

## NMDP CURRENT INVENTORY REQUIREMENTS FOR NEW CORD BLOOD UNITS

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Updated by NMDP in response to FDA HBV NAT testing requirements change February, 2017

This document is to be used in conjunction with requirements contained in the Cord Blood Bank Participation Agreement and NMDP Standards.

All of the following requirements are intended for both NMDP member and affiliated listing cord blood banks prior to final individual unit registration into NMDP computer systems.

(Please note specific member and affiliated listing requirements in items #1 and #2).

Item Number	Item	Detail	Comment
<b>Infectious Disease Marker Testing of Maternal Samples</b>			
1	Infectious Disease Marker (IDM) Testing	<p><b><u>Member CBBs</u></b>  <u>Required tests:</u> HBsAg, Anti-HCV, Anti-HIV 1/2 (or anti-HIV 1/2 plus O), HIV NAT, anti-HBc, HCV NAT, HBV NAT, Anti-HTLV I/II, Syphilis, anti-CMV Total, WNV NAT, and Chagas.  <u>Testing method:</u>  Testing must be performed using FDA licensed, approved, or cleared donor screening tests performed in a CMS approved laboratory in accordance with manufacturer's instructions and in compliance with current tissue regulations.</p> <p><b><u>Affiliated Listing CBBs</u></b>  All applicable national and local regulations must be followed.  <u>Required tests:</u> HBsAg, Anti-HCV, Anti-HIV 1/2 (or anti-HIV 1/2 plus O), HIV NAT or p24.  Where available, testing should be performed for anti-HBc, HCV NAT, HBV NAT, Anti-HTLV I/II, Syphilis, anti-CMV Total, WNV NAT, and Chagas.  <u>Testing method:</u>  It is preferred that the testing method listed above for member CBBs is used if possible.</p>	<p><b><u>Member and Listing CBBs</u></b>  Testing must be performed on a maternal sample collected within seven days (before or after) of the date of collection of the cord blood unit.</p> <p>All units must be screening test negative, with the exception of anti-HBc, Syphilis, and anti-CMV. Units that are anti-HBc positive will be accepted if HBsAg testing is negative and HBV NAT testing is negative.  Units that are Syphilis screening test positive using a non-treponemal test and negative with a treponemal supplemental test will be accepted.  Units that are Syphilis screening test positive using a treponemal test will not be accepted.</p> <p>CMV test status does not impact eligibility; anti-CMV results are communicated to the TC.</p> <p>Units that are positive for anti-HBc or Syphilis (non-treponemal) screening will be labeled as Ineligible depending on the date of collection and other factors present that may affect eligibility status.</p> <p>If tests listed as required tests under "Member CBBs" are not performed, or if they are not performed according to FDA criteria, the units will be managed as Incomplete depending on the date of collection of the cord blood unit.</p>

Health History Screening			
2	Maternal and Family	<p><u>Member CBBs</u> Must have current donor screening processes that are consistent with the FDA Guidance for Industry Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) August 2007. Screening must address a current maternal medical history, family medical history, and other available medical records including relevant and readily available physical findings and delivery records as defined by the cord blood bank.</p> <p><u>Affiliated Listing CBBs</u> Must have current donor screening processes that are consistent with applicable laws and regulations of the country of origin and address a current maternal medical history, family medical history, and other available medical records including relevant and readily available physical findings and delivery records as defined by the cord blood bank.</p>	<p>The NMDP MRQ and FMHQ are consistent with the FDA Guidance for Industry Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) August 2007. CBB equivalent documents may also be acceptable. AABB would also be considered as having an equivalent MRQ.</p> <p>The intent of the screening process is to identify potential infectious disease risk, and inherited medical conditions potentially transmitted through transplantation.</p> <p>Screening must be performed between 6 months prior and 30 days after the time of collection and must be performed in a manner that provides current relevant history information.</p>
Storage of Maternal Samples Collected at the Time of CBU Collection			
3	Serum or Plasma	Two vials of serum or non-heparinized plasma containing a minimum of 1.8 ml each should be stored at $\leq -70^{\circ}\text{C}$ .	
4	DNA	Material for preparation of $\geq 50$ $\mu\text{g}$ of genomic DNA must be collected and stored.	The CBB may store frozen cellular material, extracted DNA or filter paper blots provided the material is equivalent to or sufficient to prepare $\geq 50$ $\mu\text{g}$ of genomic DNA.
Testing on Final CBU Product, Post-processing, Pre-freezing (prior to addition of DMSO)			
5	Total Nucleated Cell Count (TNC)	TNC must be measured on a post-processing sample, reported as the number of cells $\times 10^7$ and must <u>not</u> be corrected for nRBCs.	Note: FDA licensure requires a minimum post-processing TNC of $50 \times 10^7$
6	Nucleated Red Blood Cell Count (nRBC)	nRBC must be determined on the same sample as the post-processing TNC and can be reported as either the % of total or as an absolute count.	The CBB must report the nRBC value as it is received from the testing laboratory. No additional calculations or conversions should be performed by the CBB.
7	CD34+	The CD34+ count must be determined on the post-processing sample and reported as the total number of cells $\times 10^6$ .	Note: FDA licensure requires a minimum post-processing CD34+ count of $\geq 1.25 \times 10^6$ viable CD34+ cells/unit.
8	Colony Forming Unit (CFU) Assay	CFU assays must be determined on the post-processing sample and reported as "Growth" or "No Growth" <i>with the actual count</i> .	CFU assays may include all colony types or be limited to granulocyte-macrophage (GM). CBUs with no growth will not be listed.

9	Viability	Viability must be determined on the post-processing sample and be $\geq 85\%$ .	Viability may be performed by whatever assay is commonly used in the laboratory performing the test. Note: FDA licensure requires $\geq 85\%$ viable nucleated cells (TNC).
<b>Testing on CBU Residual Samples Post-processing</b>			
10	Bacterial and Fungal Culture	CBUs must be tested for aerobic/anaerobic microbes and fungus and must exhibit "No Growth".	Testing may be performed on a residual red blood cell and/or plasma sample remaining after processing, on the final product prior to cryopreservation, or on the final product after addition of DMSO. When the culture is performed before the addition of DMSO, evidence that the DMSO was sterile must be documented.
11	Hemoglobinopathy Testing	Testing for hemoglobinopathies, including sickle cell disease and thalassemia, must be performed prior to listing CBUs. The test must utilize a method that distinguishes sickle cell disease and trait, alpha and beta thalassemia disease and trait and Hemoglobin C disease. CBUs homozygous for either sickle cell disease or thalassemia will be deferred. CBUs heterozygous for either sickle cell trait or thalassemia will be accepted.	Testing may either be performed on residual rbc material remaining post-processing or on a sample of whole cord blood prior to processing. Newborn screening is also acceptable provided that the results are available. A solubility assay for hemoglobin screening is not acceptable.  CBUs testing positive for multiple traits may be deferred. However, a particular unit with multiple traits may be used upon consultation with an expert in the field of hemoglobinopathies and with the knowledge and approval of the transplant center.
12	HLA Typing	CBUs must be typed using DNA methodology at a minimum of low resolution for HLA-A and -B, and high resolution for HLA -DRB1.	HLA typing may either be performed on residual material containing nucleated cells following processing or on a sample of whole cord blood prior to processing.
13	ABO Rh Typing	CBUs must be typed for ABO and Rh.	ABO/Rh typing may either be performed on residual rbc material remaining post processing or on a sample of whole cord blood prior to processing.
<b>Storage of CBU</b>			
14	Temperature	CBUs must be stored at temperatures $\leq -150^{\circ}\text{C}$ at all times.	Storage may occur in the liquid or vapor phase of nitrogen.
<b>Storage of Cord Blood Samples</b>			
15	Serum/Plasma	Two vials of serum or non-heparinized plasma containing a minimum of 1.8 ml each should be stored at $\leq -70^{\circ}\text{C}$ .	The material for these samples may come from residual material (undiluted) following volume reduction.
16	DNA	Material for preparation of $\geq 50$ $\mu\text{g}$ of genomic DNA must be collected and stored.	The CBB may store frozen cellular material, extracted DNA or filter paper blots provided the material is equivalent to or sufficient to prepare $\geq 50$ $\mu\text{g}$ of genomic DNA.

Viable Cell Requirements (CBU)			
17	<p>Viable Cells</p> <p>Aliquot = sample representative of the final product</p>	A minimum of three aliquots of cells each containing a minimum of $1 \times 10^6$ cells must be cryopreserved and stored at $\leq -150^\circ\text{C}$ .	<p>Aliquots must include at least two contiguous segments – additional aliquots may include any that contain a cryoprotectant and are stored in the same manner as the CBU.</p> <p>Note: For CBBs in the US, licensure requirements may indicate that an appropriately labeled reserve sample representative of the final product is maintained as a reserve/retention sample, beyond the minimum requirements specified here, consistent with a CBB's Biologic License Application (BLA).</p>
18	Contiguous Segments	All CBUs must have at least two contiguous segments containing a minimum of 100 $\mu\text{l}$ each.	<p>One segment will be used for HLA confirmatory typing.</p> <p>One segment (additional segment or same as HLA segment if enough material) will be used for additional testing at the time of release of the unit for transplant (ex. TNC, viability, CFU). Alternatively, TNC and viability may be performed from an aliquot stored separately from the CBU.</p> <p>Every attempt should be made to leave one segment attached to the unit for shipment to the transplant center.</p> <p>Note: For CBBs in the US, licensure requirements may indicate that an appropriately labeled reserve sample representative of the final product is maintained as a reserve/retention sample, beyond the minimum requirements specified here, consistent with a CBB's Biologic License Application (BLA).</p>