

SHORT APPLICATION FOR ETHICS APPROVAL HUMAN SUBJECT HEALTH RECORD/DATABASE RESEARCH

Registry Methodology

Background

North American Pediatric Renal Trials Collaborative Studies (NAPRTCS) is a research effort that was organized in 1987 by a group of physicians and surgeons committed to the success of pediatric renal transplant. In 1992, the study was expanded to include pediatric patients who receive maintenance hemodialysis or peritoneal dialysis therapy. In 1994, data collection began on patients with chronic renal insufficiency (CRI), defined as Schwartz calculated creatinine clearance ≤ 75 mL/min 1.73m. The group represents a collaborative effort between centers in the United States, Canada, and Latin America. NAPRTCS works to study the clinical course and natural history of patients with renal dysfunction and continue following these patients as they move among the end-stage renal disease (ESRD) therapeutic modalities, and to collect and analyze information to advance the science of pediatric renal transplant. Participation in this registry is voluntary. The Data Coordinating Center (DCC), located at The EMMES Corporation, is responsible for data collection and analyses. The registry is supported by educational and research grants made available by sources such as Novartis Pharmaceutical Corporation, AMGEN Inc., and Genentech, Inc.

Due to the voluntary nature of this registry, there are no contracts or grants between the funding agencies and the participating transplant centers. Letters of Agreement are required by the NAPRTCS Foundation to ensure that participating centers comply with Good Clinic Practice with regards to data collection and submission. Participating Centers are required to follow their local Institutional Review Board's (IRB) requirements for participating in this endeavor. Many of the participating centers have executed a Registry Participation Agreement (*Appendix A*) with NAPRTCS.

NAPRTCS has established oversight committees to ensure that policies pertaining to the Registry are conducted in an organized and consistent manner. A copy of the NAPRTCS organizational chart is attached (*you may attach a copy of the NAPRTCS Organizational Chart and call it Appendix B*). The President is a member of the Board of Directors (BOD), the majority of whom are physicians or surgeons from NAPRTCS centers. The BOD is responsible for the scientific integrity of registry, as well as approving all operational issues pertaining to NAPRTCS. A Publication Committee has oversight responsibility for publications and presentations using NAPRTCS data. Study data submitted become the property of NAPRTCS and belong collectively to all participating centers.

NAPRTCS has four functioning organizational bodies: the BOD, DCC, Participating Clinical Centers and the Affiliated Labs Committee (ALC). The Organizational Chart details the structure of the DCC and BOD. The Participating Clinical Centers are listed in Appendix C, (*you may attach a copy of the NAPRTCS Directory and call it Appendix C*)

To date, over 12,000 patients have been registered in NAPRTCS. One hundred and fifty four centers participate, including seven from Canada. NAPRTCS contributes to publications and presentations that impact the medical community it is intended to affect (*you may attach a copy of the NAPRTCS Bibliography and call it Appendix D*). Each year an Annual Report is published and distributed to participating Centers, and presented at the Annual Meeting.

Hypotheses or Questions

The specific objectives of NAPRTCS are:

- to characterize patient survival, graft survival and patient morbidity (e.g., infections, rejections, hospital stay) among pediatric renal allograft recipients, dialysis and chronic renal insufficiency patients, and to correlate these measures of outcome with clinical variables such as graft donor source, immunosuppressive treatment received, dialysis treatment received, chronic renal insufficiency treatment received and selected patient characteristics;
- to characterize and follow trends in immunosuppressive therapy;
- to characterize the side effects of various immunosuppressive regimens;
- to characterize the incidence, risk factors, diagnosis, treatment and outcome of Targeted Adverse Events;
- to follow growth of children who receive renal allografts, dialysis, or care for chronic renal insufficiency, correlating growth with treatment received, age at onset of therapy, prior therapies and other patient characteristics;
- to answer relevant questions that address the health and progression of children with renal dysfunction.

Methods

NAPRTCS is comprised of participating Centers who will have responsibility for enrolling patients and collecting follow-up information on patient outcomes. In addition to the Centers, the DCC will provide support for logistical, data capture, quality-control monitoring, and statistical design and analysis.

Data collection is the responsibility of each participating center. Patient entry criteria include:

- A pediatric patient is defined as a patient who will not have reached his/her 21st birthday prior to enrollment in the Cooperative Study.
- All pediatric patients who received a renal allograft in a participating center on or after January 1, 1987 will be eligible for enrollment.
- All pediatric patients receiving maintenance dialysis at a participating pediatric transplant center are eligible for enrollment.
- All pediatric patients with an estimated GFR by the Schwartz method of $<75 \text{ mL/min/1.73 m}^2$ will be eligible for enrollment.
- Pre-CRI patients with FSGS, or other diseases as determined by the study investigators.

Statistical Analysis

The NAPRTCS analysis plan is designed to carefully monitor study accrual, data quality and timeliness, patient eligibility rates, adverse reactions and other outcomes. While detailed analyses of studies are performed periodically, study progress is monitored continuously. Technical and administrative reporting requirements of NAPRTCS consist of both interim and final reports of the scientific efforts.

The analysis plan for NAPRTCS includes data quality, study progress, adverse experience and patient outcome analyses. A comprehensive annual report summarizing data received is issued to each participating center (*you may attach a copy of the Table of Contents for the NAPRTCS Annual Report and call it Appendix E*). In addition, annual reports summarizing key aspects of the registry's experience compared to individual center experience is issued. Database assessments are performed by the DCC to evaluate database quality on a regular basis. In addition to these planned analyses, the DCC will expect to conduct various unplanned analyses precipitated by evolving registry needs. Requests for such analyses will be reviewed and approved by the Special Studies Committee.

DATA COLLECTION FORMS are attached (*you may attach a copy of the NAPRTCS Forms and call them Appendix F*).

IF YOU ARE PLANNING ON EXTRACTING SOCIODEMOGRAPHIC INFORMATION, E.G., RACE OR ETHNICITY, PLEASE PROVIDE JUSTIFICATION.

Sociodemographic data is extracted for the purposes of characterizing diseases and immunologically-driven complications such as graft rejection.

CONSENT TEMPLATE

The North American Pediatric Renal Transplant Cooperative Studies (NAPRTCS) is a multi-center registry that collects information on children with renal disease and renal transplant at treatment centers in North America.

PRIMARY INVESTIGATOR

Invitation to Participate

Your child or dependent is invited to participate in this research study. The following information is provided in order to help you make an informed decision about whether or not to participate. If you have any questions, please do not hesitate to ask.

Basis for Subject Selection

Included in the registry are all pediatric patients receiving dialysis at participating centers and children with chronic renal insufficiency or those who have or who need renal transplantation. A goal of NAPRTCS is to register and follow >80% of the children who receive renal allografts at pediatric renal disease treatment centers in North America.

Purpose of Study

The purpose of the study is to enter scientific data on care and treatment of pediatric renal disease and transplantation into a national registry. Collecting this data into one nationwide registry is expected to improve medical care of children including those who have received renal transplants.

Explanation of Procedures

Medical information, including test results, that are routinely obtained on children with renal disease and children who have received renal transplants will be provided to NAPRTCS. No extra testing is done on children simply because they participate in NAPRTCS. Information about your child shall be given to NAPRTCS on several different forms, which NAPRTCS has given to us. Your child will be identified on these forms by _____.

All patients participating in NAPRTCS will have information collected following their initial evaluation and at regular periods subsequently (typically 6 months) until the patient transfers to another center, resigns or is removed from the study. The information includes blood test results, physical symptoms, information on height and weight, donor information, complications, type of immunosuppression and other medications, and length of hospitalization.

PARENT'S INITIALS

More detailed information will be collected with any episode of organ rejection or for some adverse events. This information will include physical symptoms, blood test results, biopsy results, and treatment.

Information will also be collected if a NAPRTCS participant transfers to another transplant center, if the investigators are no longer able to collect data on the NAPRTCS participant, or upon death of the NAPRTCS participant.

Potential Risks and Discomforts

There should be no risk or discomfort for your child should he/she participate in this study.

Potential Benefits to Subjects

The accumulation of information on pediatric renal transplant in a uniform fashion is expected to benefit subjects by improving the overall quality of care.

Potential Benefits to Society

The accumulation of information of pediatric dialysis, treatment for chronic renal insufficiency or who have or who need renal transplantation in a uniform fashion is expected to benefit society by providing information about outcomes from different clinical practices.

Alternatives to Participation

If you desire not to have your child participate in this study, the care of your child will not be affected.

Financial Obligation

There is no cost to you for participating.

Assurance of Confidentiality

Any information obtained during this study which would identify your child will be kept strictly confidential. Information obtained in this study will be furnished to the Data Coordinating Center. The information obtained in this study may be published in scientific journals or presented at scientific meetings, however, your child's identity will be kept strictly confidential.

Rights of Research Subjects

Your child's rights as a research subject have been explained to you. If you have any additional questions concerning your rights, you may contact: _____, MD Primary Investigator Telephone - _____

If you have any questions about your rights as a research subject, you may contact:

PARENT'S INITIALS

Voluntary Participation and Withdrawal

You are free to decide not to participate in this study or to withdraw your child at any time without adversely affecting your relationship with the investigator(s) or the **(insert name of institution here)**. Your decision will not result in any loss of benefits to which you are otherwise entitled.

Documentation of Informed Consent

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a copy of this form for my records and future reference.

Study subject (age 12-18): _____ **PRINT NAME**

Study subject: _____ **SIGNATURE**

_____ **DATE**

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I give permission for my child to participate in this study. I have received (or will receive) a copy of this form for my records and future reference.

Parent/Guardian: _____ **PRINT NAME**

Parent/Guardian: _____ **SIGNATURE**

_____ **DATE**

PERSON OBTAINING CONSENT

I have read this form to the subject and/or the subject has read this form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information.

_____ **PRINT NAME AND TITLE**

_____ **SIGNATURE**

_____ **DATE**

My signature as witness certifies that the parents/legal guardians signed this consent form in my presence as his/her voluntary act and deed.

_____ **PRINT NAME OF AUDITOR WITNESS**

_____ **TITLE**

_____ **SIGNATURE OF AUDITOR WITNESS**

_____ **DATE**