PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

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PROTOCOL TITLE

Helping Olfaction and Nutrition On Renal Replacement (HONORR)

FUNDING

Leslie Fang Translational Award (Internal Funding) and the Executive Committee on Research (ECOR)

VERSION DATE

May 26, 2017

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

Malnutrition and cachexia are prevalent in end stage renal disease (ESRD) and in chronic kidney disease (CKD) patients and are associated with increased morbidity and mortality. Food aversion is a major contributor to anorexia and malnutrition in ESRD and CKD and it also impacts the quality of life. Olfactory dysfunction has been shown to contribute to food aversion in ESRD and CKD patients. Since up to 80% of a meal's flavor is attributed to olfactory input, loss or alteration of smell leads to loss or alteration of taste in ESRD and CKD patients and at present there are no effective therapies to treat smell and/or taste disorders in ESRD and CKD patients.

In patients with other causes of olfactory dysfunction such as congenital hyposmia and traumatic brain injury, intranasal theophylline has been shown to be effective in improving olfactory defects via increasing nasal mucus levels of cAMP and cGMP, second messengers critical for optimal smell sensation. However, the efficacy of nasal theophylline to improve olfaction in ESRD and CKD patients has not been investigated and the effects of nasal theophylline treatment on the nutritional parameters are unknown in ESRD and CKD patients.

Aim: To examine the efficacy and safety of nasal theophylline treatment to improve olfaction and nutrition in ESRD and CKD patients

Hypothesis: Nasal theophylline treatment improves olfaction and nutrition in ESRD and CKD patients with olfactory defects by via increasing intracellular cAMP and cGMP levels.

A previous pilot clinical trial demonstrated that intranasal theophylline is safe and effective in improving olfactory deficits in congenital hyposmia and traumatic brain injury, however, it has not been examined in ESRD and CKD patients. We will conduct a pilot single arm open-label clinical trial (n=45) of 6 weeks duration to examine the safety of nasal theophylline in the following groups of patients with olfactory defects: hemodialysis-dependent ESRD patients, peritoneal dialysis dependent ESRD patients, CKD patients, and patients with normal kidney function. We will investigate whether nasal theophylline improves olfaction and nutritional status in trial participants. Patients with normal kidney function who have olfactory defects will be recruited to determine whether the effects of nasal theophylline are different in patients with normal kidney function compared to patients with kidney disease.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Uremic anorexia and malnutrition are common in ESRD and CKD patients and remain major predictors of morbidity and mortality. Anorexia and food aversion are also predominant patient reported outcomes in this population and they significantly impair ESRD and CKD patients' quality of life. Loss or alteration of olfactory function has been shown to cause food aversion and appetite suppression in ESRD and CKD patients. Until now, studies designed to improve nutrition and anorexia in ESRD and CKD patients have largely focused on the taste function and have ignored the contribution of olfaction. However, up to 80% of a meal's flavor is attributed to olfactory input, and this sets the target for our proposed study that will examine whether olfactory defects in ESRD and CKD patients can be corrected by administering intranasal theophylline.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

Study design: Pilot open-label single arm clinical trial

Study population: We will prospectively enroll 20 hemodialysis-dependent ESRD patients with olfactory defects, 10 peritoneal dialysis dependent ESRD patients with olfactory defects, 10 CKD patients with olfactory defects, and 5 patients with normal kidney function with olfactory defects in this clinical trial over 2-year study period (total n=45). Study subjects will be identified from the current ongoing prospective obsevational study titled "Role of Olfaction in End Stage Renal Disease, Chronic Kidney Disease, and Health" (Protocol #: 2014P002461). A physician colleague or research nurse will

initially explain the study to potential patients and patient will be approached by the Investigator if patient is interested. Patients will also be offered an opportunity to take home the Consent Form, and call back if they wish to participate.

Clinical trial eligibility criteria are outlined in Table 1.

Table 1

Inclusion criteria	Exclusion criteria
-Adult (age >18 years) -ESRD requiring chronic outpatient hemodialysis or ESRD requiring chronic outpatient peritoneal dialysis or CKD or normal kidney function -Able to provide written consent -Defects in smell identification and/or smell threshold detection as measured by "Scratch-and-sniff" University of Pennsylvania Smell Identification Test (UPSIT) and Smell Threshold Test during the ongoing prospective study (Protocol #: 2014P002461)	- Prior allergic reaction to theophylline - Patients currently treated with theophylline for clinical indication - Pregnancy or lactation - Patients hospitalized at the time of study enrollment -Patients with hypokalemia at baseline

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

Study Procedures: Patients meeting the eligibility criteria will be consented and will self-administer 20 µg intranasal theophylline (theophylline methylpropyl paraben in a 0.4-mL saline solution) once daily (in the morning) into each naris for a total of 6 weeks. The study medication will be provided by Foundation Care. Patients will be instructed to direct the spray superiorly into the nasal cavity but not posteriorly into the nasopharynx. This technique will be practiced before study initiation with sterile saline at baseline study visit (study visit 0). The baseline study visit will take approximately 2 hours. Follow-up will occur every 2 weeks (study visits 1, 2, and 3) and each follow-up visit will take approximately 1.5 hours.

Following procedures will be conducted during study visits:

1) History and physical by a study staff physician at study visits 0, 1, 2, and 3. Data to be collected during these visits are summarized in Table 2 below.

Table 2

Category	Data collected
Demographic information	Age, sex, race
Medical history	Cause(s) of ESRD and CKD, coronary disease, chronic heart failure, previous arrhythmia, cerebrovascular disease, peripheral vascular disease, diabetes mellitus, pulmonary disease, neurologic disease, psychiatric disease, musculoskeletal disease, gastrointestinal and hepatic diseases, cancer, eye disease, hepatitis, dialysis start date
Vital signs	Blood pressure, heart rate, weight, height, waist circumference
Dialysis prescription	Time, dialyzer, dialysate composition, blood flow
Medications	List of medications
Vascular access history	Type and location of current access, number of prior temporary and permanent accesses
Hospitalizations	Dates, diagnosis, and procedures for each interval hospitalization
Subjective assessment of smell	Rating overall smell abilities on a scale of 0 to 100

2) Subjective global assessment, a tool that assesses nutritional status based on features of the history and physical examination, will be conducted at study visits 0, 1, 2, and 3.

3) "Scratch-and-sniff" University of Pennsylvania Smell Identification Test (UPSIT) test will be administered at study visits 0, 1, 2, and 3. This test uses cards with odorants on them, which study subjects try to identify. We will use the test that is made commercially available by Sensonics, Inc.

   This test is a comprehensive 40-item test and will be administered by study investigators. It is the most reliable (test-retest r=0.94) and accurate olfactory test available.

   This test provides an absolute indication of smell loss. Norms from

nearly 4,000 men and women spanning the entire age range provide a basis for examinee percentile rank. This test is available in multiple languages: American English, Arabic, British English, Chinese (Simplified), Chinese (Traditional), Dutch, French, German, Italian, Japanese, Portuguese, and Spanish.

Estimated time burden for this test: 15 minutes each subject

The test is validated in subjects with age range from 18 to 85 years.

Odors used:
Pizza Cinnamon Paint Thinner
Gum Gasoline Grass
Menthol Strawberry Smoke
Cherry Cedar Pine
Motor oil Chocolate Grape
Mint Gingerbread Lemon
Banana Lilac Soap
Clove Turpentine Natural Gas
Leather Peach Rose
Coconut Root Beer Peanut
Onion Dill Pickle Wintergreen
Fruit Punch Pineapple Watermelon
Licorice Lime
Cheddar Orange

4) Smell threshold test will be administered at study visits 0, 1, 2, and 3. This test involves subjects smelling phenyl ethyl alcohol in various concentrations ranging from -10 log vol/vol to -2 log vol/vol to determine smell threshold. Norms based upon hundreds of subjects; 75%, 95%, and 99% confidence intervals provided for each decade of age. Estimated time burden for this test: 20 minutes each subject.

5) Assessment of adverse events at study visits 1, 2, and 3. Study subjects will be specifically asked regarding adverse events such as nausea, restlessness, tremors, nose irritation, seizures, sleep disturbances, palpitations, and headaches. Physical examination will be conducted to determine heart rate and to assess tremors. Adverse events will be characterized as probably related, probably not related, or unknown and all adverse events will be reviewed by the data safety monitoring board (DSMB).

6) Collection of blood samples (plasma and serum, 10 mL each) will be done at study visits 0, 1, 2, and 3.

7) Saliva (5 ml) and nasal mucus (5 ml) will be collected at study visits 0 and 3.

   Salivary samples will be collected into plastic cups during the study visit (at study visits 0 and 3).

   For nasal mucus samples, subjects will be provided plastic cups to collect nasal mucus over the next 2 days (at study visits 0 and 3). The samples will be kept refrigerated at 4°C and courier pick-up will be arranged to get samples shipped to study investigators.

Patients will store the study drug in refrigerators at temperatures between 35F and 46F (2C and 8C).

Sample processing and assays: The study coordinator will spin and aliquot blood samples immediately after they are collected and store them in refrigerators. Serum levels of albumin, pre-albumin, blood urea nitrogen, and transferrin, and cholesterol will be measured to assess nutritional status from each study visit sample. Plasma levels of theophylline will be measured using fluorescence polarization from samples collected at study visits 1, 2, and 3 to ascertain whether theophylline levels reach detectable range with intranasal administration in ESRD and CKD patients and in patients with normal kidney function.

Nasal mucus and salivary samples will be centrifuged at 17,000 to 19,000*g* in a cold centrifuge, the supernatant will be transferred to plastic tubes and stored at -20°C until assayed by a sensitive 96-plate spectrocolorimetric immunoassay to determine levels of cAMP and cGMP.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

Nasal theophylline is not standard of care treatment for patients with olfactory defects. At present, there are no effective therapies to treat olfactory defects in the ESRD and CKD patients.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

We will minimize risks of nasal theophylline by excluding subjects with allergy to theophylline and those who are on theophylline therapy for any

clinical indication. We will exclude patients with hypokalemia at baseline. Pregnant and breast-feeding women will be excluded.

All data collected will be coded with a unique study ID number to ensure patient confidentiality.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

Nasal theophylline is overall a safe therapy. Potential adverse effects include nausea, restlessness, tremors, seizures, sleep disturbnaces, palpitations, and headaches. Patients will be specifically asked about these and any other adverse events at study visits 1, 2, and 3 and physical examination will be conducted to determine heart rate and to assess tremors. Adverse events will be characterized as probably related, probably not related, or unknown and all adverse events will be reviewed by the data safety monitoring board (DSMB).

Subjects will be removed from the study for for unacceptable adverse events.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

There is a potential to further anemia in this typically anemic population through additional blood sampling, however, this risk will be minimized by restricting blood collection to only 20 mL at each visit.

Pregnant and breast-feeding women are excluded from this study.

Nasal theophylline is overall a safe therapy. Potential adverse effects include nausea, restlessness, tremors, seizures, sleep disturbnaces, palpitations, and headaches. Patients will be specifically asked about these and any other adverse events at study visits 1, 2, and 3 and physical examination will be conducted to determine heart rate and to assess tremors. Adverse events will be characterized as probably related, probably not related, or unknown and all adverse events will be reviewed by the data safety monitoring board (DSMB). Subjects will be removed from the study for for unacceptable adverse events.

Because theophylline together with caffeine or alcohol can increase the side effects caused by theophylline, subjects will be instructed to limit intake of caffeine and alcohol while enrolled in the study.

Risks to privacy and confidentiality will be minimized by providing each subject with a unique subject identifier. The link between subject and ID number will be stored in a password protected database, and only accessible to the study PI.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

The benefits of nasal theophylline administration have not been studied in ESRD and CKD patients. At present, there is no effective treatment for olfactory defects in ESRD and CKD patients. Through this pilot trial we hope to gain insights into the efficacy and safety of nasal theophylline administration in ESRD and CKD patients. Data from this trial will set the stage for future larger randomized controlled trials.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

Men, women, and minorities are encouraged to participate. Because risks to a developing fetus or nursing infant are not documented, lactating or pregnant women are excluded from the study. Women of childbearing age will be asked to practice birth control during the duration of the study.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Non-English speaking subjects will be allowed participation in this study. Interpreter services will be provided as needed. We will follow the procedure outlined in PHRC policy for obtaining and documenting informed consent of subjects who do not speak English. We also have multilingual (Chinese, French, Spanish, Hindi) co-investigators in the study who are able to communicate with foreign speaking subjects.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English

https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Study subjects will be identified from the current ongoing prospective observational study titled "Role of Olfaction in End Stage Renal Disease, Chronic Kidney Disease, and Health" (Protocol #: 2014P002461). A physician colleague or research nurse will initially explain the study to potential patients and patient will be approached by the Investigator if patient is interested. Patients will also be offered an opportunity to take home the Consent Form, and call back if they wish to participate. Consent will be obtained by a licensed physician investigator.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

To compensate subjects commensurate with their level of participation, we will pay each subject $25 for each completed visit. Ideally, subjects will complete the entire study, which involves 4 study visits, and will be compensated a total of $100.00. We will pay for parking in the hospital garage during study visits.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Eligible subjects will be identified from the current ongoing prospective observational study titled "Role of Olfaction in End Stage Renal Disease, Chronic Kidney Disease, and Health" (Protocol #: 2014P002461). We will ask a physician colleague or research nurse to initially explain the study to potential patients and patient will be approached by the Investigator if patient is interested. We will also offer patients an opportunity to take home the Consent Form, and call back if they wish to participate. Either the Principal Investigator or co-investigator or research nurse or research coordinator will approach the subjects for potential participation in this trial following approval by their attending nephrologists. Informed consent will be obtained by the research nurse or the Principal Investigator or the co-investigator, who will assist the subject in understanding the risks and benefits and a signed informed consent will be mandatory. We will reinforce with the subjects that participation is voluntary, that they do not have to participate, and the decision not to participate will not affect their care, now or in the future. Consent of subjects who do not speak English will be obtained and documented following the procedures outlined in the PHRC Policy.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

We will record episodes of nausea, restlessness, tremors, seizures, sleep disturbances, palpitations, and headaches. Subjects will be withdrawn per the recommendation of the Principal Investigator or the primary nephrologist.

A data safety monitoring board (DSMB), including 2 clinicians and 1 statistician, will assess potential adverse events.

Compliance will be determined by interview at study visits 1, 2, and 3.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

Data obtained during the course of this study will be reviewed by the Principal Investigator and co-investigators weekly. We will utilize Partner's electronic system to notify us of an admission, or visit to the Emergency Department by an enrolled subject. The investigator will assess and record any adverse event in detail including the date of onset, description, severity, time course, duration and outcome, relationship of the adverse event to study drug, an event diagnosis, if known, and any action(s) taken. All adverse events will be followed to a satisfactory conclusion.

Any adverse events, regardless of their relationship to the study protocol, or drugs, will be reported to the Partner's IRB within the required timeframe as outlined by the Partners Human Research Committee Investigator' Responsibilities Guidelines.

Unanticipated problems involving risks to subjects or others including adverse events will be reported to the PHRC in accordance with PHRC unanticipated problems reporting guidelines.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who

will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

Lab results will be transcribed from the laboratory printouts to the database by two people using a check and balance method. We will utilize the secure web-based application, REDCap, to complete data collection for each enrolled subject. Data will be entered electronically by the research nurse or study coordinators at each visit when possible, thus minimizing the potential for transcription errors. The data manager will review the electronic CRF's for accuracy and completeness, and review with the research nurse every two weeks. The data manager is responsible for monitoring the integrity of the database. Demographic data, and data obtained from the questionnaire is stored in both electronic and paper format. The coded hardcopies are stored in a locked, secured file cabinet.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

Each patient will be given a unique study number, and all specimens and data collected will reflect this study number, and be stripped of patient's medical record number. The principal investigator will store the database linking the subject's demographic information and study numbers in a separate secure password protected database.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

De-identified specimens will be sent to external research collaborators in the event that an assay cannot be performed within Partners.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Specimens and data will be stored at Partners. Subjects may withdraw specimens and/or data by requesting to do so in writing, however, data or samples that have already been shared or used in this research will not be able to be withdrawn.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Not applicable at this time.