PART B
STUDY DESCRIPTION

TITLE OF PROTOCOL	**Mechanisms of Weight Loss with SGLT2 Inhibition**		
Principal Investigator	**Jody Dushay, MD**		
Co-Investigators			
Mailing Address	**330 Brookline Ave, Boston MA 02215**		
E-Mail Address	**jdushay@bidmc.harvard.edu**		
P.I.'s Telephone	617-667-1996	P.I.'s Pager 95649	Fax: 617-667-7060
Sponsor/Funding Source	**Janssen Scientific Affairs, LLC**		

B1. PURPOSE OF PROTOCOL

The primary purpose of this study is to examine change in body weight in individuals with type 2 diabetes and overweight or obesity treated with the SGLT2 inhibitor canagliflozin compared to placebo. Secondary objectives include investigation of changes in resting energy expenditure, body composition, glycemia, metabolic markers, and food intake with SGLT2 inhibition.

B2. SIGNIFICANCE AND BACKGROUND FOR THE STUDY

Canagliflozin is a sodium-glucose transporter subtype 2 (SGLT2) inhibitor that was approved by the FDA for the treatment of Type 2 diabetes in March, 2013. Canagliflozin, at the doses of 100mg and 300mg daily, improves blood sugar control by a novel mechanism which causes the kidneys to block reabsorption of about 50-80 grams of glucose. Canagliflozin lowers the renal threshold for glycosuria and causes excess glucose to be excreted in the urine.

Canagliflozin is also associated with a 3-5% reduction in body weight among obese individuals with type 2 diabetes. Weight loss appears to be most rapid during the first 18 weeks of treatment and sustained over 104 weeks of treatment. The mechanisms of weight loss with canagliflozin are not completely understood. The increased energy expenditure associated with glycosuria is typically 300-400 kcal/day, however the magnitude and duration of this energy loss has not been carefully studied. Specifically, it is not known whether canagliflozin changes resting metabolic rate (RMR), and there are few published data on the change in body composition associated with canagliflozin therapy. Careful investigation of the magnitude and duration of changes in energy expenditure during canagliflozin treatment is clinically relevant as it may inform recommendations about lifestyle modification, including a reduced calorie diet and physical activity.

References

Leiter LA, Yoon KH, Arias P, Langslet G et al. 2014. Canagliflozin Provides Durable Glycemic Improvements and Body Weight Reduction Over 104 Weeks Versus Glimepiride in Patients With Type 2 Diabetes on Metformin: A Randomized, Double-Blind, Phase 3 Study. *Diabetes Care* [Epub ahead of print]

Forst T, Guthrie R, Goldenberg R, Yee J, Vijapurkar U, Meininger G, Stein P 2014. Efficacy and safety of canagliflozin over 52 weeks in patients with type 2 diabetes on background metformin and pioglitazone. *Diabetes Obes Metab*. May;16(5):467-77. Epub Mar 12.

H. E. Bays; R. Weinstein; G. Law; W. Canovatchel 2014. Canagliflozin: Effects in overweight and obese subjects without diabetes mellitus. *Obesity* 22(4): 1042-1049.

Stenlof K, Cefalu WT, Kim KA et al. 2013. Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. *Diabetes, Obesity and Metabolism* 15:372-382.

F. J. Lavalle-Gonzalez; A. Januszewicz; J. Davidson; C. Tong; R. Qiu; W. Canovatchel; G. Meininger 2013. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. *Diabetologia* 56(12): 2582-2592.

D. Vasilakou; T. Karagiannis; E. Athanasiadou; M. Mainou; A. Liakos; E. Bekiari; M. Sarigianni; D. R. Matthews; A. Tsapas 2013. Sodium-Glucose Cotransporter 2 Inhibitors for Type 2 Diabetes: A Systematic Review and Meta-analysis. *Annals of Internal Medicine* 159(4): 262-274.

G. Schernthaner; J. L. Gross; J. Rosenstock; M. Guarisco; M. Fu; J. Yee; M. Kawaguchi; W. Canovatchel; G. Meininger 2013. Canagliflozin Compared With Sitagliptin for Patients With Type 2 Diabetes Who Do Not Have Adequate Glycemic Control With Metformin Plus Sulfonylurea: A 52-week randomized trial. *Diabetes Care* 36(9): 2508-2515.

J. P. H. Wilding; G. Charpentier; P. Hollander; G. González-Gálvez; C. Mathieu; F. Vercruysse; K. Usiskin; G. Law; S. Black; W. Canovatchel; G. Meininger (2013). "Efficacy and safety of canagliflozin in patients with type 2 diabetes mellitus inadequately controlled with metformin and sulphonylurea: a randomised trial." International Journal of Clinical Practice

B3. DESCRIPTION OF RESEARCH PROTOCOL

A. Study Design – Overview, Methods, Procedures

This is a randomized, double-blind, placebo-controlled parallel design study in which 42 subjects will be randomized (1:1) to treatment with canagliflozin 300mg or placebo once daily for 18 weeks. The study will include 7 outpatient visits which will take place in the Harvard Catalyst Clinical Research Center at BIDMC. The funding source for this study is Janssen Scientific Affairs, LLC; Janssen Scientific Affairs, LLC is also providing canagliflozin for this study.

Our primary endpoint is change in body weight. Secondary endpoints are change in resting metabolic rate measured using indirect calorimetry, change in body composition using DXA scans changes in serum markers of metabolism and inflammation, and change in hunger and satiety using visual analog scales. We will also analyze change in caloric intake using food logs.

Study procedures include a screening visit, an enrollment visit (study week 0), follow-up visits at study weeks 2, 4, 8, and 12, and a final visit at study week 18.

Screening visit: Screening procedures will occur after an overnight fast and will include a full medical history: history of diabetes care and blood sugar control; review of body weight history; review of current medications; a physical exam including height, weight, blood pressure and heart rate; a blood test to measure CBC, electrolytes, kidney function, liver function, thyroid function, cholesterol levels, hemoglobin A1C, and markers of metabolism and inflammation. We will also collect a urine sample for measurement of glucose andcreatinine. We will also measure urine glucose and creatinine levels.

Women of childbearing age will have a urine pregnancy test unless they are over age 50 and have not had a menstrual period in more than 2 years, or have had a surgical procedure which makes it impossible to become pregnant (hysterectomy). If the pregnancy test is positive, the subject will not be allowed to enroll in the study.

Enrollment visit (Study Week 0): The enrollment visit will occur after an overnight fast and will include measurement of vital signs, body composition, and resting metabolic rate. We will also distribute blood sugar logs, visual analog scales, and food logs, and we will do a 24-hour food recall assessment.

Vital signs: For all visits, vital signs will include weight (with the subject wearing a hospital gown), blood pressure lying down and standing, heart rate lying down and standing, and waist circumference.
Body composition:.We will measure body composition using a Dual Energy X-ray Absorptiometry (DXA) scan.
Resting metabolic rate: Resting metabolic rate (RMR) is the number of calories a person's body burns while at rest. Subjects will lay in bed and breathe comfortably without falling asleep for about 20 minutes. After this, we will place a large plastic dome over the subject's head, including the nose and mouth, and we will measure the air the subject inhales and

exhales for about 20 minutes. By measuring oxygen consumption and CO2 production, we can calculate resting metabolic rate.
Blood sugar logs: We will provide blood sugar logs for subjects to record blood sugar levels at least once every day. If subjects already have their own blood sugar logs which they use regularly, they will be allowed to continue to use those during the study.
Visual analog scales: Subjects will be asked to draw a vertical line through a 10cm horizontal line, with one end representing hunger and the other end representing fullness. They will complete these in the fasting state and in the full state (2 hours after a meal) once per week, and at every study visit.
Food recall and food logs: Subjects will be asked to name all of the food eaten in the 24 hours prior to the screening visit so that we can understand baseline eating habits.

Follow-up visits: Study weeks 2, 4, 8, 12

Follow-up visits will occur after an overnight fast and will include

A urine pregnancy test if this was required at the screening visit
A review of adverse effects, changes in medical history, blood sugar logs and compliance with study treatment/placebo
Measurement of vital signs
Collection of a urine sample for measurement of glucose andcreatinine.
Measurement of resting metabolic rate
Collection of food logs, blood sugar logs, and visual analog scales

Final study visit (Study week 18)

The final study visit will occur after an overnight fast. Study procedures at this visit are the same as those done at the enrollment visit, above.

Adverse Event Definitions and Classifications

Unlisted (Unexpected) Adverse Event/Reference Safety Information

An adverse event is considered unlisted if the nature or severity is not consistent with the applicable product reference safety information. For canagliflozin the expectedness of an adverse event will be determined by whether or not it is listed in the Investigator's Brochure.

Special Reporting Situations
Safety events of interest on a sponsor study drug that may require expedited reporting and/or safety evaluation include, but are not limited to:

- Overdose of a sponsor study drug
- Suspected abuse/misuse of a sponsor study drug
- Inadvertent or accidental exposure to a sponsor study drug
- Medication error involving a sponsor product (with or without subject/patient exposure to the sponsor study drug, eg, name confusion)

Special reporting situations will be recorded in the CRF. Any special reporting situation that meets the criteria of a serious adverse event will be recorded on the serious adverse event

page of the CRF.

Procedures

All Adverse Events

All adverse events and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the subject's last study-related procedure (which may include contact for follow-up of safety). Serious adverse events, including those spontaneously reported to the investigator within 30 days after the last dose of study drug, will be reported.

All events that meet the definition of a serious adverse event will be reported as serious adverse events, regardless of whether they are protocol-specific assessments.

All adverse events, regardless of seriousness, severity, or presumed relationship to study drug, will be recorded using medical terminology in the source document and the CRF. Whenever possible, diagnoses will be given when signs and symptoms are due to a common etiology (eg, cough, runny nose, sneezing, sore throat, and head congestion will be reported as "upper respiratory infection"). Study investigators will record in the CRF their opinion concerning the relationship of the adverse event to study therapy. All measures required for adverse event management will be recorded in the source document.

The sponsor assumes responsibility for appropriate reporting of adverse events to the regulatory authorities. The sponsor will also report to Janssen Scientific Affairs, LLC all serious adverse events that are unlisted (unexpected) and associated with the use of the study drug. The sponsor will report these events to the appropriate Independent Ethics Committee/Institutional Review Board (IEC/IRB) that approved the protocol unless otherwise required and documented by the IEC/IRB.

Serious Adverse Events

All serious adverse events occurring during the study must be reported to Janssen Scientific Affairs, LLC by study-site personnel within 24 hours of their knowledge of the event.

All serious adverse events that have not resolved by the end of the study, or that have not resolved upon discontinuation of the subject's participation in the study, must be followed until any of the following occurs:

• The event resolves
• The event stabilizes
• The event returns to baseline, if a baseline value/status is available
• The event can be attributed to agents other than the study drug or to factors unrelated to study conduct
• It becomes unlikely that any additional information can be obtained (subject or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

Suspected transmission of an infectious agent by a medicinal product will be reported as a serious adverse event. Any event requiring hospitalization (or prolongation of hospitalization) that occurs during the course of a subject's participation in a study must be reported as a serious adverse event, except hospitalizations for the following:

• Hospitalizations not intended to treat an acute illness or adverse event (eg, social reasons such as pending placement in long-term care facility)
• Surgery or procedure planned before entry into the study (must be documented in the CRF). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered serious adverse events. Any adverse event that results in a prolongation of the originally planned hospitalization is to be reported as a new serious adverse event.

Disease progression should not be recorded as an adverse event or serious adverse event term; instead, signs and symptoms of clinical sequelae resulting from disease progression/lack of efficacy will be reported if they fulfill the serious adverse event definition.

Adverse Events of Interest

Specific adverse events or groups of adverse events will be followed as part of standard safety monitoring activities. These events will be reported to Janssen Scientific Affairs, LLC within 24 hours of awareness irrespective of seriousness (ie, serious and nonserious adverse events) following the procedure described above for serious adverse events and will require enhanced data collection.

Major Hemorrhage

Major hemorrhage is defined as any hemorrhagic event that is Grade 3 or greater in severity or that results in 1 of the following: intraocular bleeding causing loss of vision, the need for a transfusion of 2 or more units of red cells or an equivalent amount of whole blood, hospitalization, or prolongation of hospitalization.

Intracranial Hemorrhage

Any intracranial hemorrhage adverse event, including subdural hematoma/hemorrhage, epidural hematoma/hemorrhage and intracerebral hemorrhage, of any grade severity, will be captured as an event of special interest.

Other Malignancies

In addition to all routine AE reporting, all new malignant tumors, including solid tumors, skin malignancies and hematologic malignancies, are to be reported for the duration of study treatment and during any protocol-specified follow-up periods including post-progression follow-up for overall survival.

Pregnancy

All initial reports of pregnancy will be reported to Janssen Scientific Affairs, LLC by study-site personnel within 24 hours of knowledge of the event. Abnormal pregnancy outcomes (eg, spontaneous abortion, stillbirth, and congenital anomaly) are considered serious adverse

events and will be reported as a Serious Adverse Event. Any subject who becomes pregnant during the study will discontinue further study treatment.

Because the effect of the study drug on sperm is unknown, pregnancies in partners of male subjects included in the study will be reported by the study-site personnel within 24 hours of their knowledge of the event.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

PRODUCT QUALITY COMPLAINT HANDLING

A product quality complaint (PQC) is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, ie, any dissatisfaction relative to the identity, quality, durability, or reliability of a product, including its labeling or package integrity. A PQC may have an impact on the safety and efficacy of the product. Timely, accurate, and complete reporting and analysis of PQC information from studies are crucial for the protection of subjects, investigators, and the sponsor, and are mandated by regulatory agencies worldwide.

Procedures

All initial PQCs must be reported to Janssen Scientific Affairs, LLC by the study-site personnel within 24 hours after being made aware of the event.
If the defect is combined with a serious adverse event, the study-site personnel must report the PQC to Janssen Scientific Affairs, LLC according to the serious adverse event reporting timelines. A sample of the suspected product should be maintained for further investigation if requested by Janssen Scientific Affairs, LLC.

B. Statistical Considerations

Sample Size Justification: There are no published data on change in resting metabolic rate with canagliflozin treatment. We therefore calculated sample size based on change in body weight, our primary outcome. Published data show approximately 3kg placebo-corrected weight loss after 12 weeks of treatment with canagliflozin compared to placebo in individuals with type 2 diabetes and obesity (Stenlof et al, 2013). Based on a 3 kg difference in body weight between canagliflozin and placebo and a SD of 3.3, the probability that this study will detect a treatment difference at a two-sided 0.05 significance level is 80% if we have 42 study completers. We plan to screen 60 subjects in order to enroll approximately 50 subjects (8-10 screen failures) and obtain 42 study completers (approximately 8-10 dropouts). Data from subjects who complete at least 12 weeks of treatment will be used in the final analysis.

Data analysis: Descriptive statistics with 95% confidence intervals will be used to describe baseline characteristics of the study population. The primary endpoints of change in body weight and BMI will be analyzed using an analysis of covariance (ANCOVA) model. We will use repeated measures analysis of variance to assess changes in body weight and resting metabolic rate at each study visit/timepoint. We will also analyze change in body composition between baseline and end of study. Treatment group will be the fixed effect and corresponding baseline values at the start of each treatment period will be the covariates. We will stratify based on baseline BMI, glycemic control (A1C), and diabetes treatment (lifestyle vs pharmacologic treatment at baseline). The least squares mean differences between treatments (canagliflozin vs placebo) and the associated 95% confidence intervals will be estimated based on this model.

Secondary endpoints will be analyzed using an ANCOVA model as above. The least squares mean differences between treatments and the associated 95% confidence intervals will be estimated based on this model.

We will enroll subjects who are treated at baseline with sulfonylureas or metformin or basal insulin, but will aim to enroll a majority of subjects treated with lifestyle alone to minimize the effects of other agents on body weight. Additionally, we will only enroll subjects with stable body weight (change in body weight less than 3% for at least 3 months prior to the screening visit), which will minimize the effect of different background diabetic regimens on body weight. Subjects who drop out prior to week 8 of treatment will not be included in the final analysis.

C. Subject Selection

Inclusion criteria

1. Type 2 diabetes
2. BMI 25-45 kg/m2
3. Hemoglobin A1C > 6% but < 9%
4. Normal renal function (GFR > 60)
5. Age 18-75

Exclusion criteria

1. Type 1 diabetes
2. History of recurrent UTI or mycotic genital infections
3. Treatment with a GLP1 agent for type 2 diabetes
4. Pregnant or breastfeeding
5. 5. Individuals with A1C < 6.5% who are taking sulfonylurea or insulin

B4. POSSIBLE BENEFITS

It is not possible to say whether subjects will benefit from participation in this study.

B5. POSSIBLE RISKS AND ANALYSIS OF RISK/BENEFIT RATIO

More Common

As of 28 March 2015 approximately 12367 subjects have received canagliflozin in completed or ongoing studies of 12 weeks or longer.

• Hypoglycemia (low blood sugar) in subjects taking other medications associated with hypoglycemia. If canagliflozin is taken with another medicine that can cause low blood sugar, such as a sulfonylurea, the risk of getting low blood sugar is higher. The dose of sulfonylurea medicine may need to be lowered during the study, and study doctors will be in communication with subjects' doctors outside the study. Hypoglycemia is very common and may occur in more than 1 in 10 people on canagliflozin.

• Dizziness or lightheadedness upon standing**:** These symptoms may occur from a decrease in blood pressure, can occur soon after starting canagliflozin, and are more likely to occur in people on medicines to lower blood pressure including diuretics (water pills such as furosemide), on a low salt diet, older patients or those who have reduced kidney function. While you are participating in this study, you should try to avoid becoming dehydrated and you should speak to the study doctor about any changes in your diet or other medications. This side effect may occur in up to 1 in 20 people on canagliflozin, or slightly more frequently in those at risk as described above.

For Women: Vaginal yeast infections and vaginal itching: You may have symptoms such as vaginal itching, burning, irritation, odor or discharge. This side effect may occur in slightly more than 1 in 10 women on canagliflozin.

For Men: Yeast infection at the head of the penis - You may have symptoms such as penile itching, irritation, burning, swelling, foul smelling discharge or pain. In 0.3% of men who are not circumcised, this could lead to swelling of the foreskin, and require circumcision. The side effect of yeast infection may occur in up to 1 in 20 men on canagliflozin.

Increased urination and thirst – Symptoms might include feeling thirsty, having a dry tongue, urinating more frequently or in larger amounts, an urgent need to urinate or more frequent urination at night. These side effects may occur in up to 1 in 20 people taking canagliflozin.

Urinary tract infections – Symptoms of urinary tract infections may include burning with urination, discomfort in passing urine, or fever. This side effect may occur in up to 1 in 20 people on canagliflozin.

Allergic reaction including rash or hives – These events can occur shortly after starting canagliflozin, are generally not serious or associated with other serious symptoms, such as breathing problems. This side effect may occur in up to 1 in 20 people on canagliflozin.

Less Common

Constipation – The side effect of constipation may occur in slightly more than 1 in 50 people on canagliflozin.

Nausea - The side effect of nausea (stomach queasy) may occur in slightly more than 1 in 50 people on canagliflozin.

Bone fractures may occur in up to 1 in 50 people per year on canagliflozin.

- Laboratory changes that have been observed in clinical studies with canagliflozin
  - Increase in the LDL, or "bad", cholesterol.
  - Increase in serum potassium, phosphate and/or hemoglobin; decreases in serum urate can also occur. These changes are generally not serious and not associated with serious symptoms.
  - A change in lab tests associated with kidney function might occur. These changes have generally been temporary and may relate to hydration status. During the study, we regularly monitor kidney function.
  - There may be side effects with the use of canagliflozin that are not yet known.

    Side effects in patients not involved in clinical studies who have been prescribed canagliflozin to treat their diabetes include those below. It is difficult to know specifically how often these side effects occur or always be certain if they are more likely to occur as a result of canagliflozin because these were not reported in the manner similar to data collection in a clinical study.
  - Serious allergic reactions, including those with the symptoms of swelling of the face, throat, and/or tongue or breathing problems.
  - Changes in lab tests associated with kidney function. Cases of severe decreases in kidney function have been reported more commonly in patients who were dehydrated.

- **Diabetic ketoacidosis** - The blood may show increased levels of blood acids called ketones. Sometimes this can occur even if blood sugar levels are not very high (e.g., less than 250 mg/dL [13.9 mmol/L]). Symptoms may include difficulty breathing, nausea, vomiting, abdominal pain, confusion, fruity-smelling breath, and unusual fatigue or sleepiness. This side effect may occur in up 1 in 1000 people with Type 2 diabetes.

○

Risks Associated with Blood Draw: The risks and discomforts of blood drawing from a vein include the possibility of pain or bruising at the site of the blood draw, occasional feeling of lightheadedness, and rarely, infection at the site of the blood draw.

Risks Associated with Indirect calorimetry: Subjects may feel a sense of suffocation when they are laying underneath the large plastic dome.

Risks Associated with DXA scan: This research study involves exposure to radiation from body composition scans. This radiation exposure is **not** necessary for medical care and is for research purposes only. This is in addition to the radiation exposure that you will receive as part of standard care. Using the standard way of describing radiation exposure, from participating in this study subjects will receive a total of 0.04 mSv.

For comparison, the average person in the United States receives a radiation exposure of 3 mSv per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that subjects will receive from participation in this research study is about the same amount that he/she would normally receive in about one week from these natural sources.

One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4 (or 25 percent). The increase in the chance of getting a fatal cancer, as a result of the radiation exposure received from this research study, is less than 1 in 25,000 (or much less than 1/100th of a percent). Therefore, the total risk of fatal cancer may be estimated to increase from 25 percent to 25.01 percent. This additional risk is too small to be measured and is generally regarded as insignificant.

Another concern some people may have about radiation exposure is the effect on fertility or on the possibility of causing harm to future children (i.e., genetic effects). The doses a subject will receive in the study are well below the known levels needed to affect fertility or cause genetic effects.

Pregnant and lactating women are not eligible for participation because it is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

Canagliflozin has been tested for its ability to cause harm to the fetus during pregnancy or cause birth defects. These studies have been done in animals. The studies that have been completed do not indicate that canagliflozin is associated with birth defects.
Nonetheless, women who are pregnant, lactating or intend to become pregnant during the study will be not allowed to participate in the study. Women who could possibly become pregnant must have a negative pregnancy test prior to starting the study drug and report immediately to the study site if they suspect they are pregnant during the study.

If a female subject is able to have children and is heterosexually active, she must use birth

control (contraception) during the study. Birth control methods that can be used while in this study include: avoiding sex, birth control pills, birth control injections or patch, intrauterine device, barrier method (for example, condoms or diaphragm) combined with spermicide (foam, cream, or gel), or the male partner is sterile (e.g. sperm tubes are cut or blocked). The type of birth control used must be discussed with the study doctor before a subject begins the study. The study doctor must approve the method before the subject can enter the study.

If a subject becomes pregnant during the study, she will be required to tell the study doctor immediately. She will have to stop taking the study drug. The doctor will provide advice about medical care and will ask the subject to allow him/her to collect information about the pregnancy and the health of the baby.

If a male subject's partner becomes pregnant, he must notify the study doctor.

B6. RECRUITMENT AND CONSENT PROCEDURES

Recruitment

Potential subjects will be recruited from the BIDMC, the Joslin Diabetes Center, and from the greater Boston area using print and online advertising.

Consent

Written informed consent will be obtained at the screening visit by one of the study investigators. Subjects will be provided with ample time in a private setting to read the informed consent document and ask questions about study procedures.

Subject Protection

Vulnerable populations, including children and pregnant women, will not be recruited and will not be allowed to participate in this study.

B7. STUDY LOCATION

Privacy

All study visit will occur in a private setting in the Harvard Catalyst Clinical Research Center at BIDMC.

B8. DATA SECURITY

All hard copies of PHI will be kept in subject binders stored in file cabinets in a locked office to which only study staff have access. All electronic data will be stored on a password-protected shared drive behind the BIDMC firewall, to which only study staff have access. All identifiers will be destroyed 6 months after publication of manuscripts that result from this study.

B9 Multi-Site Studies

Is the BIDMC the coordinating site? ☐ Yes ☐ No **N/A**

Is the BIDMC PI the lead investigator of the multi-site study? ☐ Yes ☐ No

B10 Dissemination of Research Results

We will provide research results to subjects by informing them by mail or email when any manuscripts are published.