AMERICAN
ASSOCIATION
OF BLOOD BANKS

November 30, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr. Room 1-23
Rockville, MD 20857

Re: Docket No 97N-0497 Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood Hematopoietic Stem/Progenitor Cell Products; Request for Comments

Dear Docket Officer:

The American Association of Blood Banks (AABB) is the professional society for over 8,000 individuals involved in blood banking and transfusion medicine and represents approximately 2,000 institutional members, including blood collection centers, hospital-based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.

The AABB has recently published the first edition of Standards for Cord Blood Services. These Standards became effective October 1, 2001 and the requirements must be met in order to obtain AABB accreditation. The AABB submits these Standards for Cord Blood Services in response to the FDA request for proposed product standards. The format of Standards for Cord Blood Services is to state the general quality Standards at the beginning of each chapter, followed by the technical requirements

The AABB has previously submitted Standards for Hematopoietic Progenitor Cell Product Services, and intends to submit the third edition of that publication for FDA consideration as soon as it is published.

97N-0497 C15

8101 Glenbrook Road ♦ Bethesda, MD 20814-2749 ♦ Phone: (301) 907-6977 ♦ Fax: (301) 907-6895
Web site: www.aabb.org ♦ Email: aabb@aabb.org

The AABB appreciates the opportunity to comment on this draft guidance. Any questions may be directed to Kay Gregory, Director Regulatory Affairs, at 910-842-2790 or kayg@aabb.org.

Sincerely,

Dale Malloy

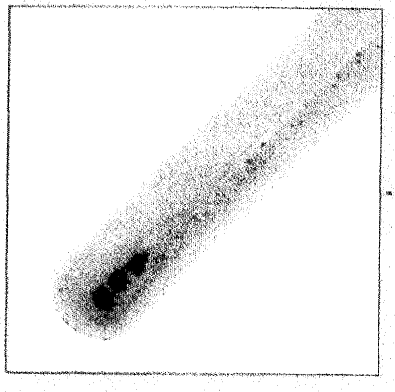
Dale Malloy DPA, MT(ASCP)SBB
President

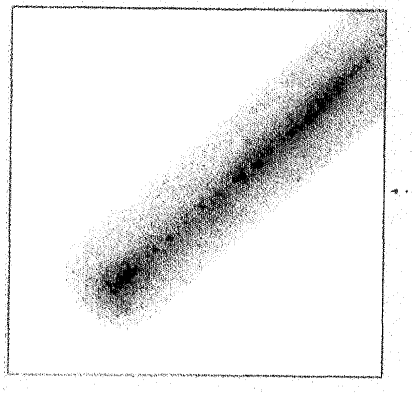
Enclosures

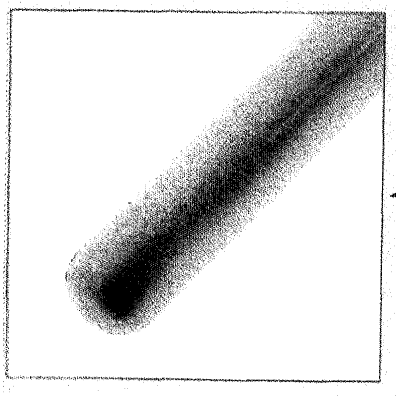
8101 Glenbrook Road ♦ Bethesda, MD 20814-2749 ♦ Phone: (301) 907-6977 ♦ Fax: (301) 907-6895
Web site: www.aabb.org ♦ Email: aabb@aabb.org

Standards for

Cord Bloo







AMERICAN
ASSOCIATION
OF BLOOD BANKS

American Association of Blood Banks

STANDARDS FOR CORD BLOOD SERVICES

First Edition

American Association of Blood Banks
8101 Glenbrook Road
Bethesda, Maryland 20814-2749
United States of America

ISBN 1-56395-144-4
Printed in the United States

Standards Program Committee

Members

Jay Menitove, MD, Chair
Linda A. Chambers, MD
David W. Gjertson, PhD
Jed B. Gorlin, MD
N. Rebecca Haley, MD
Teresa Harris, MT(ASCP)SBB
Bonni Hazelton, PhD
Linda Issitt, MT(ASCP)SBB
Paula J. Santrach, MD
Virginia M. Vengelen-Tyler, MBA, MT(ASCP)SBB, CQA(ASQ)

Liaisons

Accreditation Program Committee, Susan Wilkinson, EdD, MS, MT(ASCP)SBB
Armed Services Blood Program Office, Lt. Col. Michael Fitzpatrick, MT(ASCP)SBB
Food and Drug Administration, Larry Fenner, MT(ASCP)SBB, Jong-Hoon Lee, MD
International Liaison, German LeParc, MD
Technical Manual Committee, Mark Brecher, MD

Quality Management Subcommittee

Linda A. Chambers, Chair
Nicholas Bandarenko, MD
Lucia M. Berte, MA, MT(ASCP)SBB, CQA(ASQ)
Alice Carey, MS
Cheryl Conley, PhD
Rosalie Dvorak-Remis, MHS, MT(ASCP)SBB
Catherine Finke, MA, MT(ASCP)SBB
Betsy W. Jett, MT(ASCP)
Regina M. Leger, BA, MT(ASCP)SBB, CQMgr(ASQ)

Cord Blood Standards Program Unit

Members

Linda A. Issitt, MT(ASCP)SBB, Chair
Cynthia A. Fisher, MBA
Laura Gindy, MT(ASCP)SBB
Kevin F. Long, MS, MT(ASCP)SBB
Ellen Mackintosh, BSMT, MT(ASCP)
Richard Meagher, PhD
Nancy Rebecca Haley, MD
Terry Perlin, PhD

Liaisons

Geralyn M. Meny, MD
Nicholas Bandarenko, MD
Dennis L. Confer, MD
Ronald N. Harkey
Ellen F. Lazarus, MD
Zbigniew M. Szczepiorkowski, MD, PhD

Consultant

Thomas Lane, MD

PREFACE

The American Association of Blood Banks (AABB) has been developing standards for blood banks and transfusion services for over 40 years. With the endorsement of the AABB Board of Directors, the AABB is pleased to present the 1st edition of these *Standards for Cord Blood Services*.

The role of the Standards Program Committee (SPC), an umbrella committee, is to oversee the creation, development, and revision of all AABB standards and to harmonize and ensure consistency in AABB's standard-setting activities. The Cord Blood Standards Program Unit was created in 2000, when the AABB Board of Directors elected to expand the Standards Program Committee to draft standards for cord blood services. The SPC consists of a chair, two subcommittees, and specialty program units. The Quality Management Subcommittee (QMS) ensures that all quality management concepts incorporate a consistent message. The standards program units create the technical standards based on a review of the current scientific and medical data, when available. The program units are: blood banks and transfusion services, hematopoietic progenitor cell services, immunohematology reference laboratories, cord blood services, parentage testing laboratories, and perioperative autologous blood programs. The subcommittees and program units work together to ensure that the standards and guidance content, particularly as it relates to quality management concepts, and format are consistent with the goals of the AABB.

The AABB's interest in expanding the cord blood standards coincides with recent advances in transplant technology, as well as increased public awareness of the therapeutic benefits of cord blood.

Under this format, general quality standards are stated at the beginning of each chapter, and technical requirements follow. Wherever possible, the program unit has made every effort to ensure that the requirements presented in this document reflect a compromise between the recognition that cord blood services programs operate differently from one another and that,

simultaneously, the standardization of certain criteria is an important and necessary step in this process.

The SPC has made a clear distinction between standards and guidance. The *Cord Blood Standards* contain requirements that must be implemented by accredited AABB institutions. Standards are signified by the term "shall." All guidance to these *Cord Blood Standards* will be published with guidance for the *Standards for Hematopoietic Progenitor Cell Services* in a separate document to better clarify what is expected (required) vs what is recommended. The intent of guidance is to provide rationales for standards or examples of how standards might be implemented.

The AABB believes that the implementation of such quality driven management requirements, challenging as they may be, will benefit both cord blood programs and their patients. Further, implementation of these *Cord Blood Standards* should help open communication between cord blood service personnel.

I would like to extend a thank you to all members of the Cord Blood Standards Program Unit for all their effort, dedication, expertise, and hard work that went into writing these standards. A mere 7 months elapsed between the time the group was appointed and the completion of their assignment. They did a phenomenal job in a short time and I thank each and every one of them. It was a pleasure to work with such a dedicated group. A special thanks to our AABB staff who did an excellent job in organizing meetings and conference calls, providing guidance when needed and keeping up with the multitude of changes in writing the standards.

Linda A. Issitt, MT(ASCP)SBB
Chair, Cord Blood Standards Program Unit

INTRODUCTION

These *Standards for Cord Blood Services* have been prepared by the Cord Bood Standards Program Unit, (which was originally a work group of the Hematopietic Prognitor Cell Standards Program Unit), the Quality Management Subcommittee, and the Standards Program Committee of the American Association of Blood Banks to maintain and enhance the quality and safety of collection, processing and cryopreservation of cord blood, and to provide a basis for accreditation by the AABB. The effective date of the 1st edition of *Cord Blood Standards* for purposes of the activities of the AABB is October 1, 2001.

Some terms or phrases are specifically defined for purposes of these *Cord Blood Standards*. The term "shall" is used to indicate a mandatory statement and describe the single acceptable activity or method; failure to meet the specified requirement would constitute a nonconformance under the Accreditation program of the AABB. The word "should" is used to indicate a recommendation. The term "may" is used to reflect an acceptable method or practice that is recognized but not required. The phrase "the cord blood service shall establish policies" or "have a process" indicates that the institution must have a specific policy or process relating to the applicable issue, and does not necessarily require implementation of a prescribed practice. A glossary is included, the terms of which are defined to reflect usage in the context of these *Cord Blood Standards*, not general usage. Terms listed in the glossary are underscored when first used in the text.

Cord Blood Standards represents performance requirements that may be exceeded in practice. Many organizations working in special situations can, and should, be more rigorous in their internal requirements. There may be legal requirements of federal, state, and local governments that apply as well. *Cord Blood Standards* have been developed on the basis of good medical practice and, when available, scientific data. Although the majority of the standards are in compliance with applicable federal laws and requirements, no assurances can be given that compliance with *Cord Blood Standards*

TABLE OF CONTENTS

1. MANAGEMENT RESPONSIBILITY

1.1 Quality Policy

The cord blood service's executive management shall define and document the cord blood service's policy for achieving and maintaining quality in donor selection, collection, processing, storage, distribution, and transplantation and/or the provision of services ("hereinafter the collection, processing, storage, distribution, and transplantation of cord blood and the provision of related services"). The quality policy shall describe the cord blood service's objectives for quality and its commitments to quality. The cord blood service's executive management shall ensure that this quality policy is understood, implemented, and maintained at all levels of the organization.

1.2 Organization

1.2.1 Responsibility and Authority

The cord blood service shall define and document the responsibility, authority, and relationship of personnel who perform, verify, or manage work covered by these *Cord Blood Standards*, particularly for personnel who:

1) Ensure that the collection, processing, storage, distribution, and transplantation of cord blood and provision of related services conform to specified requirements (see Section 2.1, General).
2) Identify, and maintain records of, any problems related to the quality system, the collection, processing, storage, distribution, and transplantation of cord blood and provision of related services.
3) Initiate, recommend, or implement corrective action to these problems.
4) Verify the implementation and assess the effectiveness of corrective action.

5) Control further collection, processing, storage, distribution, or transplantation of cord blood and the provision of provision of related services until the problem has been corrected.

1.2.2 Resources

The cord blood service shall identify resource requirements and provide adequate resources to perform, verify, and manage any activity covered by these *Cord Blood Standards*.

1.2.3 Management Representative

The cord blood service's executive management shall appoint a member of management who, irrespective of other responsibilities, shall have defined authority for ensuring that the cord blood service establishes, implements, and maintains a quality system that meets the requirements of these *Cord Blood Standards*. This individual shall report to executive management on the performance of the quality system. This report shall be the basis for management review and improvement of the quality system.

1.2.4 Management Review

The cord blood service's executive management shall review the quality system at defined intervals that ensure the system meets the requirements of these *Cord Blood Standards*. Records of these reviews shall be maintained in conformance with Section 16, Control of Records.

1.2.5 Management Responsibility and Qualifications

1.2.5.1 Executive Management

The cord blood service shall define executive management. Executive management shall have responsibility and authority for the cord blood service's operations and the authority to establish

or make changes to the cord blood service's quality policy and quality system.

1.2.5.1.1 Medical Director

The cord blood service shall have a medical director who is a licensed physician and qualified by training and/or experience (in procurement, processing, and cryopreservation). The medical director shall have responsibility and authority for all medical aspects of the cord blood service that are related to the provision of cord blood and related services.

1.2.5.1.2 Laboratory Director

The cord blood service shall have a laboratory director with a relevant doctoral degree who is qualified by training and/or experience. The laboratory director shall have responsibility for all technical aspects of the cord blood service that are related to the provision of cord blood and related services.

1.2.5.2 Job Qualifications

The cord blood service shall identify appropriate qualifications for each job position that affects quality.

2. QUALITY SYSTEM

2.1 General

The cord blood service shall establish, document, and maintain a quality system to ensure that the collection, processing, storage, distribution, and transplantation of cord blood and provision of related services conform to specified requirements. The cord blood service shall prepare a quality manual that incorporates or references the requirements of these *Cord Blood Standards*, incorporates or references detailed cord blood service processes and procedures, and outlines the structure of the documentation used in the quality system.

2.2 Quality System Policies, Processes, and Procedures

The cord blood service shall develop, document, and effectively implement policies, processes, and procedures for the quality system to ensure that the requirements of these *Cord Blood Standards* are satisfied.

2.3 Quality Planning for New or Changed Products or Services

The cord blood service shall define and document how the requirements of these *Cord Blood Standards* will be ensured for each new or changed product or service. The documentation shall be in a format that suits the nature of the change and the cord blood service's operations.

2.4 Annual Review of Policies, Processes, and Procedures

Annual review of each policy, process, and procedure that affects the quality of the cord blood service shall be performed by the medical director or designee. Records of these reviews shall be maintained in conformance with Section 16, Control of Records.

3. AGREEMENT REVIEW

3.1 General

The cord blood service shall establish and maintain policies, processes, and procedures for reviewing agreements to provide cord blood units and services to the cord blood service's customers.

Note 1: For issues relating to the acquisition of input cord blood units or services by a cord blood service, see Section 6, Obtaining Materials (Including Cord Blood) and Services.

3.2 Review

Before acceptance of a verbal or written agreement, the agreement shall be reviewed by the cord blood service to ensure that:

1) The customer's requirements are adequately defined.
2) Any differences between the agreement requirements and the cord blood units or services offered under the agreement are resolved.
3) The cord blood service has the capability to meet the agreement requirements.

3.3 Changes to Agreements

The cord blood service shall define how changes to agreements are made and communicated to affected cord blood service personnel.

3.4 Records

Records of agreements and reviews of, or changes to, agreements shall be maintained in conformance with Section 16, Control of Records.

3.5 Agreements Relating to Cord Blood

3.5.1 Agreements to Collect Engraftment Data and Outcomes of Transplantation

Prior to issuing a cord blood unit for transplantation, the cord blood service shall have an agreement with the transplant center or intermediary facility to ensure that engraftment data and information on adverse events potentially linked to the transplanted cord blood unit are collected and provided to the cord blood service.

3.5.1.1 Agreements to collect engraftment data shall define the relevant outcome data that will be provided to the cord blood service. Standards 3.5.4 and 17.3 apply.

3.5.2 Informed Consent

The cord blood service shall obtain informed consent of the birth mother and, if applicable, the legal custodian(s) (hereinafter referred to as "the consenters") in conformance with AABB reference Standard 3R-A and applicable law. Informed consent records shall be maintained in conformance with Section 16, Control of Records.

3.5.2.1 The informed consent process shall begin before collection and be completed within 48 hours of collection.

3.5.3 Disposition Agreements

There shall be agreement(s) between the cord blood service and any consenters, the intended recipient (if one has been identified) and the transplanting physician (if any) regarding the terms and length of storage and terms for disposition of the cord blood unit.

3.5.3.1 Unless otherwise addressed in the agreement, the following requirements shall be met prior to the time of discard.

3.5.3.1.1 If an intended recipient dies or no longer needs the unit, the transplant physician shall notify the cord blood service regarding the release of the unit to inventory.

3.5.3.1.2 Related or Autologous Units
If the cord blood service is notified that the intended recipient has died or no longer needs the cord blood, the cord blood service shall make a good-faith effort to contact the donor or the donor's legally designated surrogate regarding the continuing need for storage.

3.5.3.2 Any medical therapy to be provided by the cord blood service shall be ordered by the patient's physician. Orders shall contain sufficient information for positive identification of the patient.

3.5.4 Divided Responsibilities
Agreements between facilities shall define the responsibility of each party for record retention.

4. DESIGN CONTROL

4.1 General

The cord blood service shall establish and maintain policies, processes, and procedures to control and verify the design of new or changed cord blood units or services to ensure that the design goals and specified requirements are met.

4.2 Design Goals

The cord blood service shall identify, document, and review design goals and requirements. Incomplete, ambiguous, or conflicting requirements shall be resolved with those responsible for creating the requirements.

4.3 Design and Development Planning

The cord blood service shall identify how design output will meet design goals. The appropriate organizational and technical groups, including groups responsible for software or hardware processes, shall be identified and consulted during the planning process.

4.4 Design Output

Design output shall:

1) Be documented in a manner that permits verification of the output against design goals and requirements.
2) Meet the design goals.
3) Contain or make reference to acceptance criteria.
4) Meet the characteristics of the design that are critical to the safety and efficacy of a new or modified cord blood unit or service.

Records shall be maintained in conformance with Section 16, Control of Records.

4.5 Design Review

Where applicable, reviews of the design output shall be planned and conducted at appropriate stages of design. Records shall be maintained in conformance with Section 16, Control of Records.

4.6 Design Verification

Design verification shall be performed to ensure that the design output meets the design goals. Records shall be maintained in conformance with Section 16, Control of Records.

4.7 Design Validation

Design validation shall be performed to ensure that the cord blood unit or service consistently conforms to defined requirements. Records shall be maintained in conformance with Section 16, Control of Records.

4.8 Design Changes

All design changes shall be identified, documented, reviewed, and approved by appropriate personnel before their implementation. Records shall be maintained in conformance with Section 16, Control of Records.

4.8.1 There shall be a process for qualifying a test methodology for implementation.

4.9 Design Approvals

Research and related services performed under a research protocol that involves the provision of cord blood units intended for transplantation shall be performed only after approval by an Institutional Review Board (IRB) and, where applicable, under an Investigational New Drug (IND) protocol or Investigational Device Exemption (IDE). Records of approvals shall be maintained in conformance with Section 16, Control of Records.

4.9.1 Research Results

Records of research results, including expected and unexpected clinical effects, shall be maintained in conformance with Section 16, Control of Records.

5. DOCUMENT CONTROL

5.1 General

The cord blood service shall establish and maintain policies, processes, and procedures to control all documents that relate to the requirements of these *Cord Blood Standards*.

5.2 Document Approval and Distribution

The cord blood service shall review and approve all documents prior to issuance. The document control process shall ensure that:

1) Documents are identified with the current revision status.
2) Appropriate documents are available at all locations where operations covered by these *Cord Blood Standards* are performed.
3) Invalid or obsolete documents are not used.
4) Any archived obsolete documents are suitably identified as such.

5.3 Document Changes

Changes to documents shall be reviewed and approved in the same manner as the original review and approval, unless a different process or procedure is specifically established. Individuals authorized to review and approve changes shall have access to all background information necessary to conduct the review and approval.

5.4 List of Documents

The cord blood service shall maintain a master list of all policies, processes, and procedures that relate to the requirements of these *Cord Blood Standards*.

5.5 Format

Policies, processes, and procedures shall be in a standardized format, in conformance with the cord blood service's requirements. Additional policies, processes, and procedures, such as those in an operator's manual, may be incorporated by reference.

5.6 Document Retention

The cord blood service shall have a process to determine which, if any, documents shall be archived or made obsolete. Copies of archived policies, processes, and procedures shall be retained. Standard 16.4 applies.

6. OBTAINING MATERIALS (INCLUDING CORD BLOOD) AND SERVICES

6.1 General

The cord blood service shall establish and maintain policies, processes, and procedures to ensure that purchased, donated, or otherwise acquired materials or services conform to specified requirements.

Note 2: Purchased, donated, or otherwise acquired materials include but are not limited to, cord blood, cord blood intended for further processing, containers, test kits, and reagents. Services include activities required to maintain cord blood service equipment and instruments.

6.2 Evaluation of Suppliers

The cord blood service shall:

1) Evaluate and select any supplier of a material or service that is intended for incorporation into cord blood or services, or that affects the quality of the cord blood or services, on the basis of the supplier's ability to meet specified requirements.
2) Define the type and extent of control required over the supplier. The type and extent of control shall depend upon the type of product or service, the impact of the product or service on the quality of the final cord blood unit or final service, and the previous performance of the supplier.
3) Maintain records of acceptable suppliers in conformance with Section 16, Control of Records.
4) Report to management personnel with contracting authority when a supplier fails to meet specified requirements.

6.3 Purchasing Information

Purchasing documents shall contain information that clearly describes the product or service ordered. The cord blood service shall review and approve purchasing documents for adequacy of the specified requirements prior to release.

Note 3: This section applies only to cord blood laboratories that have the authority to review and/or approve purchasing documents.

6.4 Verification of Purchased Products

6.4.1 Certificate of Analysis

For material that comes into contact with the cord blood, the cord blood service shall obtain a certificate of analysis from the supplier.

6.4.2 Test Kits

Appropriate FDA-licensed, -approved, or -cleared donor screening tests shall be used, when available.*

* Fed Regist 1999;64:52696-723 [Proposed 21 CFR 1271.80(c)].

7. CONTROL OF PATIENT-SPECIFIC (AUTOLOGOUS OR RELATED ALLOGENEIC) CORD BLOOD UNITS

7.1 General

The cord blood service shall establish and maintain policies, processes, and procedures to control 1) the qualification of autologous and related allogeneic donors; 2) testing of patient-specific cord blood units for infectious diseases, and 3) disposition of patient-specific cord blood units.

Note 4: See Section 9, Process Control, for the remainder of the process control requirements related to collection, processing, storage, release, and administration of cord blood units for patient-specific donations.

7.1.1 The cord blood service shall report to the consenters, the intended recipient, and the recipient's physician, if applicable, any cord blood units that are lost, damaged, or otherwise unsuitable for transplantation. Records shall be maintained in conformance with Section 16, Control of Records.

7.2 Control of Patient-Specific (Autologous or Related Allogeneic) Cord Blood Units

7.2.1 Qualification of Mothers of Autologous and Related Allogeneic Donors

The cord blood service shall maintain written qualifications for acceptance of birth mothers of autologous and related allogeneic donors in conformance with reference standards 9R-A and 9R-B.

7.2.2 Testing of Patient-Specific Cord Blood Units for Infectious Diseases

The cord blood service shall perform tests intended to prevent disease transmission in conformance with reference standard 10R-A.

7.2.3 Disposition of Patient-Specific Cord Blood Units

The cord blood service shall define the length of storage and terms of disposition of patient-specific cord blood units. Standard 3.5.2 applies.

8. CORD BLOOD UNIT AND SAMPLE IDENTIFICATION AND TRACEABILITY

8.1 General

The cord blood service shall establish and maintain policies, processes, and procedures that ensure the identification and traceability of each cord blood unit and sample from the donor, through all processing steps, to its final disposition.

8.2 Cord Blood Unit and Sample Identification

8.2.1 Traceability and Unique Identification

A unique alphabetical (alpha) and/or numeric system shall be used that will make it possible to trace any cord blood unit or sample from source to final disposition, and to recheck records applying to the specific cord blood unit, including investigation of reported adverse reactions. The unique identification shall not be obscured, altered, or removed and shall be traceable to the donor.

8.2.1.1 If replaced with another unique alpha and/or numeric identifier, the cord blood service shall make it possible to link the current unique alpha and/or numeric identifier to the previous unique alpha and/or numeric identifier.

8.2.2 Unique Identification of Intermediate Facility

If an intermediary facility assigns or affixes a local, unique numeric or alphanumeric identification to the cord blood unit, the label shall be affixed to the cord blood unit and shall identify the facility assigning the identification.

8.2.3 Limit of Two Unique Identifications

No more than two unique numeric or alphanumeric identifications shall be visible on a cord blood unit, ideally that

of the originating cord blood service and that of the final cord blood service. It may be necessary to remove or obliterate identifications assigned by intermediate cord blood services.

8.3 General Labeling Requirements

Each cord blood unit shall be labeled in conformance with reference standard 8R-A. The donor's name shall be included on the label if it assists in the appropriate identification of the cord blood unit. When the unit is shipped or issued, the labeling information required by reference standard 8R-B shall accompany the cord blood unit.

8.3.1 Abbreviated Labels

If a container cannot accommodate a complete label as defined in reference standard 8R-A, an abbreviated label shall be affixed to the container. See reference standard 8R-A.

8.3.2 Maternal or Cord Blood Sample Identification

The cord blood service shall maintain records identifying the individual drawing the sample, the date and time of collection, and sample source. Records shall be maintained in conformance with Section 16, Control of Records.

8.3.3 Circular of Information

A Circular of Information shall be made available to clinical staff, as appropriate.

8R-A. Requirements for Cord Blood Unit Labels and Labeling Prior to Issue and Shipping

Element	Collection Container Label*	Processing Labeling Information†	Cryopreservation Label‡	Abbreviated Label§
Name of Product	X	X	X	X
Date of collection	X		X	
Time of collection, if applicable	X			
Unique alpha and/or numeric identifier	X	X	X	X
Name of collection service	X		X	
Cord blood unit volume			X	
Names/volumes of anticoagulants and other additives	X		X	
For patient-specific cord blood unit, name or identifier of intended recipient	X, if applicable		X, if applicable	
Phrase: "For Autologous Use Only"			X, if applicable	
Phrase: "For Use by Intended Recipient Only"			X, if applicable	
Phrase: "Do Not Irradiate"	X		X	
Recommended storage temperature	X		X	
Expiration date/time			X, if applicable	
Name of contact person, name of institution, address and telephone number (including emergency number) of receiving cord blood service		X		
ABO group and Rh type of cord blood unit (allogeneic)			X	
Biohazard label (see 10R-B)	X, if applicable		X	

*This information shall be included on/with the cord blood unit at the time of collection.
†This information shall be included on the label during processing steps (includes manipulation).
‡This information shall be included on/with the cord blood (eg, tie tag) prior to cryopreservation. If these elements will not fit on container, they may be included in the container package.
§This represents the minimal information that shall be affixed to the container.

8R-B. Labeling Requirements Upon Shipping or Issuing Cord Blood Units

1. Summary of processing records,* infectious disease testing results, and testing records, including name, address, and emergency contact information for releasing facility.
2. Warning label(s) for potentially toxic or volatile packing materials, including dry ice or liquid nitrogen.
3. Expiration time of systems or materials used for temperature control.
4. Instructions for receiving and opening container.
5. Name, address, and phone number of contact person at receiving facility.
6. Circular of Information and product information.†
7. Notification of biohazardous materials (see reference standard 10R-B).

*Fed Regist 1999;64:52696-723 [Proposed 21 CFR 1271.3(x)].
†Includes but is not limited to: Investigator's brochure, or written description of product.

9. PROCESS CONTROL

9.1 General

The cord blood service shall identify, plan, and validate the policies, processes, and procedures that affect the quality of cord blood units and services. These processes and procedures include the collection, processing, storage, and disposition of cord blood and the provision of related services. The cord blood service shall ensure that these policies, processes, and procedures are carried out under controlled conditions. Controlled conditions shall include:

1) Use of policies, processes, and procedures for the collection, processing, storage, and distribution of cord blood and provision of related services.
2) Use of suitable equipment and a suitable working environment.
3) Compliance with policies, processes, and procedures, and external standards.
4) Monitoring and control of suitable process parameters and cord blood unit characteristics.
5) Approval of processes and equipment.
6) Criteria for acceptable results.
7) Control of equipment.

9.1.1 Use of Materials and Supplies

Materials used during collection, processing, storage, distribution, or administration shall be sterile and without excess toxicity and shall, whenever possible, be approved for human use by the Food and Drug Administration (FDA).

9.1.1.1 If not approved for human use by the FDA, materials shall be either:

a. Approved by the IRB or an external review board with or without IND or IDE acceptance, as required.

b. Within toxicity limits established by the medical literature and current practice for the specified purpose

9.1.1.2 If the cord blood collection container is not FDA-cleared, it shall have at least one port that can be entered aseptically.

9.1.2 Proficiency Testing

The cord blood service shall participate in a Health Care Financing Administration (HCFA)-approved proficiency-testing program, if available, for each analyte tested by the bank. If there is no external HCFA-approved proficiency testing program an analyte, there shall be a process or procedure for determining accuracy and reliability of test results. Section 10 applies. Records shall be maintained in conformance with Section 16, Control of Records. (Section 19.2, Application of Statistical Techniques applies.)

9.1.3 Quality Control

The cord blood service shall establish a program of quality control that is sufficiently comprehensive to ensure that reagents and equipment function as required.

9.1.4 Use of Aseptic Methods

The cord blood service shall use aseptic methods that provide maximal assurance of a sterile process.

9.1.6 Validation of Policies, Processes, and Procedures

The cord blood service shall validate all policies, processes, and procedures prior to use. Records shall be maintained in conformance with Section 16, Control of Records.

9.1.7 Security of Facility

The cord blood service shall ensure that access to the facility is limited to authorized personnel.

9.2 Computer Systems Used in Process Control

A process shall be developed and implemented to support the introduction of new software, hardware, or databases, or modifications of existing software, hardware, or databases relating to the requirements of these *Cord Blood Standards*. This process shall include:

1) Risk analysis, training, validation, implementation, and evaluation of postimplementation performance.
2) Description of system maintenance and operation.
3) Documentation that is written in language that is understandable to the user.
4) A system for display and verification of data before final acceptance when data are added or altered.
5) Description of how modifications to the system are authorized and documented.

9.2.1 Records of the following shall be maintained:

1) Validation of system software, hardware, databases, and user-defined tables.
2) Fulfillment of life-cycle requirements for internally developed software.*
3) Numerical designation of system versions, if applicable, with inclusive dates of use.
4) Monitoring of data integrity for critical data elements.

9.2.2 Alternative Process Control Systems

The cord blood service shall have an alternative system that ensures continuous operation in the event that computerized data and computer-assisted functions are not available. The alternative system shall be tested periodically.

*FDA Guidance dated January 13, 1997, "Reviewer Guidance for a Premarket Notification Submission for Blood Establishment Computer Software." (http://www.fda.gov/cber/gdlns/swreview.txt)

9.3 Donor Qualification Process

9.3.1 Qualification of the Donor and the Birth Mother

The cord blood service shall define the criteria for qualification of an allogeneic donor's birth mother in conformance with reference standard 9R-A. Exceptions to the donor qualification process shall require written approval by the medical director. (For the qualification of birth mothers of autologous and related allogeneic donors, Standard 7.2.1 applies.)

9.3.2 The donor qualification process shall be confidential.

9.4 Collection of Cord Blood

9.4.1 Collection Methods

The cord blood service shall have policies, processes, and procedures for acceptable collection methods.

9.4.1.1 Collection methods shall ensure the safety of the birth mother and the donor.

9.4.2 The identification of the birth mother, the donor, and associated placenta shall be verified prior to collection of the cord blood.

9.5 Cell Processing

9.5.1 General

9.5.1.1 Test Suppliers

Tests required by these *Cord Blood Standards* shall be performed in a bank accredited by the American Association of Blood Banks or other equivalent accrediting body, certified by HCFA, or licensed or registered by the FDA.

9R-B. Criteria for additional testing shall be established by the cord blood service.

9.5.2.4 Review of Processing Record
After completion of processing, the cord blood service director shall review the processing record of each cord blood unit in a timely manner.

9.5.3 Testing of Cord Blood from Allogeneic Donors
The cord blood service shall ensure that the determinations for HLA antigens have been performed. This information shall be available to the intended recipient's physician, when applicable, and the transplant program. The cord blood service shall address the management of HLA type compatibility.

9.5.3.1 HLA
Major histocompatibility antigens (HLA-A, -B, and -DR antigens) shall be determined by a laboratory that is accredited by the American Society of Histocompatibility and Immunogenetics (ASHI) or by an equivalent organization.

9.5.3.1.1 The medical director shall define acceptable levels of resolution of HLA typing by DNA-based methods.

9.5.4 Cryopreservation Methods
The cord blood service shall use cryopreservation methods known to preserve cord blood unit viability, recovery, and potency.

9.5.4.1 Rate Controlled Cryopreservation
If a rate controlling device is used for the cryopreservation method, the cord blood service shall monitor the cooling rate.

9.5.4.2 Alternative Cryopreservation Methods
If an alternative cryopreservation method is used, records of the method and outcome of validation shall be maintained in conformance with Section 16, Control of Records.

9.5.4.3 Cryopreserved Sample Aliquots
To enable future testing, sample aliquots shall be cryopreserved and retained under the same storage conditions as the cellular product.

9.5.4.4 Records
The cord blood service shall maintain cryopreservation records in conformance with reference standard 9R-C and Section 16, Control of Records.

9.6 Cord Blood Unit Release from Storage Facility

The cord blood service shall inspect the conditions of cord blood units prior to release from storage. Records shall be maintained in conformance with reference standard 9R-D and Section 16, Control of Records.

9.7 Administration of Cord Blood to the Patient

The cord blood service shall have a process to review the procedures employed in the interim between unit release and administration. Minimally, such procedures shall address:

1) Temporary product storage when necessary.
2) Thawing procedures.
3) Procedures for unambiguous identification of the intended recipient.
4) Procedures for safe and timely administration of the cord blood.

9R-A. Requirements for Qualification of Biologic and/or Birth Mothers of Donors

Measures for qualification of mothers of donors (including related cord blood donations for future allogeneic related use) for collection shall include:

A. Health History Assessment

1. A personal and family medical history of the biologic mother of the prospective cord blood donor's mother shall be obtained prior to, or within 48 hours before or after, the collection. The history of the donor's mother shall include an evaluation of risk factors for and clinical evidence of relevant communicable disease agents and diseases including at a minimum the following:
   a. Human immunodeficiency virus (HIV).
   b. Hepatitis B virus (HBV).
   c. Hepatitis C virus (HCV).
   d. Creutzfeldt-Jakob disease (CJD) and other human transmissible spongiform encepholapathies.*

   If the medical history is obtained more than 48 hours before collection, the health history shall be reviewed for changes in infectious disease exposures in the birth mother.

2. The cord blood donor's biologic mother shall be questioned regarding a family history (biologic mother, biologic father, or sibling) of genetic disorder that may affect the recipient.
3. In the case of a surrogate mother, a medical history of the surrogate shall also be obtained and documented.

B. Testing of Donor. A screening test for hemoglobin disorders that may affect the recipient shall be included.

* Fed Regist 1999;64:52696-723 (Proposed 21 CFR 1271.75).

9R-B. Processing Tests

A. The following processing tests shall be performed on each cord blood unit:
   1. CD34 analysis.
   2. Total nucleated cell count.
   3. Percent viability.
   4. ABO group and Rh type.
   5. Bacterial culture.

B. The following postprocessing tests shall be performed on each cord blood unit before cryopreservation:
   1. Total nucleated cell count.
   2. Percent viability.
   3. Final cord blood unit volume.

9R-C. Cryopreservation Records

The following cryopreservation records shall be maintained for each cord blood unit:

1. Starting unit product and volume.
2. Relevant cell count.
3. Cell viability.
4. Cryoprotectant solution and volume.
5. Cooling record from controlled-rate freezing, if applicable.
6. Endpoint temperature of cooling.
7. Location of cord blood unit and stored test aliquots.

9R-D. Verification of Cord Blood Units When Released from Storage

The following information shall be recorded at the time of cord blood unit release from storage:

1. Name of product.
2. Unique alpha and/or numeric identifier.
3. Date and time of release from storage.
4. If patient-specific cord blood unit, name and/or identifier of intended recipient.
5. Contact cord blood service personnel to whom the cord blood units were shipped, and/or name of contact person(s) at transplant program.
6. Condition of shipping container and cord blood unit.
7. Name or identifier of person(s) releasing cord blood unit from storage.

10. INSPECTION AND TESTING

10.1 General

The cord blood service shall establish and maintain policies, processes, and procedures for inspection and testing activities to verify that the specified requirements for cord blood units and services are met. Records of inspection and testing activities shall be maintained in conformance with Section 16, Control of Records.

10.2 Inspection and Testing on Receipt of Incoming Materials

10.2.1 Inspection of Incoming Materials Prior to Use

The cord blood service shall ensure that incoming materials (with the exception of cord blood) that are incorporated into the final cord blood unit or that directly affect the quality of a cord blood unit are not used until they have been inspected or otherwise verified as conforming to requirements. Verification shall be in accordance with policies, processes, and procedures.

Note 5: Cord blood units with pending infectious disease testing results are excluded from standard 10.2.1, as it is permissible to begin processing them before receipt of results.

10.2.2 Determination of Extent of Inspection

In determining the amount and nature of inspection required upon receipt of any material, consideration shall be given to the amount of control exercised at the supplier's premises and the recorded evidence of conformance provided.

10.2.3 Incoming Materials Released for Emergency Use

Where a material is used on an emergency basis, prior to verification, the material shall be positively identified and recorded in conformance with Section 16, Control of Records, to permit immediate recall and replacement in the event that it is later determined not to conform to established requirements.

10.3 Inspection and Testing of Cord Blood Units

10.3.1 In-Process Inspection and Testing of Cord Blood Units

The cord blood service shall:

1) Inspect and test the cord blood unit during processing as required by policies, processes, and procedures.
2) Quarantine the cord blood unit until any required inspection and tests have been completed or necessary reports received and verified, except when the cord blood unit is released pursuant to standard 10.2.3.

10.3.2 Final Inspection and Testing of Cord Blood Units

The cord blood service shall carry out all final inspection and testing for cord blood units in accordance with policies, processes, and procedures. These policies, processes, and procedures shall require that all specified inspection and tests, including those required for materials and in-process cord blood unit, have been carried out and that the results meet specified requirements.

10.3.2.1 No material or cord blood unit shall be released until the activities specified in processes or procedures, and the associated records have been completed. Reference standard 9R-D applies.

10.4 Inspection and Testing of Services

The cord blood service shall carry out all inspection and testing for services, including testing services, in accordance with policies, processes, and procedures. These policies, processes, and procedures shall require that all specified inspections and tests, including any that might be required during the provision of the service, have been carried out and that the service meets specified requirements.

Note 6: Services may include contracted laboratory testing services or reference laboratory services.

10.5 Inspection and Test Records

The cord blood service shall maintain records in conformance with Section 16, Control of Records, that provide evidence that the cord blood unit or service has been inspected or tested and the service has been provided in accordance with specified requirements. These records shall show clearly whether the cord blood unit or service has passed or failed any inspection or tests or whether a service has been provided in accordance with specified requirements.

Where a cord blood unit fails to pass any inspection or test, the policies, processes, and procedures for control of the nonconforming cord blood unit, standard 13.2.1 shall apply. Where a service fails to pass any inspection or test, the policies, processes, and procedures for a nonconforming service, standard 13.2.2 shall apply.

Records shall identify the individual(s) responsible for the release of the cord blood unit or provision of the service, as appropriate.

10.6 Infectious Disease Testing

10.6.1 Tests Intended to Prevent Disease Transmission

10.6.1.1 Testing Sample of Cord Blood Donor's Mother
The cord blood service shall collect a sample from the donor's birth mother within 48 hours of cord blood collection. The cord blood service shall perform tests intended to prevent disease transmission on the sample in conformance with reference standard 10R-A.

10.6.1.2 Positive or Reactive Infectious Disease Tests Results
Cord blood units or maternal blood samples with a confirmed positive or repeatedly reactive test for HIV, HBV, HCV shall not be released except under extraordinary circumstances that are approved by the medical director on a case-by-case basis. Standard 13.2.1.1.1 applies.

10.6.1.2.1 The cord blood service shall ensure communication of abnormal or repeat reactive test results in conformance with reference standard 10R-C.

10.6.2 Accreditation of Testing Facilities
Tests required by these *Cord Blood Standards* shall be performed in a bank accredited by the AABB or other equivalent accrediting body, certified by HCFA, or licensed or registered by the FDA.

10R-A. Infectious Disease Testing

Testing for the following infectious diseases shall be performed on a blood sample obtained from the donor's birth mother.

1. HBV.
2. Human T-cell lymphotropic virus (HTLV-I/II).
3. HIV-1/2.
4. HCV.
5. Cytomegalovirus.
6. Syphilis.

10R-B. Biohazard Labels

The cord blood service shall affix biohazard labels to cord blood units according to the following scenarios:

1. If results of infectious disease testing includes one of the following:

Test	Test Result
HBsAg	Confirmed positive or is repeatedly reactive, and a confirmatory test is not performed
HIV-1-Ag	Repeatedly reactive
Anti-HIV-1	Confirmed positive or is repeatedly reactive, and a confirmatory test is not performed
Anti-HIV-2	Repeatedly reactive
Anti-HCV	Confirmed positive or is repeatedly reactive, and a confirmatory test is not performed
Anti-HBc	Repeatedly reactive
HTLV-I/II	Repeatedly reactive

2. If the health history screening of the donor's mother reveals high-risk for exposure to relevant transmissible diseases.

10R-C. Notification of Test Results

Source of Sample	Test Result	To be Notified
Maternal blood or cord blood	Abnormal results	Mother, mother's physician (if defined in agreement and/or informed consent)

11. CONTROL OF EQUIPMENT

11.1 Control of Equipment

The cord blood service shall establish and maintain policies, processes, and procedures to control, calibrate, and maintain critical equipment, where applicable, that is used to inspect, measure, or test whether cord blood units (incoming, in-process, or final) conform to the requirements established by the cord blood service. Inspection, measuring, and test equipment shall be used in a manner that ensures that the measurement limitation is known and is consistent with the measurement capability that is required.

Note 7: "Equipment that measures" includes measuring devices, such as thermometers, pipettes, cell cytometers, and balances.

11.2 Control Processes and Procedures for All Equipment

The cord blood service shall:

1) Identify all equipment that can affect cord blood unit or service quality, and calibrate and adjust, at prescribed intervals or prior to use, using certified equipment that has a known valid relationship to nationally recognized standards. Where no such standards exist, the basis for calibration shall be recorded.
2) Prior to use and at prescribed intervals, calibrate and adjust equipment.
3) Define the process employed for the calibration of equipment, including details of equipment type, unique identification, location, frequency of checks, check method, acceptance criteria, and the action to be taken when results are unsatisfactory.
4) Identify equipment so that the calibration status can be determined.

5) Maintain calibration records for equipment in conformance with Section 16, Control of Records.
6) Ensure that the handling, maintenance, and storage of equipment so that the equipment remains fit for use.
7) Safeguard equipment from adjustments that would invalidate the calibration setting.
8) Assess the conformance of cord blood units and services provided when equipment is found to be out of calibration. Records shall be maintained in conformance with Section 16, Control of Records.

11.3 Control Processes and Procedures for Inspection, Measuring, and Test Equipment

For equipment used to inspect, measure, or test, the cord blood service shall also:

1) Determine the measurements to be made and the accuracy and precision required and then select appropriate equipment that is capable of meeting those requirements.
2) Assess the validity of previous inspection and test results when equipment is found to be out of calibration. Records shall be maintained in conformance with Section 16, Control of Records.
3) Calibrate the equipment using certified equipment that has a known valid relationship to nationally recognized standards. Where no such standards exist, the basis for calibration shall be recorded.
4) Ensure that environmental conditions are suitable for the calibrations, inspections, measurements, and tests carried out.

12. INSPECTION AND TEST STATUS

The inspection and test status of all materials and cord blood shall be identifiable throughout collection, processing, storage, and distribution to ensure that only materials and cord blood units that have passed the required inspections and tests are released.

The inspection or test status of all cord blood shall be identified by suitable means to indicate the conformance or nonconformance. In the case of a nonconformance, the reason for the nonconformance shall be identified and documented.

13. DEVIATIONS AND NONCONFORMING CORD BLOOD UNITS AND SERVICES

13.1 Deviations

The cord blood service shall have a process to ensure the capture, assessment, investigation, and monitoring of events that deviate from accepted policies, processes, or procedures or that fail to meet the requirements of the facility, these *Cord Blood Standards*, or applicable laws and regulations. Deviations shall be reported in accordance with specified requirements.*

13.2 Control of Nonconforming Cord Blood Units or Services

The facility shall establish and maintain policies, processes, and procedures to prevent the unintended use or release of nonconforming materials and cord blood units or services. This control shall provide for identification, documentation, evaluation, segregation (when practical), and disposition of nonconforming materials and cord blood units. The cord blood service shall establish and maintain policies, processes, and procedures to address nonconforming services. Deviations shall be reported as required in accordance with specified requirements.

13.2.1 Review and Disposition of Nonconforming Materials and Cord Blood Units

The responsibility for review of and authority for the disposition of nonconforming materials or cord blood units shall be defined. A nonconforming material or cord blood unit shall be evaluated for appropriate disposition in accordance with policies, processes, and procedures. A nonconforming material or cord blood unit shall be one of the following:

*Fed Regist 2001;66:1508-79 (Proposed 21 CFR 1271.350).

1) Reworked to meet the specified requirements.
2) Accepted by the customer, after disclosure of the nonconformance.
3) Relabeled, in conformance with applicable requirements.
4) Destroyed.

Cord blood units that are determined after release not to conform to specified requirements shall be reported to the transplanting cord blood service or patient's physician. The description of any nonconformance that has been accepted shall be documented. Records shall be maintained in conformance with Section 16, Control of Records.

Reworked cord blood units shall be re-inspected in accordance with policies, processes, and procedures.

13.2.1.1 Nonconforming Cord Blood Units

The cord blood service shall ensure that units are not released until the medical director discusses deviations from established processes and procedures that may affect the safety and efficacy of the unit with the recipient's physician. Records shall be maintained in conformance with Section 16, Control of Records.

13.2.1.1.1 Nonconforming Infectious Cord Blood Units

The cord blood service shall ensure that cord blood units that are nonconforming due to positive cultures and/or positive or repeatedly reactive markers for tests required under Section 10, Inspection and Testing, are administered only with the informed consent of the recipient or legal custodian, if applicable, and the approval of

the recipient's physician. Records shall be maintained in conformance with Section 16, Control of Records.

13.2.1.2 Shipping Nonconforming Infectious Cord Blood Units

When cord blood units with positive markers for the infectious agents listed in reference standard 10R-B will be shipped, the cord blood service shall notify the transplantation program and the patient's physician.

13.2.2 Review and Disposition of Nonconforming Services

The responsibility for review of and authority for the handling of nonconforming services shall be defined. A nonconforming service shall be evaluated for appropriate action in accordance with policies, processes, and procedures. A nonconforming service may be repeated or accepted by the customer.

Where required by agreement, the proposed repeat of a service that does not conform to specified requirements shall be reported to the customer. The description of any nonconforming service that has been accepted shall be recorded in conformance with Section 16, Control of Records, to denote the actual condition.

Repeated services shall be reinspected in accordance with policies, processes, and procedures.

13.2.3 Adverse Events

The cord blood service shall establish a process for the detection, reporting, and evaluation of adverse reactions to donations and administration. Records of such events, and the related investigations, evaluations, and notifications, shall be maintained in conformance with Section 16, Con-

trol of Records. Deviations shall be reported as required in accordance with specified requirements.

13.2.3.1 Recipient adverse reactions attributable to the transplantation of cord blood, including but not limited to the transmission of infectious diseases and failure to engraft, shall be reported to the cord blood service for evaluation.

13.2.3.2 Adverse events shall be tracked and analyzed for trends and repeated frequent deviations. Standard 3.5.1 applies.

13.2.4 Collections from Nonconforming Donors

Collection of cord blood from donors that do not meet all qualification criteria shall be approved by the medical director on a case-by-case basis. Records shall be maintained in conformance with Section 16, Control of Records.

14. CORRECTIVE AND PREVENTIVE ACTION PLANS

14.1 General

The cord blood service shall establish and maintain policies, processes, and procedures for implementing corrective and preventive action plans. Management personnel shall review relevant information on corrective or preventive actions taken.

Any corrective or preventive actions taken to eliminate the causes of actual or potential nonconformances shall be proportional to the magnitude of problems and the risks encountered.

The cord blood service shall implement any changes to the policies, processes, and procedures resulting from corrective and preventive action. Records shall be maintained in conformance with Section 16, Control of Records.

14.2 Corrective Action

The process for corrective action shall include:

1) The effective handling of deviation reports and cord blood unit nonconformances.
2) Investigation of the cause of nonconformances relating to cord blood unit, process, and the quality system. Records shall be maintained in conformance with Section 16, Control of Records.
3) Investigation of customer complaints.
4) Determination of the corrective action needed to eliminate the cause of nonconformances.
5) Ensuring that corrective action is taken and that it is effective.

14.3 Preventive Action

The process for preventive action shall include:

1) The use of appropriate sources of information, (such as cord blood unit or service quality, assessment results, proficiency testing results, quality control records, customer complaints, and aggregate data) to detect, analyze, and eliminate potential causes of nonconformances.
2) Determination of steps needed to deal with any problems requiring preventive action.
3) Initiation of preventive action and application of controls to ensure that it is effective.

15. STORAGE, DISTRIBUTION, AND TRANSPORTATION

15.1 General

The cord blood service shall establish and maintain policies, processes, and procedures for storage, distribution, and transportation of materials, in-process, and final cord blood units.

15.2 Storage

The cord blood service shall use designated storage areas to limit deterioration of and prevent damage to materials, in-process, and final cord blood units. The cord blood service shall control access to such areas and control removal of cord blood units from these areas.

In order to detect deterioration, the condition of material and cord blood units in stock shall be assessed at appropriate intervals.

15.2.1 Storage Conditions

The cord blood service shall store cord blood from the time of collection to the point of distribution. The storage duration and temperature shall be for periods of time and at temperatures that are designed to preserve the viability, recovery, sterility, and potency of the cord blood. There shall be provisions for power failures and other disruptions.

15.2.1.1 Undesirable Storage Temperatures

The cord blood service shall take proper action before cord blood units reach undesirable temperatures.

15.2.2 Storage Devices

15.2.2.1 Location of Cord Blood Units Within a Storage Area

The cord blood service shall ensure it can locate any cord blood unit within storage areas.

15.2.2.2 Segregation of Cord Blood Units

The cord blood service shall store and segregate cord blood units in a manner that minimizes the possibility for cross-contamination or unintended release of untested cord blood units and cord blood units that require biohazard labels, as listed in reference standard 10R-B.

15.2.2.3 Security of Stored Cord Blood Units

Storage devices shall be located in secure areas.

15.3 Distribution and Transportation

The cord blood service shall use policies, processes, and procedures for handling materials and cord blood units that are intended to limit deterioration and prevent damage. The cord blood service shall control packing to the extent necessary to ensure conformance with specified requirements. The cord blood service shall arrange for protection of the quality of the material and cord blood units during transport and after final inspection and release.

15.3.1 Transportation between Facilities

The cord blood service shall select appropriate modes of transportation for cord blood. The urgency of the request shall determine the need for special shipping and handling requirements of the cord blood units. Processes and procedures shall be validated to ensure that temperatures have not gone out of the accepted range for the duration of shipping.

15.3.1.1 Transportation of Potentially Infectious Cord Blood Units

The cord blood service shall ensure that the transportation and labeling of biohazardous or potentially infectious cord blood units complies with applicable legal requirements (Department of Transportation, Customs, International Air Transport Association, etc).

15.3.2 Records of Receipt

Transport records shall include receiving facility's record of the receipt and condition of the unit on arrival.

16. CONTROL OF RECORDS

16.1 Original Records

The cord blood service shall establish and maintain policies, processes, and procedures for identification, collection, indexing, access, filing, storage, maintenance, and disposition of records.

Records shall be maintained to demonstrate that a material, cord blood unit, or service conforms to specified requirements and that the quality system is operating effectively. Pertinent records from suppliers shall be an element of this information.

All records shall be legible and shall be stored and retained in such a way that they are readily retrievable. Records shall be stored in a suitable environment to prevent damage or deterioration and to prevent loss. Retention time of records shall be established and recorded.

Records shall be maintained and protected from accidental or unauthorized modification.

16.2 Copies of Records

Prior to destruction of the original records, the cord blood service shall ensure that copies of records in any medium are verified to be copies of the original records.

16.3 Confidentiality

The cord blood service shall ensure the confidentiality of donor, employee, and recipient records.

16.3.1 A system designed to prevent unauthorized access and ensure confidentiality of donor and patient records shall be established and followed.

16.4 Record Retention

Records shall be retained for appropriate periods of time in conformance with reference standard 16R-A.

16.4.1 The cord blood service shall determine the appropriate retention time for records not included in the reference standard 16R-A.

16R-A. Record Retention for Cord Blood Services

A. Records that shall be retained indefinitely by the cord blood service include:

1. Cord Blood Donor Records
   a. Identifying information sufficient to attempt to identify and contact the donor or donor's mother and/or father, if available.
   b. Informed consent of the donor's mother.
   c. Medical history, interview, additional relevant information regarding the donor's mother and the infant donor, where applicable.
   d. Interpretation of donor's ABO group and Rh type.
   e. Interpretation of tests for infectious disease markers performed on a sample from the donor's mother or from the donor.
   f. Collection facility.
   g. Individual responsible for collection of the cord blood unit.
   h. Individual responsible for collection of maternal blood samples.

2. Facility Records. Identifying information for all facilities providing:
   a. Donor selection information, cord blood unit collection, processing or testing.
   b. Recipient selection information, testing, record-keeping, or administration of cord blood.

3. Processing Records
   a. Physician authorization for collection and processing, if required.
   b. Product name, unique alpha and/or numeric identification, preparation volume and additives, date of collection, and date of processing.
   c. Details of cord blood unit processing, including the responsible individual and the following results:

16R-A. Record Retention for Cord Blood Services (continued)

1) Measurements of established collection and processing parameters.
2) Manipulations other than minimal.
3) Name, lot number, and expiration date of all critical reagents and supplies used during processing.
4) Labeling, including initials of personnel performing any container transfer.

d. Verification of the accuracy of the final container label prior to issue.
e. Name and address of processing facility.
f. Authorization to release quarantined cord blood units.

4. Storage and Disposition Records for Each Unit
   a. Reissuance, if applicable, including temperature records of shipment, receipt, and storage.
   b. Final disposition, including:
      1) Method (released, discarded, research, transplant).
      2) Date.
      3) Identification of individual performing disposition.

5. General Records
   a. Names, signatures, and initials of identification codes, and inclusive dates of employment of those authorized to sign or initial or review reports and records.
   b. Technical personnel
      1) Employee qualifications.
      2) For each employee, name, signature, and inclusive dates of employment.
   c. Deviations and resulting corrective action.
   d. Reports of nonconforming or mislabeled cord blood units or adverse reactions, including reports of investigation.
   e. Records required by agreement. Standard 3.5.4 applies.

16R-A. Record Retention for Cord Blood Services (continued)

B. Records that shall be retained for 10 years after disposition of the cord blood unit include:

1. Storage temperature charts and records, including temporary transport storage.
2. Quality control records
   a. Calibration of equipment.
   b. Performance checks of equipment and reagents.
   c. Periodic check of sterile technique.
   d. Periodic tests of transport equipment.
   e. Quality control testing results, interpretation, and corrective action for out-of-range values.
   f. Results of external proficiency testing, if performed.
   g. Validation of equipment.
   h. Validation of procedures and processes.
3. General Records
   a. Technical personnel
      1) Training and continuing education.
      2) Periodic competency testing.
   b. Maintenance records for equipment, including preventive maintenance.
   c. Sterilization of supplies and reagents.
   d. Disposition of rejected supplies and reagents.

17. QUALITY ASSESSMENTS

17.1 Quality Assessments

The cord blood service shall perform quality assessments that verify whether the quality system and the collection, processing, storage, distribution, and transplantation of cord blood and the provision of related services comply with requirements; and that determine the effectiveness of the quality system.

The cord blood service shall establish and maintain policies, processes, and procedures for scheduling and conducting external and internal quality assessments. These internal quality assessments shall verify whether the quality system and the collection, processing, storage, distribution, and transplantation of cord blood and the provision of related services comply with requirements and shall determine the effectiveness of the quality system.

Internal quality assessments shall be planned on the basis of the importance of the activity to the quality of the cord blood unit or service. The results of the internal assessments shall be reviewed by personnel independent of those having direct responsibility for the activity being assessed.

The results of internal quality assessments shall be reviewed by executive management. The results of the assessments shall be recorded in conformance with Section 16, Control of Records, and reviewed by the personnel having responsibility for the area being assessed. The management personnel responsible for the area shall take timely corrective action on nonconformances found during the assessment.

Follow-up action shall verify and record the implementation and effectiveness of the corrective action and preventive action taken. Executive management shall review the results of quality assessments.

17.2 External Quality Assessments

The cord blood service shall successfully participate in an external quality assessment program. The results of quality assessments shall be reviewed by executive management. Records shall be maintained in conformance with Section 16, Control of Records.

17.3 Engraftment Data and Outcomes of Administration and Transplantation

The cord blood service shall review information relating to administration and transplant outcomes defined in agreement to include:

a. Adverse reactions related to infusion.
b. Engraftment.
c. Survival.
d. Occurrence of graft-vs-host disease.

Standard 19.2 applies.

17.3.1 The cord blood service shall identify additional criteria, if any, that are relevant to transplant outcome evaluations.

18. TRAINING

18.1 General

The cord blood service shall establish and maintain policies, processes, and procedures for identifying training needs and provide for the training of all personnel performing activities affecting quality. Personnel performing specific assigned tasks shall be qualified on the basis of appropriate education, training, or experience. Records shall be maintained in conformance with Section 16, Control of Records.

18.2 Competence

Evaluation of continued competence shall be performed. Records shall be maintained in conformance with Section 16, Control of Records.

19. STATISTICAL TECHNIQUES

19.1 Identification of Need

The cord blood service shall identify the need for statistical techniques required to establish, control, and verify process capability and cord blood unit characteristics.

19.2 Application of Statistical Techniques

When statistical techniques are used, the cord blood service shall establish and maintain policies, processes, and procedures to implement and control the application of the statistical techniques.

20. SAFETY

20.1 General

The cord blood service shall establish and maintain policies, processes, and procedures designed to minimize risks to the health and safety of employees, donors, volunteers, and, where applicable, patients and other persons affected within the work environment. Suitable quarters, environment, and equipment shall be available to maintain safe operations.

The policies, processes, and procedures shall address biological, chemical and, where applicable, radiation safety and appropriate intervention to mitigate exposure, and shall include a system for monitoring training and compliance.

Cord blood and other biohazardous materials shall be handled and discarded in a manner that minimizes the potential for human exposure to infectious agents.

20.1.1 Collection and Processing Environments

The cord blood service shall have criteria for acceptable collection and processing environments. All areas where activities covered by these *Cord Blood Standards* are performed shall meet applicable state and federal requirements.*

20.2 Compliance with External Safety Requirements

The cord blood service shall comply with all applicable requirements relating to safety issued by the Centers for Disease Control and Prevention, the Food and Drug Administration, and the Occupational Safety and Health Administration.

*Fed Regist 2001;66:1508-79 (Proposed 21 CFR 1271.190-195).

GLOSSARY

Agreement: A contract, order, or understanding between two or more parties, such as between a facility and one of its customers.

Agreement Review: Systematic activities carried out by the supplier before finalizing the agreement to ensure that requirements are adequately defined, free from ambiguity, documented, and achievable by the supplier.

Analyte: Substance or chemical constituent that is assayed.

Assessment: A systematic explanation to determine whether actual activities comply with planned activities are implemented effectively, and achieve objectives. Assessments usually include a comparison of actual results to expected results. Types of assessments include external assessments, internal assessments, peer review, and self assessments.

Biologic Mother: The woman who is the source of the fertilized ovum.

Birth Mother: The woman carrying the infant to term.

Calibrate: To set or align measurement equipment against a known standard.

Collection: The act of obtaining the cord blood.

Competence: Ability of an individual to perform a specific task according to procedures.

Conformance: Fulfillment of requirements. Requirements may be defined by customers, practice standards, regulatory agencies, or law.

Consenters: Individual(s) whose consent is obtained for cord blood collection activities, including but not limited to birth mother, biologic mother, surrogate mother, and any legal custodians (when applicable).

Cord Blood: The portion of the blood of a fetus or neonate that remains in the placenta or umbilical cord following delivery of the

neonate and clamping of the umbilical cord. Umbilical cord blood is typically rich in HPCs.

Cord Blood Service: Facility involved in any of the following activities: collection, processing, and storage of cord blood products. May consist of more than one collection site.

Cord Blood Unit: The HPCs collected, processed, and cryopreserved for subsequent use as a clinical transplantation product.

Corrective Action: An activity performed to eliminate the cause of an existing nonconformance or other undesirable situation in order to prevent reoccurrence.

Critical Equipment/Materials: A piece of equipment or material that can affect the quality of the facility's products or services.

Customer: The receiver of a product or service. A customer may be internal, ie, another department within the same organization, or external, ie, another organization.

Design Control: Process to direct, control, verify, and validate the design of a product or service.

Design Goals: A list of physical and performance requirements, including regulatory and customer requirements, that must be included when designing a new product or service.

Design Output: The results of a design effort. The finished design output consists of documents used to meet physical and performance requirements defined in design goals for the product or service, and includes packaging and labeling specifications, if applicable.

Design Validation: Checks performed to confirm that a newly implemented or changed process or procedure consistently produces acceptable results.

Deviation: An unexpected or unplanned undesirable event.

Deviation Report: The record of a nonconformance unrecognized at the time of product release, such as the acquisition of postdonation information.

Distribution: To transfer a finished product or deliver a service to an external customer.

Document *(noun):* Written or electronically captured information and work information relied on as the basis or support of organizational function and work instruction. Documents include quality manuals, policies, processes, procedures, or forms. Documents are not the same as records.

Equipment: A durable item used in a process or procedure. Examples of equipment include production equipment, such as a centrifuge, or inspection, measurement, or test equipment, such as a thermometer, that determines whether a product or service conforms to established requirements.

Establish: To define, document, and implement.

Executive Management: The highest level personnel within an organization, including employees and independent contractors, who have responsibility for the operations of the organization and who have the authority to establish or change the organization's quality policy. Executive management may be an individual or group of individuals.

Facility: The part of the organization that is assessed and accredited by the AABB. A location or operational area within an organization. AABB accreditation is granted to specified facilities for specific activities.

Final Inspection and Testing: An activity such as measuring, examining, or testing one or more characteristics of a product or service that compares the results with specified requirements in order to establish whether conformity is achieved for each characteristic.

Inspect: To measure, examine, or test one or more characteristics of a product or service and compare results with specific requirements.

Intermediary Facility: Any facility other than the original cord blood service and transplant program that manipulates or performs any activity covered by these *Cord Blood Standards*.

Label: An inscription affixed to a product for identification.

Labeling: Information that is required or selected to accompany a product, which may include content, identification, description of processes, storage requirements, expiration date, cautionary statements, or indications for use.

Legal Custodian: Person legally responsible for donor until age of majority.

Maintain: To keep in the current state.

Material: A good or supply item used in a process or procedure to prepare the final product or service. Reagents are a type of material.

Medical Therapy: The direct provision of a medical intervention ordered by a physician, eg, therapeutic phlebotomy, issuing a unit for transfusion, collecting hematopoietic progenitor cells by apheresis.

Nonconformance: Failure to meet requirements.

Organization: An institution, or part thereof, that has its own functions and executive management.

Output: The product or service that results from performing a process or procedure.

Policy: A documented general principle that guides present and future decisions.

Procedure: A series of tasks usually performed by one person according to instructions.

Process: A set of related tasks and activities that accomplish a work goal, ie, that transforms input into output products and services.

Process Control: Efforts made to standardize and direct processes in order to produce predictable output.

Product: A tangible result of a process or procedure. Products may be divided into materials or input products (eg, reageants) and output products. Notice that a blood component ready for compatibility testing is an output product for a blood center, but a material or input product for a transfusion service.

Proficiency Testing: The structured evaluation of laboratory test results that encompass the suitability of processes, procedures, equipment, materials, and personnel.

Qualification: The aspects of an individual's education, training, and experience that are necessary to successfully meet the requirements of a position.

Quality: Characteristics of a product or service that bear on its ability to meet requirements, including those defined during agreement review.

Quality Control: Testing routinely performed on materials and equipment to ensure their proper function.

Quality Manual: A document that describes the facility's quality policies, objectives, practices, resources, and activities.

Quality Planning: Activities that identify the requirements and the intended method of achieving those requirements prior to the production of a new or changed product or service.

Quality Policy: The overall vision, intentions, and direction of an organization to achieve quality that is formally expressed by top management.

Quality System: The organizational structure, responsibilities, policies, processes, procedures, and resources established by executive management to achieve the quality policy.

Quarantine *(verb):* To isolate nonconforming materials or products in a clearly marked area so that they cannot accidentally be used in a downstream process.

Reagent: A substance used to perform an analytic procedure. A substance used (as in detecting or measuring a component or preparing a product) because of its biological or chemical activity.

Record *(noun):* Information captured in writing or through an electronically generated medium that provides objective evidence of activities that have been performed or results that have been achieved, such as test records or audit results. Records do not exist until the activity has been performed and documented.

Reference Standards: Specified requirements defined by the AABB (see Specified Requirement). Reference standards define how or within what parameters an activity shall be performed and are more detailed than quality system requirements.

Regulation: Law promulgated by federal, state, or local authorities.

Related Allogeneic/ Autologous: Private donor, ie, not available to the public.

Release: Removal of product from quarantine or in-process status for distribution.

Service: An intangible result of a process or procedure.

Shall: A term used to indicate a requirement.

Specified Requirements: The expectations for products or services. Specified requirements may be defined by customers, regulatory agencies (such as the FDA), practice standards, or accrediting organizations (such as the AABB).

Standard: A set of specified requirements upon which a facility may base its criteria for the products, components, and/or services provided.

Statistical Techniques: Established mathematical methods used to collect, analyze, and present data.

Supplier: An organization that provides a material or service.

Surrogate Mother: The woman who carries the ovum of another woman.

System: A subgroup of related activities preformed by a particular organization. Activities dealing with maintaining product and service quality are organized into "quality system."

Traceability: The ability to follow the history, application, or location of a product or service by means of recorded identification.

Transplant Program: The facility involved in receipt and thawing of a cord blood unit, infusion, and patient data monitoring.

Trend: A movement of measurement data in a specific direction over time.

Validation: Demonstration that something produces the desired result. The results of a new or changed processes are checked in order to validate the process.

Verification: Affirmation of the accuracy of something. New or changed processes are verified against the design goals before being implemented.

INDEX

T

V

AMERICAN
ASSOCIATION
OF BLOOD BANKS

8101 Glenbrook Road • Bethesda, Maryland 20814-2749
www.aabb.org

013115

ISBN 1-56395-144-4

AMERICAN ASSOCIATION OF BLOOD BANKS
8101 Glenbrook Road • Bethesda, Maryland 20814-2749

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dirve, Room 1-23
Rockville, MD 20857

Return Postage Guaranteed

Address Correction Requested