RESEARCH PROTOCOL

TITLE: **ASFA Registry Study (version 092315)**

RESEARCH PLAN

A. Specific Aims

To establish a registry for rare diseases treated by apheresis or rare indications treated by apheresis in more common diseases.

B. Background and Significance

There is very little information on the safety and efficacy of apheresis on the treatment of rare diseases (1-3). Much of our current outcome information comes from small, single institution based, retrospective case series, with safety information derived from large studies based on more commonly treated diseases (1-14). In addition, rare diseases which are seen in both in children and adults may have a different natural history in children (3-5). Although there are several current registries of apheresis procedures, none describe clinical outcomes and safety in rare diseases, nor describe in the detail the technical aspects of the procedure. (15-17). Similarly to rare diseases treated by apheresis, safety and efficacy information is also lacking in common diseases treated rarely by apheresis.

The American Society for Apheresis (ASFA) is an international group of practitioners and researchers in the field of apheresis. The rare diseases treated by this group and other practitioners or rare indications treated by apheresis in more common diseases in the field, if carefully studied, and combined into a registry would do much to advance the knowledge of treatment and safety of apheresis in these diseases. The registry will be sponsored by ASFA.

C. Preliminary Studies

None.

D. Research Design and Methods

There will be two parts to this study prospective and retrospective. A maximum total of 20,000 patients from both retrospective and prospective from all centers, with 2000 patients from all centers (both retrospective and prospective) for each disease or indication will be studied.

Prospective study:
This part will involve prospective data collection that will allow entry of laboratory and clinical information on patients undergoing apheresis for rare diseases or rare indications for more common diseases. Study endpoint will include collection of data anticipated to take approximately 20 years at most depending on disease or indication.

Retrospective study:
The second part will be a retrospective data collection study going back 10 years from the initial approval of the study at this institution.

The type of information that will be collected will include (for each series of treatments):

- Age (yr) at start of apheresis treatments
- Gender
- Ethnicity
- Dates of apheresis treatments
- Number and frequency of apheresis treatments
- Type of replacement fluid needed for each apheresis
- Volume of exchange
- Clinical status (symptoms)/ prior to and after each apheresis treatment
- Medications prior to start of and during plasmapheresis:
- Date and results of relevant laboratory testing and/or pathology results
- Clinical outcomes

In addition, we will note the medications used during and prior to each procedure (See appendices for each disease being studied.)

Because this is a registry study, no extra testing or blood draws will be performed.

REDCap (Research Electronic Data Capture), a secure, web-based application designed exclusively to support data capture for research studies will be used to collect the data. The REDCap project (http://project-redcap.org/) was initiated at Vanderbilt

University and includes more than 70 active institutional partners from both U.S and international institutions. Data will be housed at the REDCap database located at Children's National Medical Center in Washington, DC.

Recommendations for analysis of the registry data and future diseases/indications to be studied will be determined from members of the Research Subcommittee of the Applications Committee of the American Society of Apheresis (ASFA) on an annual basis or as designated by the subcommittee with results presented at the ASFA annual meeting.

E. Study Population –(Gender and Minority Inclusions):

Study population will include all participants with either rare diseases treated by apheresis or rare apheresis indications in participants with more common diseases. There will no gender or ethnic minority exclusions. Current diseases/indications to be studied will be Wilson's disease, Neuromyelitis optica, MUSK positive Myasthenia Gravis, Thrombotic Thrombocytopenic Purpura, atypical HUS, Sickle Cell Disease, Focal Segmental Glomerulosclerosis, ABO incompatible liver transplantation, leukemia, and disease/conditions requiring extracorporeal photopheresis. In addition, therapeutic apheresis complications will also be studied.

F. Human Subjects (Risks & Benefits)

Prospective study:
Participants will be identified by referrals from clinical services to the apheresis service for consideration of apheresis. After the apheresis service has made a decision to begin treatment, participants will be asked by the apheresis physician if they would like to participate in the registry. To avoid coercion and to provide privacy, participants will be given the opportunity to review the consent in a private room after the patient's condition has stabilized. Because some participants will be children and because of the clinical condition of the participant, a waiver of assent will be requested for those who cannot physically or mentally give assent. However, it should be noted that assent will be obtained whenever possible, preferably when the child is able, typically at the end of the apheresis treatment.

Retrospective study
For the retrospective part of the study (to capture those patients previously treated and not currently treated), a waiver of consent will be requested because of the difficulty of obtaining consent from a patient that may have been treated years earlier. Enrollment of these participants will come from review of apheresis records at the institution.

G. Risks and Side Effects:

The major risks of the study will be related to loss of confidentiality. To minimize this risk, unique participant numbers will be assigned to participants and no identifiable information

will be collected (except to collect and collate clinical and laboratory data). At each study site, the principal investigator or designee will keep a log of the study ID linking to patient's medical record or other identifiable information, but patient's medical record No. or date of birth will not be entered in the database. In addition, all data will be entered into REDCap (Research Electronic Data Capture), a secure, web-based application designed exclusively to support data capture for research studies will be used to collect the data from individual sites. The REDCap project (http://project-redcap.org/) was initiated at Vanderbilt University and includes more than 70 active institutional partners from both U.S and international institutions. Apheresis specialists entering data into the database will not know that identify of other patients from other institutions entered into the registry. No identifiable information will be entered into the database.

H. Benefits:

There are no direct benefits to participants. The major benefit is understanding what is the safety and efficacy of plasmapheresis for rare diseases, and the safety of apheresis for rare indications in more common diseases.

I. Outside Consultants/Collaborators

Members of the AFSA Research subcommittee including the Study PI for the registry: Edward Wong (Children's National Medical Center), Division of Laboratory Medicine, 111 Michigan Avenue, NW, Washington, DC 20010, Telephone: (202) 476-5338.

J. Contractual Agreements

There will be contractual data use agreement between the PI and ASFA regarding responsibilities and expectations of each. See appendix.

K. Costs To Subjects:

None

L. Conflicts Of Interest:

None

M. Confidentiality:

See risk and benefits section above.

N. Subject Compensation:

None

O. Facilities and Equipment

Institutional hospital information systems, institutional apheresis flowsheets and records.

P. References & Literature Cited

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Q. Appendix

RedCap PDF data entry forms for each disease or indication
PI data use agreement form with ASFA

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