Cover Page for Protocol with Statistical Plan

Official Title:	Preserving Lean Body Mass During Weight Loss In Elderly Obese Patients With GLP-1 Receptor Agonist Treatment
NCT number:	NCT05302596
Document Type:	Study Protocol and Statistical Analysis Plan
Date of the Document:	11/22/2022

University at Buffalo
The State University of New York
University at Buffalo Institutional Review Board (UBIRB)
Office of Research Compliance | Clinical and Translational Research Center Room 5018
875 Ellicott St. | Buffalo, NY 14203
UB Federalwide Assurance ID#: FWA00008824

Complete Research Protocol (HRP-503)

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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 6, 21, 22, 24, 25, 26 and 27 do not apply.*
    - *For exempt research: Section 6 may not apply. Section 6.1 will still apply if there is a study intervention.*

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 Example
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:

Include the full protocol title.

Response:

Preserving Lean Body Mass During Weight Loss In Elderly Obese Patients With GLP-1 Receptor Agonist Treatment

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response: Husam Ghanim, PhD

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ghanim@buffalo.edu

SECONDARY INVESTIGATORS:

Paresh Dandona, M.D., Ph.D.

Manav Batra, MD,

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response: V2 11.22.2022

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
2	11/22/2022	Change in team members and inclusion in UB-PIR listing	No

FUNDING:

Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.

Response:

CTSI Translational Pilot Studies Program Grant

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: The protocol is funded by CTSI pilot studies grant

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 and Endocrinology

1.0 Study Summary

Study Title	Preserving Lean Body Mass During Weight Loss In Elderly Obese Patients With GLP-1 Receptor Agonist Treatment
Study Design	Single-center, prospective, controlled, randomized and open label study
Primary Objective	To investigate the effect of the semaglutide addition to standard of care weight loss intervention (personalized lifestyle and exercise) in elderly obese subjects on body weight and body composition as assessed by DEXA
Secondary Objective(s)	1. To assess between group differences in gene expression related to adipose tissue lipolysis and changes in mitochondrial metabolism. 2. To assess between group differences in muscle strength as evaluated by both biceps arm strength and quadriceps leg strength. 3. To assess between group differences in measured and patient reported side effects including hypoglycemia,

	gastrointestinal concerns, injection site irritation and any physical activity limitations.
Research Intervention(s)/ Investigational Agent(s)	Standard of care weight loss program with or without semaglutide weekly s.c. injection for 16 weeks
IND/IDE #	N/A
Study Population	Elderly obese patients: age: ≥65 years, BMI ≥30 Kg/m^2 AND waist circumference for women: > 80cm and for men: > 90cm
Sample Size	16
Study Duration for individual participants	Up to 4 months
Study Specific Abbreviations/ Definitions	GLP-1 Receptor Agonist: GLP-1RA DEXA: Dual energy X-ray absorptiometry

2.0 Objectives*

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

Response:

PRIMARY OBJECTIVE

To investigate the effect of the semaglutide addition to standard of care weight loss intervention (personalized lifestyle and exercise) in elderly obese subjects on body weight and body composition as assessed by DEXA compared to age and gender matched control group on standard of care weight loss intervention only.

SECONDARY OBJECTIVES

1. To assess between group differences in gene expression related to adipose tissue lipolysis and changes in mitochondrial metabolism.
2. To assess between group differences in muscle strength as evaluated by both biceps strength and quadriceps leg strength.
3. To assess between group differences in measured and patient reported side effects including hypoglycemia, gastrointestinal concerns, injection site irritation and any physical activity limitations.

2.2 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:

We hypothesize that:

Hypothesis 1: We hypothesize that the addition of semaglutide treatment to the standard weight loss intervention will lead to greater weight loss, while, importantly, also enhancing the proportion of lean (muscle) mass in comparison to standard intervention alone.

Hypothesis 2: We hypothesize that the addition of semaglutide will be associated with a gene expression profile favorable for increased lipolysis. Furthermore, we hypothesize semaglutide treatment will be associated with greater energy utilization and increased mitochondrial reserve in the adipose tissue relative to standard intervention alone.

Hypothesis 3: We hypothesize that semaglutide treatment added to standard weight loss intervention will improve muscle strength relative to standard intervention.

Hypothesis 4: We hypothesize that semaglutide can be safely added to a standard weight loss intervention program in obese elderly patients.

3.0 Scientific Endpoints*

3.1 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

1- Body weight: Change from baseline will be calculated at 8 and 16 weeks

2- Body composition by DEXA: Change from baseline in total body fat (kg), total fat-free mass (kg), lean mass (kg) and bone mass (kg), bone mineral density (BMD) and lean body mass to total fat mass ratio will be calculated at weeks 16.

SECONDARY ENDPOINTS:

1) Adipose tissue metabolism and energy expenditure: Subcutaneous abdominal fat biopsies will be collected and assayed for A: RNA expression levels (by RT-PCR) of genes related to lipolysis (AGTL and HSL), lipid storage and mobilization (PPARs and PGC-1a) and mitochondrial thermogenesis (β-adrenergic receptors, CPT-1, UCP-1 and UCP-2). B: freshly collected adipose tissue samples will also be processed to assess mitochondrial basal and maximal metabolism as well as mitochondrial reserve will be measured using the Seahorse XFP energetic flux Analyzer.

2) Blood samples will be assayed for CBC, CMP, and lipid profile and for serum insulin, free fatty acids, glycerol, and lipoprotein lipase concentrations.

3) Muscle strength: at least 2 measures of muscle strength will be collected: biceps and quadriceps muscle strength using MicroFET2 dynamometer.

4) Patient reported side effects and responses to age-appropriate quality of life questionnaire will be used to assess any adverse events and changes to quality of life and mobility.

4.0 Background*

4.1 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: Americans are living longer and obesity rate is on the rise. These two trends add up to an increase in the number of obese older people (1, 2). Both obesity and aging are associated with increased risk of chronic diseases such as type 2 diabetes, hypertension, cardiovascular diseases and cancer (3). Obesity is also independently associated with all-cause mortality (4, 5). Abdominal obesity is also associated with accelerated muscle strength decline (6) Therefore weight loss is typically recommended to lower many of these risks. However, weight loss in older patients is a more complex issue. Aging process is associated with loss of muscle mass and increase in fat mass and increasing the risk of sarcopenia (7). Approximately 25% - 33% of all weight lost in older adults during intentional weight loss interventions is fat-free mass (lean body mass and bone mass) (8, 9), which further contributes to sarcopenia and increases risk for impaired activity, disability, and frailty (10, 11). Therefore, providers can be discouraged from recommending losing weight in this population. On the other hand, existing evidence suggests that intentional weight loss should be recommended in older people specifically when obesity-related comorbidities exist, including those with functional limitations or metabolic complications such as metabolic syndrome, type 2 diabetes, and cardiovascular disease (12, 13). The current therapeutic options for weight management in older adults do not generally differ from those offered to younger or middle-aged people but personalized regular resistance exercise combined with adequate protein intake is usually advised to mitigate the risk of further reductions to lean mass (12). Unfortunately, very little is done to emphasize the importance of exercise, and/or poor adherence in the elderly lead to poor mitigation of weight loss induced sarcopenia. Therefore, weight loss intervention that targets fat mass reduction while preserving lean mass is clearly needed in older patients.

GLP-1RAs are drugs approved for use in type 2 diabetes to manage hyperglycemia. They are also known, with semaglutide approved, for inducing weight loss by reducing the appetite slowing the release of food from the stomach and increasing feelings of fullness after eating. We have previously shown that treatment with liraglutide, a GLP-1 RA, improved glycemic control and led to significant weight loss in obese type 1 diabetic patients (14). Our data reveal that weight loss was attributable to the loss of total body fat, including visceral fat, while there was no change in lean body mass as assessed by dual-energy x-ray absorptiometry (DEXA). Additionally, this was associated with increased expression of genes involved in lipolysis, lipid oxidation and thermogenesis in the adipose tissue including ATGL, CPT-1, PPARα, PPARγ, UCP-2 and Dio-2 (14). Our observations are supported in part by basic research suggesting that GLP-1 RA induced weight loss involves central and peripheral mechanisms, which increase adipose tissue metabolism and thermogenesis (15, 16). Additional studies have also demonstrated, albeit with significant variability, a fat mass targeted weight loss in response to GLP-1 RA treatment in obesity (17). There has been only one previous report in a form of a series of cases that looked at the effect of liraglutide on weight loss in *elderly* obese patients with type 2 diabetes (18). In this study, liraglutide treatment was associated with reductions in fat mass and android fat and preserved the muscular tropism (18). None of these studies prospectively investigated the effect of these drugs on weight loss and body composition in *older* obese patients. Therefore, GLP-1 RAs

use to safely combat obesity and preserve muscle mass, and potentially improve muscle strength, in older obese patients requires further investigation.

The basis for hypothesizing that GLP-1RA can improve proportion of lean body mass while reducing overall body weight is based in part on our data in obese type 1 diabetes patients treated with liraglutide (14). The hypothesis is also based on basic research in animal models suggesting that GLP-1 RA actions in the brain triggers many of its effects on the adipose tissue. GLP-RA administered directly in the brains of mice lead to reduced body weight and increased brown adipose tissue (BAT) thermogenesis through activation of GLP-1 receptors in the hypothalamus which increased activity of sympathetic fibers innervating BAT. This was combined with increased expression of genes upregulated by adrenergic signaling and required for BAT thermogenesis, including PGC1a and UCP-1 (15) and browning of white adipose tissue (16). This data supports an independent effect of GLP-1 RA on increasing energy expenditure and thermogenesis in the adipose tissue, which can potentially translate to fat mass targeted weight loss.

Our study will be the first prospective randomized and controlled study to investigate the ability of semaglutide (the most potent GLP-1 RA) to induce the desired weight loss while preserving lean mass in elderly obese patients and to investigate mechanisms involved. This approach capitalizes on basic research concepts and supported by human data.

4.2 Include complete citations or references.

Response:

1. Arias E, Rostron BL, and Tejada-Vera B. United States life tables, 2005. Natl Vital Stat Rep. 2010;58(10):1-132.
2. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
3. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, and Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health. 2009;9:88.
4. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, and Heath CW, Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med. 1999;341(15):1097-105.
5. Flegal KM, Kit BK, Orpana H, and Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2013;309(1):71-82.
6. de Carvalho DHT, Scholes S, Santos JLF, de Oliveira C, and Alexandre TDS. Does Abdominal Obesity Accelerate Muscle Strength Decline in Older Adults? Evidence

From the English Longitudinal Study of Ageing. J Gerontol A Biol Sci Med Sci. 2019;74(7):1105-11.

7. Roubenoff R. Sarcopenic obesity: the confluence of two epidemics. Obes Res. 2004;12(6):887-8.
8. Willoughby D, Hewlings S, and Kalman D. Body Composition Changes in Weight Loss: Strategies and Supplementation for Maintaining Lean Body Mass, a Brief Review. Nutrients. 2018;10(12).
9. Beavers KM, Beavers DP, Nesbit BA, Ambrosius WT, Marsh AP, Nicklas BJ, et al. Effect of an 18-month physical activity and weight loss intervention on body composition in overweight and obese older adults. Obesity (Silver Spring). 2014;22(2):325-31.
10. Villareal DT, Banks M, Siener C, Sinacore DR, and Klein S. Physical frailty and body composition in obese elderly men and women. Obes Res. 2004;12(6):913-20.
11. Rodriguez-Gomez I, Manas A, Losa-Reyna J, Alegre LM, Rodriguez-Manas L, Garcia-Garcia FJ, et al. Relationship between Physical Performance and Frailty Syndrome in Older Adults: The Mediating Role of Physical Activity, Sedentary Time and Body Composition. Int J Environ Res Public Health. 2020;18(1).
12. Coker RH, and Wolfe RR. Weight Loss Strategies in the Elderly: A Clinical Conundrum. Obesity (Silver Spring). 2018;26(1):22-8.
13. McTigue KM, Hess R, and Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment. Obesity (Silver Spring). 2006;14(9):1485-97.
14. Ghanim H, Batra M, Green K, Abuaysheh S, Hejna J, Makdissi A, et al. Liraglutide treatment in overweight and obese patients with type 1 diabetes: A 26-week randomized controlled trial; mechanisms of weight loss. Diabetes Obes Metab. 2020;22(10):1742-52.
15. Lockie SH, Heppner KM, Chaudhary N, Chabenne JR, Morgan DA, Veyrat-Durebex C, et al. Direct control of brown adipose tissue thermogenesis by central nervous system glucagon-like peptide-1 receptor signaling. Diabetes. 2012;61(11):2753-62.
16. Beiroa D, Imbernon M, Gallego R, Senra A, Herranz D, Villarroya F, et al. GLP-1 agonism stimulates brown adipose tissue thermogenesis and browning through hypothalamic AMPK. Diabetes. 2014;63(10):3346-58.

5.0 Study Design*

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

Response:

This will be a single center, prospective, open label, randomized and controlled pilot study to investigate the effects of semaglutide addition to a standard weight loss intervention program for 16 weeks on body weight and composition, adipose tissue metabolism and muscle strength compared to the standard weight loss program alone in elderly obese patients.

6.0 Study Intervention/Investigational Agent

6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

Response:

- Semaglutide, a once-weekly injection GLP-1 RA. Starting dose of 0.25mg titrated up to 1mg dose. This dose is approved for type 2 diabetes management with higher doses approved for obesity management. Experimental arm
- Standard of Care (SOC) weight loss intervention (personalized lifestyle and exercise) administered to both experimental and control group.

6.2 Drug/Device Handling: If the research involves drugs or device, 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.

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

The study drug will be stored in locked refrigerator in the research building at 1000 Youngs Road, Suite 105, Williamsville, NY. The study drugs will be accessible by authorized study personnel only (physicians, nurses and laboratory staff) and amount of drug dispensed to the patient will be properly documented in the charts.

6.3 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:

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research 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:

According to FDA guidelines, the investigator/sponsor of this research considers the use of semaglutide in this research exempt from IND requirement. All regulation will be followed according to FDA and IRB.

7.0 Local Number of Subjects

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

Response:

16

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

Response:

We expect to screen 20 to 22 patients

7.3 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:

Preliminary assessment suggests up to 20 elderly obese patients visit the Diabetes and Endocrinology Center and Geriatrics clinics per month. We anticipate that a majority (60%, 12) will be eligible and off which 33% (4) will agree to participate in the trial.

8.0 Inclusion and Exclusion Criteria*

*8.1 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- Males and females age: ≥65 years

2- BMI ≥30 Kg/m^2 AND waist circumference for women: > 80 cm and for men: > 90 cm

3- Stable body weight (no more than ±3 kg change during the 3 months prior to screening)

4- Able to participate in personalized physical activities and dietary instructions.

5- Participant must be able to read, write, and understand the English language and be able to provide written consent.

*8.2 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. Current diagnosis of weight changing condition including cancer, gastrointestinal conditions or eating disorders
2. GLP-1R agonists use within last 6 months
3. Diagnosis of type 1 or 2 diabetes
4. Impaired cognitive function (VA-St. Louis University Mental Survey (VA-SLUMS) score ≤ 19)
5. History of chronic/idiopathic acute pancreatitis
6. Personal/family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2
7. Previous surgical treatment for obesity
8. Smoking or use of any nicotine products
9. Use of any medication that could interfere with trial results especially weight management drugs
10. Anticipated change in lifestyle (e.g., dietary, exercise or sleeping pattern) other than provided by the study.
11. Hepatic disease or cirrhosis
12. Aspartate Aminotransferase (AST) > 3X Upper limit of normal (ULN) *and/or* Alanine aminotransferase (ALT) > 3X ULN
13. Inability to give informed consent
14. History of gastroparesis
15. History of serious hypersensitivity reaction to these agents
16. Alcoholism
17. Patients with retinopathy
18. Participation in any other concurrent interventional clinical trial

8.3 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: NA

☐ Adults unable to consent

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

☐ Pregnant women

☐ Prisoners

8.4 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 will not have non-English speaking individuals in this study. We have patients that English is a second language, but they can read, write and understand it. This population is less than 10% of the total population.

9.0 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.

9.1 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.

*9.2 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.

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

Response:

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

*9.4 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").

*9.5 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.

*9.6 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:

No specific populations or vulnerable groups will be targeted. All subjects enrolled in this study will be of legal adult consenting age with the ability to speak, read and interrupt the English language. Subjects will have the ability to speak with the research team regarding any questions or concern they have before signing the consent. Subjects will be made aware that this study is voluntary, and they are able to stop participating at any time they feel uncomfortable. Subjects will not be pressured into participating and their clinic standard of care will remain the same if they participate or choose not to participate.

10.0 Eligibility Screening*

*10.1 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:

After obtaining partial HIPAA waiver, patient charts will be screened according to the study inclusion and exclusion criteria by our trained clinical staff and physicians. In addition, 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 clinics. 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. The research coordinator will contact interested patients and those meeting the inclusion and exclusion criteria based on preliminary phone evaluation (phone-script attached) will be invited to participate in the study. All personal information will be kept confidential and locked in the coordinator office. In addition, interested subjects who are informed about the study through the online listing or those referred by other physicians will be contacted and evaluated for potential participation.

Prospective participants who pass the phone screening will be scheduled to An in-person screening visit. At the screening visit, they will be asked to read 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 and a copy provided for their record. 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 (about 25 ml) will be taken to evaluate HbA1c, CBC and CMP. Patients daily eating and exercise habits will be collected and reviewed for determining lifestyle intervention. 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.

11.0 Recruitment Methods

☐ **N/A:** This is a record 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.

11.1 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, patient doctor interaction at the time of their visits to 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
4. 1000 Youngs Road, Suite 105, Williamsville NY 14221
5- Patients can be also referred by other physicians and providers.
Participants will also be recruited through researchmatch.org and the study will also be listed on UB's Study Information Portal (SIP) website.

Patient records will be reviewed at the time of clinical encounter to identify potentially eligible individuals. If a participant is identified during clinical encounter, physicians will speak to them about their interests in participating in research.

This study will be publicized on the UB Participate in Research (PIR) portal (www.research.buffalo.edu/portal/clinicaltrial/) while in the active recruitment period. Once study accruals have been met, the study will be removed from the portal. A lay title and study description will be included on the portal and have been included as an attachment in Click for approval. Once approval is received, the study will be populated onto the portal and will receive its own unique hyperlink. The UB PIR Portal was determined to be not research involving human subjects (see STUDY00006316 for more information).

11.2 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 in a private room where no one else can hear the conversation. If the patient agrees, their information will be given to the research coordinator to be contacted for further evaluation. No personal information will be shared without patient's approval and will not be used for any purpose except for this research. All personal information will be kept confidential and locked in the coordinator office.

11.3 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:

No paper, audio or video advertisement will be used. Patients will be identified through screening of clinical charts from investigators clinics and through researchmatch.org and UB's SIP website.

12.0 Procedures Involved*

*12.1 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.

Response: Eligible and qualified patients will be randomized 1:1 (using Excel, Microsoft Inc. randomization function) in pairs (8 pairs) matched by age and BMI within 5% and by gender to one of two open-label interventions. Priority of enrollment will be to match already existing and non-matched pair(s) before starting new ones. However, participants will not need to wait until they are matched to be enrolled in the study. The two open-label interventions are:

1- Control group: Standard of care weight loss program that includes lifestyle changes and personalized exercise and dietary education.

2- Semaglutide group: semaglutide (up to 1mg) once weekly injection added to the standard of care weight loss program. Semaglutide dose will be started at 0.25 mg dose during the baseline visit and doubled every 2 weeks up to 1mg dose or up to maximum tolerable dose. Patients will be instructed on how to inject themselves with the drug and how to increase the dose. At every visit, number of injections taken and doses will be collected. Semaglutide dose escalation is faster than recommended in the product label and during clinical use but is consistent with our current studies approved by FDA. During this faster dose escalation, we will be monitoring the subject more extensively (4 weeks and 8 weeks), compared to clinical practice, for any side effects including if they experience any GI side effects, and subjects will be kept at the maximum tolerable dose up to 1mg/week.

At the baseline visit, and for all other visits, patients will come fasting (10 -12 hours) to the research center. Patients will visit the research center at 4 weeks (safety visit), 8 weeks and at 16 weeks (final study assessment visit). Blood (about 25 ml), body weight and other vitals, adverse events including hypoglycemia (blood sugar <70 mg/dl) will be collected at all visits. Fat biopsy aspiration, DEXA scans, muscle strength measurement and age-appropriate quality of life questionnaire (Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF) will be performed at 0- and 16-weeks visits.

All patients will receive instructions at the beginning of the study on weight loss nutritional program and appropriate physical activity to be performed for the next 16 weeks. The program will be based, in-part, on dietary and exercise habits collected at screening visit. For the entire duration of the study, participants will maintain a daily diary to document food and exercise activities to ensure compliance with lifestyle program provided. At the 4- and 8-weeks visits, the daily diary will be reviewed for food and exercise activities, and instructions will be provided again to reinforce intervention.

Patients will be provided with glucose meter and glucose strips to measure fingerpick blood glucose. For the entire duration of the study, patients will be asked to measure their blood sugars at least one time after exercise and to record any hypoglycemic events (glucose <70mg/dl) in their diary, Patients will be instructed to record any other untoward side effects like nausea, vomiting, changes in appetite and other experiences in the diary. 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.

Subject will receive phone calls at 2- and 12-weeks following start of treatment to collect any safety data and at 2 weeks after the end of the treatment. The subjects will then be discharged from the study. Patients will be instructed to call the research center anytime they have a question or side effects.

Standard of care weight loss program:

Patients will be instructed to implement dietary and exercise program for the next 16 weeks and to record their activities on daily food and exercise diary provided.

1- Energy intake should be reduced by 500–750kcal/day.
2- Dietary fat should be reduced to 30% of total energy intake maximally.
3- Meal replacements (if used) will be consumed during breakfast and lunch.
4- Dinner consisted of conventional food and participants will be encouraged to eat fruits and vegetables within their calorie limit.
5- Participants should ingest 1.0–1.5g of protein/kg/day and spread consumption equally throughout the day. A leucine-enriched balanced amino acid supplement can be used.
6- Subjects will be instructed to perform aerobic, muscle-strengthening, flexibility, and balance exercises. Minimally, this should include moderate-intensity aerobic activity for 30 minutes five days per week or vigorous-intensity aerobic activity for 20 minutes three days a week, 10–15 repetitions of 8–10 major muscle group strengthening exercises two or more nonconsecutive days each week, 10 minutes of flexibility activities at least two days a week, and balance exercises three times a week for fall prevention.

Fat aspiration procedure:

Subcutaneous fat tissue aspiration will be performed on abdomen at a 10 cm distance from the umbilicus under sterile conditions and local anesthesia. 0.5-3 gm tissue will be aspirated and cleared from blood and fluids contaminants by centrifugation. The upper adipose tissue will be collected into a separate sterile tube, washed twice with

cold sterile PBS and centrifuged to remove the PBS. Total RNA, nuclear extracts and total cell lysates will be prepared from the adipose.

DEXA scans: Patients will visit an off-site imaging center (Seton Imaging, Amherst, NY) for this test.

12.2 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:

Study Measures (table 1):

1- Body weight will be measured with calibrated scale available in the research center. Patient will be wearing one outer layer of clothing and no shoes. Change from baseline will be calculated at 8 and 16 weeks

2- Body composition by DEXA: DEXA scans will be performed to collect data on total body fat (kg), total fat-free mass (kg), lean mass (kg) and bone mass (kg) and bone mineral density (BMD). Lean body mass to total fat mass ratio will be calculated at every visit. Changes from baseline will be calculated at week 16.

3- Adipose tissue metabolism and energy expenditure: Subcutaneous abdominal fat biopsies will be collected and assayed for A: RNA expression levels (by RT-PCR) of genes related to lipolysis (AGTL and HSL), lipid storage and mobilization (PPARs and PGC-1a) and mitochondrial thermogenesis (β-adrenergic receptors, CPT-1, UCP-1 and UCP-2). B: freshly collected adipose tissue samples will also be processed to assess mitochondrial basal and maximal metabolism as well as mitochondrial reserve will be measured using the Seahorse XFP energetic flux Analyzer. This will be performed at baseline and at 16 weeks.

4- Blood samples will be assayed for CBC, CMP, and lipid profile and for serum insulin, free fatty acids, glycerol, and lipoprotein lipase concentrations. This will be performed at baseline and at 8 and 16 weeks.

5- Muscle strength: Biceps and quadriceps muscle strength will be collected as the average of 3 measurements using the MicroFET2 dynamometer. For these assessments, participants will be asked to take a seat and either lift an arm or kick a leg straight while be restrained by the MicroFet2 device – allowing collection of force generated. This will be performed at baseline and at 16 weeks.

6- Patient reported side effects and responses to age-appropriate quality of life questionnaire will be used to assess any adverse events and changes to quality of life and mobility and will be compared to baseline.

Table 1: Study visits and measurements

Visit #		1	2	3	4
Week# (±2-7days)	-4 to 0	0	4	8	16
Study Procedures	Screening	Randomization/start interventions			End of Study
History	X				
Physical	X				
Vitals including body weight	X	X	X	X	X
CBC, CMP	X	X	X	X	X
Dietary and exercise education		X	X	X	
Study drug titration		X	X		
Dispense medications		X	X	X	
Adverse Event reporting		X	X	X	X
DEXA imaging		X			X
Research blood endpoints		X		X	X
Fat biopsy		X			X
Muscle strength testing		X			X
Quality of life questionnaire		X			X

12.3 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:

1- Quality of Life Questionnaire

2- Source Documents will be used to collect data during visits

3- MicroFET2 dynamometer will be used to measure muscle strength

4- Daily Diary (to collect food and exercise and other events).

12.4 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 will be accessed using HIPAA partial waiver and signed informed consent HIPAA authorization.

*12.5 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.

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

Response:

Not Applicable. 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.

13.0 Study Timelines*

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

Response:

up to 4 months

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

Response:

Up to 5 months

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

Response:

11 months

14.0 Setting

14.1 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 and at the

CTRC located in 875 Ellicott St. Buffalo NY14203, Division of Endocrinology, Diabetes and metabolism, Department of Medicine. Both facilities are locked facilities with limited access and with security cameras installed outside and inside the facilities. Keys or swipe cards are needed to access the facilities. The Diabetes Research Center has private exam rooms available for physical exam, fat biopsy collection and other rooms needed to conduct procedures needed for the study. Study coordinator and registered nurse are available during visits for data collection and blood work. One of the investigators will be available during visits to address patients' related issues. CTRC location is a fully equipped laboratory with Equipment include ultra-low freezers for sample storage, preparation and analysis using ELISA and PCR. All offices were study and patients' information is stored have locked cabinets and password-secured computers for protection of data with access limited to study personal

The VA (3495 Bailey Avenue, Buffalo, NY 14215) location will be utilized to conduct mitochondrial basal and maximal metabolism as well as mitochondrial reserve using the Seahorse XFP energetic flux Analyzer. The VA Lab facility is fully secured with access limited to facility users and research staff.

14.2 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.

15.0 Community-Based Participatory Research

15.1 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.

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

Response:

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

16.0 Resources and Qualifications

*16.1 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. The PIs, CO-investigators and research team have conducted similar studies in this patient population using similar agents and have the expertise to execute the study protocol and manage any adverse events. All team members are experts in their fields with extensive published records.

Dr Ghanim (PhD, Biochemistry) will supervise regulatory and IRB filings, overall execution of the protocol, sample collection, processing and perform gene expression analysis. Dr Ghanim will advise participants on lifestyle changes, perform muscle strength tests and perform adipose tissue/mitochondrial respiration assays. Dr Ghanim will also perform data and statistical analysis, interpret data and write manuscripts.

Drs Paresh Dandona and Manav Batra (MDs, Endocrinologists) will support clinical protocol execution, patients' management and clinical data related to safety and dose escalation of the study Drug. They will also participate in data interpretation and manuscript writing. Dr. Batra will also perform fat biopsy collection. In collaboration with Dr Ghanim and Troen, they will also provide personalized exercise and dietary instructions and education to all patients enrolled in the study at baseline and at 8 weeks.

Jeanne Hejna, (LPN, Research Nurse/coordinator): will be responsible for patient consenting, protocol executions, drug dispensing and recording (in consultation with Endocrinologists), blood sample collection and maintaining all study documents and records.

Describe other resources available to conduct the research.

16.2 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 monthly research meetings are conducted to discuss the recruitment rate, resolve and discuss issues related to the conduct, safety, analysis of samples and discuss study and related publications. PI is expected to spend 15% of his academic time on this research. The co-investigators and study coordinator provide coverage to the research related activity during regular hours.

16.3 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 patients 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 physicians who will be available to address any adverse effects or other questions during the course of the study

16.4 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:

Before beginning of enrollment all research staff will be asked to review the protocol and a training session will be conducted to provide protocol details, explain technical points, and answer staff questions. All training sessions will have a sign in sheet to document such training. Continuous education through training meetings, conferences and discussions will continue through the study period and when revisions are made to protocol.

17.0 Other Approvals

17.1 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.

18.0 Provisions to Protect the Privacy Interests of Subjects

18.1 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. Patient who qualifies 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 privately for a possible telephone screening and ask if time is appropriate for this discussion.

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. Additionally, a partial HIPAA waiver will be obtained to access medical records when screening for patients.

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 room in the research unit and will be allowed to discuss the consent in detail with the research coordinator and or study doctor. Patient will be 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 before partial HIPAA is obtained or informed consent is signed.

18.2 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 partial HIPAA waiver

19.0 Data Management and Analysis*

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

Response:

Analytical plan:

Measurements taken on a continuous scale will be summarized by range, median, means and standard deviations. Categorical measurements will be summarized using percentages, various types of cross-tabulations, and proper graphical presentations. Type-I error will be set to 5%, i.e. α=0.05, for all the statistical tests. Baseline values for patients' demographics and concomitant illnesses will be compared using parametric or non-parametric tests. The primary endpoint will be to compare the between group differences in lean body mass/total fat mass ratio changes from baseline at 16 weeks. Secondary end points will include the additional study measures listed above assessed as the difference between groups at 8 and 16 weeks.

Statistical analysis will be carried out using SPSS and SigmaStat software (SPSS, IL). All data will be expressed as mean ± S.E of arbitrary units and percent change is calculated from the means for mRNA gene expression. To evaluate similarity between the study groups, baseline values for subject's demographics will be compared using appropriate parametric and non-parametric tests based upon the nature of the data.

19.2 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:

There are no previous studies investigating the effect of semaglutide in the age group specifically, however semaglutide was shown to induce significant weigh loss (about 5%) predominantly from body fat mass in obese subjects. Therefore, with an estimated difference between semaglutide group and standard of care only group of about 50% in the primary endpoint, a sample size of 8 patients in each group (semaglutide vs control) should provide at least 80% power to detect a significant difference (α = 0.05), provided the standard deviation of the residuals (variability) is not greater than half the estimated difference between the groups.

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

Response:

Two investigators and study coordinator will double check the accuracy of collected data. All laboratory testing will be standardized using references and standards.

20.0 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**.*

*20.1 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 research department and lab. All subject data collected after enrollment in study will be stored in a coded format. Documents related to IRB correspondences, consent forms and other paper documents with patients' identifiable information, including the master list/code key containing patient identifiers, will stored in locked cabinet in a locked office. Additional paper documents containing coded patients' data will be stored in separate binders in a different locked cabinet.

Digital coded data will be stored in password locked computers accessible by study team only.

20.2 A. How long will the data be stored?

Response:

1. IRB correspondence (approval, determination letters) as well as any signed consent documents should be maintained for at least 3 years after the study has been closed.

2. Any master list/code key containing patient identifiers should be deleted 3 years after the study related analysis has ended.

3. Working data analysis files that contain no identifiable information will be maintained indefinitely. Researchers may continue to use such stored data to further develop this research concept

20.3 A. Who will have access to the data?

Response:

Those investigators, nurses, and laboratory staff that are on all involved in this study and listed on IRB submission will have access to the data.

20.4 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 can handle transfer of data.

20.5 A. How will the data be transported?

Response:

Coded DEXA data from Seton imaging will be emailed to study coordinator and PI. All data are stored at study performance sites only and is not transported unless it is being archived. At that point files will be transferred to Iron Mountain for storage and archiving.

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 21.0)*

20.6 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 coded specimens will be stored in the laboratory located at the CTRC located in 875 Ellicott St. Buffalo NY14203. Samples will be stored in a locked -80^{o} C freezer.

20.7 B. How long will the specimens be stored?

Response:

Specimen storage has no expiration date and will be stored for a minimum of 7 years. Researchers may continue to use stored specimens to further develop this research concept

20.8 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 specimens

20.9 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 specimens and can handle transfer of samples

20.10 B. How will the specimens be transported?

Response:

Samples will be transported by the laboratory technician which will be hand delivered using dry ice in a properly labeled Styrofoam container.

21.0 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.

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

Response:

The principal investigator and co-investigators will review the data every 3 months to assess the safety and potential benefits to the participant. The investigators will assess other risks including the physical, psychological, social and economic harm to these patients. The investigators will carefully watch for any invasion of privacy and breach of confidentiality.

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

Response:

Efficacy data:

1- Body weight: Change from baseline will be calculated at 8 and 16 weeks

2- Body composition by DEXA: Change from baseline in total body fat (kg), total fat-free mass (kg), lean mass (kg) and bone mass (kg), bone mineral density (BMD) and lean body mass to total fat mass ratio will be calculated at weeks 16.

3- Adipose tissue metabolism and energy expenditure: Subcutaneous abdominal fat biopsies will be collected and assayed for A: RNA expression levels (by RT-PCR) of genes related to lipolysis (AGTL and HSL), lipid storage and mobilization (PPARs and PGC-1a) and mitochondrial thermogenesis (β-adrenergic receptors, CPT-1, UCP-1 and UCP-2). B: freshly collected adipose tissue samples will also be processed to assess mitochondrial basal and maximal metabolism as well as mitochondrial reserve will be measured using the Seahorse XFP energetic flux Analyzer.

4- Muscle strength: at least 2 measurements of muscle strength will be collected: Biceps and quadriceps muscle strength using MicroFET2 dynamometer.

Safety Data:

1- CBC and CMP data will be reviewed for any untoward outcomes.

2- Patient reported side effects including hypoglycemia, GI side effects, injection site reaction will be used to assess any adverse events

21.3 Describe any safety endpoints.

Response:

1- Hypoglycemia (glucose <70mg/dl) as reported by patients.
2- Frequency and severity of GI side effects
3- Mobility related events including, falls, fractures, dizziness, and loss of balance.
4- injection site reactions
5- Adipose tissue biopsy site swelling or other complications.

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

Response:

Safety event and side effect will be recorded on case report forms during the visit. We also encourage participants to call us if they develop any adverse reaction.

21.5 Describe the frequency of safety data collection.

Response:

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

21.6 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

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

Response:

Safety data will be reviewed every three months throughout the duration of the study.

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

Response: N/A- this is a pilot study that may not have enough participant to draw statistical conclusions for safety data.

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

Response:

No interim analysis is planned for efficacy so termination of study will be related to safety. Significant increases in severe hypoglycemic (glucose<55mg/dl or requiring assistance) events or severe side effects related to study drug are possible, although not likely, causes that might trigger termination of study. Serious adverse reactions/side effects from fat biopsy procedure might trigger revision of protocol to eliminate fat biopsy collection. Study can be terminated if IRB or CTSI suspends this research

22.0 Withdrawal of Subjects*

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

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

Response:

- Serious adverse GI reactions to semaglutide
- Sever hypoglycemic events
- lack of adherence to weight loss program or lack of compliance to study medication.

22.2 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 PI can stop investigational study treatment or remove participants from the trial without participants approval. If a patient participation is terminated or the patient withdraws consent and decide not to participate in the study, she/he will be asked to undergo a final study visit for his/her safety. Final blood sample collection, DEXA scan and fat biopsy procedures may be performed if patient agrees. 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.

22.3 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 necessary, they will be asked to complete an end of study visit for their safety.

23.0 Risks to Subjects*

23.1 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:

- The risks associated with the study blood draw are generally considered to be minimal. All subjects will be informed of the complication of venipuncture, which includes mild bruising at the site, which should resolve in few days. They will also be informed about the possibility of infiltration at the time of performing blood draws in which case another venipuncture at different site will be performed and this may lead to bruising at more than one sites. Serious risks associated with venipuncture 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.
- The risks involved with fat biopsy procedure are also very minimal. This procedure is performed under local anesthesia and therefore study subjects might experience momentary discomfort at the time of giving local anesthesia. There is a small risk of bleeding at the site of incision, but this will be controlled with cotton gauzes and pressure. The risk of infection is very rare as the procedure is done under sterile conditions.
- Potential side effects of GLP-1 RA, like semaglutide, include GI side effects including nausea (especially when you start using semaglutide); vomiting, stomach pain, loss of appetite; diarrhea; or constipation.

- The risk of hypoglycemia appears to be low with semaglutide, however, it could increase when combined with exercise or lower food intake as proposed in this study.
- In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. However, it received FDA-approval for the treatment of type 2 diabetes in 2017 following large Phase 3 trials including the cardiovascular safety trial SUSTAIN-6. Based on the above rodent studies, semaglutide is contraindicated in those with a personal or family history of medullary thyroid carcinoma and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). However, following review of human data with GLP-1RAs, FDA does not require or suggest routine monitoring of serum calcitonin/ thyroid ultrasound in people treated with semaglutide.
- Injection-site reactions: Serious injection-site reactions, with or without bumps (nodules), have happened in some people who use GLP-1RAs but are less frequent with semaglutide. Injection-site reactions have rarely required surgical intervention. Participants will be instructed to report any injection site reactions including nodules to study investigators.
- Kidney injury: GLP-1 RA might cause acute kidney injury in patients without underlying renal disease especially in patient who had experienced nausea, vomiting, diarrhea or dehydration.
- Severe allergic reaction (anaphylaxis) to study drug ingredients may accrue in rare cases.
- There might be other unforeseen risks associated with the use of semaglutide in this age population.
- Exercise related events including, falls, fractures, dizziness, and loss of balance.
- 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.

23.2 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 25 ml of blood on each study visit. We will follow standard sterilization procedures. Safety data will be collected at screening and during the study.

- To lessen risk of hypoglycemia, patients will be instructed to not exercise before mealtime and up to 1hr after meals. For the entire duration of the study, patients will be asked to measure their blood sugars at least one time daily after exercise. Patients will maintain a diary to record any hypoglycemia and other untoward side effects like nausea, changes in appetite and other experiences. Patients will be instructed to consume a small sugary drink or small, sweet snack if blood sugar is

>70mg/dl and to repeat the test in 30 min. They will be also instructed to call the Diabetes Center to speak to a study investigator directly in case of any problem or untoward side effects. They will be specifically asked to call if they have hypoglycemia (blood sugar <70 mg/dl) on more than one occasion.

- Injection site reactions and complications from fat biopsy collection will be monitored. If injection site reaction is observed or reported patient will be instructed to alternate semaglutide injection site.

- Risk of acute kidney injury or renal function impairment: CBC, CMP, including kidney function test will be performed at screening and every visit of the study (table 1). Additional testing will be performed in patients who suffer from sever nausea or GI symptoms or hypovolemia.

- To reduce the risk of injury due to exercise patients will be instructed to perform warm up and cool down stretching exercises. Subjects will also be advised to stop exercise in the event of unexpected pain, dizziness or discomfort and to contact the study team.

Research team will monitor patients for side effects and other unwanted outcomes through phone calls, patients own reporting and during visits.

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

Response: Any adverse effects of semaglutide not currently known may be some of the unforeseeable risks.

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

Response:

NA, this study is not recruiting women of childbearing age.

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

Response:

NA

24.0 Potential Benefits to Subjects*

24.1 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:

While following a weight loss dietary and exercise program with or without study drug can lead to weight loss, the short duration of the intervention may reduce the magnitude of such benefit. Participants in this study may not directly benefit from the biomarker assessments and the results will not be reported in their clinical record.

25.0 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.

25.1 ***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 billed to their insurance, paid by patient or 3rd paying party.

25.2 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

26.0 Economic Burden to Subjects

26.1 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 during visits will be covered by research funds. Cost of adherence to weight loss program (dietary and exercise needs) is the responsibility of the participants.

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

27.0 Compensation for Participation

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

Response:

- Screen: $0
- Visit 1: blood draw ($25), fat biopsy ($75), DEXA ($25)
- Visit 2: blood draw ($25)
- Visit 3: blood draw ($25)
- Visit 4: blood draw ($25), fat biopsy ($75), DEXA ($25)
- Completed daily diary: $50/study (prorated if not fully completed)

*Total compensation for all completed visits: $ 350.00

☐ **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.

28.0 Consent Process

28.1 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 29.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*

☐ ***No*** *(If no, Skip to Section 29.0)*

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

Response:

All participants will come to the research department at Diabetes and Endocrinology research 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

28.3 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 require time to decide and or discuss partaking in a research study, the subject will be given said time.

28.4 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 that may affect patients' participation, the patient may be re-consented to ensure patient ongoing consent.

28.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *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 28.8)*

28.6 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 8.4 of this protocol.

Response:

NA

28.7 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, how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study, and any process to ensure ongoing consent. 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 28.9)

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

Response: In addition to reviewing medical records for any diagnosis of impaired cognitive function, the study team will evaluate participants responses during the screening process as an indicator of their cognitive function.

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 28.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 28.9 and 28.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 28.11 and 28.12).*

28.9 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)."

28.10 ***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:

This research will not be conducted outside the state of NY

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

- *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:

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

Response:

28.12 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 29.0)*

28.13 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:

28.14 ***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:

NA

28.15 Describe whether parental permission will be obtained from:

Response:

NA

☐ 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)."

28.16 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:

NA

*28.17 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:

NA

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

Response:

NA

29.0 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.

29.1 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:

29.2 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:

30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 31.0)

30.1 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).

31.0 Multi-Site Research (Multisite/Multicenter Only)*

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

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

Response:

*31.2 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as the following. See "WORKSHEET: Communication and Responsibilities (HRP-830).":*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately in accordance with applicable federal regulations and local laws.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

31.3 Describe the method for communicating to engaged participating sites (see "WORKSHEET: Communication and Responsibilities (HRP-830)"):

- *Problems (inclusive of reportable events)*
- *Interim results*
- *Study closure*

Response:

*31.4 If this is a multicenter study **where you are a participating site/investigator**, describe the local procedures for maintenance of confidentiality. (See "WORKSHEET: Communication and Responsibilities (HRP-830).")*

- *Where and how data or specimens will be stored locally?*
- *How long the data or specimens will be stored locally?*
- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

Response:

31.5 If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described elsewhere in the protocol.

- *Describe when, where, and how potential subjects will be recruited.*
- *Describe the methods that will be used to identify potential subjects.*
- *Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)*

Response:

32.0 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.

*32.1 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 in Diabetes Research center or in -80 freezers at the research laboratory (875 Ellicott St, CTRC) for at least 7 years

The research staff (study personnel including coordinator) only will be authorized to access data and or specimens. Data and specimens might be used in future assessments related to the advancement of this research subject.

32.2 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.

32.3 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:

No data or specimens will be released to any party outside research team.