Attachment A
Statement of Work # 2

Carilion Medical Center, a Virginia nonprofit corporation located at 1906 Belleview Avenue, Roanoke, Virginia 24014 ("Institution"), and TechLab, Inc. having a principal place of business at 2001 Kraft Drive, Blacksburg, VA 24060-63664 ("Sponsor") have entered into a Master Research Services Agreement effective the 20th of April, 2015 (the "Agreement").

In accordance with the Agreement, Sponsor and Institution are entering into this Statement of Work ("Statement of Work") as of the 8th of February, 2016 (the "Effective Date") pursuant to the terms and conditions set forth below (Sponsor and Institution each a "party" and collectively, the "parties").

1. *General Terms.*

(a) The terms and conditions of the Agreement are incorporated herein by reference and shall govern the parties' rights and obligations under this Statement of Work. Capitalized terms not otherwise defined in this Statement of Work shall have the meaning attributed to such terms in the Agreement.

(b) Sponsor and Principal Investigator have developed a protocol for the performance of a Study in accordance with Protocol titled "Fecal Lactoferrin to Quantify Musocal Inflammation in Inflammatory Bowel Disease" ("Protocol"), attached hereto as Exhibit A and incorporated by reference herein.

(c) Sponsor and Principal Investigator have developed a study budget for the performance of the referenced protocol, attached hereto as Exhibit B and incorporated by reference herein.

2. *Scope of Research Services.* Institution shall provide its employees, Dario Sorrentino, MD and Marrieth Rubio, MD, to oversee the performance of the Study pursuant to the Protocol at Institution and serve as Principal Investigator.

3. *Payments.* Sponsor shall pay Institution for performance of Research Services in accordance with the terms of the Protocol, and this Statement of Work as specified in the Fee Schedule, within 30 days of receipt of an invoice and upon receipt of the Research Report. Payments to Institution under this Statement of Work shall be sent to the following:

PAYEE NAME:	Carilion Medical Center
PAYEE ADDRESS:	Research and Development
	101 Elm Ave SE, 2nd Floor
	Roanoke, VA 24013
TAX ID NUMBER:	54-0506332

CONTACT INFORMATION:	Jennifer Chapman 540-224-4742 jtchapman@carilionclinic.org

4. *Counterparts and Execution.* This Statement of Work may be executed in counterparts, each of which shall be deemed an original instrument, and all of which shall constitute a single agreement. The parties may execute this Statement of Work by facsimile or electronically transmitted signature, and such facsimile or electronically transmitted document, including the signatures thereon, shall be treated in all respects as an original instrument bearing an original signature.

5. *Fee Schedule.* (Example) will be included in the study budget (Exhibit B)

Service Description	Charge	Frequency	Estimated Total	Comments
1. Supplies				
2. Shipping and Handling				
3. Sample Storage				
4.				
5.				

6. Subject Injury. No applicable.

IN WITNESS WHEREOF, the parties hereto have entered into this Statement of Work by their duly authorized representatives as of the Effective Date above.

Carilion Medical Center

Signature Date

Daniel P. Harrington, M. D.
Vice President – Academic Affairs

TechLab, Inc.

Signature 9/23/2016
Date

Robert M. Day
Chief Operating Officer

Exhibit A
Protocol
(as provided by Sponsor and Principal Investigator)

A. TRIAL PARAMETERS.

BACKGROUND: Traditionally, the activity of inflammatory bowel disease (IBD) has been monitored by the severity of clinical symptoms. Currently, a paradigm shift in practice has occurred towards using endoscopy, a parameter more objective than symptoms. However, endoscopy is both expensive and invasive, and often unwelcome by patients. Recent studies have shown that fecal biomarkers, such as calprotectin and lactoferrin, are effective indicators of mucosal inflammation and injury.

OBJECTIVE: The purpose of this retrospective study is to establish a correlation between lactoferrin levels and mucosal inflammation in patients with IBD. Our hypothesis is that lactoferrin levels correlate strongly with the degree of mucosal inflammation and are reliable surrogate markers to monitor disease activity and determine clinical management.

SPECIFIC AIMS:

- Correlate lactoferrin levels to mucosal inflammation as well as disease location and extent as assessed by endoscopy and histology.
- Correlate lactoferrin levels with the clinical severity of disease and disease progression.
- Establish cut-off lactoferrin levels associated with disease remission and relapse as assessed by endoscopy, clinical, and biochemical parameters.

METHODS: The International Classification of Diseases-9 (ICD-9) for CD (555.xx) and UC (556.xx), in combination with medications for IBD treatment, will be used in a query of patients that are both within the Epic database and treated by Dr. Sorrentino—the principal IBD specialist and Dr. Rubio- a member of the IBD team, utilizing lactoferrin to monitor IBD symptoms at Carilion Clinic.

Endoscopic findings will be quantified using the Simple Endoscopic Score for Crohn's Disease (SES-CD) and the endoscopic component of the Mayo clinical score (DAI) for UC to grade the degree of disease severity. Histological findings will be categorized by disease activity into active enteritis, active crypt destructive colitis, chronic colitis, or quiescent colitis. Active enteritis as well as active crypt destructive colitis will further be divided into mild, moderate or severe based upon disease activity upon review by our expert pathologist Dr. Grider. To adequately compare lactoferrin levels to the degree of mucosal inflammation and injury, the time period between fecal biomarker collection and endoscopy must occur within 30 days of each other. This is less than the average time period used in previous studies.

EXPECTED OUTCOMES: We expect that lactoferrin levels will correlate strongly with the degree of mucosa inflammation as determined by endoscopic and histological

findings. We plan to show that measured lactoferrin levels can be used as a reliable surrogate marker for monitoring IBD activity and guiding management

Estimated start date: 1 of September, 2016

Estimated completion date: 31 of August, 2017

B. SUMMARY OF DESIGN:

This retrospective study involves all patients who have been diagnosed with IBD (either ulcerative colitis, Crohn's disease, or undetermined colitis), have been under the care of either Dr. Sorrentino and/or Dr. Rubio and have had their IBD symptoms monitored through the measurement of fecal lactoferrin levels. These IBD patients would have had at least one colonoscopy for scoring of Crohn's disease within 30 days of lactoferrin analysis as well as the availability of tissue sections of biopsies taken at time of colonoscopy. Control groups will include patients who were diagnosed with Irritable Bowel Syndrome (IBS) and who have had fecal lactoferrin levels measured.

C. STUDY MILESTONES:

Location of the project: This project will be conducted at CRMH and Riverside 3 locations, and data analysis conducted at TechLab.

Scope of Work:

Dr. Sorrentino, Dr. Rubio, Dr, Gazo and Dr. Nguyen, with the help of a research coordinator, will be reviewing each chart to determine the level of inflammation, mucosal injury, and disease severity in mucosal tissue. Endoscopic pictures taken at either Carilion Roanoke Memorial Hospital (CRMH) or Carilion Roanoke Community Hospital (CRCH) are stored within the Olympus Endoworks 7.4 server. **Dr. Rubio** will search through this database and retrieve pictures from each endoscopy that patients in our study have received. **Dr. Rubio** will give a score to each picture based on the photos and endoscopy reports; scoring will also be based upon magnetic resonance imaging (MRI) or CT scan/general diagnostic radiology image results for Crohn's disease patients. The following clinical endoscopic scoring systems will be utilized: the Simple Endoscopic Score for Crohn's Disease (SES-CD) and the endoscopic component of the Mayo Clinical score (DAI) for ulcerative colitis (Tables 1 and 2)3. The SES-CD, a 56-point scale, and the endoscopic DAI, a 3-point scale, are both used clinically to measure disease activity4. Endoscopy scores established in previous studies will be used to indicate disease activity. The SES-CD defines the following terms: remission (0-2), mild inflammation (3-6), moderate inflammation (7-16), and severe inflammation (>16)5. The endoscopic component of the DAI defines the following terms: normal or inactive disease (0), mild disease (1), moderate disease (2), and severe disease (3).

Tissue specimens in the form of histological slides are also available for each patient. The tissue sections from each patient sample will be reviewed by **Dr. Grider** and classified by disease activity into one of the following categories: active enteritis, active crypt destructive colitis, chronic colitis, and quiescent colitis. Moreover, active enteritis and active crypt destructive colitis will be graded as mild, moderate or severe depending upon disease activity. Disease activity is measured by such factors as erosion, ulceration, neutrophilic involvement of crypts and surface mucosa as well as crypt distortion. **Dr. Grider** will be blinded to the lactoferrin levels of each patient to ensure an unbiased analysis of the histological samples.

James Boone and Kim Love will be receiving de-identified data from retrospective study which includes data from patient EMRs, endoscopy and histological scoring results and will conduct data and statistical analysis.

Responsibilities	**Institution**	**Comments**
Collection of retrospective data	CMC	
Data Analyses	Tech Lab	
Manuscript preparation for publication	CMC and Tech Lab	
Publications/Presentations/Posters	CMC and Tech Lab	

Exhibit B
Study Budget
(as provided by Sponsor and Principal Investigator)

There is no budget associated with this retrospective study and all work will be done in-kind.