be transferred to anyone not working on the Approved Project without the prior written permission of Foundation, provided that nothing herein shall prevent Company from meeting its obligations pursuant to any applicable law, or

from meeting any obligation requiring the Materials to be made available in connection with publication of the results of the Approved Project. Company may request additional use of the Provided Items but no such additional use shall occur without prior written permission of Foundation and, upon such written permission such additional use shall be an Approved Project.

2. Storage and Access to/Use of Materials. Company shall safeguard storage of the Provided Items and prevent its use or disclosure in violation of this Agreement. Only the PI, and individuals appropriately trained in the handling of sensitive Materials under the PI's supervision, will have access to and use the Provided Items.

3. Compliance; Notice of Withdrawal. PI shall use the Provided Items in compliance with all applicable laws. If Company receives written notice from Foundation that a patient, as identified using the unique coded identifier, whose Materials has been provided, wishes to withdraw permission for use of such Materials (a "Notice of Withdrawal"), then PI only shall use such Materials to the extent necessary to protect the integrity of the Approved Project.

4. Notifications of Breaches and Security Incidents. Company shall notify Foundation in writing as soon as possible, but in no event more than three (3) calendar days, after becoming aware of any breach or, or security incident involving Provided Items. Company shall be deemed to be aware of any breach or security incident as of the first day on which such breach or security incident is known to any of its officers or employees. Company shall cooperate in good faith, at its own cost and expense, in the investigation by Foundation of any breach or security incident.

(a) Prompt Corrective Actions. Company shall: (i) take prompt corrective action to remedy any breach or security incident, and (ii) mitigate, to the extent practicable, any harmful effect of a use or disclosure of Provided Items in violation of this Agreement.

(b) Notification of Corrective Action and Provision of Policies. Company will provide written notice as soon as possible but no later than ten (10) calendar days from the date that Company provided notice to Foundation, of: (i) the actions taken by Company to mitigate any harmful effect of such breach or security incident; and (ii) the corrective action Company has taken or shall take to prevent future similar breaches or security incidents.

5. Intellectual Property Rights ("IPRs"); New Materials/information; New Resources.

(a) Claim of IPRs. Company and/or PI may claim IPRs on inventions or discoveries involving use of the Provided Items provided that Company and PI shall not claim any IPRs or any ownership rights, or permit any claim or assertion of IPRs or ownership rights, in any of or any part of, the Materials.

(b) Non Targeted Materials. If the Approved Project generates results not directed at a particular hypothesis, but rather is a preliminary exploration of the Materials ("Non

Targeted Materials"), then, with respect to such Non-Targeted Materials, upon the earlier of: (a) one hundred eighty (180) days after the last grant of Materials to PI; (b) acceptance of an Approved Project manuscript for publication; or, (c) filing of a patent application, Company shall provide to Foundation in writing: (i) information about the status of the Approved Project, including identification of any New Resource (defined in Subsection (d)); and (ii) new raw Approved Project Materials in a manner that retains linkage of such Materials to the Materials, which new raw Approved Project Materials may be released to third party researchers in connection with new research projects.

(c) Targeted Materials. If the Approved Project generates Results directed at one or more particular hypotheses ("Targeted Materials"), then, with respect to such Targeted Materials, upon the earlier of: (a) five hundred forty (540) days after the last grant of Materials to PI; (b) acceptance of an Approved Project manuscript for publication; or, (c) filing of a patent application, Company shall provide to Foundation in writing: (i) information about the status of the Approved Project, including any New Resource; and, (ii) new raw Approved Project Materials in a manner that retains linkage of such Materials to the Materials, which new raw Approved Project Materials may be released in connection with new research projects.

(d) New Resources. If PI and/or Company creates any novel resources (which shall include new Materials, information and results) useful to scientific researchers that arise from use of the Materials, including without limitation that may be protectible as an IPR ("New Resources"), then Company shall notify Foundation and, if requested by Foundation, provide a copy of all such New Resources to Foundation at cost and without markup, for at cost distribution to scientists performing research into the causes of and cures for IBD, and provided that (i) any New Resource that is not new raw Approved Project Materials that may be commercializable by Company only shall be made available by Foundation to non-commercial organizations, (ii) this sublicensable license shall be subject to Sections 5(b) and (c), (iii) such distribution will not grant to any third party any other right to such New Resources; and (iv) any recipient of such New Resources shall agree to substantially similar terms and conditions as the ones set forth in this Agreement, including without limitation release and indemnification of Company and PI as contributor for receipt, storage and use of any New Resource.

6. **Notice**. Any notice required or permitted by this Agreement shall be made by one Party to the other Party as follows:

to Foundation:

Orlando Green
Senior Manager, Grants & Contracts
Crohn's & Colitis Foundation
733 Third Avenue, Suite 510
New York, NY 10017
E: ogreen@crohnscolitisfoundation.org
T: (646) 943-7505

to: Company

9. No Representations or Warranties. EACH PARTY MAKES NO REPRESENTATIONS OR WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, WITH

RESPECT TO THE MATERIALS OR OTHER SUPPLIED MATERIALS, INCLUDING WITHOUT LIMITATION ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE, OR THAT THE MATERIALS OR OTHER SUPPLIED MATERIALS WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK OR OTHER PROPRIETARY RIGHTS. ALL MATERIALS AND OTHER SUPPLIED MATERIALS ARE PROVIDED ON AN "AS IS" BASIS.

9. Risk of Liability/Indemnification. Each Party shall assume all risk of and hereby does release the other Party, including without limitation, Foundation, IBD Plexus, its members, contributors, and their directors, officers, employees and agents (collectively, the "Releasees"), from all liability related to access to, storage and use of any Materials and other materials supplied to it by the other Party (the "Activities") and, only if Company is permitted by law to do so, each Party shall and hereby does indemnify, defend and hold Releasees harmless from and against all liability relating to the Activities, except to the extent that any such liability is caused by the gross negligence or willful misconduct of any of the Releasees.

11. Remedies for Violation. Any material violation of these terms and conditions shall constitute good cause for Foundation to immediately revoke permission granted for use of the Materials and, upon such written notice from Foundation, Company and PI shall promptly cease all such use and at the election of Foundation return or destroy all such Materials. Company agrees that any material violation of these terms and conditions may cause Foundation to pursue any and all available legal remedies.

The Parties, by their duly authorized representatives, agree to the foregoing:

Crohn's Colitis Foundation

_____
Name
Title
Date

Company

_____
Name
Title
Date

Principal Investigator

_____

Name:
Title:
Date:

Exhibit A – Provided Items
Exhibit B – Approved Proposal