Protocol including Statistical Analysis Plan
Official Title: Efficacy of Vaccination Against Seasonal Influenza in Individuals with the Metabolic Syndrome
NCT Number: NCT02653495
Version/Date of Document: Version 1.11 (05/07/2017)

Study Application (Version 1.11)

1.0 General Information

*** Please enter the full title of your study:**

Efficacy of Vaccination Against Seasonal Influenza in Individuals with the Metabolic Syndrome

*** Please enter the study short title:**

Impact of Metabolic Syndrome on Flu Vaccine Efficacy

Is this Study using Subject Management?

(•) Yes ( ) No

2.0 Add Lab/Dept(s)

2.1 List departments associated with this study:

Primary Dept?	Department Name
(•)	**RUH** - Laboratory of Virology and Infectious Disease (Rice)
( )	**RUH** - Research Facilitation Office
( )	**RUH** - Rockefeller University Hospital

3.0 Assign key study personnel(KSP) access to the study

3.1 * Please add a Principal Investigator for the study:

Andreo, Ursula, PhD

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Rice, Charles, Ph.D.
Clinical- Co-Investigator
Rosenberg, Brad R, MD, PhD
Clinical- Co-Investigator
Walker, Jeanne Marie, MSN/NP-C
Clinical- Co-Investigator

B) Research Support Staff

Brassil, Donna, MA, RN, CCRC
Study Coordinator
Dowd, Kathleen, BSN, RN, CCRC
Study Coordinator
Johnson, Amber
Research Pharmacist
MacArthur, Robert B, PharmD MS
Research Pharmacist

3.3 * Please add a Study Contact:

Andreo, Ursula, PhD
Brassil, Donna, MA, RN, CCRC
Dowd, Kathleen, BSN, RN, CCRC

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

4.0 Rockefeller University Conflict of Interest

4.1

Investigator Financial Conflict of Interest
All KSP (unless they have done so in the past 12 months) must complete and update promptly a Rockefeller University Significant Financial Interest Disclosure at http://mycoi.rockefeller.edu/. Prompt disclosure means within 30 days of discovering or acquiring a Significant Financial Interest, and as early as possible in the development of this protocol. If a KSP discloses a significant financial interest that may constitute a conflict of interest with respect to the proposed study, he or she must E-mail a copy of the Lay Summary of the study to Teresa Solomon (solomot@rockefeller.edu). Doing so will allow the process of addressing the potential COI to proceed in step with the development of the study protocol. Tardiness or non-compliance with this requirement will very likely cause delay in submission of the study for IRB review.

Institutional Conflict of Interest
As early as possible the PI or designee preparing this application must log in to https://icoi. rockefel ler.edu/account/login.php, which lists entities in which The Rockefeller University has a direct financial interest. If the proposed study involves any entity on that list the PI or designee must E-mail the entity involved and a copy of the Lay Summary to Ms. Teresa Solomon so that the process of addressing the potential Institutional COI can proceed in step with the development of the study protocol.

5.0 External Personnel

5.1 List external personnel who will be working on the study:

Name	Institution	Telephone	E-mail	Role
Stasi Lubansky, DNP, ANP, CDE, CTTS	Weill Cornell Medical College	[redacted]	[redacted]	Consultant

6.0 Delegation of Authority

6.1 Enter authorized activities for all Rockefeller University personnel named on the study.

Activity Codes:

1. Informed consent
2. Inclusion / exclusion criteria
3. Medical / medication history
4. Perform physical exam
5. Skin assessments and photos
6. Study drug dispensing
7. Study drug administration
8. Study drug reconciliation
9. Study drug compliance
10. Administer study questionnaire(s)
11. Subject recruitment
12. Perform assays
13. Specimen / sample analysis
14. Lumbar puncture
15. Femoral line placement
16. Central line placement
17. Insulin clamp procedure
18. Leukapheresis
19. Sigmoidoscopy
20. Fat biopsy
21. Skin biopsy
22. Conduct sleep study
23. Diet design and preparation
24. Nutritional assessment and counseling
25. Addition of PABA to food
26. Data analysis
27. Data review
28. Data management
29. Maintain regulatory documents / files
30. Complete CRF's

Add up to three additional authorized activities specific to this study:

31: Adverse Event assessment

32:

33:

Activity Codes Continued:

34. Behavioral Testing
35. Bod Pod
36. Bone Marrow Aspiration
37. Neuropsychological Testing
38. Conduct Focus Group
39. Conduct Smell Study
40. Genetic Counseling
41. Apply EEG Electrodes
42. Olfactometer Test
43. Study Participant Teaching
44. Resting Energy Expenditure
45. Source Document Review & Correction
46. Medical Photography
47. Write/Sign LIP orders

Enter delegation of authority for Rockefeller University Key Study Personnel:

Name	Title	Authorized Activities	Start Date	End Date
Andreo, Ursula, PhD	PI	2, 12, 13, 26, 27, 28	09/01/2015	

Rice, Charles, Ph.D.	Co-Investigator	27	09/01/2015
Rosenberg, Brad R, MD, PhD	Co-I	26, 27	09/01/2015
Brassil, Donna, MA, RN, CCRC	Facilitator	1, 2, 3, 29, 43, 45	09/01/2015
Dowd, Kathleen, BSN, RN, CCRC	Coordinator	1, 2, 3, 29, 43, 45	09/01/2015
Walker, Jeanne Marie, MSN/NP-C	NP	1, 2, 3, 4, 31, 43, 47	09/01/2015
MacArthur, Robert B, PharmD MS	Research Pharm	6, 8	03/17/2017
Johnson, Amber	Research Pharm	6, 8, 9	03/17/2017

Enter delegation of authority for additional Rockefeller University Key Study Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No records have been added				

Enter the authorized activities for External Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No records have been added				

7.0 Study Description

7.1 * Lay Summary

Please provide a summary of your study in lay language. The summary should be no more than a half page (500 words or less) and should contain a clear statement of the rationale for the study.

The development of industrialization with increased food consumption and sedentarity has given rise to an obesity pandemic, which affects up to 30% of the population in countries like US, these populations being at greater risk for cardiovascular diseases, and diabetes. More than obesity per se, visceral obesity is associated with metabolic diseases (**1**) that cluster together and clinically defined metabolic syndrome (MetS). MetS comprises individuals with at least three of the 5 of the following factors: abdominal obesity, high blood triglycerides, low HDL ("good cholesterol"), high blood pressure and elevated fasting glucose (**2**). Metabolic syndrome is associated with a low-grade inflammation or metaflammation characterized by an infiltration of immune cells particularly in the adipose tissue, the liver and the pancreas (**3**) that is thought to be responsible for the induction of insulin resistance. It is thought that obesity predisposes to other diseases such as cancer, asthma but only little attention has been given to infectious diseases (**4**, **5**). Studies have shown that obesity increases the risk of severe influenza infection (**6**) and associated death and reduces the efficacy of influenza vaccine in the obese population (**7**) but yet, the molecular mechanisms have not been described. Immune dysfunctions associated with obesity are suspected to play a major role but obesity is often associated with respiratory disorders that could directly explain the increased susceptibility to influenza infection (**8**). Also, metabolically healthy obesity is less associated with metaflammation (**9**). Therefore, we would like to focus particularly on metabolic syndrome, and determine how it influences immune response to viruses.
We are thus hypothesizing that differences in the innate immune responses between individual with or without metabolic syndrome impact viral infection and vaccine outcome. Recent studies involving complex biological analysis and computational modeling have shown that the ability of an individual to positively respond to influenza vaccine can be molecularly predicted by looking at markers in the blood cells (**10-12**). We will perform seasonal influenza vaccination in people with or without metabolic syndrome to determine if the late adaptive response assessed by antibodies titers is different between the two groups and correlates with the early immune response assessed by gene expression profile in whole blood cells.
Healthy nutritional habits along with increased physical activities should be best at preventing the development of metabolic syndrome but socio-economical issues are slowing the implementation of these changes. Therefore, as metabolic syndrome is raising public health concerns, it is important to understand why the metabolic syndrome affects susceptibility to diseases. The project we propose will contribute to a better understanding of the inflammatory phenotype associated with metabolic syndrome and establish for the first time if it affects the immune protection against infectious diseases and particularly against influenza virus infection. Our results are important to determine if the population affected by metabolic syndrome should receive anti-influenza treatment in priority in the context of a severe influenza epidemic.

7.2 * Public Health Impact Statement

Provide a brief plain language statement (100 words or less) of the value of the research proposed and its potential impact on population health. Additional instructions located in Help.

Metabolic syndrome (MetS) is the combination of unhealthy metabolic factors associated with obesity that confer an increased risk for cardiovascular disease and diabetes. Influenza vaccine has been shown to be less protective in obese individuals without assessment of their metabolic status. We would like to study the influenza vaccine response in people with and without MetS. We believe our study might help develop vaccines of better efficacy for this population and understand immune deficiencies associated with metabolic syndrome and obesity.

7.3

*** Submission Request Category**

Please indicate:

Full Review

8.0 Clinical Trial Registration

8.1

Clinical Trial Registration

The types of studies listed below must be registered at **www.ClinicalTrials.gov /> *before* enrolling the first participant in order to be in compliance with federal regulations and preserve the opportunity to publish the study in journals that adhere to the ICMJE guidelines. Please check the answer that best applies.**

- ○ Study involves testing of FDA regulated drugs or biologics (See HELP)
- ○ Study is funded by the NIH, and meets the definition of a "clinical trial" (see HELP)
- ◉ Study meets the ICMJE definition of a "clinical trial" (See HELP)
- ○ None of the above

If you selected 1, 2, or 3, you must register your trial with ClinicalTrials.gov through the Rockefeller University institutional account. Please contact the Clinical Research Support Office x7408 for assistance.

9.0 Study Overview/Summary

9.1 * Who initiated this study?

Please specify one:

- ◉ Principal Investigator Initiated
- ○ Industry Initiated
- ○ Other

If other, please specify:

9.2 * This study in collaboration with:

- ○ Weill Cornell Medical College
- ○ Memorial Sloan-Kettering Cancer Center
- ○ Both Weill Cornell Medical College and Memorial Sloan-Kettering Cancer Center
- ◉ Neither Weill Cornell Medical College nor Memorial Sloan-Kettering Cancer Center

Please note: If any of the first three options is checked, you will be prompted to attach the **Tri-Institutional Study Specific Financial Disclosure** and the **IRB of Record** forms later on in the submission. Links to these forms can be found in the Help link to the right.

9.3 * Are other institutions involved in the study?

- ◉ 1. No
- ○ 2. Yes, and a federal, industry or private organization is administratively coordinating the study.
- ○ 3. Yes, however, a federal, industry or private organization is not administratively coordinating the study.

If #3 was selected above, please provide the following for each involved institution:

Name of Other Institution	Date of Approval by Other Institution	Date of Pending Approval by Other Institution	Date of Expiration at Other Institution

No records have been added

9.4 * Is this a multi-center trial?

○ Yes ◉ No

9.5 * Who (What) is to be studied?

☑ Human Subjects - including coded samples and/or data with links to Identifiers
☐ Deidentified Samples - unable to be linked to identifiers by receiver
☐ Data Only - unable to be linked to identifiers

9.6 *Study Type:

◉ Interventional
○ Observational

9.7 The initial date of IRB approval was:

11/25/2015

9.8 * What is the expected duration of the study?

3 years

9.9 * Are any of the following agents to be used in the study?

Check all that apply:

☑ Drug FDA Approved
☐ Approved Drug for Off-Label Purpose
☐ Investigational New Drug
☐ Biologic Agents
☐ Nutritional Supplements
☐ Placebo
☑ Vaccines
☐ No Agents

9.10 * Are investigational devices to be used in the study?

○ Yes ◉ No

If Yes, please specify:

○ A Significant Risk Device
○ A Non-significant Risk Device

9.11 Special Research Procedures

Does the study propose to directly involve participants in the following special research procedures?

☐ Recombinant DNA
☐ Gene Therapy

If either item is checked, please see Help for details.

9.12 * Radioactive Isotopes Involved

Will subjects be exposed to any radiation other than routine x-rays solely for clinical care purposes?

○ Yes ◉ No

10.0 Interventional

10.1 *Interventional, please specify:

- (•) Open Label
- ( ) Single Blind
- ( ) Double Blind
- ( ) Other

If Other, specify:

All participants seen at RU will receive the flu vaccination.

11.0 Objectives and Rationale

11.1 * Overview

Briefly state the ***purpose of this study***. Give enough background and rationale to provide both scientists and lay members of the IRB and ACCTS with the basis for exposing human subjects to the risks involved.

Metabolic syndrome is associated with a chronic inflammatory state that is thought to be determinant in the development of diabetes and cardiovascular events. Excess energy intake results in a hypertrophy of the adipose tissue that generates the production of pro-inflammatory molecules like TNF alpha, and IL-6, which turn on the immune response. This results in infiltration of immune cells like macrophages and natural-killer (NK) cells in the adipose tissue. As oppose to inflammation triggered by a pathogen, chronic inflammation or metaflammation induced in the context of excess nutrient intake does not resolve and directly leads to a decrease of insulin sensitivity. As energy imbalance persists and metabolic syndrome progresses, not only the adipose tissue, but also the liver, the pancreas, and the muscles are sites of inflammation and insulin resistance (**3**). The role of key immune molecules, such as pathogen sensors like toll-like receptors (TLR) in metabolic syndrome and obesity has been demonstrated by showing that their ablation in mice conferred protection against insulin resistance (**13**). Thus, classical pathways of inflammation used to activate the immune system in the context of an infection are primed in the context of metaflammation. This leads us to speculate that these pathways might be altered and less prone to react in the event of an infection (**3**).

To support our hypothesis, several studies have demonstrated that during the 2009 influenza H1N1 pandemic, obesity was associated with more severe infection and death (**6**, **14**). The mechanism is likely immune mediated but has not been determined yet (**15**). Also, it has been reported that obese people might be less protected by influenza vaccination (**7**). The area of systems biology has considerably contributed to a better understanding of vaccine efficacy (**10**, **16**). Gene expression studies using peripheral blood can predict vaccine response to influenza (**10**, **11**). High vaccine response correlates with the expression of interferon signaling (genes like STAT1, IRF9) and antigen processing and presentation. To test our hypothesis, we contacted the authors of a study published in Cell in 2014 (**12**) and obtained the BMI of the patients. The study demonstrated the ability to predict the influenza vaccine response using several parameters. We focused on the immune response based on antibody titers and the gene expression profile at D0 and D1. We separated the individuals in 2 groups: one group of lean (BMI<25) and one group overweight and obese (BMI>25). The two groups contained 25 and 17 individuals respectively. We observed a trend towards an inverse correlation of the immune response to influenza vaccine with increasing BMI. Also, we analyzed the differential gene expression profile between D0 and D1 between the two groups. JUN Kinase, Stat1 and IRF1 were among the most up-regulated genes in the lean group but not in the overweight and obese group. When comparing the two groups using ingenuity pathway analysis, the role of PKR in interferon response, Toll like receptor signaling, Natural killer cell signaling were more activated in the lean group compare to the overweight and obese group. These results indicated that the innate immune response induced by the vaccine might be attenuated in the overweight and obese group. BMI was the only factor used for this analysis and we did not have access to any metabolic marker. Obesity is not necessarily associated with an unhealthy metabolic status. Therefore, we would now like to focus on metabolic syndrome as it better correlate with an unhealthy metabolic status. Our aim is to determine if metabolic syndrome attenuates the immune protection induced by the vaccine and establish the molecular mechanism of antiviral immune deficiency associated with metabolic syndrome. We would like to know if differences between people with and without metabolic syndrome can be seen at the molecular level and correlate with differences in antibody titers. We believe our study will contribute to 1/ better understand vaccine efficacy 2/ establish if the low-grade chronic inflammation associated with metabolic syndrome impacts the systemic immunity against viral infection.

11.2 * Engaging Stakeholders: Describe any plans to engage other stakeholders (Scientists, practitioners, patients, advocacy groups, etc.) for hypothesis generation, or feasibility purposes.

The following staff at RU are engaged in the develoment of this study: Paul Cohen,MD; Jan Breslow, MD; Peter Holt,MD; Jose Aleman, MD, PhD, Taia Wang,MD; and Brad Rosenberg, MD.

11.3 * Hypothesis

Describe the ***research hypothesis*** in a single sentence.

We are hypothezing that immune dysregulation associated with obesity and metabolic syndrome affect the influenza vaccine immune response putting these populations at risk for a more severe infection outcome.

11.4 * Aim(s)

Indicate how you will ***address the hypothesis*** (e.g., to compare groups, to estimate a parameter, to ascertain feasibility). Since the sample size determination is usually based on the primary aim only, the primary aim should be sufficient to justify the study.

Antibody response post influenza vaccine will be compared between subjects with the metabolic syndrome and healthy lean controls

11.5 * Primary Outcome(s)

Indicate which ***variable(s)*** will be assessed to judge the primary specific aim. Give measurement units, if applicable.

Antibody titers and vaccine response (hemagglutin)

11.6 * Secondary Outcome(s)

Indicate which ***additional variable(s)*** will be assessed to judge the secondary outcome(s). Give measurement units, if applicable.

Gene expression profile
Cytokines
Chemokines

11.7 * Methods and Procedures

Please provide a description of the laboratory and clinical analyses and procedures that will be performed. Include the role of external collaborators and consultants when appropriate.

Participants will be seen at Rockefeller University as outpatients. There will be two (2) cohorts, namely those with the metabolic Syndrome who have not been treated and healthy volunteers.
The Metabolic Syndrome will be determined according to the NHLBI Guidelines.
SCREENING VISIT #1
Consent
Medical history
Physical examination including height and weight to determine BMI, and waist circumference
Vital Signs - If the initial blood pressure is above 150/90 mmHg upon arrival to the OPRC, a second B/P will be taken by the LIP during the screening process. The average of the two readings will be the enrollment criterion.
POCT - HIV
POCT - urine pregnancy test
Labs: HbA1c - (1) 3.0 ml lavender tube
Hepatitis Panel - (1) 8.5ml SST marble top tube
Comprehensive metabolic & CRP – (1) 8.5 ml SST marble top tube
CBC - 3 ml lavender top tube
Gene expression – (3) 2.5ml Pax RNA tube (total 7.5ml).
Influenza A & B antibodies – (1) 10ml red top tube
Total blood volume to be drawn for screening visit 1 = 40.5ml .
Instructions to return fasting for 8 hours prior to the next visit.
SCREENING VISIT #1-A
(for those participants who previously screen failed and are now eligible secondary to change in inclusion/exclusion criteria)
Re-consent (if necessary)
Repeat of all study requirements for screening visit #1.
SCREENING VISIT #2 (within 2 weeks of screening visit #1)
Adverse event assessment
Fasting Labs: Glucose, lipids and triglycerides) - (1) 3.5ml gold top tube

STUDY VISIT #1 (Day 0)((within 1 month of screening visit #2)(+/- 1 week)
Labs: venous blood sample for gene expression (3) 2.5ml Pax RNA tubes (total 7.5ml)
Cytokines (9ml for plasma (purple EDTA tube), 10 ml for serum (red top tube); ***labs drawn prior to flu vaccine)**

POCT - urine pregnancy test
Adverse event assessment
Administration of the influenza vaccine intramuscularly (IM): Vaccination with quadrivalent 2016-2017 vaccine A/California/7/2009 (H1N1); A/Hong Kong/4801/2014 (H3N2); B/Brisbane/60/2008(B/Victoria lineage); B/Phuket/3073/2013 (B/Yamagata lineage). Participants of normal weight will be injected IM with a needle of 1 to 1.5 in length. Obese individuals (defined as BMI>25) generally will require the use of a 2 in length needle to assure that the injection reaches the muscle. The needle length used for injection will be documented in the medical record.
Total blood volume to be drawn for visit #1 = 26.5ml
STUDY VISIT #2 (Day 1 with no window)
Labs: gene expression profile (blood volume = 7.5 ml)
Adverse event assessment
STUDY VISIT #3 (Day 7 (+/-1 day)
Labs: gene expression - (3) 2.5ml Pax RNA tubes (total 7.5ml)
Research Blood: Cytokines (9ml for plasma (purple EDTA tube), 10ml for serum (red top tube)
Total amount of blood drawn for visit #3 = 26.5ml
Adverse event assessment
STUDY VISIT #4 (Day 28 +/- 2 days)
Labs: gene expression - (3) 2.5ml Pax RNA tubes. (total 7.5ml)
Influenza A & B antibodies – (1) 10ml red top tube
Research Blood: Cytokines (9ml for plasma (purple EDTA tube), 10ml for serum (red top tube)
Total blood volume to be drawn for study visit #4 = 36.5ml)
Adverse event assessment
STUDY VISIT #5 (Telephone visit) (Day 60 +/- 7 days)
Adverse event assessment
STUDY VISIT #6 (Day 90 +/- 7 days)
Labs: gene expression (3) 2.5ml Pax RNA tubes. (total 7.5ml)
Influenza A & B antibodies – (1) 10ml red top tube
Research Blood: Cytokines (9ml for plasma (purple EDTA tube), 10ml for serum (red top tube)
Total blood volume for study visit #6 = 36.5ml
Adverse event assessment
Unscheduled Study Visits:
Study subjects may be asked to return to the RUH OPRC for additional bloodwork taken in the event of abnormal or missing labs.
RESEARCH LABS

Analyze blood sample and serum for evaluation of the immune response to influenza:
1/ Hemagglutination inhibition assay
Determine antibody titers against each strain of influenza included in the quadrivalent 2016-2017 vaccine: A/California/7/2009 (H1N1); A/Hong Kong/4801/2014 (H3N2); B/Brisbane/60/2008(B/Victoria lineage); B/Phuket/3073/2013 (B/Yamagata lineage) as described in similar studies (**10**, **11**).
Neutralization assay
Determine the presence of specific neutralizing antibodies to influenza viruses in human sera following the protocol described by the WHO.
http://www.who.int/influenza/gisrs_laboratory/2010_12_06_serological_diagnosis_of_influenza_by_microneutralization_assay.pdf
3/ RNA-seq analysis of the peripheral blood
RNA was obtained from peripheral blood using PAXgene RNA stabilization tubes places at -80C post collection. RNA purification Quality of the RNA was assessed using the Agilent Bioanalyzer from the Genomic resource center. RNA-seq analysis will be performed by the Genomic resource center Illumina HiSeq 2500 Sequencing (50bp Single Read Sequencing).
Approximately 180 ml of blood (12 Tbsps.) will be obtained from each participant in the study.
Study participants whom are determined to have the metabolic syndrome will be referred to their primary care physician for treatment or will be referred to a healthcare clinic by the RUH social worker for treatment.
Stasi Lubansky, DNP, ANP, will refer potential participants to Dr. Andreo for possible entrance into this study.

11.8 * Data Analysis

Describe method(s) of data analysis. Include the role of external collaborators as appropriate.

As per recommended by the food and drug administration (17), the hemagglutination inhibition (HI) antibody assay has been used to assess vaccine activity and may be appropriate for the evaluation of the pandemic influenza vaccine. Appropriate endpoints may include: 1) the percentage of subjects achieving an HI antibody titer ≥ 1:40, and 2) rates of seroconversion, defined as the percentage of subjects with either a pre-vaccination HI titer < 1:10 and a post vaccination HI titer > 1:40 or a pre-vaccination HI titer ≥ 1:10 and a minimum four-fold rise in post-vaccination HI antibody titer. Previous study have built models using both HAI and neutralization assays to determine vaccine responsiveness.

The RNA-seq analysis will be run with the help of the Genome resource center as well as the expertise of Brad Rosenberg listed as a collaborator of this project.

11.9 * Explain the rationale for the choice of statistical measures and the number of subjects proposed for the study, including the power calculations when applicable.

Since no preliminary data is available to estimate the percentage of participants achieving a determined level for the HI antibody titer and the rate of seroconversion for each group (healthy volunteers and metabolic syndrome participants) we provide an estimation of the minimum effect size for the sample size selected is able to detect. For a sample size of 40 participants, 20 at each group, a 95% significant Chi-square test will be able to detect an effect size equal or larger than 0.56 with 0.8 power. It means that a Chi-square test will be able to detect independence between groups if the distance between the observed odd ratio is larger than 1.56.
Statistical Analysis
To compare the means of antibody titers between groups (healthy volunteers and metabolic syndrome participants) a t-test at 95% significance level will be performed if the data follows a normal distribution, otherwise a non parametric Wilcoxon-Mann-Whitney test will be used.
A Chi-square test at 95% significance level will be used for the comparison of percentage of participants achieving a determined level for the HI antibody titer and rates of seroconversion. On that case if any observed frequency is smaller than 5 Fisher exact test will be used instead of Chi-square.
Expression values will be modeled using mixed-effect models, with group as fixed factor, and a random effect for each participant. FCHs for the comparisons will be estimated, and hypothesis testing conducted.

11.10 * Will samples be coded?

(•) Yes ( ) No

If Yes, Please describe coding scheme consistent with GCP. If samples will not be coded, please provide justification for this proposed departure from GCP practice.

Samples will be coded utilizing the IRB number of the study, followed by the cohort (M= metabolic H= healthy control) and a sequential 3 digit number that contains no identifiers. For example:
UAN-xxxx-M- 001, UAN-xxxx-M-002, etc.
UAN-xxxx-H- 001, UAN-xxxx-H-002, etc.

12.0 Subjects of Study

12.1 Specify age range of subjects:

* Minimum Age:
18
Maximum Age:
65
Please note: If age of subjects indicated is less than 18 years old, you will be prompted to attach a Pediatric Assent form later on in the submission process. A link to the Pediatric Assent form can be found in the Help link to the right, or this form can be downloaded later on in the submission process.

12.2 * Indicate the gender(s) of the subjects:

☑ Female

☑ Male

12.3 * Indicate projected enrollment by race and ethnicity. See Help for disease/volunteer population demographics.

Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	6	5	11
Not Hispanic or Latino	15	14	29
Ethnic Category: Total of All Subjects*	21	19	40
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	7	14
White	11	10	21
Racial Categories: Total of All Subjects*	21	19	40

12.4 * Will subjects of a specific racial/ethnic group be excluded from participation?

○ Yes ◉ No

If Yes, please specify:

☐ Caucasian
☐ African-American
☐ Hispanic
☐ Asian
☐ Other

Reason for the exclusion:

○ The condition being studied does not occur in the selected group(s)
○ Other

If Other, please specify:

12.5 Gender/Minority Exclusion Justification

All research involving human subjects should be designed and conducted to include members of both genders and members of minority groups, unless a rationale and justification is provided. Please provide such justification below:

12.6 Vulnerable Populations

Indicate whether any of the following populations will be included in the study:

☐ Children
☐ Pregnant Women
☐ Cognitively Impaired Persons
☑ RU Employees
☑ RU Students
☐ Fetal Tissue or Embryonic Stem Cells
☐ Induced Pluripotent Stem Cells
☐ Other:

If you checked any of the above, give a brief explanation of the need to use these particular individuals:

Special precautions will be used in recruiting employees of the Rockefeller University to minimize the possibility of undue influence. Rockefeller University employees will be made aware of the study through flyers rather than directed presentation to selected groups. Subjects will be reassured that refusal to participate in the study will not affect their studies or employment in any way

If the subject is a Rockefeller University employee, does she/he work within the Laboratory of the Principal Investigator or Co-Investigator(s)?

- (•) Yes
- ( ) No
- ( ) N/A

If the subject is a Rockefeller University student, does she/he work within the Laboratory of the Principal Investigator or Co-Investigator(s)?

- (•) Yes
- ( ) No
- ( ) N/A

12.7 ***What is the total number of evaluable participants you plan to enroll at Rockefeller University Hospital over the course of the entire study?**

40

12.8 ***** **What is the total number of participants who will need to sign consent *at Rockefeller University Hospital over the course of the entire study* to result in the desired number of evaluable subjects?**

100

12.9 ***** **What is the total number of participants you plan to sign consent *at Rockefeller University Hospital in the next year?***

100

12.10 ***** **What will be the total number of evaluable participants *at all sites over the course of the entire study?***

40

12.11 Inclusion Criteria

Please list subject inclusion criteria:

Order Number	Criteria
1	**METABOLIC SYMDROME COHORT** Any evidence of NHLBI Guidelines for Clinical Identification of the Metabolic Syndrome: (must have 3 or more of the following risk factors): Abdominal Obesity, given as a waist circumference: - Men >102 cm (>40 in) - Women > 88 cm (>35 in) Triglycerides ≥150 mg/dl HDL Cholesterol: - Men < 40 mg/dl - Women <50 mg/dl Blood Pressure ≥130/ ≥85 mm Hg or on antihypertensive medication Fasting Glucose ≥ 100 mg/dl
2	**HEALTHY CONTROLS** BMI 18.5 - 25 kg/m^2 HDL female > 50 mg/dL, male > 40 mg/dL fasting glucose < 100 mg/dL triglycerides <150 mg/dL, waist circumference of a female < 88 cm, male < 102 cm) Blood pressure ≤ 120/80 May be on antihypertensive medication

12.12 Exclusion Criteria

Please list subject exclusion criteria:

Order Number	Criteria
1	Currently undergoing treatment for the metabolic syndrome
2	Blood Pressure > 150/90

3	NSAIDs and/or Aspirin ingestion within the last 14 days
4	Hepatitis A, B and C
4	Self-reported history of any active autoimmune diseases
5	Self-reported ingestion of statins within the last 3 months
6	Self-reported antibiotic use within the last 3 months
7	Anti-inflammatories including biologics and corticosteroids within last 3 months(nasal spray and topical applications are OK)or Omega 3 Fatty Acids.
8	Self-reported hx of cancer treatment within the last year
9	Allergy to eggs
10	History of Guillain-Barre syndrome
11	Pregnant (determined by POCT at Screening visit #1 and Study visit #1).
12	HIV positive
13	Self-reported history of receiving the flu vaccination after June 1, 2016.
14	Any self-reported infection in the week of the visit except the first two visits (Screening visit 1 and Screening visit 2) and the last visit (Study visit #5) that could be rescheduled.
15	Any medical, psychological or social condition that, in the opinion of the Investigator, would jeopardize the health or well-being of the participant during any study procedures or the integrity of the data.

13.0 Study Plan

13.1 * Describe the study plan:

Select a template: Template 1 ▼ Select an arm: Screening Visits ▼

Procedure/Task Name	CPT Code	Screening ...	Screening ...
Clinical Procedures			
Adverse Event Assessment			
Adverse Event /Serious Adverse Event Assessment			1
Assessments (Nursing)			
Assess for changes in general health status			1
Blood Pressure Seated		1	
Concomitant Medications			

*** What is the total number of outpatient visits for all subjects projected for the next year?**

240

*** What is the average length of each outpatient visit (in hours)?**

2

*** What is the total number of Day Patients visits for all subjects projected for the next year?**

0

*** What is the average length of each Day Patient visit (in hours)?**

0

*** What is the total number of inpatient days for all subjects projected for the next year?**

0

13.2 *Number of Patients per arm

Study Arm	Number of Patients
Healthy Controls	20
Test Cohort	20

Test Cohort	20

14.0 Study Drugs

14.1 * List all the medications, study drugs, biological agents, solutions and supplements needed to conduct the study:

See Help for link to Rockefeller University Research Pharmacy web page for additional information.

View Details	Drug Name		FDA Approved	IND Number
⊟	**Trade Drug Name:**	Fluarix Quadrivalent		
	Generic Drug Name:	Influenza Vaccine	Yes	
	Investigational Drug Name:			

Trade Drug Name:	Fluarix Quadrivalent
Generic Drug Name:	Influenza Vaccine
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	GlaxoSmithKline
Is the Drug FDA Approved:	Yes
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose Range:	0.5mL prefilled syringe

View Details	Drug Name		FDA Approved	IND Number
⊟	**Trade Drug Name:**	Fluzone Quadrivalent		
	Generic Drug Name:	Influenza Vaccine	Yes	
	Investigational Drug Name:			

Trade Drug Name:	Fluzone Quadrivalent
Generic Drug Name:	Influenza Vaccine
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	Sanofi Pasteur
Is the Drug FDA Approved:	Yes
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose Range:	0.5mL prefilled syringe

14.2 * Will the study involve the use of a placebo?

○ Yes ◉ No

If yes, complete A and B.

A. Is there a proven effective therapy for the condition under study?

○ Yes ○ No

If Yes, please specify:

B. Please give a justification for the use of the placebo.

15.0 Consent Procedure

15.1 * This study will use the following types of informed consent:

- [ ] Informed Consent Form Standard - a standard consent form with instructions for adapting it to your study
- [ ] Consent Form Genetic- a consent form designed for a study where genetic testing (as defined by NYS law) is to be done in the CURRENT study
- [x] Consent for studies including genome wide sequencing
- [ ] Pediatric Assent Form (To be used in addition to Consent) for Pediatric patients
- [ ] Other (e.g., waivers)

Links to the **Standard Consent**, **Genetic Testing Consent** and the **Pediatric Assent** forms can be found in the Help link to the right, or these forms can be downloaded later on in the submission process.

15.2 * Indicate the consent process to be used.
(See Help for CCTS SOP)

Describe how the required information is being presented to subjects (consent form, orally, information sheet, etc.). Attach a copy of what is being presented to subjects (usually the ICF and Assent forms).

Prior to the initiation of any study related procedures, the potential participants will be given a copy of the most recent IRB stamped and approved informed consent to read. Additionally, the PI or study staff member who has been designated to consent will discuss the specifics of the study including but not limited to the purpose of the research, procedures, time commitment, required tasks, test article or device, alternative treatments, benefits, risks, confidentiality etc. in a comprehensible (non-scientific) manner, using language readily understandable by the participant. Participants will be told that participation is voluntary and that, if they do not consent, they will not be penalized. The person consenting will assure the voluntariness of the participant.

Describe the circumstances under which consent will be obtained, where the process will take place and any waiting period between informing the prospective participant and obtaining consent.

A private, confidential setting will be provided for the potential participant to read and discuss the informed consent free from coercion, undue influence or constraints of time. All participants will be given a chance to ask questions and express concerns. They will be given the option to take the consent home and discuss it with family, friends, and /or health care providers. After a participant and the person conducting the consenting signs and dates the consent, the participant will be given a copy of the signed informed consent form.
An enrollment note will be written in the source document as to who obtained consent, how, when, were questions asked and answered, and that a copy of the informed consent was given to the participant.

Describe the experience of the investigators designated for this task in the DOA in obtaining consent from subjects.

The following staff, J. Walker, K. Dowd and D. Brassil have extensive experience consenting human participants for participation in research studies.
Ursula Andreo will undergo consent form training. This competency is based on attending a consenting class which includes regulations, the do’s and don’ts and didactic role playing. It also includes observing the consenting process as performed by an experienced consenter and then consenting a participant to participate in a research study while being observed by the experienced consenter.

How will it be determined that the subjects or the subjects' authorized representatives understand the information presented?

The "Teach Back" method will be used in the clinical research setting to ask research participants to repeat or “teach back” the information, concepts and directions that the staff member has attempted to convey to the participant. This method is used to assess comprehension and retention of protocol requirements, adverse event information, risks and benefits, and the participant's rights described in the Informed Consent process.

If English is not the subjects' native language, how will written and/or verbal translation be provided?

For unexpected or isolated participants who are candidates for this study, but for whom English is not a primary language, a translator provided through Pacific Interpreters will be used to facilitate the explanation of the study.

Will any subjects be cognitively impaired so that they may not have the capacity to give consent?

- ( ) Yes
- (•) No

If yes, Describe the procedures to be used to determine the individual subject's capacity to provide consent.

For subjects where it has been determined that they lack the capacity to give consent, describe the provisions for obtaining consent from the subjects' legally authorized representative.

NA

15.3 * Based on the demographics, will this study's subject population require foreign language consent form?

- ( ) Yes
- (•) No

If Yes, please list the language(s):

15.4 * This study's consent procedure will require the following waivers:
(See Help for additional information.)

- ( ) Waiver of one or more elements of informed consent, 45CFR46.116(d)
- ( ) Waiver of documentation of informed consent, 45CFR46.117(c)
- (•) No waiver is requested

If a waiver is requested, please explain:

15.5 * Does this study include videotaping, photography or other electronic recording of human subjects?

○ Yes ◉ No

If Yes, please specify:

16.0 Recruitment and Advertising

For assistance consult CRSO to create a robust Recruitment Plan see Help.

16.1 * What is the plan for recruitment?

Overview:
The CRROSS will prescreen up to 100 volunteers in order to enroll 20 with a metabolic syndrome and 20 healthy controls to achieve the goal of 40 evaluable participants at study completion. Healthy controls will be age matched (+/-5 years) and gender matched to the metabolic syndrome participants.
Feasibility and Assessment:
Incentives: 1) Compensation for efforts; 2) Altruism; 3) Free FDA-approved flu vaccine **Challenges:** 1) Many individuals do not self-identify as having metabolic syndrome (may not know diagnosis); 2) Multiple visits within the first week; 3) Lengthy gap between 5th and 6th visit, which may result in attrition, 4) Participants must have untreated metabolic syndrome.
Issues relevant to rapid accrual: *Availability of the target population*: A previous study that recruited a similar population (JWA-0786) required prescreening 325 individuals for the investigator to enroll 28 participants across the span of 2 years. The age upper limit of the current study, age 50, limits the eligible population. A NHLBI publication of prevalence by age group of metabolic syndrome of participants in the HUNT2 study suggests that the eligible population will increase (+30% for men, +40% for women) by including the 50-59 year old age group. A feasibility query of the Research Participant Repository reveals 17 potentially eligible volunteers of age 18-50, as well as an additional 22 potentially eligible volunteers aged 51-59. These volunteers are predominantly male due to restrictions of prior studies. *Study burdens*: Another study (TWA-0804) enrolled healthy volunteers to receive FDA-approved vaccines, with a similar duration and shorter between-visit follow-up period; that study enrolled 86 on-study of whom 15 dropped out before the 3 month final visit. *Time Constraints:* Due to vaccination and multiple visits in the first few days, Day 0 visits cannot occur on Fridays. Also, the flu season is limited; interest in the flu vaccine will likely wane by March so the enrollment window is brief.
Projected enrollment timeline: Recruitment initiation will begin as soon the study receives IRB approval, likely in the first or second week of November. The investigator's target of completing accrual by April 2016, which would allow for 5-6 months achieving complete study enrollment. This would require the enrollment of 10 participants (5 metabolic syndrome and 5 age matched controls) per month. The study requires 2 screening visits (1 week start-up lag). The enrollment timeline is ambitious, even assuming a steady flow of participants and likely only feasible using the Repository population and potentially expanding the age range. Based on previous recruitment experience of this population, CRROSS would predict 12- 15 months for study accrual, however given ResearchMatch and Repository resources, 6 months is ambitiously feasible.
Recruitment Implementation:
Advertising development and placement- CRROSS will develop and send out the IRB approved campus email to recruit individuals on campus. Internet outlets will include craigslist.com, centerwatch.com, rucares.org, researchmatch.org, and others as appropriately identified. **Local newspapers**-advertisements may be placed in local newspapers (i.e., Metro). **Centralized Call Management** – CRROSS will work with the research team to develop a protocol-specific pre-screening script based on IRB approved protocol eligibility criteria to prescreen volunteers who call 1800RUCARES. Potentially eligible candidates will be passed onto the study team for further screening. CRROSS staff will also call volunteers based on Repository queries described above. Research teams are responsible to provide timely updates on pre/screening outcomes (through iRIS, etc.) to keep CRROSS strategies on target. **Research Volunteer Repository Database** – The investigator has agreed to associate protocol UAN-[REDACTED]48, the Research Volunteer Repository Protocol, enabling the CRSO to query the existing volunteer database to identify a list of potential volunteers who have agreed to be contacted for future studies and who meet basic eligibility criteria. The CRROSS will contact potential volunteer as allowed to determine interest and will refer eligible and interested volunteers to the study coordinator/investigator. In parallel, the research team will seek and document the granting or denial of permission to contact volunteers about future studies.
Compensation plan:
Total compensation: $300

Screening Visit 2	Visit 1	Visit 2	Visit 3	Visit 4	Visit 6
$20	$40	$50	$50	$60	$80

Unscheduled Study Visits:
- Additional study visits will be compensated $25 per visit for bloodwork taken in the event of abnormal or missing labs.

16.2 *From the date of final IRB approval, how long will it take to complete enrollment of the study?

◉ 6 Months
○ 12 Months
○ 18 Months
○ 24 Months
○ More than 2 years (specify in years)

16.3 This Study

◉ Involves an intervention or comparison and a defined enrollment target
○ Is a natural history study with expected annual enrollment over many years
○ Is an exploratory mechanistic study
○ Other

16.4 This Study will enroll:

○ Healthy volunteers
○ Individuals affected with a specific disease/disorder

Individuals affected with a specific disease/disorder

Both

16.5 * Do you plan on using the Research Participant Repository (RKO-0648) ?

Yes No

16.6 * Are you screening or recruiting from or through a record review of an existing patient database of a healthcare provider?

Yes No

16.7 * Please describe how the Recruitment Plan addresses recruitment of the volunteers consistent with the demographics of the condition under study:

CRROSS staff will recruit participants to match the racial and ethnic diversity of this study population. The demographics of the RKO-0648 repository have been consistently similar (2009-2013) to the demographics reported in the NYC 2010 census. Through our plan to utilize our call management service and query the RKO-648 repository, we anticipate being able to enroll participants who match the disease demographics projected in the application.

16.8 * Do you plan to advertise directly to potential volunteers? (As opposed to relying on practitioner referrals or flyers to practitioners)

Yes No

16.9 * Do you plan to use the free, web-based volunteer registry, ResearchMatch.org, as a recruitment tool?

Yes No

17.0 Research Participant Repository (RKO-0648)

17.1 This protocol, will be linked with the Research Volunteer Screening/Recruitment Data Repository run by the Recruitment staff and the Clinical Research Support Office (protocol RKO-0648-1008).

In order to participate in the generation of the Repository the PI will enter into a Collector/Collaborator agreement regarding the Repository. The role of Collector/Collaborator is to contribute to the Repository the name, contact and demographic information, recruitment referral information, and screening outcome information, as well as appropriate protocol specific screening information, of volunteers who are screened by telephone or in person for entry into the protocol regardless of the screening outcome. In addition to screening volunteers for the PI's current study, verbal consent will be obtained from the volunteers regarding their willingness to be contacted in the future about possible additional research studies. This permission may be obtained by the Recruitment office staff through the central Call Center. If the PI receives calls directly from participants for initial prescreening, then the PI is responsible for collecting the required information and conveying it to the Recruitment staff for data entry. The consent or withholding of permission will be recorded in the Repository as will the name of the person who obtained the permission. A volunteer's permission or declination will not affect their eligibility for my current protocol, or future protocols. The Recruitment staff of the Clinical Research Support Office may gather the Repository information and request the verbal consent of the volunteer for re-contacting on my behalf as part of our recruitment plan.

In order to benefit from the Repository, the PI will enter into a Recipient/Collaborator agreement with the Repository. The Recipient/Collaborator may receive from the Repository pre-screened lists of potentially eligible subjects for his/her study as a means to facilitate recruitment. The Recruitment staff will prepare the Repository queries according to the protocol eligibility requirements and available Repository information, and may re-affirm permission to re-contact volunteers as necessary. The PI may use the information and names in the list from the Repository only for the current study and may not save the list to use for a future study of his/her own, nor may he/she share the list with colleagues for other studies."

18.0 Utilization of ResearchMatch.org

18.1 Utilization of ResearchMatch.org for Recruitment

Basic information regarding this tool:

- **ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University. There is no cost for researchers at participating institutions in the ResearchMatch.org Network to use ResearchMatch.org. The Vanderbilt IRB provides oversight for ResearchMatch.org as a recruitment tool and this has been documented within the ResearchMatch.org IRB Letter of Understanding which was executed by Dr. Gotschlich in October, 2009. However, individual requests to use ResearchMatch.org as a recruitment tool must be submitted to this institutions' IRB.**

Registration:

- **This recruitment tool may be utilized once the PI or research staff registers for recruitment access through ResearchMatch.org and the Institutional Liaison provides approval.**
- **The ResearchMatch.org Institutional Liaison will review the study information and evidence of IRB approval. He/she will set the researcher's expiration date to mirror that of the study's IRB approval.**

Search Capability:

- **After being granted recruitment access, the researcher can search for appropriate matches amongst the non-identifiable ResearchMatch.org Volunteer profiles in the system. He/she can enter study inclusion/exclusion criteria in the ResearchMatch.org Search Builder which will yield a list of potential matches to the study's criteria.**

Contacting ResearchMatch.org Volunteers:

- **Once yielding a list of potential matches (ResearchMatch.org Volunteers), the researcher will send out IRB-approved content that will be the initial recruitment message that these volunteers receive about the study through ResearchMatch.org. The study's recruitment message will be inserted into the standard ResearchMatch.org electronic notification that informs possible matched Volunteers that he/she has been identified as a potential match for the study. The secure ResearchMatch.org clearinghouse will route this standard ResearchMatch.org email notification. These potential matching volunteers will have the option of replying yes, no, or not respond through a set of quick links available in this notification to the study announcement. THE CONTACT MESSAGE WILL NOT INCLUDE THE STUDY'S DIRECT CONTACT INFORMATION (e.g. EMAIL, PHONE). By responding yes, the Volunteer has authorized ResearchMatch.org to release his/her contact information to the researcher. The researcher will be responsible for managing this contact information as called for by this IRB-approved study protocol.**

Study Management in ResearchMatch.org:

- **Researchers (and the Liaison) can view information regarding his/her study's status in ResearchMatch.org (e.g. number of volunteers contacted for the study via ResearchMatch.org to date, response rate of volunteers, etc.). ResearchMatch.org will also be collecting aggregate data regarding the status of ResearchMatch.org volunteers within the study. Volunteers consent to this within the ResearchMatch.org Volunteer Agreement. This information will allow the researcher to indicate where the Volunteer currently stands within the recruitment process and thus will help the researcher monitor the utility and effectiveness of using this resource (e.g. Did not contact, Not eligible, Enrolled, Completed, etc.).**

19.0 Potential Benefits to Subjects

19.1 * **Will participation in this study provide direct benefits to the subject?**

(•) Yes ( ) No

19.2 If Yes, describe the potential direct benefits:

Volunteers will receive without cost an FDA-approved vaccine.

20.0 Potential Risks to Subjects

20.1 * **Describe any potential risks: physical, psychological, social, legal or other and assess their likelihood and seriousness. Indicate risks both to the subjects and to the embryo or fetus if the subject is or may become pregnant. Please provide the potential risks below:**

Influenza Vaccine (IM administration):
- Most common (≥10%) injection-site reactions were injection site tenderness, pain, swelling and arm stiffness.
- Most common (≥10%) systemic adverse events were headache and myalgia.
- Life-threatening allergic reactions from vaccines are very rare. If they do occur, it is usually within a few minutes to a few hours after the shot.
- In 1976, a type of inactivated influenza (swine flu) vaccine was associated with Guillain-Barré Syndrome (GBS). Since then, flu vaccines have not been clearly linked to GBS. However, if there is a risk of GBS from current flu vaccines, it would be no more than 1 or 2 cases per million people vaccinated. This is much lower than the risk of severe influenza, which can be prevented by vaccination.

Potential risks associated with venipuncture include discomfort or pain, ecchymosis, bleeding, phlebitis and infection at the needle insertion site. Additional risks include lightheadedness and a vasovagal response.
Psychological affect of MetS diagnosis although this will be presented as a positve to be aware and to make healthy life style changes .

21.0 Procedures to Minimize Risks

21.1 * **Describe the procedures for protecting against or minimizing any potential risks, and include an assessment of their likely effectiveness. Include a discussion of confidentiality safeguards, where relevant, and arrangements for providing medical treatment, if needed.**

Study volunteers will be monitored for a minimum of 20 minutes after receiving their vaccination
All blood will be drawn by trained professionals using sterile technique
The influenza vaccine will be administered by an RN or LIP.
Persons with allergy to eggs will be excluded from the study
Persons with a history of Guillian-Barre' syndrome will be excluded from the study.

22.0 Alternative Methods or Treatments

22.1 * **Describe alternative methods or treatments for the disease(s) under study, if any, that were considered and why they will not be used:**

they will not be used:

The study participant can obtain an influenza vaccine from other sources, such as from their PCP, pharmacies, clinics.

23.0 Data and Safety Monitoring

This section describes the Data and Safety Monitoring Plan (DSMP) required of each protocol undertaken at the CCTS according to HRPP and NIH policies Notice 98 -084 and Notice 00-038, as cited in Help Sections below. Depending on the level or risk and trial phase, some protocols will need Data and Safety Monitoring Boards.

23.1 * Overall Risk Classification

An estimate of risk is necessary to evaluate the adequacy of the planned monitoring. The HELP section provides guidance in making the risk assessment.

Read the risk definitions and examples of risk in the HELP section and select the risk category that best describes the current study.

If your assessment differs from the definitions the HELP section, describe any factors that modify your judgment of the overall risk in the text box after the risk designation.

- ○ MINIMAL RISK
- ○ LOW RISK
- ◉ MODERATE RISK
- ○ SIGNIFICANT RISK

Please provide any optional description(s):

23.2 Protocols Involving Minors

The chance of direct benefit to the child, or to understanding a disorder not otherwise understood, may be major factors in justifying more than minimal risk in research involving children.

Based on the above definitions, please specify your study's risk classification below:

- ○ NOT GREATER THAN MINIMAL RISK (the risk of daily life to a healthy child living in a safe environment) 45 CFR 46.404
- ○ GREATER THAN MINIMAL RISK WITH DIRECT BENEFIT TO SUBJECT; 45 CFR 46.405
- ○ GREATER THAN MINIMAL RISK, NO DIRECT BENEFIT, BUT BENEFIT TO UNDERSTANDING OF SUBJECT'S DISORDER; 45 CFR 46.406
- ○ RESEARCH NOT OTHERWISE APPROVED PRESENTING OPPORTUNITY TO UNDERSTAND, PREVENT OR ALLEVIATE SERIOUS PROBLEM AFFECTING CHILDREN 45 CFR 46.407 (cannot be approved by IRB; requires public comment)

23.3 DSMB

1. The NIH requires that all SIGNIFICANT RISK protocols have a **Data and Safety Monitoring Board** and provide information about the expertise and independence of that Board
2. Phase III trials require a Data and Safety Monitoring Board,
3. A DSMB may be appropriate for some Phase I and II protocols. (See Help for examples.)
4. It is the investigator's responsibility to report to the IRB, the findings and recommendations of the DSMB as they become available.

Please specify:

- ○ A DSMB is required for this study
- ◉ A DSMB is not required for this study
- ○ Unsure

If a DSMB is required, please indicate why:

- ☐ Significant Risk
- ☐ Study Design - Phase III
- ☐ Study Design - Placebo Controlled
- ☐ Study Design - Multicenter Trial
- ☐ Study Design - Other Factor

If other factor, please specify:

If other factor, please specify:

If a DSMB is required, select one:

- ○ An independent DSMB has been constituted; the members, mission charter, schedule for meetings, and a listing of the data to be reviewed by the DSMB will be attached.
- ○ A DSMB has not yet been constituted; the PI will consult the IRB and/or CRSO for assistance in assembling a DSMB.

If a DSMB is not required, but is being constituted for other reasons, please explain:

23.4 * Safety Review

Select one:

- ◉ Safety Review is conducted as follows: Laboratory results for research volunteers will be reviewed in a timely manner, usually within 24 hours of receipt by a licensed practitioner. The potential clinical significance of any abnormal finding will be documented in the medical and research record(s), and an appropriate plan or referral developed. The PI's review of safety issues at research team rounds will be documented in the meeting minutes.
- ○ Protocol Specific

If Protocol Specific, please describe safety review for protocol tests and procedures that require other than routine review. For example, an EKG taken to detect emerging conduction problems might require immediate safety review.

23.5 Monitoring

Monitoring Personnel: See Help Bubble to the right.

Internal Monitoring

The PI or his/her designee shall conduct internal monitoring to assure the safe and proper conduct of the protocol and all the elements list above in monitoring, following the general principles of quality management. The intensity and frequency of internal monitoring will depend on the protocol risk to subjects, the experience of the PI and research team, rate of enrollment, and specific details of the protocol.

Internal monitoring of informed consent and eligibility documentation will be conducted by the research team shortly after enrollment begins. Internal monitoring activities will be documented by logs, meeting minutes or other systematic means.

Specify the research team members who will conduct the internal monitoring of the study (see Help for who may monitor):

U. Andreo, K. Dowd

For new investigators: Internal monitoring should be conducted at least monthly by new investigators until there are essentially no findings to correct at each review.

External Monitoring

* Is external monitoring planned for this protocol?

- ◉ Yes
- ○ No
- ○ Unsure

If external monitoring is planned, please specify (see Help for who may monitor):

- ○ (Significant Risk) External monitoring will occur at least every six weeks unless there is no enrollment
- ◉ (Moderate Risk) External monitoring will occur at least quarterly
- ○ (Low or Minimal Risk) External monitoring will occur at least annually

If external monitoring is planned, please specify the name of the monitor:

CRSO will determine the monitor for this study

- ☑ Note that copies of external monitoring reports must be supplied to the IRB and the CRSO as soon as they are made available

Additionally, audits of the research records of minimal, moderate or significant-risk protocols may be performed by the CRSO staff on a random basis or as part of a prospectively identified auditing plan.

23.6 Adverse Event Classification

Adverse events are classified by definition, severity, and association with the investigational trial.

Definition of an Adverse Event
Any unfavorable or unintended sign (including abnormal lab findings), symptom or disease temporally associated with the use of a medical treatment or procedure, or protocol, regardless of whether it is considered related to the medical treatment or procedure or protocol.

Definition of a Serious Adverse Event
Any unanticipated event that involves the following:
- o results in death
- o is life-threatening
- o requires hospitalization or prolongs existing hospitalization
- o results in persistent or significant disability/incapacity

o is any medical event which requires treatment to prevent one of the outcomes listed above
Other events can be classified as "serious adverse events" at the discretion of the PI.

Definition of Anticipated/Expected Adverse Event

Any adverse event, which has been reported in the Investigator's Brochure, package insert, safety reports, clinical protocol, consent form or listed in the NCI agent-specific Expected Adverse Event List[3], is classified as an expected adverse event. The investigator must provide the available data of known adverse events and toxicities that have been associated with the study drug, device, intervention, or procedures. This information helps to define the level of risk of the trial and enables safety monitoring. A minimal risk trial may not have any defined risks and a statement to that effect is sufficient to meet the DSMP requirements.

Definition of an Unanticipated/Unexpected Adverse Event
Any adverse event that is not consistent with the known, predicted possible effects of the research protocol. An unexpected adverse event varies in nature, intensity or frequency from information on the investigational product provided in the Investigator's Brochure, package insert, safety reports, clinical protocol, or listed in the consent form.

Definition of an Unanticipated Problem (UaP)
A UaP is an event or circumstance that meets all the following three criteria: [1] the nature, severity, frequency of the event(s) or information was not expected in the descriptions in the study documents or the characteristics of the subject population being studied; [2] there is a reasonable possibility that the procedures involved in the research caused or are linked in a significant way to the problem; [3]the event or information suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized (including physical, psychological, economic, or social harm.

Grade and Relatedness of Adverse Events:

Adverse Events are graded for severity and scored for relatedness to the protocol, according to a published scale. Several standardized AE Reporting scales are available. (See Help for links to these scales.)

* Please indicate the scale you intend to use:

- ○ CTC v2.0 (http://ctep.info.nih.gov/reporting/ctc.html)
- ○ CTCAE v3.0 (http://ctep.info.nih.gov/protocolDevelopment/electronic_applications/docs/ctcaev3.pdf)
- ◉ CTCAE v4.0 (http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf)
- ○ AIDS Clinical Trials Group (http://aactg.s-3.com/)
- ○ Other

If Other, please specify:

23.7 Reporting Adverse Events

All AEs will be reported to the IRB at least annually.

Reporting Serious AEs

☑ Serious Adverse Events, (SAEs) will be reported to the IRB according to policy, within two working days of identification of the SAE.

Select all that apply:

☐ SAEs will be reported to the Sponsor and or ESCROW

SAEs will be reported to the sponsor within how many days of the event?

☐ SAEs will be reported directly to the FDA, per 21 CFR 312

SAEs must be reported directly to the FDA within 7 days of the event by the investigator/sponsor.

☐ SAEs will be reported to another entity

Describe:

Reporting Unanticipated AEs:

Select all that apply:

☑ UAEs will be reported to the IRB

UAEs that are related and greater than moderate severity must be reported to the IRB according to policy, within two working days of identification of the UAE.

☐ UAEs will be reported to the Sponsor

UAE will be reported to the sponsor within how many days of the event?

☐ UAEs will be reported to the FDA, per 21 CRF 312

UAEs will be reported to the FDA, per 21 CRF 312, within 15 days.

☐ UAEs will be reported to another entity

Describe:

23.8 Reporting Unanticipated Problems

☑ Unanticipated problems involving risks to subjects or others severe will be reported to the IRB and the CRSO within five working days.

23.9 CLIA/CLEP

Only laboratory and research tests that are CLIA/CLEP certified or waived may be used to determine eligibility, shared with research volunteers, and used in clinical decision making.

Select if applicable:

☑ This study includes tests that are not CLIA/CLEP certified; the results of such tests will not be used in clinical decision making, or to determine eligibility, or shared with subjects or their health care providers.

23.10 Tissue Repository

Human Tissue and Data Repositories collect, store, and distribute human tissue materials and or data for research purposes. Repository activities involve three components: (i) the collectors of tissue samples\data; (ii) the repository storage and data management center; and (iii) the recipient investigators.

* Select one:

◉ I DO NOT intend to collect, store, and distribute human tissue materials for research purposes

○ I DO intend to collect, store, and distribute human tissue materials for research purposes, therefore this protocol entails the Operation of a Tissue Repository. The IRB requires that the protocol specify the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

If you do intend to collect, store, and distribute human tissue materials, you will be asked to upload the following documents later on in the submission:

- A Sample collection protocol (for tissue collector collaborators to follow) and informed consent document for distribution to tissue collectors and their local IRBs.
- A Certificate of Confidentiality (to protect confidentiality of repository specimens and data).
- A Recipients Agreement describing the commitment of the recipient to preserve the anonymity of the samples shared.

24.0 Toxicity Management and Stopping Rules

24.1 * Describe any drug toxicity or other conditions under which the participation of a subject or the conduct of the study would be stopped in order to maximize safety (e.g., toxicity management and stopping rules):

A severe allergic reaction to the Flu vaccine.

*** Indicate withdrawal criteria and procedures below:**

Volunteers may be involuntarily withdrawn from this study if they experience a signficant adverse event.

25.0 Compensation/Costs

25.1 *Will any compensation be offered to participants in return for their participation, e.g., direct payment, medical care, tests, etc.?

○ No

◉ Yes (Please describe)

Participants will be compensated as follows:
Screening visit 1 - No compensation
Screening visit 2 - $20
Study visit 1 - $40
Study Visit 2 - $50

Study Visit 3 - $50
Study Visit 4 - $60
Study Visit 5 (telephone visit) - No compensation
Study Visit 6 - $80
Total = $300.
Study participants will be compensated an additional $25 for an unscheduled study visit.

25.2 * Will there be any costs to participants associated with their participation in research?

○ Yes ◉ No

If so, please explain:

26.0 Bibliography

26.1 * Enter your bibliography below:

1. Gesta S, Tseng YH, Kahn CR. Developmental origin of fat: tracking obesity to its source. Cell. 2007;131(2):242-56. doi: 10.1016/j.cell.2007.10.004. PubMed PMID: 17956727.
2. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640-5. doi: 10.1161/CIRCULATIONAHA.109.192644. PubMed PMID: 19805654.
3. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Annual review of immunology. 2011;29:415-45. doi: 10.1146/annurev-immunol-031210-101322. PubMed PMID: 21219177.
4. WHO. Obesity and overweight. WHO Factsheet 311 [updated January 2015.]. Available from: **http://www.who.int/mediacentre/factsheets/fs311/en/**.5. Karlsson EA, Beck MA. The burden of obesity on infectious disease. Experimental biology and medicine. 2010;235(12):1412-24. doi: 10.1258/ebm.2010.010227. PubMed PMID: 21127339.
6. Zhou Y, Cowling BJ, Wu P, Chan WM, Lee SY, Lau EH, et al. Adiposity and influenza-associated respiratory mortality: a cohort study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2015;60(10):e49-57. doi: 10.1093/cid/civ060. PubMed PMID: 25645211.
7. Sheridan PA, Paich HA, Handy J, Karlsson EA, Hudgens MG, Sammon AB, et al. Obesity is associated with impaired immune response to influenza vaccination in humans. International journal of obesity. 2012;36(8):1072-7. doi: 10.1038/ijo.2011.208. PubMed PMID: 22024641; PubMed Central PMCID: PMC3270113.
8. Sivapalan P, Diamant Z, Ulrik CS. Obesity and asthma: current knowledge and future needs. Current opinion in pulmonary medicine. 2015;21(1):80-5. doi: 10.1097/MCP.0000000000000119. PubMed PMID: 25405670.
9. Stefan N, Haring HU, Hu FB, Schulze MB. Metabolically healthy obesity: epidemiology, mechanisms, and clinical implications. The lancet Diabetes & endocrinology. 2013;1(2):152-62. doi: 10.1016/S2213-8587(13)70062-7. PubMed PMID: 24622321.
10. Nakaya HI, Wrammert J, Lee EK, Racioppi L, Marie-Kunze S, Haining WN, et al. Systems biology of vaccination for seasonal influenza in humans. Nature immunology. 2011;12(8):786-95. doi: 10.1038/ni.2067. PubMed PMID: 21743478; PubMed Central PMCID: PMC3140559.
11. Bucasas KL, Franco LM, Shaw CA, Bray MS, Wells JM, Nino D, et al. Early patterns of gene expression correlate with the humoral immune response to influenza vaccination in humans. The Journal of infectious diseases. 2011;203(7):921-9. doi: 10.1093/infdis/jiq156. PubMed PMID: 21357945; PubMed Central PMCID: PMC3068032.
12. Tsang JS, Schwartzberg PL, Kotliarov Y, Biancotto A, Xie Z, Germain RN, et al. Global analyses of human immune variation reveal baseline predictors of postvaccination responses. Cell. 2014;157(2):499-513. doi: 10.1016/j.cell.2014.03.031. PubMed PMID: 24725414; PubMed Central PMCID: PMC4139290.
13. Osborn O, Olefsky JM. The cellular and signaling networks linking the immune system and metabolism in disease. Nature medicine. 2012;18(3):363-74. doi: 10.1038/nm.2627. PubMed PMID: 22395709.
14. Louie JK, Acosta M, Samuel MC, Schechter R, Vugia DJ, Harriman K, et al. A novel risk factor for a novel virus: obesity and 2009 pandemic influenza A (H1N1). Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52(3):301-12. doi: 10.1093/cid/ciq152. PubMed PMID: 21208911.
15. Milner JJ, Beck MA. The impact of obesity on the immune response to infection. The Proceedings of the Nutrition Society. 2012;71(2):298-306. doi: 10.1017/S0029665112000158. PubMed PMID: 22414338.
16. Li S, Nakaya HI, Kazmin DA, Oh JZ, Pulendran B. Systems biological approaches to measure and understand vaccine immunity in humans. Seminars in immunology. 2013;25(3):209-18. doi: 10.1016/j.smim.2013.05.003. PubMed PMID: 23796714; PubMed Central PMCID: PMC3797847.
17. administration FaD. Guidance for Industry: Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines.

27.0 Appendices

27.1 Enter your appendices below:

28.0 Funding

28.1 * Do you have sufficient financial resources to support your study?

◉ Yes ○ No

If No, explain:

An application for a pilot grant has been submitted.

28.2 If this study is/was a CTSA-funded pilot, please specify dates of funding:

From date:

To date:

28.3 Specify funding by Rockefeller University, industry sponsor and/or grant:

	Sponsor	Funding
Rockefeller University	Rice Laboratory	☑
Industry		
Grant		
Pilot Award		

28.4 List grants in which this study is named:

PHS or Non-PHS	Program	Grant Number	Grant Name	From Date	To Date

No records have been added

29.0 Clinical Services

29.1 *What is the general health status of your study group(s)?

- ☑ Well/Minimally Ill
- ☐ Moderately Ill
- ☐ Severely Ill
- ☐ Other
- ☐ Not Applicable

If other than Well/Minimally Ill, please describe:

29.2 * Does your study group have special care needs?

○ Yes ◉ No

If Yes, specify:

- ☐ Assistance with ambulation
- ☐ Wound care
- ☐ Assistance with ADL
- ☐ Other

If Other, please describe:

29.3 * Does your study have special equipment needs?

○ Yes ◉ No

If Yes, please describe:

29.4 * Will you require storage space on the clinical units for supplies to conduct this study?

○ Yes ◉ No

If Yes, please describe:

29.5 * Is special training of hospital staff required?

○ Yes ◉ No

If Yes, please describe:

30.0 Pharmacy Services

30.1 * Does the study require Pharmacy Services?

◉ Yes ○ No

If No, please proceed to next section.

30.2 Types of pharmacy services required:

☑ Dispensing
☐ Randomization
☐ Aseptic technique training
☐ Other

If Other, please specify:

30.3 Dispensing:

☐ Sponsor supplied drugs
☑ Investigator supplied drugs
☐ Pharmacy supplied drugs
☐ Other

If Other, please describe:

30.4 Type of medication(s):

☐ Oral
☐ Anergy panel
☑ Injectable
☐ Other

If Other, please specify:

If Injectable, please specify:

☑ Monday-Friday 8:30AM-5PM
☐ Off-hours [all other days/times]

30.5 Compounding: (including mixing medications)

☐ None
☐ Capsule
☐ Placebo
☐ Liquid oral formulation
☐ Development of new dosage forms
☐ Injectable
☐ Ointment, gel, cream or other external product(s)
☐ Other

If Other, please specify:

31.0 Bionutrition

31.1 * Will study require patient meals?

○ Yes ◉ No

If Yes, please specify:

Standard ☐ Inpatient ☐ Outpatient

Therapeutic	☐ Inpatient ☐ Outpatient
Research Diet	☐ Inpatient ☐ Outpatient
Formula Diet	☐ Inpatient ☐ Outpatient

Nutrient(s) to be controlled (specify):

31.2 Will meal times be altered?

○ Yes ○ No

If Yes, please explain:

31.3 Will food be provided to caregiver, parent or significant other?

○ Yes ○ No

31.4 For metabolic diets, is diet homogenization required for nutrient analysis by independent lab?

○ Yes
○ No
○ N/A

32.0 Clinical and Translational Research Facilitation Office

32.1 Indicate Clinical and Translational Research Facilitation Office assistance requested and/or received in the development of this study:

Protocol Navigation	☑ Requested ☑ Received
Development of consent(s) with research coordinator	☑ Requested ☑ Received
Creation of source documents	☑ Requested ☑ Received
IRB/ACCTS submission	☑ Requested ☑ Received
Initiation Meeting	☑ Requested ☑ Received
Create and maintain regulatory binder	☑ Requested ☑ Received
Internal monitoring	☑ Requested ☐ Received

	Requested	Received
Provision of research coordinator from the Facilitation Office.	☑	☑
Data entry services	☐	☐
Creation of CRF's	☐	☐
Other	☐	☐

If Other, please explain:

33.0 Clinical Research Support Office Resources (CRSO)

33.1 Indicate CRSO assistance requested and/or received in the development of the study:

	Requested	Received
Data and Safety Monitoring Plan	☐	☐
Informed Consent	☐	☐
Recruitment and Advertising	☑	☑
IND Application	☐	☐
Study Monitoring	☐	☐

If Other, please indicate:

34.0 Research Design and Biostatistics Resources

34.1 Indicate Biostatistics assistance requested and/or received in the development of this study:

	Requested	Received
Development of experimental design	☐	☐
Sample size determination (# of subjects)	☑	☑
Randomization schedule	☐	☐
Data analysis	☐	☐
Development of new statistical techniques for data analysis	☐	☐
Other	☐	☐

34.2 Please select the Biostatistician on this Protocol:

- ○ J[redacted] Correa da Rosa, PhD
- ◉ Sam[redacted]arcet, PhD
- ○ Mayte Su[redacted] Farinas, PhD
- ○ Knut M Wittkow[redacted] PhD, ScD
- ○ Other

If other please specify:

35.0 Biomedical Informatics Resources

35.1 Indicate BioInformatics assistance requested and/or received in the development of this study:

	Requested	Received
Data storage outside of iRIS	☐	☐
Database other than iRIS/Oracle	☐	☐
Database design	☐	☐
Application design	☐	☐
Software other than iRIS	☐	☐
Special computer hardware	☐	☐

Microarray analysis software	☐	☐
Microarray analysis software training	☐	☐
Pathways analysis software	☐	☐
Other	☐	☐

If Other, explain:

35.2 If you are/will be using microarray analysis software, specify:

- ☐ Genespring
- ☐ Other

If Other, specify:

35.3 If you are/will be using pathway analysis software, specify:

- ☐ Ingenuity
- ☐ Pathways Studio
- ☐ Other

If Other, specify:

36.0 Translational Immunomonitoring Resource Center

36.1 Indicate if you plan or did use the following TTCL resources:

	Plan To Use	Used
Sample handling and preparation for immunological studies	☐	☐
Feasibility determination of markers for immunophenotyping of surface and cytoplasm antigens, functional studies and DNA analysis by flow cytometry	☐	☐
Protocols for flow cytometry and Luminex assays	☐	☐
Training for BD LSR II (flowcytometer) and Luminex instruments	☐	☐
Multiparametric analysis of flow cytometry and Luminex data	☐	☐
Other	☐	☐

If Other, explain:

37.0 HIPAA Form

37.1 A study's specific HIPAA form signed by the volunteer is required for institutions that are HIPAA covered entities so that they may communicate Private Health Information (PHI) to the Investigator.

Below, Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University are listed so that that they may report laboratory results and X-ray readings respectively. If you foresee that any other entity may need to provide PHI then add them to the field highlighted in green.

37.2 Name of Study:

Efficacy of Vaccination Against Seasonal Influenza in Individuals with the Metabolic Syndrome

37.3 Principal Investigator:

Ursula Andreo, PhD

37.4 Funding Source[1]:

Rice Laboratory

[1] The funding source does not appear on the final HIPAA form unless the source is an industry sponsor.

Who may obtain, use, and/or disclose your health information?

The following persons and organizations may obtain, use, or disclose health information about you.

- The Principal Investigator(s) listed at the top of this form, and persons who assist the Investigator(s) in carrying out the research
- Each research site for this study, including The Rockefeller University, and the research management and support staff and the medical staff at each site
- Health care providers who have provided in the past, or currently provide, health care services to you
- Laboratories and other persons and organizations that will analyze your health information and/or biological samples as part of this study, including Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University

Other entities that may need to provide PHI:

- Members and staff of the Institutional Review Board and other boards and committees that watch over research at The Rockefeller University
- Members and staff of The Rockefeller University's Office of Sponsored Research
- The sponsor(s) of the research, named above, and persons who watch over the research for the sponsor(s)
- The United States Food and Drug Administration, other government agencies, regulatory entities and Rockefeller University consultants that watch over the safety, effectiveness, and quality of research and/or fund The Rockefeller University Hospital
- Others (as described here):

What information will be obtained, used, or disclosed?

The persons and organizations listed above may obtain, use, and disclose:

- Information about you that is created or collected during the research study (but not including any HIV-related information)
- Health information in your medical records that is relevant to the research study (but not including any HIV-related information)
- **And**, if checked below:

___ HIV-related information (this includes any information indicating that you have had an HIV-related test or have HIV infection, HIV-related illness, or AIDS, as well as information that could indicate you may have been exposed to HIV)
___ Other information (as described here) _____

- Other information (as described here):

By signing this form, you give permission to the persons and organizations listed above to obtain, use and disclose your health information noted above.

How will your health information be used?

The health information noted above, as well as information shown by the boxes checked above (if any), may be obtained, used, and disclosed to:

In addition, the above named investigators, The Rockefeller University, and the above named sponsors may obtain, use, and disclose your information as needed for your treatment or as permitted by the informed consent form for the research study.

- conduct the research study explained to you during the informed consent process; and
- assure the quality, safety, and effectiveness of the research study

Please note that the persons and organizations listed above may re-use or further disclose your information if they are permitted by law to do so.

What are your rights?

It is your right to refuse to sign this authorization form. If you do not sign this form, you will not be able to participate in the research study. Your health care outside the study will not be affected. The payment for your health care and your health care benefits will not be affected. If you sign this authorization form, you will have the right to withdraw it at any time except to the extent that the persons and organizations listed above:

- have already taken action based upon your authorization;
- need the previously collected information to complete analysis and reports of data for this research; or

- will continue to use and disclose previously collected information as permitted by the informed consent form signed by you (except as to HIV-related information, for which disclosure to new persons or organizations will not occur unless permitted by federal or state law).

If you withdraw the authorization, you will not be permitted to continue taking part in the research study. This authorization form will not expire unless you withdraw it. If you want to withdraw this authorization, please write to the above named investigators.
You have a right to see and copy your health information described in this authorization form in accordance with The Rockefeller University's policies; in certain circumstances where the integrity of the study will be affected, you will not be able to obtain your health records in this study until the study has been completed.
You will receive a copy of this form after you have signed it.

Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that such information may not be shared without your approval unless permitted by federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (212) 480-2493 or the New York City Commission of Human Rights at (212) 306-7450. These agencies are responsible for protecting your rights.

Your signature

I have read this form, and all of my questions have been answered. By signing below, I acknowledge that I have read and accept all of the information above.

_____
Signature of participant or participant's legal representative

_____
Date

_____
Printed name of participant

_____
Printed name of legal representative (if applicable)

_____
Representative's relationship to participant

THE STUDY PARTICIPANT OR HIS OR HER PERSONAL REPRESENTATIVE MUST BE PROVIDED WITH A COPY OF THIS FORM AFTER IT HAS BEEN SIGNED.

38.0 End of Application Form

38.1 The study application form is complete. The next step in the submission process is to gather attachments before proceeding to the submission form.

The following submission reports are generated in the Lab/Dept Reports menu, Submission Reports section:

- **Delegation of Authority** (if applicable, and if not previously generated)
- **HIPAA form** (if applicable)
- **CCTS Utilization Report** (required for all submissions)
- **Study Progress Report** (if the study has been managed in iRIS for a minimum of one year, generate the Progress Report from the report menu in iRIS. if the study has not been managed in iRIS for one year, complete the Progress Report located on the IRB website.)

All other required forms can be downloaded from the corresponding sections' help links above or from the IRB website.