CHAPTER 2. SCREENING AND RECRUITMENT

2.1 Population

The total number of subjects to be entered in the study at all study sites will be 140.

2.2 Screening/Recruitment Plan

Subjects will be recruited from patients evaluated at, referred to, and followed at the Childhood Liver Disease Research and Education Network (ChiLDREN) study sites, which have been consented and enrolled into the ChiLDREN prospective database study (PROBE) and found to have biliary atresia. The Principal Investigator (PI) or Clinical Research Coordinator (CRC) will recruit the subject's parent(s) or legal guardian(s) during clinic visits, or during an inpatient admission to the hospital when exploratory laparotomy and portoenterostomy are being planned for diagnosis and treatment of biliary atresia. If the subject's parent(s) or legal guardian(s) are not approached about the clinical trial before surgery, recruitment may also occur within 72 hours of the portoenterostomy. The investigator will discuss the study design, benefits and possible risks with the family. Printed information about the study and the informed consent form will be given to the family; questions about the study will be answered.

The Institutional Review Board (IRB)-approved consent will include:

- Purpose of the trial.
- Research procedures used in the trial.
- Responsible parties and investigators.
- Potential benefits.
- Risks of participation.
- Right to refuse to be in the study.
- Right to withdraw from the study under no penalty.
- Contact numbers and information about the responsibility for injury and payment for medical care.

2.3 Eligibility/Exclusion Criteria

All infants enrolled in the ChiLDREN prospective database study (PROBE) who undergo portoenterostomy or the gall bladder Kasai operation (portocholecystostomy) for biliary atresia will be eligible for the trial.

Eligibility: fulfillment of the inclusion/exclusion criteria. This data must be collected at recruitment. The CRCs will need to enter this data into the ChiLDREN website and complete the eligibility Case Report Form (CRF) S11.

2.3.1 Inclusion Criteria

- Portoenterostomy or gall bladder Kasai operation for biliary atresia within the previous 72 hours.
- Post-conception age ≥36 weeks.
- Weight at enrollment ≥2000 gm.
- Written informed consent to participate in the study obtained prior to or within 72 hours of completion of portoenterostomy. (Note: Families of potential subjects may be approached prior to the portoenterostomy.)

2.3.2 Exclusion Criteria

- Known immunodeficiency.
- Diabetes mellitus (glucose ≥200 mg/dL).
- Presence of significant systemic hypertension for age (persistent systolic blood pressure ≥112 mmHg).
- A serum indirect (unconjugated) bilirubin ≥5 mg/dL for infants under 4 weeks of age or ≥7 mg/dL for infants between 4 and 8 weeks of age.
- Known sensitivity to corticosteroids.
- Documented bacteremia or other tissue infection, which is felt to be clinically relevant.
- Known congenital infection or disease with herpes simplex virus, toxoplasmosis, or cytomegalovirus inclusion disease of the liver.
- Infants whose mother is known to have human immunodeficiency virus infection.
- Infants whose mother is known to be HBsAg or hepatitis C virus positive.
- Infants with other severe concurrent illnesses such as neurological, cardiovascular, pulmonary, metabolic, endocrine, and renal disorders that would interfere with the conduct and results of the study.
- Any other clinical condition that is a contraindication to the use of corticosteroid (e.g., bowel perforation).
- Infants who have received the live attenuated rotavirus vaccine (e.g. Rotateq) within 5 days prior to proposed administration of study drug.
  - Infants who have received the live attenuated rotavirus vaccine (e.g. Rotateq) within 5 days prior to proposed administration of study drug are excluded from the study. Infants who have received the vaccine prior to this interval should not receive their first dose of steroids until a total of 5 days post vaccination has elapsed.

In the unlikely event that the diagnosis of biliary atresia is established during exploratory laparotomy, but the surgeon did not perform a portoenterostomy (as may occur in cases of advanced cirrhosis), the patient will not be eligible for this study.

2.4 Exceptions to the Inclusion/Exclusion Criteria

Whenever the answer to an inclusion criterion is no or to an exclusion criterion is yes (even if the condition for the exclusion is fulfilled), an exception/exemption will be required.

When a PI is aware that a request for exception/exemption will be necessary, they can email the Data Coordinating Center (DCC) to have the Exemption Committee review the request prior to obtaining informed consent from the subject. The email should include a sequence number (Exx) for case identification, the exclusion criterion violated and the reason that an exemption is being requested. If approved and the subject is recruited, the Exemption Form would be completed at the time of consent and the DCC will indicate on it the approval of the request. (In order to enter data in the Exemption Request, Form 15, go to the Screening or Baseline section of the subject's CRF on the website.)

The Steering Committee (SC) requests that the DCC email the Exemption Committee with the results of the exemption vote. Pat Robuck from the National Institutes of Health (NIH) requests to be cc'd on these emails.

NOTE: If a subject has been consented and then a question about eligibility arises, please use Form 15. If ineligible, the research subject ID cannot be reused.

2.4.1 Details about Certain Eligibility Criteria

- **Blood pressure**: One of the START ineligibility criteria is significant hypertension, but there is no place provided to record the blood pressure. The blood pressure can be taken any time during the preceding 24 hours and therefore should be available in the hospital record. When this is not possible, the CRC may write the actual blood pressure on Form S11 next to the criterion and note that there is no other source document.

- **Criteria for bilirubin at the time of recruitment/eligibility:** A subject is eligible if at the time of recruitment the known bilirubin is in the eligible range. This blood draw may be from prior to the day of consent. The result of a blood draw that is known after consent does not affect eligibility.

- **Request for a protocol exemption:** If the subject does not meet eligibility criteria, the study site may submit a protocol exemption (form 15). This data is entered into the ChiLDREN website and is forwarded to the Exemption Committee. A response is forward to the study site within 2 days.

2.5 Screening/Enrollment Logs

The Screening/Enrollment Logs form can be either printed off of the ChiLDREN website or developed independently by study-sites to capture the essential information. In either circumstance, it should be kept up to date throughout the study.

- **Screening Form:** An essential document that records all individuals who entered pre-screening or screening and details the reasons why an individual was not enrolled. The screening log demonstrates the lack of bias in the selection of subjects and the investigator's attempt to enroll a representative sample of subjects. This log should be completed separately for each study.

- **Enrollment Log/Master Participant Log:** An essential document that records the enrollment of subjects. The Enrollment Log contains the study subject name or initials, study ID # and informed consent date. This log should be kept in a secured location with procedures in place regarding who has access to remove and under what conditions. With today's computer systems, this log may be an extension of an automated screening log or may be generated by the computer.