PROTOCOL TITLE:

Include the full protocol title.

Response: Anti-inflammatory and ROS Suppressive Effects of the Fiber supplementation to a High Fat High Carbohydrate Meal and fiber supplementation alone in obese patients with type 2 diabetes

PRINCIPAL INVESTIGATOR:

Response:

Paresh Dandona, MD

Division of Endocrinology, Department of Medicine

Phone: 716-535-1850

Email: pdandona@kaleidahealth.org

Sub Investigators:

Chi Tang, MD

Husam Ghanim, PhD

Itivrita Goyal, MD

VERSION:

Include the version date or number.

Response:

05/09/2017

NCT02868788

Complete Research Protocol (HRP-503)

Table of Contents

Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 19, 20, 22, 23, 24, 25, 31, and 32 do not apply.*
    - *For exempt research: Sections 31 and 32 do not apply.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

Response: This study does not involve multiple participant groups

Intervention Group:
Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

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GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response:

Endocrine Fellows Foundation

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Location:Diabetes Endocrinology Research Center of WNY

Address:1000 Youngs Road, Suite 105, Williamsville NY 14221

Department: Diabetes Endocrinology

1.0 Objectives

1.1 Describe the purpose, specific aims, or objectives of this research.

Response: To study the effects of fiber supplementation to high fat high carbohydrate (HFHC) meal and the effects of fiber supplementation alone on inflammation and insulin sensitivity

1.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

HYPOTHESIS A:

HFHC meal causes an acute inflammatory and oxidative stress response in mononuclear cells (MNC) and adipose tissue of obese patients with type 2 diabetes mellitus (T2DM) versus HFHC meal plus fiber and fiber alone.

Aim A1: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on the levels of inflammatory mediators and indices of oxidative stress (intra-nuclear NF-κB binding activity, ROS generation by MNC, Thiobarbituric acid reactive substances (TBARS), endotoxin, free fatty acid (FFA), urinary isoprostanes, expression of TNF alpha)

Aim A2: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on the levels of Matrix Metallopeptidase 9 (MMP-9), LPS and LBP concentrations.

Aim A3: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on intracellular mediators of insulin resistance (SOCS-3, protein tyrosine phosphatase-1B (PTP-1B), TLR-4 and TLR-2).

HYPOTHESIS: B

HFHC meal causes reduced insulinogenesis and increased glucose excursion versus HFHC meal plus fiber or fiber supplementation alone.

Aim B1: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on secretion of insulin, proinsulin, C-peptide and insulin to glucose ratio.

Aim B2: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on secretion of GLP-1, GIP-1, glucagon and DPP-4.

Aim B3: To compare the effect of HFHC meal with and without fiber supplement and fiber supplement alone on gastric emptying rate.

2.0 Scientific Endpoints

2.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

Primary endpoints: change in reactive oxygen species (ROS) generated by mononuclear cells (MNC) and plasma concentration of dipeptidyl peptidase IV (DPP-IV) enzyme after meal challenge

Secondary endpoints: changes in other inflammatory and oxidative stress markers including Tumor Necrosis Factor alpha (TNF-α), Toll Like Receptor-4 (TLR-4), Toll Like Receptor-2 (TLR2), Suppressor of Cytokine Signaling 3 (SOCS-3), Protein Tyrosine Phosphatase-1B (PTP-1B), lipopolysaccharides (LPS) concentrations in plasma and changes in insulin secretion, glucose excursion and incretin level after meal challenge

3.0 Background

3.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

We have previously demonstrated that the intake of a high fat and high carbohydrate (HFHC) meal results in the induction of oxidative and inflammatory stress, which was measured as an increase in reactive

oxygen species (ROS) generated by mononuclear cells (MNC) and the expression of p47, a key subunit of NADPH oxidase, with a concomitant increase in nuclear factor κB (NFkB) binding. We also demonstrated that HFHC meal led to an increase in lipopolysaccharides (LPS) concentrations and the expression of Toll-like receptor 4(TLR-4) and lipopolysaccharide binding protein (LBP), the protein which facilitates the binding of LPS to CD14 and TLR-4. In contrast, when a fruit and fiber meal (recommended by American Heart Association, known as AHA meal) was taken, no such changes occurred. This contrasting observation raises the question whether the fruit and/or the fiber content of the latter meal has anti-inflammatory effects. We have also shown previously that the concomitant intake of orange juice prevents the pro-inflammatory effects of the HFHC meal and thus exerts anti-inflammatory and anti-oxidant effects. But we do not know whether it is due to the fiber component of orange juice.

Since atherosclerosis is chronic inflammation of the arterial wall and this inflammation is initiated by the arrival of monocytes and other mononuclear cells from the circulation into the intimal layer of the artery, the post prandial inflammatory state of the MNC may be important to atherogenesis. Therefore, a reduction in post-prandial inflammation and oxidative stress can potentially reduce atherogenesis. There are several studies demonstrating the beneficial effects of fiber intake on the prevention of cardiovascular events. While these epidemiological studies are consistent in terms of the clinical outcomes, there are limited data available to explain the mechanisms underlying these beneficial effects. It is, therefore, important that the molecular effects of fiber intake on inflammation and oxidative stress be investigated.

In addition to the anti-inflammatory effects of orange juice, fruit and high fiber meal, we have also previously observed that the magnitude of insulin secretion and the insulin/glucose ratio is significantly increased after the intake of orange juice with the HFHC meal and following the AHA meal. This was associated with an early peak in glucagon-like peptide -1 (GLP-1) concentrations and prevention of the increase in plasma concentration of dipeptidyl peptidase IV (DPP-IV) enzyme which lyses GLP-1 and gastric inhibitory polypeptide (GIP). Furthermore, inflammatory mediators, including suppressor of cytokine signaling 3 (SOCS-3), interfere with insulin signal transduction and thus mediate insulin resistance. Our previous work has shown that SOCS-3 is induced by the HFHC meal and that its increase is prevented by orange juice and by a meal rich in fruit and fiber. It is, therefore, possible that fiber intake prevent increase in SOCS-3.

This study will help elucidate the mechanism underlying the cardioprotective and anti-diabetes effect of dietary fiber by exploring a comprehensive set of inflammatory and oxidative stress markers, based on a contemporary understanding of this process. In addition, there have been very few studies that explored the immediate change in oxidative stress and incretin secretion after fiber intake. In this study, we will be able assess the short term metabolic impact

of dietary fiber at great details. The result will contribute to dietary recommendation or designing of fiber supplementation for prevention/treatment of diabetes, obesity and cardiovascular disease.

Furthermore, we will test the effect of fiber alone without HFHC meal to determine if fiber is the active component responsible for the anti-inflammatory and anti-glycemic effect of orange juice and high fiber meal. Since fiber can potentially alter gastric emptying time, which is a confounder in the metabolic parameter measurement, we will assess gastric emptying with acetaminophen absorption test. This test was validated for measurement of gastric emptying time[16].

3.2 Include complete citations or references.

Response:

1. Ceriello A, Hanefeld M, Leiter L, Monnier L, Moses A, Owens D, Tajima N, and Tuomilehto J. Postprandial glucose regulation and diabetic complications. Archives of internal medicine. 2004;164(19):2090-5.

2. Cavalot F, Petrelli A, Traversa M, Bonomo K, Fiora E, Conti M, Anfossi G, Costa G, and Trovati M. Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes mellitus, particularly in women: lessons from the San Luigi Gonzaga Diabetes Study. J Clin Endocrinol Metab. 2006;91(3):813-9.

3. Gerich JE. Postprandial hyperglycemia and cardiovascular disease. Endocr Pract. 2006;12 Suppl 1(47-51.

4. de Munter JS, Hu FB, Spiegelman D, Franz M, and van Dam RM. Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review. PLoS Med. 2007;4(8):e261.

5. Threapleton DE, Greenwood DC, Evans CE, Cleghorn CL, Nykjaer C, Woodhead C, Cade JE, Gale CP, and Burley VJ. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. BMJ. 2013;347(f6879.

6. Aljada A, Mohanty P, Ghanim H, Abdo T, Tripathy D, Chaudhuri A, and Dandona P. Increase in intranuclear nuclear factor kappaB and decrease in inhibitor kappaB in mononuclear cells after a mixed meal:

evidence for a proinflammatory effect. Am J Clin Nutr. 2004;79(4):682-90.

7. Ghanim H, Abuaysheh S, Sia CL, Korzeniewski K, Chaudhuri A, Fernandez-Real JM, and Dandona P. Increase in plasma endotoxin concentrations and the expression of Toll-like receptors and suppressor of cytokine signaling-3 in mononuclear cells after a high-fat, high-carbohydrate meal: implications for insulin resistance. Diabetes Care. 2009;32(12):2281-7.

8. Ghanim H, Sia CL, Upadhyay M, Korzeniewski K, Viswanathan P, Abuaysheh S, Mohanty P, and Dandona P. Orange juice neutralizes the proinflammatory effect of a high-fat, high-carbohydrate meal and prevents endotoxin increase and Toll-like receptor expression. Am J Clin Nutr. 2010;91(4):940-9.

9. Deopurkar R, Ghanim H, Friedman J, Abuaysheh S, Sia CL, Mohanty P, Viswanathan P, Chaudhuri A, and Dandona P. Differential effects of cream, glucose, and orange juice on inflammation, endotoxin, and the expression of Toll-like receptor-4 and suppressor of cytokine signaling-3. Diabetes Care. 2010;33(5):991-7.

10. Mohanty P, Ghanim H, Hamouda W, Aljada A, Garg R, and Dandona P. Both lipid and protein intakes stimulate increased generation of reactive oxygen species by polymorphonuclear leukocytes and mononuclear cells. Am J Clin Nutr. 2002;75(4):767-72.

11. Cho SS, Qi L, Fahey GC, Jr., and Klurfeld DM. Consumption of cereal fiber, mixtures of whole grains and bran, and whole grains and risk reduction in type 2 diabetes, obesity, and cardiovascular disease. The American journal of clinical nutrition. 2013;98(2):594-619.

12. Ross R. Atherosclerosis is an inflammatory disease. American heart journal. 1999;138(5 Pt 2):S419-20.

13. Dandona P, Ghanim H, Abuaysheh S, Green K, Batra M, Dhindsa S, Makdissi A, Patel R, and Chaudhuri A. Decreased insulin secretion and incretin concentrations and increased glucagon concentrations after a high-fat meal when compared with a high-fruit and -fiber meal. American

journal of physiology Endocrinology and metabolism. 2015;308(3):E185-91.

14. Hatano R, Ohnuma K, Yamamoto J, Dang NH, and Morimoto C. CD26-mediated co-stimulation in human CD8(+) T cells provokes effector function via pro-inflammatory cytokine production. Immunology. 2013;138(2):165-72.

15. Zhong J, Rao X, and Rajagopalan S. An emerging role of dipeptidyl peptidase 4 (DPP4) beyond glucose control: potential implications in cardiovascular disease. Atherosclerosis. 2013;226(2):305-14.

16. Willems, M., et al. (2001). "How useful is paracetamol absorption as a marker of gastric emptying? A systematic literature study." Dig Dis Sci 46(10): 2256-2262.

4.0 Study Design

4.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

This is a single center, open-labeled, crossover, controlled, randomized, prospective study. The study will be conducted at the Diabetes – Endocrinology Center of Western New York under the direction of Dr. Paresh Dandona, M.D.

15 patients with obesity and Type 2 diabetes mellitus will be enrolled to undergo meal challenges with HFHC meal, HFHC and fiber and fiber alone.

5.0 Local Number of Subjects

5.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response: 15

5.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response: 45

5.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

In our clinics, we will see about 10 patients every week that meet the inclusion criteria. We only need to recruit 15% of them over 10 weeks.

6.0 Inclusion and Exclusion Criteria

*6.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1. Men and women 18 to 80 years of age
2. Non-smoker (last cigarette at least one month ago)
3. Type 2 diabetes for at least 1 year
4. Body mass index > 30 kg/m2

*6.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1. Participation in any other concurrent clinical trials
2. Pregnancy or premenopausal women who are trying to be pregnant
3. Patients who are incompetent to give consent
4. Patients on non-steroidal anti-inflammatory drugs or steroids
5. Concurrent disease that could disrupt intestinal epithelium and increase permeability to endotoxin, ie Celiac and Crohns disease.
6. Hepatic disease (transaminase > 3 times normal)
7. Renal impairment (serum creatinine > 1.5 mg/dl)
8. History of drug or alcohol abuse
9. History of allergic reaction to acetaminophen.
10. Use of over the counter or prescribed probiotic supplements.
11. Recent or current antibiotic use.
12. Coronary artery disease (CAD): documented by history of myocardial infarction, angioplasty/stent placement, angina, exercise EKG positive for ischemia or angiographic evidence of CAD

6.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response:

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

6.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may ***not*** *be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

We have no non-English speaking patients in this population. We have patients that English is a second language, but they are able to read, write and understand it. This population is less than 10% of the total population.

7.0 Vulnerable Populations

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

7.1 For research that involves ***pregnant women,*** *safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response: We will not be using subjects from vulnerable populations ☒ **N/A**: This research does not involve pregnant women.

7.2 For research that involves ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*

NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*7.3 For research that involves **prisoners**, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

*7.4 For research that involves **persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")**, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☒ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*7.5 For research that involves **cognitively impaired adults**, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

*7.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. **Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

Not applicable

8.0 Eligibility Screening

*8.1 Describe **screening procedures** for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

📎 *Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response: Prospective participants will be asked to read and understand the consent and any questions they may have regarding the protocol will be answered. If the subject wants to participate in the study, they will be asked to sign the informed consent form. The subject's medical history and current medications will be obtained as well as their blood pressure and vitals. A physical examination will also be done. Blood samples will be taken in order to evaluate CBC, CMP, HbA1c and lipid panel and urine pregnancy status. Patients meeting all the

inclusion and exclusion criteria based on all screening tests will be enrolled in the study.

☐ **N/A:** There is no screening as part of this protocol.

9.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

9.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Participants will be identified by prescreening clinical charts, and patient doctor interaction at the time of their visit at the Diabetes Endocrinology Center of WNY. Locations include:

1. 1020 Youngs Road, Williamsville NY 14221

2. 705 Maple Road, Williamsville NY 14221

3. 462 Grider Street, Buffalo NY 14215

The study clinical team will evaluate their clinic patients for possible participation in this study according to the inclusion and exclusion criteria at the Diabetes and Endocrinology Center of WNY. Patients that may qualify for the study are referred to the research team for further eligibility evolution. Patients meeting the inclusion and exclusion criteria based on preliminary phone evaluation will be invited to participate in the study.

9.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response: Patient charts will be screened according to the study inclusion and exclusion criteria by our trained clinical staff and physicians. If the patient qualifies and is of consenting age, the physicians will speak to them about their interests in participating in research. If the patient agrees, their information will be given to the research coordinator to be contacted for further evaluation. All personal information will be kept confidential and locked in the coordinator office.

9.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

In addition to screening clinical charts, participations will be identified through; flyer advertisement and researchmatch.org

10.0 Procedures Involved

*10.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Screening Day

All subjects will have completed the following procedures prior to participating in the study:

1) Informed consent

2) Medical history

3) Physical exam

4) Baseline labs include complete blood count (CBC), comprehensive metabolic panel (CMP), Hemoglobin A1C, and lipid profile. All labs will be drawn in the fasting state

Visit 1: Subjects will arrive after having fasted overnight (10 hours) at 7 to 7:30 am. An indwelling intravenous cannula will be placed in the anterior cubital vein for blood draws. A blood sample of the research labs and a urine sample will be collected. Blood pressure, heart rate and weight will be measured. After blood draw and before the meal, patient will be asked to take a dose of 1000 mg *acetaminophen (Tylenol). Then the subject will consume either a HFHC meal or HFHC meal plus fiber (FiberOne Original cereal) or fiber alone according to*

randomization. Fiber will be consumed before and after the HFHC meal (28 grams in total, 14 grams before and after the meal) or 28 grams in total if consuming fiber alone. HFHC meal includes an egg muffin sandwich, a sausage muffin sandwich and two hash browns which contain 88g carbohydrate, 51 g fat (33% saturated) and 34 g protein. 35 ml of blood will be obtained at 1h , 2h, 3h and 5 h and 5 ml at 8 min*, 15 min, 30 min, 45 min, 75 min and 90 min. A total of 170 ml (about 12 tablespoon) blood will be collected.* A spot urine will be collected at 0, 3 and 5 hour*s*.

Visit 2: Subjects will return 1 week later after overnight fasting (10 hours) at 7 to 7:30 am. Blood pressure, heart rate and weight will be measured. Baseline blood and urine samples will be collected again and subjects will be crossed over to receive acetaminophen 1000 mg, followed by the second meal (HFHC only or HFHC with fiber or fiber alone) according to the randomization. Visit details are similar to visit 1. Blood samples will be drawn as described above.

Visit 3: Subjects will return 1 week later after overnight fasting (10 hours) at 7 to 7:30 am. Blood pressure, heart rate and weight will be measured. Baseline blood and urine samples will be collected again. Subjects will be crossed over to receive acetaminophen 1000 mg, followed by the third meal (HFHC only or HFHC with fiber or fiber alone) according to the randomization. Visit details will be the same as visit one. Blood samples will be drawn as described above. After this, the subject will be discharged from the study.

10.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

Reactive oxygen species (ROS) generated by mononuclear cells (MNC), Tumor Necrosis Factor alpha (TNF-α), Toll Like Receptor-4 (TLR-4), Toll Like Receptor-2 (TLR2), Suppressor of Cytokine Signaling 3 (SOCS-3), Protein Tyrosine Phosphatase-1B (PTP-1B), lipopolysaccharides (LPS) concentrations will be collected before meal challenge and at all time points after meal challenge. Plasma concentration of dipeptidyl peptidase IV (DPP-IV) enzyme, insulin, glucose and incretin level will be collected before meal challenge and at 1h, 2h, 3h and 5h after meal challenge. Urinary isoprostanes will be collected before meal challenge and at the end of 5 hours

10.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response: Please see forms for screening visit and for regular visit (visit 1, 2 and 3). Blood Pressure and weight are monitored every visit to ensure safety.

10.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response: electronic medical records, clinical charts and research files

*10.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response: Individual participant lab results will be disclosed to the participant upon their request. If the participant requests documentation be shared with another physician, physician office or hospital the participant must come to the research center to collect said documentation and/or the documentation can be mailed to their given home address.

*10.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

Study results will not be shared with the subjects. However, unidentifiable study results could be published in the form of a manuscript or abstract and will be reported to clinicaltrilas.gov.

11.0 STUDY TIMELINES

11.1 Describe the anticipated duration needed to enroll all study subjects.

Response: 10 weeks

11.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response: If the subject was found to meet the eligibility criteria, he/she will come to our research center for two appointments. Each appointment lasts for 5 hours and two appointments are 1 week apart.

11.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response: 18 months

12.0 Setting

12.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility,

department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

Research will be conducted at the Diabetes Endocrinology Research Center of WNY, located at 1000 Youngs Road, Suite 105, Williamsville NY 14221. The Diabetes Research Center has facilities and exam rooms available for insulin pump download, CGM device download, meal and infusion studies and presence of study coordinator and registered nurse for data collection and blood work at all times. One of the investigators will be available at all times to address patients' related issues. Equipment include ultra-low freezers for sample storage, centrifuges, microscopes for sample preparation, infusion pumps, ELISA, PCR and immunoblotting instrumentation. CTRC location is a fully equipped laboratory

12.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

13.0 Community-Based Participatory Research

13.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

13.2 Describe the composition and involvement of a community advisory board.

Response:

☒ **N/A:** This study does not have a community advisory board.

14.0 Resources and Qualifications

*14.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

All study personnel are educated, trained, and licensed as required for their delegated role in this study. All study personnel have also received the required university training and will be trained by the PI before the study starts.

Describe other resources available to conduct the research.

14.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

The principal investigator supervises the research project and weekly research meetings are conducted to discuss the recruitment rate, resolve and discuss issues related to the conduct, safety, analysis of the study and related publications. PI is expected to spend 5% of his academic time on this research. The co-investigators and study coordinator provide coverage to the research related activity for 365 days a year.

14.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

Available medical literature will be provided as deemed appropriate or requested by patient through UB libraries, Pubmed, Google scholar as all the investigators have access to medical literature through listed resources above

The patient will also have access to physician (Investigators and Co-Investigators) who will be available to address any adverse effects or other questions during the course of the study.

14.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response: Education through meetings, conferences and discussions

15.0 Other Approvals

15.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

☒ **N/A:** This study does not require any other approvals.

16.0 Provisions to Protect the Privacy Interests of Subjects

16.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

Our clinical providers involved in the study will identify potential patients for recruitment from the Diabetes-Endocrinology Center of WNY Clinics according to the inclusions and exclusion criteria and through advertisements. Patient who qualify will be asked in private during their one on one consultation time with the physician if they wish to participate in the research study. If the patient agrees, the research coordinator will contact them for a telephone screening privately. The patients who call for potential participation in the study due to advertisement flyers will be screened over the phone with the research coordinator, using our telephone screening form.

When the patient is being seen at our clinics for the first time they sign the "Consent to use and disclosure of protected health information" form which

clearly states that their protected health information (PHI) can be used for review in preparation for possible research.

If the patient passes the telephone screening, they will be asked to make an appointment to review and sign the consent. Patient will do this in a private, screen off area of the research department and will be allowed to discuss the consent in detail with the research coordinator and or study doctor. Patient will be no notified that it is completely voluntary to participate in the research study and can withdraw at any time.

We will not be accessing any medical information of the patients for whom the services are not provided by our clinic providers.

16.2 Indicate how the research team is permitted to access any sources of information about the subjects.

NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question ***does apply*** *to records reviews.*

Response: Consent of the subject and HIPAA waiver.

17.0 Data Management and Analysis

17.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

The demographic features of the population and screening lab results will be displayed in tables. Statistical analysis will be conducted using SigmaStat software version 3.1 (SPSS Inc., Chicago, IL). Data will be represented as mean±S.E. Percent change from baseline will be calculated and statistical analysis for change from baseline will be carried out using one-way repeated measures analysis of variance (RMANOVA) followed by Holm-Sidak post hoc test. Two-factor RMANOVA analysis followed by Tukey's post hoc test will be used for comparison between the 3 groups. Area under the curve for glucose, insulin, incretins and DDP-IV concentration will be calculated for each subject's samples and compared between meals by paired t- test.

17.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

Sample size determination for the overall study was based on the difference between the HFHC meal and AHA meal groups in DPP-IV concentration change from baseline. By conservatively assuming a mean difference in DPP-IV concentration of 20% between the 3 groups and a standard deviation of 15%, a sample size of 10 is sufficient to obtain a statistically significant difference ($P<0.05$) between the two groups with a power of 0.8. We also determined sample size based on the difference in the change from baseline in ROS generation by MNC following HFHC meal with and without fiber as the primary endpoint for this study. Based on our previous data ROS generation was lowered by 63±32% following AHA meal compared to HFHC meal, we now conservatively estimated a mean difference in ROS generation between HFHC meal with or without fiber of about 40% with a standard deviation of 30%. Therefore, a sample size of 15 is sufficient to obtain a statistically significant difference ($P<0.05$) between the two groups with a power of 0.8.

17.3 Describe any procedures that will be used for quality control of collected data.

Response:

Three investigators and research nurse will double check the accuracy of collected data. All laboratory testing will be standardized using references and standards

.

18.0 Confidentiality

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*18.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

All data records will be stored on password protected computers and or in locked cabinets within the Diabetes Endocrinology Research Center of WNY 1000 Youngs Road, Suite 105, Williamsville NY 14221 All subject data will be stored on a coded data collection form. The data collection form will be stored on a password protected computer in the research department with the subject files. These fileswill only be accessible by authorized study personnel.

18.2 A. How long will the data be stored?

Response:

Data and specimens storage has no expiration date and will be stored for a minimum of 7 years. The researchers may continue to rely on this for future use in research study

18.3 Data and specimens storage has no expiration date and will be stored for a minimum of 7 years. The researchers may continue to rely on this for future use in research study A. Who will have access to the data?

Response:

Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data and specimens

18.4 A. Who is responsible for receipt or transmission of the data?

Response: Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data and specimens and can handle transfer of data and samples

18.5 A. How will the data be transported?

Response:

All data are stored at one location and is not transported unless it is being archived. At that point files will be transferred to Iron Mountain for storage and archiving. Samples that are transported will be done so using dry ice in a properly labeled Styrofoam container by the laboratory technician.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☐ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 19.0)*

18.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response: The data and specimens will be stored in the laboratory located at 1000 Youngs Road, Suite 105, Williamsville NY 14221 and at the CTRC located in 875 Ellicott St. Buffalo NY14203. Samples will be stored in a locked -80º C freezer. Data will be stored on computers that are password protected.

18.7 B. How long will the specimens be stored?

Response: Data and specimens storage has no expiration date and will be stored for a minimum of 7 years. The researchers may continue to rely on this for future use in research study

18.8 B. Who will have access to the specimens?

Response: Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data and specimens

18.9 B. Who is responsible for receipt or transmission of the specimens?

Response: Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data and specimens and can handle transfer of data and samples

18.10 B. How will the specimens be transported?

Response: All data are stored at one location and is not transported unless it is being archived. At that point files will be transferred to Iron Mountain for storage and archiving. Samples that are transported will be done so using dry ice in a properly labeled Styrofoam container by the laboratory technician

19.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

19.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

We do not expect subjects to experience adverse reaction from high calorie meal or fiber supplementation. However, Patient will be under close monitoring by our staff during the entire process of meal challenge. The principal investigator Paresh Dandona, MD,PhD and co-investigators Chi Tang, MD, Husam Ghanim, PhD and Itivrita Goyal, MD will review the data every 3 months to assess the safety

and potential benefits to the participant. Furthermore, they will also assess other risks including the physical, psychological, social, legal and economic harm to these patients. The investigators listed above will carefully watch for any invasion of privacy and breach of confidentiality.

19.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Blood Pressure, Height, Weight, and adverse reaction reported by subjects are monitored every visit to ensure safety.

19.3 Describe any safety endpoints.

Response: NA

19.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

On site during the visit. We also encourage participants to call us if they develop any adverse reaction

19.5 Describe the frequency of safety data collection.

Response:

The data collection will be done at all study visits. The patitients, however, will be asked to report any adverse event or safety related information via phone as soon as it occurs.

19.6 Describe who will review the safety data.

Response: The safety data will be reviewed by the principle and sub investigators as well as the research coordinator.

19.7 Describe the frequency or periodicity of review of cumulative safety data.

Response: Safety data will be reviewed every three months during the duration of the study. Study endpoint data will be reviewed once after half of the recruited patients have completed the study and then at the end of the study.

19.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response: The statistical analysis will be carried out using student t-test, Chi-square and Wilcoxson's test for paired data

19.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

- Inability to tolerate the study meals or other adverse reaction during the meal challenge or blood draw.
- Significant high incidence of SAE (serious adverse events) and events leading to withdrawal of subjects determined based on the continuous review by the investigators.

20.0 Withdrawal of Subjects

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*20.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response: Inability to tolerate the study meals or other adverse reaction during the meal challenge or blood drawn.

20.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

The principal investigator of the study can remove a participant from the research study without their approval if for any reason he/she feels is appropriate, including: severe side effect, injury or medical condition which may place subjects at risk of further complications if you continue to participate, failure to take the medication as instructed, failure to keep your scheduled appointments, or other administrative reasons.

If any of the subjects become pregnant during the period of study, they will need to withdraw from the study.

20.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response: If a subject withdraws from the research, the data collected to that point will be used toward the research finding. If applicable the subject will have to bring back any unused research drug and or device. If necessary, they will be asked to complete an end of study visit for their safety.

21.0 Risks to Subjects

21.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

Potential risks of ingesting the HFHC meal with fiber include nausea, abdominal pain and diarrhea. The patients will be monitored closely for these symptoms at the research center.

Patients always run a risk of breach of confidentiality when doing a research trial. However, procedures are in place to minimize this risk as described in the protocol and consent.

Risks Associated with Administration of Intravenous (IV) line and blood collection:

All subjects will be informed of the complication of administration of intravenous (IV) line, which includes mild bruising at the site of IV line, which should resolve in few days. They will also be informed about the possibility of infiltration of the IV line at the time of performing blood draws in which case another IV line at different site will be secured and this may lead to bruising at more than one sites. Subjects are advised to call us if they have a lot of pain or swelling at the insertion site. Rarely some people have side effects such as low blood pressure or heart rate and allergic reaction to lidocaine including swelling of the throat. Serious risks associated with IV puncture may also include infections and thrombosis. If any of these serious side effects is observed, the patients will be asked to call us immediately or seek immediate medical help.

There are no potential additional risks for the additional 8 min blood draw and spot urine samples.

Potential risks associated with Acetaminophen are:

Skin rash, elevation of liver function tests. Derangement of kidney function tests (but usually happens with chronic overdose) and very rare anaphylaxis reactions.

21.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:.We will collect no more than 165 ml of blood on each visit. We will follow standard sterilization procedure. Safety data (vitals, CBC, CMP, urinary markers) will be collected at screening, during and at end of the study. *Patients will be instructed to call the Diabetes Center to speak to a study investigator*

directly in case of any problem or untoward side effects. The patients, however, will be instructed to report any adverse event or safety related information via phone as soon as it occurs. All adverse events will be reviewed by the PI or sub-investigators within 24 hr of reporting and all safety data will reviewed every 3 months

*21.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response: not applicable

21.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response: not applicable, we will not be enrolling pregnant participants or who may become pregnant or with in child baring years without signing the consent stating they will use at least two forms of birth control. If a participant becomes pregnant they will be withdrawn from the study immediately.

21.5 If applicable, describe risks to others who are not subjects.

Response: not applicable

22.0 Potential Benefits to Subjects

22.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response: there is no direct benefit to participating in this research study.

23.0 Compensation for Research-Related Injury

☐ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*23.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

Routinely, Buffalo General Hospital, Erie County Medical Center, and/or the University at Buffalo, State University of New York, its agents, or its employees do not compensate for or provide free medical care for human subjects/participants in the event that any injury results from participation in a human research project. In the unlikely event that they become ill or injured as a direct result of participating in this study, they may receive medical care, that will be covered by study.

23.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with ***different language regarding research related injury****, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response:

NA

24.0 Economic Burden to Subjects

24.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response: All research expenses will be covered. Participants will not be subjected to any out of pocket cost

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

25.0 Compensation for Participation

25.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response: Each subject will be compensated 60 dollars for each visit they participate. If participants complete all three study visits, total compensation will be $180.00 after completion of all study visits and procedures. The subjects will be not be paid for the screening visit. If additional visits are required for safety evaluations or to repeat blood tests, there will be no additional compensation for extra visits.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☐ **N/A:** There is no compensation for participation. This section does not apply.

26.0 Consent Process

26.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 27.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 27.0)*

26.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response: All participants will come to the research department to be consented. Participants will be placed in a private room where they can review the consent. Participant questions and or concerns will be address with a member of the study team or research doctor if applicable. The research coordinator will discuss in length the participant's requests for privacy of their PHI.

26.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response: Participants will be made aware that participating in research is completely voluntary, and they may withdraw at any time with no consequence to their routine clinic care. If the patients requires time to decide and or discuss partaking in a research study, the subject will be given said time.

26.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response: The research coordinator and study team are available to answer any question or concerns with the patient during the duration of the research trial. At each study visit, the patient is asked a series of questions to ensure they are on task with the study visits and feel comfortable. Upon departing from their study visit, the patients are told of their next visit and given detail instruction for their next visit. If study is revised or amendment or new information becomes available

about drug safety that may affect patients participation, the patient may be re-consented to ensure patient ongoing consent.

26.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

1. *The role of the individuals listed in the application who are involved in the consent process*
2. *The time that will be devoted to the consent discussion*
3. *Steps that will be taken to minimize the possibility of coercion or undue influence*
4. *Steps that will be taken to ensure the subjects' understanding*

Response:

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☒ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 26.8)*

26.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

NOTE: The response to this Section should correspond with your response to Section 6.4 of this protocol.

Response: NA

26.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response: NA

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults.
(Skip to Section 26.9)

26.8 Describe the process to determine whether an individual is capable of consent.

Response: NA

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 26.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 26.9 and 26.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 26.11 and 26.12).*

26.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

26.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response: NA

26.11 Describe the process for ***assent of the adults****:*

1. *Indicate whether assent will be obtained from all, some, or none of the subjects. If some, indicate which adults will be required to assent and which will not.*

Response:

2. *If assent will not be obtained from some or all subjects, provide an explanation of why not.*

Response:

*26.12 Describe whether **assent of the adult** subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response:

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☒ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 27.0)*

*26.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

*26.14**For research conducted outside of New York State**, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

26.15 Describe whether parental permission will be obtained from:

Response:

☐ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

*26.16 Describe whether permission will be obtained from individuals **other than parents**, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

*26.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

26.18 When assent of children is obtained, describe how it will be documented.

Response:

27.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

27.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response:

27.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

28.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 29.0)

28.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

29.0 Multi-Site Research (Multisite/Multicenter Only)

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

*29.1 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as:*

1. *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
2. *All required approvals have been obtained at each site (including approval by the site's IRB of record).*

3. *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
4. *All engaged participating sites will safeguard data as required by local information security policies.*
5. *All local site investigators conduct the study appropriately.*
6. *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

29.2 Describe the method for communicating to engaged participating sites:

1. *Problems*
2. *Interim results*
3. *Study closure*

Response:

29.3 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response:

29.4 If this is a multicenter study for which UB will serve as the IRB of record, and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods.

Response:

30.0 Banking Data or Specimens for Future Use

☐ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*30.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response:

The study data/specimens will be stored in a locked closet or -80 freezer at the research facility of the Diabetes and Endocrinology Center of WNY for up to 7 years

The research staff (study personnel including coordinator) only will be authorized to access data and or specimens

30.2 List the data to be stored or associated with each specimen.

Response:

Patient ID number, study visit information and date of collection will be stored with specimen. Other data stored will include record files of all patients participating in the study, including data collection sheets and lab results

30.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response:

The copy of the individual patient data collected during the study period will be provided to these individual patients who can choose to hand carry it to their respective physicians and a copy will be faxed to their respective clinical providers upon verbal request from the patient. The results of the completed study will be made available to the patients if requested through published manuscript Specimens and research data (unidentified) will be used by current study staff or future collaboration for other research projects with appropriate approvals.

31.0 Drugs or Devices

☐ **N/A:** This study does not involve drugs or devices. This section does not apply.

31.1 If the research involves drugs or devices, list and describe all drugs and devices used in the research, the purpose of their use, and their regulatory approval status.

Response: Acetaminophen. purpose of use is to check for gastric emptying. The drug will be used according to FDA regulations.

31.2 Describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

Response: Drugs will be stored in a locked cabinet at the research facility of the Diabetes and Endocrinology Center of WNY in ECMC. The study drug will be dispensed and documented by the research nurse, Jeanne Hejna. Training on administrating study drug and information about side effects and how to report any adverse events will be discussed with patients

If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

31.3 Identify the holder of the IND/IDE/Abbreviated IDE.

Response:

31.4 Explain procedures followed to comply with FDA sponsor requirements for the following:

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

32.0 Humanitarian Use Devices

☒ **N/A:** This study does not involve humanitarian use devices. This does not apply.

32.1 For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

Response:

32.2 For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

Response: