

Guidelines for Collection, Processing, and Storage of Cord Blood Stem Cells

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**New York State Council on Human Blood and Transfusion Services
New York State Department of Health
Wadsworth Center
P.O. Box 509
Albany, New York 12201-0509**

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Requests for copies of this publication may be directed to:

Blood and Tissue Resources Program
Wadsworth Center
New York State Department of Health
P.O. Box 509
Albany, New York 12201-0509

Phone (518) 485-5341
Fax (518) 485-5342
e-mail: BTRAXESS@health.state.ny.us
www.wadsworth.org/labcert/blood_tissue

**NEW YORK STATE DEPARTMENT OF HEALTH
COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES**

Dennis Galanakis, M.D. (Chairperson)
SUNY Health Science Center
Stony Brook, New York

Lazaro Rosales, M.D.
SUNY Health Science Center
Syracuse, New York

Robert Dracker, M.D.
North Area Pediatrics, Inc.
Syracuse, New York

Donna Skerrett, M.D.
New York Presbyterian Hospital
New York, New York

William Fricke, M.D.
Rochester General Hospital
Rochester, New York

Antonia C. Novello, M.D., M.P.H., Dr.P.H.
Commissioner of Health
New York State Department of Health
Albany, New York

Alicia E. Gomensoro-Garcia, M.D.
Maimonides Medical Center
Brooklyn, New York

Jeanne V. Linden, M.D., M.P.H.
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Albany, New York

Ms. Gloria Rochester
Queens Sickle Cell Advocacy Network
St. Albans, New York

HEMATOPOIETIC PROGENITOR CELL COMMITTEE

Robert Dracker, M.D. (Chairperson)
North Area Pediatrics
North Syracuse, New York

Rajendra N. Pahwa, M.D.
North Shore University Hospital
Manhasset, New York

Niculae Ciobanu, M.D.
Stem Cell Sciences, Inc.
New York, New York

Robert Preti, Ph.D.
Progenitor Cell Therapy, L.L.C.
Hackensack, New Jersey

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Center
New York, New York

Donna Skerrett, M.D.
New York Presbyterian Hospital
New York, New York

Jeanne V. Linden, M.D., M.P.H.
New York State Dept. of Health
Albany, New York

David L. Wuest, M.D.
Memorial Sloan-Kettering Cancer Center
New York, NY

Philip L. McCarthy, M.D.
Roswell Park Cancer Institute
Buffalo, New York

WORKING GROUP ON CORD BLOOD STEM CELL GUIDELINES

We gratefully acknowledge the efforts of the following experts in contributing to the first edition of these guidelines, published in May 1997.

Rajendra N. Pahwa, M.D. (Chairperson)
North Shore University Hospital
Manhasset, New York

Jeanne V. Linden, M.D., M.P.H.
New York State Dept. of Health
Albany, New York

Richard Berkowitz, M.D.
Mt. Sinai Medical Center
New York, New York

Robert A. Preti, Ph.D.*
Hudson Valley Blood Services
Valhalla, New York

Robert Dracker, M.D.
North Area Pediatrics
North Syracuse, New York

Cladd Stevens, M.D.
New York Blood Center
New York, New York

Niculae Ciobanu, M.D.
Stem Cell Sciences, Inc.
New York, New York

*Now at Progenitor Cell Therapy, L.L.C.
Hackensack, New Jersey

GUIDELINES FOR COLLECTION, PROCESSING, AND STORAGE OF CORD BLOOD STEM CELLS

Principles: Cord blood is defined as blood contained within the umbilical cord and blood in the contiguous placental circulation. Collection of cord blood for the express purpose of harvesting stem cells should be performed in a manner which would not alter the delivery of the infant; would not increase the likelihood of any adverse reaction in the infant or mother; and/or would not preclude appropriate medical management of the infant or mother, including collection of cord blood diagnostic specimens.

I. Donor evaluation.

A. Informed consent.

Informed consent for collection of cord blood must, in all cases, be obtained before stem cells are placed in inventory. Consent from preferably both parents, but at least one parent or a legal guardian, should be obtained. Parents should be clearly informed of all available options. The informed consent document should disclose all financial ramifications of the collection and storage procedure, and include a statement regarding limitations of any implied guarantees or warranties.

1. **Timing of informed consent.** Whenever possible, informed consent should be obtained prior to onset of labor. In all cases of *in utero* collection, consent must be obtained prior to collection.
2. **Person obtaining informed consent.** Informed consent should be obtained by an individual appropriately trained in the informed consent process, and with sufficient knowledge of all aspects of cord blood collection, processing and storage, as well as relevant applications of the stem cell product.

B. Donor Suitability Determination.

1. A personal and family medical history of the biologic mother, in all cases, and biologic father, if available, of the prospective cord blood cell donor should be obtained and documented prior to, or within 48 hours of, the collection and shall be reviewed prior to the release for infusion of the cord blood-derived cells. At the time of collection, the mother should be in good health and without evidence of active infection that may be transmissible transplacentally. The medical history should include an assessment of genetic disorders affecting, as a minimum, the genetic mother, father and siblings of the newborn.
2. A sample of blood from the donor's mother must be collected within 30 days prior to or 72 hours after donation and tested promptly for anti-HIV-1, anti-HIV-2, anti-HTLV-I/II, HBsAg, anti-HBc, anti-HCV and syphilis. Appropriate testing should be performed to demonstrate whether the mother has active CMV infection. If the original testing was prior to the onset of labor, it may be desirable to retest the mother at the time of collection to minimize the window period of any carried viral infection.

3. In the event of a positive test result for any infectious disease (other than CMV), an attempt should be made to notify the mother of the donor within five working days of the receipt of the test results by the cord blood bank. Failure to make contact with the mother for purposes of notification should not preclude the use of the cord blood for transplant. Rather, the nature of the infectious disease should determine the utility of the product. It is recommended that cord blood collected from a newborn infant whose mother has positive test results for infectious disease markers (other than for CMV) not be used for transplantation without documentation of the rationale for such use from the transplant physician and the informed consent of the patient (recipient) and/or the patient's (recipient's) guardian. If the mother is HIV positive, cord blood should not be used for allogeneic transplant.
4. Consideration should be given to testing a sample of the cord blood for infectious diseases. Such a strategy may serve as an added safeguard to ensure the identity of the cord blood.
5. Red blood cells from the infant donor or from the cord blood collected should be tested for ABO and Rh group.
6. For community cord blood collections, appropriate Class I and Class II HLA typing of the cord blood component should be performed shortly after collection and the results stored in a way that lends itself to search. Such storage of data and data retrieval should be performed in accordance with currently accepted methods. For family storage, a sample may be held in storage for subsequent HLA typing.

C. **Facility notification and authorization.** An access agreement/acknowledgment between the administration of the hospital or collection site and the licensed cord blood bank should be established prior to the collection of cord blood. Such established agreement/acknowledgment should delineate responsibilities for the collection, handling, transportation and disposition of all cord blood samples.

II. **Cord blood collection and processing methods and procedures.**

A. **Cord blood collection personnel.**

1. Cord blood collection should be performed by staff with documented appropriate training, experience, and proficiency in the technique utilized. Health professionals with experience in venipuncture, infection control, and handling of biohazardous material (e.g. physicians, nurses, licensed midwives or bone marrow technicians) should receive training sufficient to perform the procedure. Other health professional staff will require additional training.
 - a. Training.
 - 1) Standard operating procedures should be read and understood; this should be attested to by a signed statement of the staff.
 - 2) Instruction may be in person or by videotape and/or written materials.
 - 3) Training should be acquired in advance of the collection (preferably

prior to the onset of labor).

b. Experience and proficiency.

Experience may be acquired by collection of cord blood that is not intended for subsequent clinical use. For personnel other than licensed health care professionals who perform deliveries of infants, proficiency should be demonstrated by performing a minimum of five collection procedures in which cord blood is not intended for clinical use unless there is documented direct supervision by trained personnel. Proficiency should be demonstrated prior to the collection of cord blood for clinical use, and at least yearly thereafter.

B. Collection methods.

1. Procedures used should be documented to result in retention of adequate sterility and stem cell viability.
2. The collection of cord blood should not result in any deviation from normal obstetric procedures (e.g. for time of clamping).
3. *In utero* (prior to placental delivery) and *ex utero* (following placental delivery) collection methods are both acceptable and have comparable efficacy. Use of a closed or semi-closed system (bag or syringe) by venipuncture of the umbilical vein under aseptic conditions is recommended. Use of open cord vessels for collection is unacceptable.
 - a. The collection procedure should present no foreseeable harm for either the mother or child or compromise the cord blood sample.
 - b. *In utero* collection is an invasive procedure and should be performed by the obstetrician or allied health care professional responsible for delivery of the infant, with full consideration of possible adverse effects on the mother and child.
4. **Collection.** The collection of cord blood should not affect the care of the mother or child and there should be no significant deviation from normal procedures. Collections of cord blood are generally more successful if initiated within ten minutes of the birth of the infant.
5. **Labeling of cord blood.** At the completion of collection, the primary collection container should bear, at a minimum, sufficient information to identify the product, the source and destination, the donor and recipient (if known), recommended conditions for storage and transportation, and product characteristics such as anticoagulant used.

C. Processing and storage methods. Processing of cord blood should commence within 48 hours of collection. Pre-processing cord blood storage temperature should be maintained at between one degree Celsius and ambient temperature, depending on methods used.

1. **Collection and storage vessels.** Cord blood should be collected and stored in vials, bags, or other containers approved for cryopreservation of hematopoietic progenitor cells or validated by the cord blood bank to maintain viability.

2. **Separation methods.** Separation methods should be approved by the director, described in written procedures and demonstrated to be free of bacterial contamination. Methods should also be approved by the institutional review board or be well-described in the medical literature.
3. **Sterility testing.** Sterility testing for bacterial and fungal contamination should be performed on a sample collected after addition of the cryoprotectant mixture and the results evaluated as a component of quality control for the procedure. Testing may also be performed on a sample of the cord blood obtained at the time of collection.
4. **Cryopreservation.** Cells should be cryopreserved by methods detailed in written procedures using reagents approved for human use. Methods should be well described in the medical literature or approved by an institutional review board. Non-human animal colloids should not be used.
5. **Storage temperature.** After processing, cells should be stored within a temperature range of minus 196 degrees Celsius to minus 80 degrees Celsius. If the storage period exceeds one year, cells should be stored at a temperature of less than minus 130 degrees Celsius.

Cells should be stored continuously in either a mechanical freezer or liquid nitrogen tank equipped with an audible alarm.

Refrigeration devices used should be reserved for hematopoietic progenitor cells, other tissues intended for transplantation, and/or blood intended for transfusion. A backup system should be in place in the event of unexpected mechanical failure or liquid nitrogen loss.

6. **Labeling.** The final product container should be labeled and/or tagged in accordance with Department of Health regulations for labeling hematopoietic progenitor cells found in 10 NYCRR Section 58-5.6(d)(4). The label should be legible and indelible and, at a minimum, should contain the donor's identification code and, if positive for any required tests for infectious disease markers (other than tests for CMV), a biohazard label.
7. **Safeguards to prevent mixups.** The director should be responsible for implementing safeguards to prevent mixup of specimens during collection and processing.

D. **Sample retention.**

1. Two or more samples of cord blood should be retained from each donor in order to provide adequate material for confirmatory testing, additional HLA typing, and for other additional testing (other than genetic testing) that is currently not standard practice, but may become important as the field matures and more information is known about *in vitro* characteristics affecting component transplantability. It may also be desirable to save similar samples from the mother's blood.
2. It is recommended that cellular samples be either physically stored with the actual component from which derived or under similar conditions. A system

should be in place to ensure that the contents of the sample tube are actually derived from the cord blood product they intend to represent. Such assurance should be reflected in the standard operating procedures for preparation of cellular samples, labeling of sample tubes and storage containers, and for process control.

3. For all products still in storage or already transplanted, samples should be retained for an appropriate period of time. For discarded cord blood and for specimens used for research, samples need not be retained indefinitely and may be discarded at the time the cord blood is removed from inventory.

E. **Length of storage.**

1. There is no evidence at present that cells stored at minus 196 degrees Celsius in an undisturbed manner lose either *in vitro*-determined viability or biological activity. Therefore, at the current time, no expiration date need be assigned to cord blood stored continuously under liquid nitrogen.
2. For specimens whose storage may have been compromised, assessment of the accepted *in vitro* correlates for transplantability should be performed on similarly stored samples of the product prior to ablative therapy of the prospective patient. Such analyses may include colony growth assays, CD34 enumeration, viability testing, or other appropriate indices of viability acceptable to the transplant physician. Appropriate microbiologic assays should be performed. Results should be communicated to the physician responsible for the patient's care and documented.

III. **Release.** At the time of release for infusion, a tag should be attached to the container bearing information sufficient for identification of the proper recipient and the component, and clearly listing any relevant product testing. In addition, information received after, during or as a result of the processing procedure, including, but not limited to, type and volume of any additive, method(s) of manipulation, and most recent test results, should be included on the container tag or packing slip.