NMDP
INVESTIGATIONAL NEW DRUG (IND) SUPPLIER REQUIREMENTS FOR CORD BLOOD BANKS

Personnel

1. Cord blood bank (CBB) must have a designated medical director who is licensed to practice medicine in that state/region/country.
2. CBB (or affiliated registry) must have daily and emergency coverage by designated coordinator(s) who are proficient in English to provide prompt response to requests.
3. CBB must document initial and ongoing training and competence assessment for relevant skills for its staff.
4. CBB must define the qualifications and responsibilities of its staff.
5. CBB must have a process to document training for individuals who collect cord blood units (CBUs).

Maternal Donor Consent/Screening/Testing

6. CBB must obtain and document consent from the maternal donor for donation, collection, testing, and storage of the CBU for use in unrelated donor transplantation.
7. Maternal donors must not be coerced to donate CBUs, be paid to donate CBUs, or be charged fees for any aspect of the collection, donation, or storage of the CBU.
8. Maternal donor screening for high risk behavior must be performed and documented. The screening must be completed within six months prior to collection or one month after collection.
9. Medical health histories must be obtained from the infant's family (mother, father, and siblings) within six months prior to collection or one month after collection.
10. Review of readily available relevant delivery/medical records for evidence of relevant communicable disease must be documented.
11. The maternal donor must have a blood sample collected for infectious disease marker testing within seven days of CBU collection. Testing must meet national requirements and include, at a minimum, HIV 1/2 antibody, HIV antigen (p24 or NAT), Hepatitis B surface antigen, and Hepatitis C antibody testing.

Operations (Collection, Processing, Cryopreservation, and Storage)

12. Prior to making the unit available for listing, a physician or designee must evaluate the readily available relevant maternal donor medical history information, family medical history/histories, delivery records, medical information including testing results, as well as collection, processing, cryopreservation, and storage records.
13. Equipment and lot numbers of materials and reagents used in the collection, processing, cryopreservation, and storage of the CBU must be documented and traceable to the manufacturing and testing of the CBU, donor, and all related samples.
14. All materials and reagents used in the collection, processing, cryopreservation, and storage of the CBU must be approved for human use (with the exception of the DMSO used in cryoprotectants).
15. For CBUs that have been shipped for transplantation, the CBB must be able to track the unit from the donor to the patient and the patient back to the donor.

16. CBUs should be cryopreserved within 48 hours of the CBU collection.
NOTE: Historically, CBUs must have been cryopreserved within 72 hours.

17. CBUs should be stored at ≤ -150°C.
NOTE: Historically, CBUs must have been stored at ≤ -135°C.

18. CBUs must be stored in a freezer that is continuously monitored electronically for temperature.

19. CBUs must not be stored with non-human sources of blood, blood components, or tissues. CBUs with infectious disease risks identified through donor testing or maternal/family history and related records must be quarantined through physical separation (such as through overwrap or storage in vapor phase) or other methods, such as electronic designation.

Cord Blood Unit Testing

20. CBUs must test negative for microbial contamination. Current testing must include both bacterial and fungal testing.

21. CBUs (or the infant donor) should be tested for hemoglobinopathies.

22. Laboratories that perform testing on the maternal donor or CBU must be authorized, licensed, or accredited by a national regulatory agency.

23. HLA confirmatory/verification typing of a CBU must be performed at a laboratory accredited by EFI, ASHI, or CAP.

24. CBU reports must include at least the following:

- A unique identifier
- HLA typing
- ABO/Rh type
- Infant date of birth or CBU collection date
- Infant gender
- Microbial testing results
- Volume (mL)
- Maternal infectious disease marker results

Procedures

25. CBB must maintain and follow standard operating procedures (SOPs) for key manufacturing steps.

26. Documentation for each manufacturing step must be created at the time the activity is performed. Records must include the task performed, the individual performing the task, and when the task was performed. Records must be legible, indelible, complete, kept indefinitely, and retrievable in a reasonable period of time.

27. CBB must report and collaborate with NMDP in investigations for product deviations and complaints and recipient serious adverse events. NMDP will report events to the FDA and/or WMDA SEAR/SPEAR, as required.

Labeling

28. For CBUs intended for transplantation in the U.S., the label affixed to the CBU must include (at a minimum):
    - A unique identifier
    - Product name

29. For CBUs intended for transplantation in the U.S., the label or accompanying records must be in English and must include:
    - Name and address of the CBU manufacturer (CBB)
    - Storage temperate information

30. For CBUs intended for transplantation in the U.S., CBB must use the NMDP-provided paperwork to accompany the CBU at time of shipment.

Shipping

31. After final product labeling and before shipment, two individuals at the CBB (or one individual and a validated electronic equivalent) must verify the labeling and accompanying documentation for accuracy and completeness. The verification must be documented.

32. Cryopreserved products must be shipped in a liquid nitrogen dry shipper that contains adequate adsorbed liquid nitrogen to maintain temperature at least 48 hours beyond the expected arrival time at the receiving facility. The temperature of the shipping container during shipment shall be continuously monitored using an electronic data monitor or equivalent device, and the shipping container must be validated by the bank.

33. CBB must limit the contents of the dry shipper to a maximum of one CBU when shipping to the U.S.

Accreditations/Compliance with Other Agencies

34. U.S. CBBs must maintain accreditation by either AABB or NetCord-FACT for cord blood banking. Non-U.S. CBBs must maintain accreditation by AABB, NetCord-FACT, ISO, or other industry accrediting organization; or be authorized by the National Competent Authority (NCA).

35. CBB must promptly report any significant change in personnel (including, but not limited to, the medical director, coordinator, or laboratory director), facilities, accreditation, FDA registration, or support services to NMDP. Any change to accreditations, licensures, or FDA registration must be reported to NMDP no later than 15 days after the CBB receives notice of the change(s).

36. CBB must provide documentation to NMDP on an annual basis that it continues to meet the requirements specified in this document.

Administration

37. CBB (or its parent organization or national registry) must have an agreement in place with NMDP that specifies the mutual responsibilities under the IND.

38. CBB (or its parent organization or national registry) must have agreements in place with any entity that performs any step in the manufacturing process.

39. CBB /registry should maintain adequate professional and general liability insurance coverage.

NOTE: NMDP will not facilitate access to CBUs with any of the following characteristics:

- Compromised traceability to product or maternal identity suggestive of mix-up such as discrepant HLA typing
- Positive microbial culture of CBU (bacterial and/or fungal)
- Positive hemoglobinopathy testing indicating unit is
    - Homozygous for sickle cell and/or beta thalassemia disease
    - Heterozygous for both sickle cell and beta thalassemia trait
    - Positive for severe alpha thalassemia (hemoglobin H disease)
- Positive maternal or CBU infectious disease marker testing (FDA cleared/approved donor screening test or other laboratory infectious disease test as part of relevant medical records) for:
    - Human immunodeficiency virus (HIV) types 1 and 2
    - Hepatitis B Virus (HBV)
        - Hepatitis B Surface Antigen (HBsAg) test
        - HBV NAT test
    - Hepatitis C Virus (HCV)
    - T cruzi/Chagas Disease
    - West Nile Virus (WNV)
- No infectious disease marker test result for:
    - Human immunodeficiency virus (HIV) type 1/type 2 antibody test
    - HIV p24 Antigen or HIV nucleic acid test (NAT)
    - HBsAg test
    - HCV antibody test
- No bacterial sterility testing performed on unit
- Collection and storage of units in vials