# Columbia University Human Subjects Protocol Data Sheet

## General Information

| | | | |
|---|---|---|---|
| **Protocol:** | AAAR8777(M00Y01) | **Protocol Status:** | Approved |
| **Effective Date:** | 05/31/2018 | **Expiration Date:** | 05/30/2019 |
| **Originating Department Code:** | | PED Pediatrics (754000X) | |
| **Principal Investigator:** | | Zuckerman, Warren (wz2116) | |
| **From what Columbia campus does this research originate:** | | Medical Center | |
| **Title:** | Allograft as a Risk Factor for Pre-Sensitization in Patients with Congenital Heart Disease | | |
| **Protocol Version #:** | | **Abbreviated Title:** | Allograft as a Risk Factor to Pre-Sensitization in CHD |
| **Was this protocol previously assigned a number by an IRB:** | | | No |

**Is the purpose of this submission to obtain a "Not Human Subjects Research" determination?**

No

## IRB Expedited Determination

**5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnoses).**

## Attributes

**Special review type: Check all that apply or check "None of the Above" box.**

[ ]Review for 45 CFR 46.118 Determination (involvement of human subjects is anticipated but is not yet defined)

[ ]Funding review for Administrative IRB approval (such as for Center or Training Grants)

[x]None of the above

**IRB of record information: Will a Columbia IRB be the IRB that is responsible for providing review, approval, and oversight for this study?**

Yes

**Select the most appropriate response:**

**Columbia will be the IRB of record for the study procedures conducted by Columbia researchers (Note: this response will apply to most submissions).**

**Is this research part of a multicenter study?**

No

**Please indicate if any of the following University resources are utilized:**

[ ] Cancer Center Clinical Protocol Data Management Compliance Core (CPDM)

[ ] CTSA-Irving Institute Clinical Research Resource (CRR)

[ ] CTSA- Irving Institute Columbia Community Partnership for Health (CCPH)

[x] None of the above

## Background

**Abbreviated Submission:**

**The IRB has an abbreviated submission process for multicenter studies supported by industry or NIH cooperative groups (e.g., ACTG, HVTN, NCI oncology group studies, etc.), and other studies that have a complete stand-alone protocol. The process requires completion of all Rascal fields that provide information regarding local implementation of the study. However, entering study information into all of the relevant Rascal fields is not required, as the Columbia IRBs will rely on the attached stand-alone (e.g., sponsor's) protocol for review of the overall objectives.**

**If you select the Abbreviated Submission checkbox and a section is not covered by the attached stand-alone protocol, you will need to go back and provide this information in your submission.**

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**Study Purpose and Rationale:**

**Provide pertinent background description with references that are related to the need to conduct this study. If this is a clinical trial, the background should include both preclinical and clinical data. Be brief and to the point.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

Allograft tissue is often used in the surgical repair of patients with various forms of congenital heart disease (CHD). Exposure to allograft tissue carries the risk of antibody production against donor-specific human leukocyte antigens (HLA), a process known as pre-sensitization. Various studies have shown exposure to allograft tissues to be associated with the presence of anti-HLA antibodies that can persist over time. For the subset of patients with CHD whose clinical course will eventually require heart transplantation, the presence of such anti-HLA antibodies may impact graft survival and lead to poorer outcomes post-transplantation. To mitigate this risk, some centers for pediatric heart transplantation require a negative donor-specific complement-dependent cytotoxicity crossmatch (CDC-XM) prior to transplantation. As a result, pre-sensitized patients often experience

The methods of detection of anti-HLA antibodies have evolved over time from the initial complement-dependent cytotoxicity panel reactive antibody (CDC-PRA) assay that determined the level of antibody by detecting the reactivity of the patients' serum against a panel of lymphocytes obtained from people with different HLA types, to the new solid-phase flow bead techniques (such as the LuminexTM assay) that mix patient serum with latex beads bound with single HLA that enables the detection of individual anti-HLA antibodies of a specific identity and intensity. With transplantation of other organs, often times HLA typing is part of the listing process for transplantation and an HLA cross-match is performed before the organ is accepted for transplant. If the cross-match is positive, often the organ is refused for transplantation into that specific patient. In heart transplantation, centers may opt to perform a prospective cross-match as well, especially in patients determined to be high risk by the presence of pre-formed anti-HLA antibodies. The evolution of antibody detection, and the ability to detect anti-HLA antibodies of a specific identity and intensity also has allowed for the performance of a virtual cross-match in which certain donor HLA are determined to be unacceptable for transplantation based on LuminexTM testing results.

Though exposure to allograft tissue has been shown to be associated with pre-sensitization in the past, this study intends to ascertain whether exposure to allograft tissue is an independent risk

factor for pre-sensitization among CHD patients at one of the largest pediatric heart transplant programs in the world using the most current laboratory testing methods. Furthermore, we intend to report the prevalence of pre-sensitization among CHD patients exposed to allograft tissue at our center. Secondarily, this study intends to determine the type of pre-formed antibodies and the degree of sensitization achieved.

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**Study Design:**

**Describe the methodology that will be used in this study, covering such factors as retrospective vs. prospective data collection, interventional vs. non-interventional, randomized vs. non-randomized, observational, experimental, ethnography, etc.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

This study will be a retrospective chart review of all CHD patients who have undergone heart transplantation at MS-CHONY since 1/1/2011, which is the time that our immunology lab routinely began performing LuminexTM testing. For patients who underwent surgical correction, operative notes will be reviewed to determine the usage of allograft tissue. Data on patient demographics, CHD diagnosis, and cross-matches will be collected. Patients will be identified as being pre-sensitized either by LuminexTM and/or CDC-PRA testing performed on recipient serum both prior to and at the time of transplant. The primary outcome measure will be the presence of pre-sensitization in CHD patients who were exposed to allograft material versus CHD patients who were not. Secondary outcome measures that we will look at will include the type of pre-formed antibodies present at time of transplant and the degree of sensitization.

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**Statistical Procedures:**

**Provide sufficient details so that the adequacy of the statistical procedures can be evaluated including power calculations to justify the number of participants to be enrolled into the study. Definitions of subject terms such as enrolled and accrued as used for Rascal submissions can be found in the Subjects section.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

Continuous variables will be analyzed using a Student's T-test, dichotomous variables will be analyzed using Chi-Square analysis.

## Exempt and Expedited

**Is the purpose of this submission to obtain an exemption determination, in accordance with 45CFR46.101(b):**

No

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**Is the purpose of this submission to seek expedited review , as per the federal categories referenced in 45CFR46.110?**

Yes

**Is the risk of harm to which subjects will be exposed as a result of this research no more than minimal?**

Yes

**Select the category or categories of research into which study procedures fall.**

[ ] Category 1 - Clinical studies of drugs and medical devices only when condition (a) or (b) is met. (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks

associated with the use of the product is not eligible for expedited review.) (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

[ ] Category 2 - Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

PLEASE NOTE: If blood is collected through an existing catheter, you do not qualify for expedited review under this category.

[ ] Category 3 - Prospective collection of biological specimens for research purposes by noninvasive means. Examples include: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

[ ] Category 4 - Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples include: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject=s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

[x] Category 5 - Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

PLEASE NOTE: If extra tissue is being taken during a routine clinical procedure (i.e. additional tissue that is not being taken for diagnostic purposes), you do not qualify for expedited review under this category.

[ ] Category 6 - Collection of data from voice, video, digital, or image recordings made for research purposes.

[ ] Category 7 - Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

**Do all procedures fall into one or more of the categories listed above?**

Y

**NOTE: This project appears to be eligible for expedited review.**

## Funding

**Is there any external funding or support that is applied for or awarded, or are you the recipient of a gift, for this project?**

No

## Locations

| Location Type | Facility Name | Domestic or International | Geographic Location | Local IRB Ethics Approval | Local Site Approval |
|---|---|---|---|---|---|
| NewYork-Presbyterian Hospital @ Columbia | Morgan Stanley Children's Hospital | | | | |

## Personnel

| UNI/Phone | Name | Role | Department | Edit/View | Obtaining Informed Consent |
|---|---|---|---|---|---|
| wz2116<br>646-209-6123 | Zuckerman, Warren | Principal Investigator | PED Cardiology (754050X) | Edit | N |
| | **Roles and Experience:** Assistant Professor of Pediatrics | | | | |
| ag3595<br>203-895-9424 | Gomez, Andres | Coordinator | SRG Liver (755140X) | Edit | N |
| | **Roles and Experience:** Heart transplant study coordinator | | | | |
| djd2141<br>914-462-1178 | Donovan, Denis | Investigator | PED Central Admin (754020X) | Edit | N |
| | **Roles and Experience:** Pediatric Resident | | | | |
| eb2709<br>212-305-2688 | Bacha, Emile | Investigator | SRG CT (755220X) | Edit | N |
| | **Roles and Experience:** Pediatric CT surgeon, co-investigator | | | | |
| jm3874<br>212-305-3839 | McAllister, Jennie | Coordinator | SRG Liver (755140X) | Edit | N |
| | **Roles and Experience:** Heart transplant study coordinator | | | | |
| mr2306<br>212-305-6575 | Richmond, Marc Eric | Investigator | PED Cardiology (754050X) | Edit | N |
| | **Roles and Experience:** Heart transplant attending, co-investigator | | | | |

**Training and COI**

**The PI must ensure that each individual that is added as personnel has met the training requirements for this study (http://www.cumc.columbia.edu/dept/irb/education/index.html). For help identifying which research compliance trainings you may be required to take, visit the Research Compliance Training Finder.**

| UNI | Name | COI | HIPAA | HSP (CITI) | Research with Minors (CITI) | FDA-Regulated Research (CITI) | S-I | CRC | Good Clinical Practice (GCP) | GCP - Third-party tracking | Genetic Research Consent |
|---|---|---|---|---|---|---|---|---|---|---|---|
| wz2116 | Zuckerman, Warren | 05/10/2018 | 09/11/2008 | 02/23/2017 | 02/23/2017 | 02/23/2017 | | | 01/11/2017 | | |
| ag3595 | Gomez, Andres | 10/09/2017 | 11/13/2014 | 11/21/2017 | 11/19/2014 | 11/19/2014 | 11/13/2014 | 11/20/2014 | 02/03/2017 | | |
| djd2141 | Donovan, Denis | 11/09/2017 | 04/21/2014 | 06/15/2017 | 06/15/2017 | 04/21/2014 | 04/21/2014 | 04/22/2014 | | | |
| eb2709 | Bacha, Emile | 02/12/2018 | 05/20/2010 | 04/04/2018 | 05/04/2015 | 04/04/2018 | | | 04/26/2017 | | |
| jm3874 | McAlister, Jennie | 09/13/2017 | 07/29/2012 | 07/30/2015 | 07/30/2015 | 07/30/2015 | | 08/05/2012 | 02/03/2017 | | 11/03/2017 |
| mr2306 | Richmond, Marc Eric | 04/11/2018 | 06/30/2006 | 02/06/2017 | 02/06/2017 | 02/06/2017 | | | 02/28/2017 | | |

## Departmental Approvers

Electronic Signature: Warren Zuckerman (754050X) - Principal Investigator Date: 05/30/2018

Electronic Signature: Marc Eric Richmond (754050X) - Investigator Date: 05/03/2018

Electronic Signature: Jennie McAllister (755140X) - Coordinator Date: 05/08/2018

Electronic Signature: Fiona Sanders (754020X) - Department Administrator Date: 05/21/2018

Electronic Signature: Denis Donovan (754020X) - Investigator Date: 05/21/2018

Electronic Signature: Andres Gomez (755140X) - Coordinator Date: 05/11/2018

Electronic Signature: Emile Bacha (755220X) - Investigator Date: 05/03/2018

## Privacy & Data Security

**Indicate the methods by which data/research records will be maintained or stored (select all that apply):**

[ ]Hardcopy (i.e., paper)

[x]Electronic

**Where will the data be stored?**

Y

[ ]On a System

[x]On an Endpoint

**Identify what type of endpoint will be used (select all that apply):**

[x]Desktop Computer

[x]Laptop Computer

[ ]Mobile Device

[ ]Other

**Does this study involve the receipt or collection of Sensitive Data?**

Yes

**If any Sensitive Data is lost or stolen as part of your research protocol, you must inform both the IRB and the appropriate IT Security Office (CUMC IT Security if at CUMC; CUIT if at any other University campus).**

**What type of Sensitive Data will be obtained or collected? Select all that apply:**

[x]Personally Identifiable Information (PII), including Social Security Numbers (SSN)

**Will Social Security Numbers (SSNs) be collected for any purpose?**

No

[x]Protected Health Information (PHI), including a Limited Data Set (LDS)

**If any PHI is lost or stolen, you must inform both the IRB and the Office of HIPAA Compliance.**

**Indicate plans for secure storage of electronic sensitive data: check all that apply**

[ ]Sensitive data will not be stored in electronic format

[ ]Sensitive data will be stored on a multi-user system

[x]Sensitive data will be stored on an encrypted endpoint

**By Selecting an Endpoint Device and approving this protocol for submission to the IRB, the PI is attesting that the device and any removable media that may be used have been or will be registered and/or will be maintained in compliance with the University's Information Security Charter and all related policies. It is important that this information is updated, during the course of the study, as new devices are added.**

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**Provide a description of how the confidentiality of study data will be ensured, addressing concerns or protections that specifically relate to the data storage elements identified above (e.g. hard copy, electronic, system, and/or endpoint):**

Data and safety monitoring will be performed to comply with all rules set forth by Columbia University. Every effort will be made to maintain confidentiality. Data will only be recorded on computers that are encrypted and password protected in compliance with CUMC IT requirements. All study data will be kept confidential. No publication or written reports will link subject data with a name or any individual protected health information. Only the members of the research team listed in this IRB will have access to the collected information.

**Is there or will there be a Certificate of Confidentiality (CoC) for this research?**

No

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**Provide a description of the protections in place to safeguard participants' privacy while information is being collected:**

Sensitive information will be stored in compliance with Columbia University policy as detailed above. Please see above.

## Procedures

**Is this project a clinical trial?**

No

**Is this project associated with, or an extension of, an existing Rascal protocol?**

No

**Do study procedures involve any of the following?**

**Analysis of existing data and/or prospective record review**

Yes

**Audio and/or video recording of research subjects**

No

**Behavioral Intervention?**

No

**Biological specimens (collection or use of)**

No

**Cancer-related research**

No

**Drugs or Biologics**

No

**Future use of data and/or specimens**

No

**Genetic research**

No

**Human embryos or human embryonic stem cells**

No

**Imaging procedures or radiation**

No

**Medical Devices**

No

**Surgical procedures that would not otherwise be conducted or are beyond standard of care**

No

**Will any of the following qualitative research methods be used?**

**Survey/interview/questionnaire**

No

**Systematic observation of public or group behavior**

No

**Program evaluation**

No

**Will any of the following tests or evaluations be used?**

**Cognitive testing**

No

**Educational testing**

No

**Non-invasive physical measurements**

No

**Taste testing**

No

**Is there an external protocol that describes ALL procedures in this study?**

No

**Please describe ALL study procedures in detail.**

**NOTE: Be sure to detail all of the procedures above to which a "yes" response was selected. Also detail any additional procedures that may or may not fall into the categories listed above.**

All charts of patients with CHD who underwent heart transplantation at MS-CHONY since 1/1/2011 to 4/30/18 will be reviewed. Surgical operation notes will be reviewed to determine the presence or absence of allograft tissue in the previous surgical repair. Results of LuminexTM and/or CDC-PRA testing performed on recipient serum both prior to and at the time of transplant will be reviewed to identify patients who with pre-sensitization and those without. Data on patient demographics, CHD diagnosis, and cross-matches will also be obtained. Statistical analysis will be performed to compare the risk of becoming pre-sensitized in patients who were exposed to allograft tissue versus those that were not exposed.

## Analysis of Existing Data and/or Prospective Record Review

**Indicate whether the data that will be collected or utilized for the proposed study are in existence as of the current IRB submission date.**

All of the data are in existence

**Provide the date range of the existing data, documents, or records (e.g., medical charts, school records, census data)**

Beginning Date: 01/01/2011
End Date: 04/30/2018

**Note that end dates beyond the initial IRB Protocol submission date or future requests for a date parameter extension beyond the provided end date may require informed consent and HIPAA Authorization to be obtained from subjects.**

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**Data will be obtained from (select all that apply):**

[x] Columbia and/or NYP (e.g., departmental databases/systems, patient charts, Eclipsys, WebCIS, administrative/billing records, etc.)

**Select all that apply:**

[x] Data to be analyzed were or will be collected for clinical care

[ ] Data to be analyzed were or will be collected for nonresearch purposes other than for clinical care (e.g., student records, class evaluation, administrative records, etc.,)

[ ] Data originate from an IRB approved protocol

[ ] Other

[ ] Outside Columbia and/or NYP:

**Will a member of the research team be abstracting data directly from source documents?**

Yes

**If there is a data abstraction document/spreadsheet, attach it to the submission to complete study records. Though the IRB does not approve these documents, for reference purposes they are extremely helpful in understanding the scope of the proposed data collection.**

**Select the applicable responses:**

[x] The data, documents, or records to be reviewed/abstracted are those to which a member of the research team has legitimate access for non-research purposes (e.g., departmental patient database, physicians' patient clinical records, student records).

[ ] Special authorization is necessary to review the records as the research team does not have access to the data, and a request will be or has been made to access the data.

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**If any existing data was obtained from a prior research study, was any member of the current research team involved (e.g., obtained consent, performed study procedures, conducted data analysis) in the project or procedures that collected and/or used identifiable information?**

No

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**Indicate the manner in which the existing data and/or the records to be reviewed prospectively will be collected or received:**
**(Select all that apply. At least one must be selected.)**

[x] Contains direct identifiers (e.g., name, MRN, date of birth)
[ ] Coded and the research team has the key and can link the data to direct identifiers
[ ] Coded and the research team does not have access to the key to link data to direct identifiers
[ ] Prior to the receipt of the data by the research team submitting this protocol, the identifiers will be removed and no link will remain.
[ ] The information was originally or will be collected without identifiers

**If data are collected or received at any point in time with direct identifiers or linked to identifiers, then the data are considered to be identifiable, and the requirements for Informed Consent (or a waiver, if applicable) and HIPAA Authorization (or a waiver, if applicable) apply. The necessary information will need to be included in the respective sections of the submission.**

## Recruitment And Consent

### Recruitment:

**Describe how participants will be recruited:**
Not applicable

**Select all methods by which participants will be recruited:**

[x] Study does not involve recruitment procedures
[ ] Person to Person
[ ] Radio
[ ] Newspapers
[ ] Direct Mail
[ ] Website
[ ] Email
[ ] Television
[ ] Telephone
[ ] Flyer/Handout
[ ] Newsletter/Magazine/Journal
[ ] ResearchMatch
[ ] CUMC RecruitMe

**Additional Study Information: Please add a description of your study as you would like it to be displayed on the RecruitMe website.**

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### Informed Consent Process:

**Informed Consent Process, Waiver or Exemption: Select all that apply**

[ ] Informed consent with written documentation will be obtained from the research participant or appropriate representative.

[ ] Informed consent will be obtained but a waiver of written documentation of consent (i.e., agreement to participate in the research without a signature on a consent document) is requested.

[x] A waiver of some or all elements of informed consent (45 CFR 46.116) is requested.

**Waiver of consent is applicable to:**
The study in its entirety

**Select the applicable situation:**

[x]This study qualifies for a waiver of consent as per 45CFR46.116(d) as the following criteria are met in this study (provide justification for EACH of these criteria):

**(1)The research involves no more than minimal risk to the subjects**

**Provide justification:**
As a retrospective chart review (of 75 patients), there is no risk to the patient. Protection of the

confidentiality of patient health data will be minimized as previously described.

**(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects**

**Provide justification:**

As a retrospective chart review, there is no risk to the patient. Protection of the confidentiality of patient health data will be minimized as previously described. The welfare of the subjects will not be affected. All patient identifiers will be removed from the data set prior to analysis. Al patient information will be kept in a secure database encrypted with password protection, and only the study personnel will have access to the file.

**(3) The research could not practicably be carried out without the waiver or alteration**

**Provide justification:**

This research could not be practically conducted without the waiver because there are a large number of patients (75) whose charts are being reviewed, and contacting these families to obtain consent for a chart review would not be practical.

**(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation**

**Provide justification:**

Subjects will be provided with any pertinent information as needed.

[ ]This study qualifies for a waiver of consent as per 45CFR46.116(c) as the following criteria are met for this study (provide justification for EACH of these criteria):

[ ] Planned Emergency Research with an exception from informed consent as per 21 CFR 50.24.

[ ] Informed consent is not required; this is exempt research.

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**Subject Language**

Language of subjects is unknown/irrelevant (e.g., record reviews, mass mailing of surveys)

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**Capacity to Provide Consent:**

**Do you anticipate using surrogate consent or is research being done in a population where capacity to consent may be questionable?**

No

## Research Aims & Abstracts

**Research Question(s)/Hypothesis(es):**

This study hypothesizes that exposure to allograft tissue in the surgical correction of congenital heart disease results in a significantly larger percentage of patients who become pre-sensitized, as defined by the presence of pre-formed donor-specific anti-HLA antibodies, versus CHD patients who were not exposed to allograft tissue.

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**Scientific Abstract:**

Allograft tissue is often used in the surgical repair of patients with various forms of congenital heart disease (CHD). Exposure to allograft tissue carries the risk of antibody production against donor-specific human leukocyte antigens (HLA), a process known as pre-sensitization. Various studies have shown exposure to allograft tissues to be associated with the presence of anti-HLA antibodies that can persist over time. For the subset of patients with CHD whose clinical course will eventually require heart transplantation, the presence of such anti-HLA antibodies may impact graft survival and lead to poorer outcomes post-transplantation. To mitigate this risk, some centers for pediatric heart transplantation require a negative donor-specific complement-dependent cytotoxicity crossmatch (CDC-XM) prior to transplantation. As a result, pre-sensitized patients often experience longer wait list times and higher wait list mortality than their non-sensitized counterparts.

Though exposure to allograft tissue has been shown to be associated with pre-sensitization in the past, this study intends to ascertain whether exposure to allograft tissue is an independent risk factor for pre-sensitization among CHD patients at one of the largest pediatric heart transplant programs in the world using the most current laboratory testing methods, specifically the LuminexTM solid-phase assay. Furthermore, we intend to report the prevalence of pre-sensitization among CHD patients exposed to allograft tissue at our center. Secondarily, this study intends to determine the type of pre-formed antibodies and the degree of sensitization achieved.

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**Lay Abstract:**

Patients born with heart disease often require surgery in the first months or years of life. The surgical correction of congenital heart defects often requires the use of human tissue in the form of allografts. Exposure to such foreign human tissue triggers an immune response that can lead to the production of antibodies against human leukocyte antigen (HLA), a process called pre-sensitization. Pre-sensitization can have major implications later if patients ultimately require heart transplantation, as it has been shown to lead to poorer outcomes after transplant. As a result, patients who are pre-sensitized often wait longer for a transplant and have higher rates of death while waiting. We intend to determine whether the use of such allograft material in our patient population is a risk factor for pre-sensitization.

## Risks, Benefits & Monitoring

**Abbreviated Submission:**

**The IRB has an abbreviated submission process for multicenter studies supported by industry or NIH cooperative groups (e.g., ACTG, HVTN, NCI oncology group studies, etc.), and other studies that have a complete stand-alone protocol. The process requires completion of all Rascal fields that provide information regarding local implementation of the study. However, entering study information into all of the relevant Rascal fields is not required, as the Columbia IRBs will rely on the attached stand-alone (e.g., sponsor's) protocol for review of the overall objectives. .**

**If you select the Abbreviated Submission checkbox and a section is not covered by the attached stand-alone protocol, you will need to go back and provide this information in your submission.**

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**Potential Risks:**

**Provide information regarding all risks to participants that are directly related to participation in this protocol, including any potential for a breach of confidentiality. Risks associated with any of the items described in the Procedures section of this submission should be outlined here if they are not captured in a stand-alone protocol. Risks of procedures that individuals would be exposed to regardless of whether they choose to participate in this research need not be detailed in this section, unless evaluation of those risks is the focus of this research. When applicable, the likelihood of certain risks should be explained and data on risks that have been encountered in past studies should be provided.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

As this is a retrospective chart review, there is no risk to the patient. The only conceivable risk is to the confidentiality of patient data. This risk is minimized as described above.

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**Potential Benefits:**

**Provide information regarding any anticipated benefits of participating in this research. There should be a rational description of why such benefits are expected based on current knowledge. If there is unlikely to be direct benefit to participants/subjects, describe benefits to society. Please note that elements of participation such as compensation, access to medical care, receiving study results, etc. are not considered benefits of research participation.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

As a retrospective chart review, there is no immediate benefit to the client. However, the information gained from this review can have significant benefit to children undergoing heart transplantation in the future, as this can contribute to the established body of literature and relate to the suitability of donors.

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**Alternatives:**

**If this research involves an intervention that presents greater than minimal risk to participants, describe available alternative interventions and provide data to support their efficacy and/or availability. Note, participants always have the option not to participate in research.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

Not applicable

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**Data and Safety Monitoring:**

**Describe how data and safety will be monitored locally and, if this is a multi-center study, how data and safety will be monitored across sites as well.**

[ ] Abbreviated Submission - This information is included in an attached stand-alone protocol. Proceed to the next question

Data will be protected as described above. Access to study data is restricted to those researchers directly involved in data collection or analysis. All study data will be kept confidential.

## Subjects

**Unless otherwise noted, the information entered in this section should reflect the number of subjects enrolled or accrued under the purview of Columbia researchers, whether at Columbia or elsewhere.**

**Target enrollment:**

75

**Number anticipated to be enrolled in the next approval period:**

75

**Does this study involve screening/assessment procedures to determine subject eligibility?**

No

**Is this a multi-center study?**

No

**Does this study have one or more components that apply to a subset of the overall study population (e.g. Phase 1/2, sub-studies)?**

No

**Target Enrollment Demographics:**

**Population Gender**

| Females | Males | Non Specific |
|---|---|---|
| 40% | 60% | 0% |

**Population Age**

| 0-7 | 8-17 | 18-65 | >65 | Non Specific |
|---|---|---|---|---|
| 45% | 40% | 15% | 0% | 0% |

**Population Race**

| American Indian/Alaskan Native | Asian | Native Hawaiian or Other Pacific Islander | Black or African American | White | More than One Race | Non-Specific |
|---|---|---|---|---|---|---|
| 0% | 0% | 0% | 0% | 0% | 0% | 100% |

**Population Ethnicity**

| Hispanic or Latino | Not Hispanic or Latino | Non-Specific |
|---|---|---|
| 0% | 0% | 100% |

**Vulnerable Populations as per 45 CFR 46:**

**Will children/minors be enrolled**

Yes

**Note that upon "Save", you will see a link to the required "Child Involvement" page in the left side navigation menu. You must complete this page prior to submission.**

**Will pregnant women/fetuses/neonates be targeted for enrollment?**

No

**Will prisoners be targeted for enrollment?**

No

**Other Vulnerable Populations:**

[ ]Individuals lacking capacity to provide consent

[ ]CU/NYPH Employees/Residents/Fellows/Interns/Students

[ ]Economically disadvantaged

[ ]Educationally disadvantaged

[ ]Non-English speaking

[ ]Other Vulnerable populations

[x]None of the Populations listed above will be targeted for Enrollment

**Subject Population Justification:**
Population includes all pediatric patients that underwent heart transplantation at Columbia University Medical Center during the study period.

**Does this study involve compensation or reimbursement to subjects?**
No

## Child Involvement

**RISK/BENEFIT DETERMINATION**

**Please refer to the Columbia University IRB policy on research involving children for further information. (Available on the IRB websites: CUMC IRB or Morningside/LDEO IRB.)**

**'Minimal risk' means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.**

**Select the option below that best describes your study.**
No more than Minimal Risk (45 CFR 46.404/21 CFR 50.51; i.e., 'Section 404')

**Explain how the risks of the research are minimal. 'Minimal Risk' means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.**
As a retrospective chart review, there is no risk to the patient. Protection of the confidentiality of patient health data will be minimized as previously described.

**WARDS AND FOSTER CHILDREN**

**If 'Section 406' or 'Section 407' research was indicated, the inclusion of wards or foster children requires additional information and, if the research will be conducted in New York City (NYC), approval from the NYC Administration for Children's Services (ACS). Please select the appropriate option below.**
This research has not been categorized as 45 CFR 46.406 ('Section 406') or 45 CFR 46.407 ('Section 407').

**ASSENT OF SUBJECTS**

**Assent of the child is required except in limited circumstances. The first step in determining whether assent is required and/or appropriate is to assess whether the children who will participate in the study will be capable of providing assent. The next step is to determine, for children who are capable of providing assent, whether assent will be obtained or should be waived.**

**Indicate whether the children who will be enrolled in this study will generally be capable of providing assent.**
None are expected to be capable of assent.

**Please explain why none of the children will be capable of providing assent (e.g., the children will be too young or lack the capacity due to maturity, psychological state, medical or cognitive condition).**
As a retrospective chart review, there is no risk to the patient and we will be asking for a waiver of informed consent/assent.

**PARENT/GUARDIAN PERMISSION**

**Permission of parents/guardians of the children is required except in limited circumstances. Permission from**

**one parent/guardian is acceptable for research categorized as Section 404 or Section 405 unless waiver of informed consent is approved or the IRB determines that permission from both parents is warranted.**

**Select the parental permission option that applies to your study, and provide the rationale for your response if justification is requested. For most studies, one selection is appropriate, however, if more than one option applies, select all that apply.**

[ ] The permission of one parent/guardian will be obtained.

[ ] The permission of both parents/guardians will be obtained. - THIS IS REQUIRED IF YOU HAVE CATEGORIZED YOUR RESEARCH AS 45 CFR 46.406 OR 45 CFR 46.407

[ ] No parental permission will be obtained because each of the following waiver criteria for waiving parental permission apply (45 CFR 46.408(c)):

[x] No parental permission will be obtained because the involvement of children in this research meets the criteria for a complete waiver of consent (45 CFR 46.116(d)), which is requested in the “Recruitment and Informed Consent” section.

## Attached HIPAA Forms

| Number | Type | Title | Status |
|---|---|---|---|
| AAAO0762 | B | Denis Pre-sensitization study | Approve |