

CHAPTER 2

STUDY POLICIES

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2.1 ADHERENCE TO MANUAL OF PROCEDURES

The entire COBLT Study Group participates in the development, review, and acceptance of this Manual of Procedures. The manual is formally approved by the COBLT Study Steering Committee and the Data and Safety Monitoring Board (DSMB). It is essential to the success of the study that all COBLT Study investigators adhere to the procedures outlined herein. If any COBLT Study investigators find that, for whatever reason, adherence to these procedures is difficult or not possible, they should discuss the problem with the Study Chairperson or the Program Office.

2.1.1 FDA Form 1572 (Statement of Investigator)

This form must be filed to complete initial COBLT Study site registration and will be updated annually.

2.1.2 *Curricula Vitae* - Principal Investigators and Co-investigators

A current curriculum vitae or biographical sketch for each physician who will provide medical care is required upon initial site participation in the COBLT Study. Renewal will be requested annually along with resubmission of the Form 1572. The required documentation should be submitted to:

COBLT Study Medical Coordinating Center
The EMMES Corporation
401 North Washington Street, Suite 700
Rockville, MD 20850

2.2 INFORMED CONSENT

Written consents shall be obtained from each COBLT Study patient as part of enrollment. The Transplant Center must ensure that patients are adequately oriented to the objectives and procedures of the COBLT Study. Only after the investigator is satisfied that the patient understands the potential risks and benefits of participation in the COBLT Study will written consent be obtained.

Informed consent is also needed for any additional research procedures that may be part of an ancillary study and may expose the patient to risk or discomfort. The signed consent forms are placed in the patient's file at the Transplant Center.

Informed consent must also be obtained from each donor for the Cord Blood Banks and is described in the CBB SOP.

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2.3 PROTECTION OF HUMAN SUBJECTS

Prior to enrolling patients, each participating Transplant Center must submit to the Medical Coordinating Center (MCC) and the National Heart, Lung and Blood Institute (NHLBI) Project Office a completed copy of Form OF310 that has been approved by the local Institutional Review Board (IRB) and copies of the Transplant Center's local IRB-approved informed consent statements. In addition, annual IRB approval letters must be submitted to the MCC and Project Office.

2.4 DISCLOSURE OF STUDY RESULTS

The results of the trial will be made available to participating investigators at a time specified by the DSMB and as soon as beneficial or harmful effects are established or the trial has concluded. Investigators should refrain from predicting the overall results of the study from their own Transplant Center experience.

Disclosure of COBLT Study results at appropriate times to investigators, participants, the scientific community, and the public will be coordinated closely by the NHLBI and the MCC.

2.5 ACCESS TO INTERIM ENDPOINT DATA

Because knowledge of interim results of the clinical trial could compromise the efforts by Transplant Centers to enroll and maintain follow-up of study patients, reports of such results are submitted by the MCC only to the DSMB, which is responsible for monitoring the results for safety and efficacy.

2.6 SCIENTIFIC PUBLICATIONS AND PRESENTATIONS

2.6.1 Generation of Publications and Presentations

The Publications Committee will develop procedures for generating scientific publications and presentations emanating from the design and data collection of the COBLT Study. These procedures will be reviewed, amended, and approved by the Steering Committee. The Publications Committee will also invite suggestions for additional papers from COBLT Study investigators. It will also be the responsibility of the Publications Committee to make recommendations to the NHLBI for the appointment of writing teams for developing COBLT Study reports and designation of COBLT Study reports as either Primary or Secondary COBLT Study reports. The NHLBI will make the final designation of Primary or Secondary reports.

Primary COBLT Study reports deal with primary COBLT Study objectives; Secondary COBLT Study reports deal with secondary COBLT Study objectives or ancillary studies. Before publication, copies of Primary COBLT Study reports are sent to all members of the Steering Committee for information. Reprints of published reports are mailed to each center for distribution to staff and outside consultants. Reprints of each report are sent to the MCC for the COBLT Study library and the NHLBI.

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2.6.2 Editorial Review

Abstracts of papers to be presented at scientific meetings and manuscripts to be submitted for publication that deal with the design of the COBLT Study or are based on COBLT Study data, whether they pertain to a single COBLT Study center, several COBLT Study centers, or all COBLT Study centers, must be approved by the Steering Committee before presentation or publication. Reports on ancillary studies must be similarly approved. The only exception is oral presentations to local groups on the design of the COBLT Study, which do not need to be approved by the Steering Committee.

Chairpersons of writing teams, in submitting a COBLT Study report for publication, should include a copy of the approval letter from the Chairperson of the Steering Committee.

2.6.3 Authorship

The Publications Committee will develop policies for determining authorship for all other papers.

2.6.4 Acknowledgments

Primary COBLT Study reports will acknowledge the participation of the COBLT Study Transplant Centers and Cord Blood Banks who participated in the study. Membership of major committees may also be acknowledged.

Primary and Secondary COBLT Study reports will acknowledge support of the study by contracts from the NHLBI, National Institutes of Health.

2.7 ANCILLARY STUDIES

Ancillary studies are investigations that are conducted concurrently with the COBLT Study and involve COBLT Study participants. These studies must be approved by the COBLT Study Steering Committee and the DSMB.

2.7.1 Definition of Ancillary Studies

An ancillary study is research on COBLT Study patients that meets the following criteria:

- ! The research is conducted by COBLT Study investigators on COBLT Study participants, on stored cord blood units, or on cord blood units released to COBLT study investigators.
- ! The goals of the study are consistent with COBLT Study objectives and are not included among the study objectives stated in a COBLT Study Protocol.
- ! The research requires supplementary clinical observations or procedures on COBLT Study patients or cord blood units.

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- ! The COBLT Study Steering Committee, with NHLBI approval, has designated the study as a COBLT Study ancillary study, thus endorsing participation by the MCC in study development, conduct, data processing, and data analysis.

Studies involving cord blood units will not be considered ancillary if the units have been released to investigators who are not associated with COBLT. Note that units should only be released to investigators who have an IRB-approved research protocol.

Ancillary studies by individual COBLT Study investigators or groups of COBLT Study investigators are encouraged because they can enhance the value of the COBLT Study and increase the motivation and interest of investigators in the COBLT Study. However, to protect the integrity of the COBLT Study and to prevent a drain on COBLT Study resources, all proposals for ancillary studies, whether or not they involve the need for supplementary funds, must be submitted for approval to the Steering Committee and the DSMB.

2.7.2 Approval of Ancillary Studies

Approval is needed to assure that ancillary studies will not:

- ! Complicate the interpretation of COBLT Study results
- ! Result in premature release of COBLT Study outcome data
- ! Violate patients' rights
- ! Adversely affect patient enrollment or cooperation
- ! Jeopardize the public reputation of the COBLT Study
- ! Substantially divert study resources at the Transplant Centers or the Medical Coordinating Center (MCC)

Investigators wishing to conduct an ancillary study should submit a proposal through the MCC, who will distribute it to the Steering Committee. After review by the Steering Committee, the Principal Investigator (PI) of the MCC will summarize the Committee's comments and forward the proposal and comments to the Steering Committee and DSMB for secondary review, along with a copy of the comments to the applicant. If appropriate, the PI of the MCC, before forwarding the materials to the Steering Committee and DSMB, will give the applicant an opportunity to amplify, clarify, or withdraw the proposal. Amended proposals will be reviewed by the Steering Committee and the DSMB.

Proposals for ancillary studies should briefly describe the objectives, methods, and significance of the study and provide full details on procedures (e.g., laboratory procedures, examinations, questionnaires) to be carried out on patients, the extent to which visits will be prolonged, and if additional visits will be needed. The proposal should include, if appropriate, an informed consent statement.

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2.7.2.1 Funding of Ancillary Studies. If no additional funds are required, the investigator may proceed with the ancillary study as soon as it is approved by the Steering Committee and DSMB. For additional funds, the investigator may submit a research grant application to a funding agency after approval by the Steering Committee and DSMB, and after consultation with the Project Officer, NHLBI.

2.7.2.2 Publication of Ancillary Study Results. Manuscripts to be submitted for publication or presentations of ancillary study data at scientific meetings must be reviewed and approved by the Steering Committee.