Response to Public Comments for the 7th edition of Standards for Cellular Therapy Services

Please note that public comments that were submitted address the proposed Standards. The changes are best understood when the proposed Standards is compared to the final published version. The program unit has elected to make the substance of public comments that were submitted a part of this document. This document does not represent a full summary of significant changes to the 7th edition of CT Standards. Guidance within the Standards Portal provides a more in-depth explanation of all changes made to the 7th edition.

7th ed. standard # (6th ed. # if changed)	Change made?	Outcome Following Program Unit Discussion
General	No	**Comment:** I do not think it is necessary to use "policies, processes and procedures" in detailed, highly specific standards. In some cases, it is beyond overkill. For instance, you are saying that facilities should develop policies, processes and procedures for some very small details where policies and processes would normally not be indicated. For example, in 5.15.1.2: For ex-utero cord blood collections, the procurement facility shall have policies, processes, and procedures to verify the label on the collection container against the donor identification. **Outcome:** The committee noted this comment and decided that it is be better to be broad than overly specific.
General	No	**Comment:** We understand that the proposed standards covers both HCT/P products that are regulated by FDA solely under section 361 of the PHS Act (361 HCT/Ps) and HCT/Ps that are also regulated under section 351 of the PHS Act (351 HCT/Ps). Because the applicable regulations depend on a variety of factors including the product, indication for use and the stage of product development cycle, it is not possible to harmonize each standard with all potentially applicable regulations including Current Good Manufacturing Practice (CGMP) requirements. The applicable regulations for 351 HCT/Ps can be found in 21 CFR Parts 201, 202, 210, 211, 312, 600, and 610 and the regulations applicable to 361 HCT/Ps are found in 21 CFR 1271. **Outcome:** The Cellular Therapy Standards have not adopted the same framework as the FDA with regard to 351 products versus 361 products because these Standards are meant to be applicable to all facilities, not solely those in the United States. The committee notes that standards are written in such a way that do not match the regulatory structure of the FDA. Facilities are responsible for being aware of the differences in regulations depending on their Competent Authority and adhering to all local and national regulations.
General	Yes	**Comment:** It seems the Pen icon prompt is not present for the standards directed "to maintain records, policies, processes, notifications, and procedures". I am not sure if the pen icon was intended to be missing or if it was forgotten altogether. As an assessor, I would be looking for records, SOPs, policies, notifications, consents, or as applicable to address these activities. The following standards require pen symbols: 5.5, 5.11.7, 5.11.9.2, 5.16.5, 5.21, 5.26, 5.27, 5.30, 6.2.1, 6.2.2 and 8.5. **Outcome:** When the pencil symbol precedes a standard, users are required to maintain a record of that activity in order to meet the standard. In many of the standards listed above, most do not have an activity that would require that a record be kept. In the case of "policies, processes and procedures", standard 1.2.3 requires that all facilities have records of all policies, processes and procedures and therefore to include the pen symbol in every standard where they are mentioned would be redundant. The committee did review the list of standards mentioned and add a pen symbol to standards 5.11.9.2 and 8.5.

1.1.1 (New)	Yes	**Comment:** This new standard is a bit confusing regarding the use of the word "executive". It seems that that executive management in 1.1 refers to the CT facility and in 1.1.1 the executive level is meant for hospital administration. **Outcome:** The committee agreed with this comment and deleted the phrase "at the executive level."
1.1.2, 1.1.2.1, 1.1.3 (1.1.2)	Yes	The committee received several comments regarding the proposed language of the executive management requirements of procurement, processing, and clinical facilities. What follows are examples of the comments received: • The standards distinguish between the Procurement Facility and its Medical Director and the Processing Facility and its Laboratory Medical Director, yet the responsibilities of these individuals (in 1.1.2 and 1.1.3) are exactly the same in that they are both responsible for performing the determination of donor eligibility, procurement and/or processing, storage, and/or provision of the product. • We feel this is a source of confusion. Because we are a facility contracted to procure and process autologous HPC's, our Medical Director does not determine donor eligibility. The Clinical Program Director makes this determination. Therefore, we recommend that the Standards Committee consider adding "if applicable" or "as applicable" to these standards, or better yet, include an allowance for specific responsibilities to be spelled out in a formal agreement between the clinical and contracted facilities. The responsibilities defined in the proposed standard are confusing due to combining both procurement and processing facility functions. • This standard needs "and/or" construct to match the standards above and below it. **Outcome:** The committee agreed with the comments received and edited standards 1.1.2, 1.1.2.1, and 1.1.3 to delineate between the roles of the procurement facility executive management and that of processing facilities. References to "processing, storage, and/or provision of the product" have been removed from the procurement section and the clauses "determination of donor eligibility" and "procurement" have been deleted from the processing facilities standard. These standards were edited as follows: **1.1.2 Procurement Facilities** The procurement medical director shall be a member of executive management and responsible for performing the determination of donor eligibility **(or review of records related to donor eligibility if performed by another facility) and** procurement~~, processing, storage, and/or provision~~ of the product. **1.1.2.1 Procurement Medical Director** The procurement medical director(s) shall be a licensed physician qualified by training and/or experience and relevant continuing education in activities performed by the facility as required by these *CT Standards*. The procurement medical director(s) shall have responsibility and authority for medical activities related to the procurement~~, processing, and provision~~ of cellular therapy products and related services. When the medical director delegates these responsibilities to another qualified medical professional (designee), the medical director shall retain ultimate responsibility.

		1.1.3 Processing Facilities The laboratory medical director and the laboratory director shall be a member of the executive management and responsible for **the** ~~performing the determination of donor eligibility, procurement and/or~~ processing, storage, and/or provision of the product.
1.1.3.2 (1.1.2.2)	No	**Comment:** The way this standard is written requiring a PhD/MD is very specific to the USA. India, for example, the country requires that the "Laboratory In Charge" person have an advance degree, which could be a masters, with education and training. This is an example where the standard is not written to allow leeway for international regulations. **Outcome:** The committee noted this comment, however, did not make a change to the standard. The committee notes that facilities outside of the United States that have different requirements should submit a request for variance including all relevant background information showing a level of equivalence to an MD/PhD.
1.2	No	**Comment:** In CGMPs, the quality unit must be independent from the manufacturing facility and medical oversight. Furthermore, the quality unit must have the final authority and oversight for the release of the final product. The quality unit is also responsible for approving validation plans and reports. **Outcome:** The committee noted this comment and recognizes the importance of the distinctions between FDA regulations and AABB Standards. However, they did not feel a change was necessary at this time as the standards are also written for international facilities. Instead, the committee elected to explain this distinction further in guidance.
1.3	Yes	**Comment:** Add that both internal and external disasters apply; a common theme seen from assessments is people view disasters as happening to others, not on their own premises. **Outcome:** The committee agreed and added the phrase “internal and external disasters” to the standard.
2.1.4 (2.2.2)	No	**Comment:** This standard assumes that product procurement staff are employees of the cell therapy manufacturer or cord blood bank. For many cord blood banks, procurement staff collect on a contract basis or as a third party. Therefore it is inappropriate to require orientation, job-specific or quality systems related training for non-employees. **Outcome:** The committee did not intend for this standard to apply to contract procurement situations. Standards 4.3 – 4.3.7 requires that third party providers and cellular therapy facilities have agreements in place to certain criteria to ensure conformance with the *CT Standards*.
2.1.4 (2.2.2), 2.1.5	Yes	**Comment:** The first sentence of standard 2.1.4 is too long. Please consider splitting it into two sentences, or potentially rearrange standard 2.1.4 remains applicable to general training and specific requirements for procurement/processing and clinical personnel are broken out as substandards. **Outcome:** The committee agreed with the proposed changes and edited the standards such that the final language now reads as follows: **2.1.4 Training ~~for Procurement and Processing Personnel~~** The facility shall establish and maintain policies, processes, and procedures for orientation, initial and ongoing job-specific and quality-systems-related training needs**. The facility shall define the qualifications required for trainers.**

		2.1.4.1 Training for Procurement and Processing Personnel **The facility shall** ~~and~~ provide for the training of all personnel who perform product procurement or processing activities that affect product or service quality. ~~The facility shall define the qualifications required for trainers.~~ **2.1.4.2 ~~2.1.5~~ Training for Clinical Program Personnel** The facility shall ~~establish and maintain policies, processes, and procedures for orientation, initial and ongoing job- specific and quality-systems-related training needs and~~ provide for the training of all personnel who perform critical activities for the clinical program. ~~The facility shall define the qualifications required for trainers.~~
2.2	Yes	The committee received several comments regarding the movement of 5.1 #9 to appear as standard 2.2. What follows are examples of the comments received: • This is very vague; not sure what would be the specifics? • Shall ensure access" is very generic and difficult to assess. • The content of standard 2.2 does not fit under Human Resources **Outcome:** The committee agreed with the content of the comments and edited the standard to provide examples: **2.2 Access to Ancillary and Direct Patient Care Services** The clinical facility shall ensure access to medical specialty services and resources as needed for patient care**, including but not limited to:** **1) Leukoreduced/irradiated blood components for patients receiving hematopoietic stem cell transplants** **2) Pharmacy** 3) **Radiology**
3.3.3 (3.1.7)	Yes	**Comment:** I suggest saying qualified "individuals" instead of "personnel" in standard 3.3.3 since these services are often contracted out. **Outcome:** The committee agreed with the comment and made the proposed change.
3.5 (3.1.9)	Yes	**Comment:** The proposed wording for #7 is inappropriate for these Standards. We recommend the following rewording: 7) Policies, processes and procedures ~~shall be developed~~ using terminology **understandable by the system user** ~~that enables all users to perceive the meaning and intent~~. **Outcome:** The committee agreed with the comment and replaced the phrase "that enables all users to perceive the meaning and intent" with "that is understandable to the user."
3.5 (3.1.9)	Yes	**Comment:** Regarding subnumber7 we are not sure if the intent of "documentation" as it relates to policies, processes and procedures. I believe it is trying to address documents such as user manuals, validation protocols, and system administration guides that may be developed by IT specialists. Subnumber11 seems redundant per what is already required for training and competence in Chapter 2. **Outcome:** The committee added the phrase "and other instructional documents" to clarify the issue raised regarding item #7. Concerning #11, while the committee notes that this is a bit redundant, they elected to retain the standard in order to emphasize its importance in the process.

4.1.2 (New)	No	**Comment:** Please clarify whether this standard refers to all agreements (e.g. – purchasing, cleaning, etc.) or only those directly related to the cellular therapy clinical programs. We also would like to suggest an additional standard similar to 4.2.2 in the *Standards for Blood Banks and Transfusion Services*. For example: "The responsibilities for activities covered by these *CT Standards* when more than one facility is involved shall be specified by agreement." **Outcome:** The committee agreed with the intent of this comment and noted that this standard should apply to agreements that are both inter-facility and intra-facility. To address this, they edited standard 4.3 as follows: **4.3 Agreements Relating to Cellular Therapy Products** **When** ~~T~~**t**he responsibilities for activities covered by these *CT Standards* **involve** ~~when~~ more than one facility **or department**, ~~is involved~~ **there** shall be **agreements to address the following:** ~~specified by agreement~~. ~~When cellular therapy products are transferred from the control of one facility to another there shall be agreements to address the following:~~
4.3.1 (4.2.1, 4.2.2)	Yes	**Comment:** Please clarify the requirement; physician order vs. medical order. It seems there is an inconsistent use of the terms throughout the Standards. **Outcome:** The phrase "physician order" was changed to "medical order" throughout the document for consistency in recognition of the fact that other personnel can write orders (e.g., nurse practitioners) in certain situations.
4.3.1 (4.2.1, 4.2.2)	Yes	**Comment:** Should agreements for the processing and processing facility medical orders be covered in the standards? **Outcome:** The committee agreed with the comment and added a new #2 to include the responsibility of processing facilities regarding agreements for medical orders. It reads as such: **2) Responsibility of the processing facility to obtain a medical order before the processing procedure.**
4.3.1 (4.2.1, 4.2.2)	Yes	**Comment:** I am wondering if this new standard is necessary. If you decided to leave the standard, I would look carefully at subnumber 2 of this standard as it looks like it is an agreement of the clinical facility with itself, " the clinical facility ensuring…responsibility of the clinical facility.." In practice, this agreement should be a part of their standard operating procedures for administration that is covered under different standard. **Outcome:** The committee agreed with this comment that item #2 implied that the clinical facility needs an agreement with itself, and as a result it was deleted.
4.5.1, 4.5.2	Yes	**Comment:** –Regarding standard 4.5.1, we suggest deleting the word "any" and start with "Informed consent documents shall be …." With regard to standard 4.5.2 we suggest deleting the word "The" and start with "Informed consent from the donor …." Standard 4.5.1 sounds like informed consent is optional and 4.5.2 sounds like it is not. If there is intended nuance there, it may have gone over my head, I also have the same concern surrounding standards 4.6.1 and 4.6.2. **Outcome:** The committee edited the standards in question as suggested and the standards now appear as such: **4.5.1** Donor informed consent templates shall be reviewed and approved by the medical director of the facility responsible for obtaining informed consent. **4.5.2** Informed consent from the donor or a legally authorized representative shall be obtained (or initiated, for cord blood) before the procurement of cells, tissues, or organs from the donor.
4.6.2	Yes	**Comment:** What is a "legally executed document"? Is there other descriptive verbiage possible that would make this clearer?

		Outcome: In response to this comment, the committee changed the phrase from "legally executed document" to "legal record of authorization." Additional guidance on this topic is available in the Standards Portal.
4.5, 4.7 (New)	No	**Comment:** Now that donor & patient informed consent are split, will autologous patients and donors need both? Please clarify. **Outcome:** The committee noted this comment but did not feel a change to the standard was necessary at this time. Autologous donors would need to consent to both aspects of the collection and the administration. Both of these elements can be represented in the same physical document or the facility(ies) can have two separate documents. In some facilities, you will need two separate documents as different departments are responsible for the collection versus Administration. In these cases the facility may want separate consent forms.
4.5.1, 4.6.1, 4.7.1	No	**Comment:** Please add the phrase "before use" to each of these standards. **Outcome:** The committee noted this comment but did not feel a change was necessary at this time. Standard 6.1.2 already requires the review and approval of all documents before their use. Since these standards refer to an informed consent template, and not each individual's consent, then it is considered a document and not a record and would thus fall under standard 6.1.2.
4.5.1, 4.6.1, 4.7.1	Yes	**Comment:** Please add the clause "...medical director or designee to review and to approve informed consents." to all three standards. Also, since these standards are part of the Agreements section, I was not sure if they applied to the medical director reviewing and approving the blank templates used for informed consents and donor screening, applied to the agreement to address the procurement process as in the medical director is responsible for reviewing and approving each completed donor informed consent, evaluation, and screening, or applied to the procurement and donor evaluation activities starting at standard 5.11. **Outcome:** The committee added the word "templates" to all three standards that focused on informed consent (donor, authorization, and patient) for clarity.
4.8.1 (4.6.1)	No	**Comment:** Please note that contract manufacturing or testing facilities must also comply with applicable regulatory requirements. As such we suggest revising the standard to read: "Ensure that facilities providing tests or manufacturing services required by these CT Standards shall be accredited by AABB or other accrediting body and are in compliance with the applicable regulations." **Outcome:** The committee did not feel a change was necessary at this time. This addition would require all assessors to know every relevant regulation that exist in the country that they are assessing.
4.8.2 (4.6.2)	No	**Comment:** The NMDP performs a comprehensive review of cell therapy service providers used by their organization. If a facility is using the NMDP to coordinate the collection, testing, transport, etc. of cellular therapy products, is the receiving facility obligated to perform this evaluation and qualification? Can a facility use the supplier's AABB and/or FACT accreditation status as their qualification program? If the supplier is AABB and/or FACT accredited, these requirements have already been accessed by qualified assessors and deemed appropriate to achieve accreditation. Does this requirement apply to all types of donors (allogeneic, allogeneic related, and autologous)? **Outcome:** If a facility is utilizing the NMDP to acquire their cellular therapy products, the receiving facility must, through agreements, specify that NMDP has addressed these responsibilities and that NMDP itself is meeting specified requirements. The committee did not feel it would be appropriate to only use a supplier's AABB and/or FACT accreditation status as their

		qualification program as it is important to define your own specified requirements and ensure that the facility is meeting them. Finally, this standard does apply to all types of donors of cellular therapy products.
4.8.1 (4.6.1, 4.6.2), 4.8.2 (4.6.2)	No	**Comment:** With regard to standard 4.8.1, #1, is the standard asking that we verify training and qualifications for employees working at a vendor facility that manufactures materials? I would limit this to suppliers of services only. With regard to standard 4.8.2, #3, is the standard requiring that we verify training and qualifications for employees working at every other cell therapy facility that may send us products? I would limit this to service suppliers only. **Outcome:** The committee reviewed this comment but did not feel a change was needed at this time. The standards do not require that facilities verify training and qualifications, but rather it should be specified in agreements that the contracting facility has met specified requirements related to training and qualifications.
4.8.3 (4.6.3)	Yes	**Comment:** How does one assess "necessary" as stated in this standard? Does this mean to take corrective action and follow-up to see if the corrective action was effective? **Outcome:** The committee noted this comment and deleted the word "necessary" as it is difficult to assess as noted in the comment above.
Reference Standard 4.5A	No	**Comment:** The clause "Authorization to procure tissues and make them available … shall be obtained from the donor …" reads awkwardly since by definition a cadaveric donor is dead. **Outcome:** The committee did not feel a change was necessary at this time as donors are able authorize donation before they die.
Reference Standard 4.7A (Reference Standard 4.5B)	No	**Comment:** We feel that it is overly prescriptive to require that only health care professionals are capable of presenting information and answering questions about cellular therapy procurement (cord blood) or about the informed consent process. Any appropriately trained individual familiar with applicable cellular therapy procedures should be suitable to present information pertaining to donor informed consent and answer questions. **Outcome:** The term "qualified health professional" was used in this instance to ensure that patient safety is paramount and that an unqualified individual is not performing this activity. The committee felt it was important to require a certain level of knowledge both about the process and medically during the consent process so that the individual donating could feel comfortable that the information received comes from a qualified individual.
5.1	Yes	**Comment:** I would add "donor" to the parent standard so it reads "and optimize **donor &** patient safety." **Outcome:** The committee agreed with this comment and made the change.
5.1	No	**Comment:** How does one"… optimize patient safety."? Is it done by the list of the seven items listed below in this standard? **Outcome:** The committee noted this comment but did not feel a change was necessary at this time. Optimizing patient safety should be one of the ultimate goals of the program and all elements in the quality system should work together to achieve this, including the processes that are controlled as described in standard 5.1.
5.2.1	No	**Comment:** Please note that according to cGMPs and cGTPs validation of process changes must be completed and approved before implementation. Therefore we suggest revising standard 5.2.1 as follows: The facility shall identify the reasons for a change and obtain the appropriate approval(s) before implementation. Any changes that may affect the safety of the patient or the identity, purity, potency, or efficacy of the cellular therapy product shall be validated **before the administration procedure or the distribution and issue of products for administration,** respectively

		Outcome: The committee did not feel it was necessary to add the bolded phrase at this time as they believe that the requirement in the first sentence to "obtain the appropriate approval before implementation" ensures that change control must be completed before the process is implemented.
5.3	No	**Comment:** According to cGMPs, analytical methods or assays must be validated, while standard 5.2.3 addresses process validation only, can you clarify this for me? **Outcome:** In AABB Standards, you qualify a device and validate a process, you do not validate tests or equipment. As such, the committee did not feel a change was necessary at this time.
5.4.5 (5.4.5.1)	Yes	**Comment:** As there is only one standard under standard 5.4.5, we suggest moving the two sentences currently listed under 5.4.5.1 up to 5.4.5 and not using having a standard 5.4.5.1. **Outcome:** The committee agreed with the suggestion and combined the content of standard 5.4.5.1 with the header of standard 5.4.5 to appear as new standard 5.4.5.
5.5.1	No	**Comment:** Suggest moving the phrase "if applicable" to before the word "gases" as follow: 8) Acceptable control limits for temperature and humidity, and **if applicable, for** gases such as oxygen and CO2, when applicable. **Outcome:** The committee reviewed this comment, and noted that temperature and humidity may not always be applicable. Therefore leaving this phrase at the end of subnumber 8 allows "when applicable" to apply to the entirety of the standard..
5.6.1, 5.17.1.4	Yes	**Comment:** The descriptions in these standards and the definition for traceability in the glossary only refer to "tracing to the source or original cellular therapy product" and "final disposition". The requirements for tracking from donor to recipients and vice versa are not addressed. According to the 1271 regulations, the tracking system must enable tracking of the HCT/Ps from donor to the consignee or final disposition and vice versa (1271.290(b)) and the distinct identification code must facilitate effective tracking from the donor to the recipient and the recipient to the donor (1271.290(c)). **Outcome:** The committee noted this comment and edited the standard to be less product-centric and to clarify that traceability should be bi-directional. It was edited as follows: ***C*** **5.6.1 Traceability and Unique Identification** A numeric or alphanumeric system shall be used that will make it possible to trace any cellular therapy product or sample from **donor/**source to **recipient/**final disposition **and back to the donor/source** and to review records applying to the specific cellular therapy product or sample, including those related to reported adverse events. This unique identification shall not be obscured, altered, or removed.
5.7	Yes	**Comment:** "Systems" are usually bigger than policies, processes and procedures, and it seems to me that the overall concern of this standard is control of the label stock inventory and label templates. To better address this, I suggest making the following edits: 5) **The control of label inventory and templates, including discard**. ~~The system for discard of labels.~~ **Outcome:** The committee agreed with the suggested wording and made the change.
5.7.3	Yes	**Comment:** Cellular products with a biological license, including licensed cord blood products, are subject to the bar code label requirements (21 CFR 201.25). The bar code, at a minimum, must contain the appropriate National Drug Code (NDC). Only for certain minimally manipulated licensed biological products (e.g. unrelated umbilical cord blood), does the FDA

		consider exemption requests from the barcode rule and the use of ISBT 128 in lieu of NDC. The ISBT 128 product name and identification appear to be harmonized with the labeling requirements applicable to 361 HCT/Ps. **Outcome:** The committee noted this comment but did not think that a change was necessary at this time.
5.10	No	**Comment:** We suggest re-ordering the wording of this standard so that we limit deterioration, but prevent everything else as follows: "… in order to ~~prevent mix-ups and~~ limit deterioration **and prevent mix-ups**, contamination, improper distribution of cellular therapy products …." **Outcome:** The committee noted this comment but chose to retain the language as written as it would be difficult to prevent contamination and improper distribution.
5.10.3	Yes	**Comment:** It has historically been considered minimally acceptable for the level & temperature of LN_2 storage tanks to be taken once a day as long as there is a validated alarm system in place. However, this has not been considered acceptable for vapor phase storage. Even if the storage has a validated alarm system I would contend that continuous monitoring & periodic documentation (electronic documentation acceptable) of liquid nitrogen level or temperature be required at least based on the blood bank convention of at a minimum every 4 hours (even for liquid LN_2 storage) The 29th edition of Standards for Blood Banks and Transfusion Services state: BB/TS 29th Edition Standards state: *5.1.8.1.3 For storage of blood and blood components the temperature shall be continuously monitored and recorded at least every 4 hours* *5.1.8.1.3.1 If blood or blood components are stored in an open storage area, the ambient temperature shall be recorded at least every 4 hours.* Continuous monitoring ought to result in the ability to confirm appropriate temperature at any particular point in time (at least within the required 4 hours) by looking at the electronic (or written) records. This cannot be confirmed simply by an absence of alarms. Continuous monitoring does not refer only to monitoring for alarm conditions. **Outcome:** Based on this comment standard 5.10.3 was edited to clarify that continuous monitoring does not simply imply a system that tracks temperatures and alarms when undesirable temperatures are reached, but rather also requires the recording of data points at defined intervals. Intervals are stipulated in new standards 5.10.3.1 and 5.10.3.2 depending on the nature of the storage device in order to define minimum requirements depending on the nature of storage. The standards read as follows: **5.10.3** Storage devices containing cellular therapy products and critical materials shall have a system to continuously monitor and **also** record at defined intervals the temperature and/or liquid nitrogen levels. **5.10.3.1 The temperature of freezers where cellular therapy products are immersed in liquid nitrogen shall be recorded every 24 hours at a minimum.** **5.10.3.2 The temperature of freezers and refrigerators where cellular therapy products are not immersed in liquid nitrogen shall be recorded every four hours at a minimum.**

5.11	No	**Comment:** What do we do in the scenario he donor in question travels to Angola every 4 weeks for work and the donor is deemed eligible as there is no evidence of RCDADs was found in the donor's medical records, health history, PE or infectious disease testing. The health history screening questionnaire was properly documented with all required details related to travel specifically in question #24. NMDP policy is to notify the transplant center of the malaria risk in such case, however we do not require that the product be labeled with a biohazard tag. In this scenario, the apheresis center in question labeled the product from this donor with a biohazard tag because of the malaria risk per their policy and AABB requirements. Please clarify what AABB requires for labeling a product like this. **Outcome:** The intent of these standards is not to require these types of donors to be ineligible; however, it is important that the information is captured and relayed to the clinical site. If a facility chooses to a deem a donor ineligible, they are allowed to exceed the requirements of these AABB Standards. To clarify this distinction, a footnote was added to the items for Malaria, Chagas, and Rabies in Reference Standards 5.11B-5.11E that reads as follows: **[10]As of this date, the FDA does not consider these risk factors to render donors ineligible; facility policies must define how health history risks identified for these diseases affect eligibility determination.**
5.11.1.1 (5.12.2)	Yes	**Comment:** In standard 5.11.1.1 I would add a cross reference to reference standard 5.11.B to read, "…in conformance with reference standards 5.11A & 5.11B." Reference standard 5.11B is the table that tells you what to do in order to accomplish and complete donor suitability. **Outcome:** The committee agreed with this suggestion and added these cross references in question. The standard now reads as follows: **5.11.1.1** Before any procurement procedure, the procuring facility shall obtain final approval and documentation by the donor's physician, or by another physician who is not directly involved with the care of the recipient, that the donor is suitable to proceed with donation, in conformance with Reference Standards 5.11A, General Requirements for Cellular Therapy Product Donors; **5.11B, Clinical Evaluation and Laboratory Testing of Living Allogeneic Donors; and 5.11C Clinical Evaluation and Laboratory Testing of Autologous Donors.**
5.11.1.1 (5.12.2)	No	**Comment:** Please revise this standard to state "Before any procurement procedure**, except Cord blood,** the procuring facility..." The rationale behind the change is that the final donor suitability determination may be completed after the collection of the cord blood. **Outcome:** The committee noted this comment but did not feel a change was needed at this time. The new Standards Portal will allow facilities that focus on cord blood to filter the CT Standards accordingly and would ensure that this standard does not appear once the profile is set.
5.11.3.1	Yes	**Comment:** I have two questions, aren't the samples collected from the donor (or birth mother), considered the product? Secondly, to have 7 days in the first sentence and then call out both 7 days and 30 days in the three line items below could cause confusion, as such I suggest removing the "7 days" from the first sentence, and adding a 4th line item stating "All other cell therapy products: Collect within 7 days before or after procurement". **Outcome:** The committee did not feel a change was necessary to the structure of this standard. However, the committee did clarify that samples are collected from the donor not the product and it was edited as such: **5.11.3.1** The collection of samples for infectious disease testing shall be completed within 7 days before or after procurement. Samples ~~from~~ **associated with** the products listed below shall be collected **from the donor**

		within the following timeframes:
5.11.3.3, 5.11.3.3.1	Yes	**Comment:** This process should include an evaluation of the donor for clinical situations in which plasma dilution may be sufficient to affect the test results as such, we suggest clarifying the standard. Also, the reference in standard 5.11.3.3.1, to the FDA guidance can be deleted because it is already listed in standard 5.11.3.3. **Outcome:** The committee did not feel a change was necessary at this time but this issue could be explored further in guidance in the future. They did, however, delete the reference to FDA guidance in 5.11.3.3.1.
5.11.3.6	Yes	During the comment period the committee received the following comments to standard 5.11.3.6: • Inconsistencies between regulatory recommendations and accreditation standards are an on-going issue for accredited facilities. Please provide the rationale for allowing anti-HBc or HBV DNA when FDA currently recommends anti-HBc testing (see http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm151757.htm). • HBV DNA testing instead of testing for anti-HBc doesn't meet the current requirements in the 1271 regulations. As explained in the DE guidance, FDA currently considers HBsAg and anti-HBc to be adequate and appropriate tests for HBV. HBV DNA may be performed in addition to HBsAg and anti-HBc. **Outcome:** The committee noted that this addition to the standard needed to be clarified. The committee therefore elected to remove this reference from standard 5.113.6 and in its place created a new Standard 5.11.3.6.1, which was added to clarify that the use of HBV DNA for infectious disease testing is approved for use in some countries though the FDA regulations do not allow its use in lieu of HBsAg and anti-HBc testing in the United States. The new standard reads as follows: **5.11.3.6.1 For facilities located outside of the United States, HBV DNA testing is acceptable in place of anti-HBc testing.**
5.11.3.6	No	**Comment:** This addition of the clause, "antibody to cytomegalovirus" implies that CMV testing is to be performed for each collection. If a donor is known to be antibody positive from a previous test (for example for an autologous donor) we believe that it would be unnecessary to repeat the testing for any subsequent collections. **Outcome:** The committee noted this comment and, while they did not feel a change was necessary to the standard itself, will explain this issue further in guidance.
5.11.6	Yes	**Comment:** A final determination of donor eligibility can only be made if all the required donor screening and testing has been completed in accordance with the regulations, therefore, for clarity, we suggest deleting the reference to "determination of eligibility is incomplete" in standard 5.11.6(1). Also we suggest the deletion of subnumber of standard 5.11.6as standard 5.11.9 already covers cases when donor eligibility determination has not been completed. **Outcome:** The committee made the suggested changes and deleted the phrase "or that the determination of eligibility is incomplete." Additionally, the committee deleted item #3 and moved it to become new standard 5.11.9.1.1.
5.11.7.1	Yes	**Comment:** Standard 5.11.7.1 uses the term "repeat reactive infectious disease test results." The phrase "repeat reactive" should be removed because when the testing laboratory reports a reactive test it has already been repeated. Some facilities think this means the sample can be redrawn and if negative then that is the final result and it should be noted that this phrase does not appear in the BB/TS Standards. **Outcome:** The committee agreed with the comment and removed the word "repeat."

5.11.9	No	**Comment:** For clarity, we suggest revising the standard to read: "For allogeneic donors, if the donor screening, testing and the donor eligibility determination have not been completed, the product may be used if there is a documented urgent medical need." **Outcome:** The committee noted this comment but felt that this concept was already covered by standard 5.11.10.
5.11.9.1	No	**Comment:** We suggest deleting standard 5.11.9.1 because it implies that it would be an acceptable practice not to perform donor testing in accordance with the regulations, or if that is not possible, please revise the standard to read "……test kit, the donor eligibility determination cannot be completed." **Outcome:** The committee felt that this standard is appropriate as written and should be left as written because this situation occurs in facilities that AABB currently accredits.
5.11.9.2	Yes	**Comment:** We suggest revising this standard to read: "The facility shall complete the donor eligibility determination **during or after the use of the product**, if possible, or indicate in the associated records the justification for the eligibility **determination** not being completed….." **Outcome:** The committee agreed with the suggestion and edited the standard as requested.
5.11.10	Yes	**Comment:** In addition to the specific Warning statements, there are other requirements applicable to products from donors for whom donor eligibility has not been completed. For clarity, it may be better to include them in this section. The following are the additional requirements that could be included: -Results of any required donor screening and testing that has been completed and a list of any donor screening and testing that has not yet been completed must accompany the product. -Physician using the product must be notified that the donor screening and testing were not completed and the notification must be documented (1271.60(d)(3)). **Outcome:** The committee noted this comment and added a cross-reference to standard 5.23.2 to emphasize the items that must accompany the product at issue when the donor eligibility determination is incomplete. Standard 5.11.9.2 already addresses notification of physicians regarding screening and testing that is not completed.
5.11.11	Yes	**Comment:** According to the requirements in 1271.370(c)(4), instructions for use related to the prevention of the introduction, transmission, or spread of communicable diseases must accompany the product. This requirement is applicable to all products including those that are for autologous use; therefore, we suggest adding a reference to this in the standard. **Outcome:** The committee agreed with this comment added a cross-reference to reference standard 5.8.5A.
5.12.5	Yes	**Comment:** With regard to this standard, how do I assess the safety of the donor, mother, and baby? Should this be worded as follows: "**The procurement facility shall have policies, processes, and procedures to assess the donor medical status to ensure health and safety.** ~~Procurement procedures shall ensure the safety of the donor.~~ Criteria for discontinuation of procurement due to medical **condition or** complications shall be specified. **The procurement medical director shall be notified of medical complications of the donor. Standard 7.0 applies**" **Outcome:** The committee noted this comment and elected to broaden the standard as they agreed it was unrealistic to "ensure" the safety of the donor. It was edited as follows: **5.12.6 The procurement facility shall have policies, processes, and procedures that are designed to protect the health and safety of the donor.** ~~Procurement procedures shall ensure the safety of the donor.~~ Criteria for discontinuation of procurement due to medical complications shall be specified.

5.18.2.1.1 (5.17.1.1.1.1)	Yes	**Comment:** Revise to state: "One individual and one electronic device that is validated to fulfill labelling identification function could be used." **Outcome:** The committee made the suggested change to be consistent with requirements in other sets of AABB Standards. The standard now reads: **5.18.2.1.1** The identity of the cord blood product and segment(s) shall be confirmed by two individuals **or one individual and an electronic device that has been validated to fulfill the labeling identification function(s)** when integrally attached segments are removed.
5.18.2.2 (5.17.3)	Yes	**Comment:** This standard states that "cord blood products stored for greater than one year shall be stored at temperatures at or below -150ºC". Please note that for licensed HPCs, cord blood, the FDA guidance document recommends that cryopreserved products be stored at ≤150ºC in liquid or vapor phase of liquid nitrogen regardless of the length of storage time. **Outcome:** The committee agreed with the suggestion and edited the standard as follows: **5.18.2.2** **Cryopreserved** cord blood products ~~stored for greater than one year~~ shall be stored at temperatures at or below –150 C **in liquid or vapor phase of liquid nitrogen**.
5.19 (New)	Yes	**Comment:** a) Could this standard please state that viable cell recovery of the relevant cell population(s) is required b) Could this standard please be expanded to indicate that the stability studies are instrumental to complying with Reference Standard 5.7.1A Line 10 and 5.9.1 #7 **Outcome:** a) The committee agreed with the suggestion and included the phrase "of the relevant cell population" to standard 5.19.2.1 b) The committee did not feel a reference to standard 5.9.1 #7 was appropriate because one facility will not have direct oversight for the supplier's expiration/stability program. The facility responsible for processing steps and storage assigns the product an expiration date based on their stability program.
5.19.1 (New), 5.19.3 (New)	No	**Comment:** The committee received a number of similar comments on these standards. They include: • Is the expiration date required to be based on the facility's studies on its own products and does it need to cover different processing methods and storage conditions? Will the facility be allowed to base an expiration date on relevant literature? Will the requirement for an expiration date apply to HPC, Apheresis and HPC, Marrow? Similarly for Somatic Cells will the facility be able to base any evidence in support of an expiration date on literature? Could there please be a specific standard addressing expiration date labeling and not simply a footnote to Reference Standard 5.7.1A? • Please provide guidance on how to establish expiration dates for products that are being stored for up to 10 years, particularly for products that are already in storage. It would be difficult to identify material for stability testing that was not saved specifically for this purpose in many facilities with limited storage space. Is it acceptable to use expiration dates cited in the literature? • "If cryopreserved products are to be stored past their assigned expiration date, the facility shall have policies, process and procedures to re-assign and re-label product expiration dates according to documented stability program data." Please provide guidance on how to extend stability testing for products that may be stored up to 10 years. Is it acceptable to extend expiration dates based on studies cited in the literature?

		Outcome: A new facility may not have enough inventory and internal data on which to base a stability program, and such a facility could use publications and literature to justify initial expiration timeframes and to meet the requirement for a stability program. However, the facility's stability program must grow and must include data and criteria based on actual product testing; use of literature and publications cannot be the sole basis for expiration dates nor can they serve as the facility's stability program. Further guidance will be provided on these issues in the Standards Portal.
5.19.3 (New)	Yes	**Comment:** The committee received a number of similar comments on these standards. They include: • We request that this standard clarify that cells can be retained past expiration, but cannot be used for infusion beyond the expiration without further justification. A suggested revision is: "If cryopreserved products are stored **and used for infusion** past their assigned expiration date…" • The requirement to re-label cryopreserved cells is unrealistic. The standard should be revised to require the facility to document the review and approval for product retention past the expiration date. • Recommended Wording: **5.19.3** If cryopreserved products are to be stored past their assigned expiration date, the facility shall have **documentation of review and approval of product retention** ~~policies, processes, and procedures to re-assign and re-label product expiration dates according to documented stability program data.~~ **Outcome:** The committee noted these comments and edited the standard in order to emphasize the need for further review of products distributed after their original expiration. Standard 5.19.3.1 was added to clarify the need to re-label products if they are re-assigned expiration dates. Reference Standard 5.7.1A line 10 clarifies that re-labeling (if performed) would need to be accomplished prior to distribution, but the letter "A" means that the label just has to be attached (i.e. through use of a tie tag), - it does not have to be permanently affixed. **5.19.3** If cryopreserved products are to be ~~stored~~ **distributed** past their assigned expiration date, the facility shall **have processes for review and approval of product release**. ~~have policies, processes, and procedures to re-assign and re-label product expiration dates according to documented stability program data.~~ **5.19.3.1 If facilities re-assign product expiration dates based on documented stability program data, the facility shall have policies, processes, and procedures to re-label products with new expiration dates. Reference Standard 5.7.1A Requirements for Labeling of Cellular Therapy Products applies.**
5.21.1 (New)	Yes	**Comment:** Please clarify: the facility or the product must meet requirements? **Outcome:** Both the facility and the product need to meet specified requirements, but the committee elected to re-word standard 5.21.1 to emphasize the need for approval rather than the critical characteristics for release. It now reads as follows: **5.21.1** ~~The facility shall define critical donor and product characteristics for which documented approval by the medical director or designee and, if applicable, the recipient's physician are required before a product is made available for distribution.~~ **Products shall not be made available for distribution or listed on a registry until the medical director or designee, and the quality representative have approved the release of the product.**

		~~**5.21.1.1** The facility shall meet specified requirements before cellular therapy products are listed on a product registry.~~
5.21.2.1	No	**Comment:** The committee received a number of similar comments on these standards. They include: • Revise to state "4) The procurement order**, except cord blood,** was obtained" Rationale: Requirement is not relevant to cord blood donations. • How would this apply to a cord blood unit that was not a directed donation? Maybe add "if applicable." **Outcome:** The committee noted these comments but did not think changes to the standard were necessary at this time. Instead, the committee decided to write further guidance about whether item #4 applies to cord blood products in the Standards Portal.
5.22.1 (5.19.2)	Yes	**Comment:** It is assumed that cord blood banks (and others) must send thawing and administration instructions along with their products at distribution. Is this a correct assumption? It does not appear to be required in the CT Standards. If it is a requirement could it please be stated unambiguously? **Outcome:** The committee felt that thawing instructions would be included in the instructions for "handling and preparation" of products. To make this more clear, the committee elected to make the following edits: **5.22.1** Instructions shall be ~~provided~~ **made available** for the handling ~~and~~, storage, **and preparation** of products ~~after distribution~~ **for administration**.
5.22 (5.19.1), 5.23 (5.20)	Yes	**Comment:** Under 5.22, 5.23, I do not believe that HLA matching should be reviewed prior to distribution or issue. Any onus for ensuring HLA compatibility should be placed on the clinical team who should review the necessary information prior to selecting the donor. I do not think laboratory directors with limited HLA training can adequately perform that review especially in complicated cases such as cord blood transplants with mismatches. The laboratory director would assume that if the donor identity is correct then the HLA is correct. **Outcome:** The committee edited these standards to make it clear that the distributing facility needs to at least verify that a determination of compatibility was made even if they are not responsible for performing HLA testing. The standards now read as such: ✎***C*5.22 Distribution** Upon request for distribution, the following items shall be reviewed: 5) **Documentation of** compatibility **for the selected donor** a) ABO and other blood group and type antigen compatibility, if applicable. b) HLA compatibility, if applicable. ✎***F*5.23 Product Issue** 5) **Documentation of** compatibility **for the selected donor** a) ABO and other blood group and type antigen compatibility, if applicable. b) HLA compatibility, if applicable.
5.24.1.1 (New)	Yes	**Comment:** Not all products trigger the need for HLA typing. **Outcome:** The committee noted this comment and added the phrase "if applicable" to the standard.
5.24.1.2 (New)	Yes	**Comment:** It is unclear how this would apply to cord blood. Clarification required.

		Outcome: The committee added language clarifying that this standard applies to "HPC, Apheresis and HPC, Marrow" only.
5.24.2 (New)	Yes	**Comment:** Does this apply only to transplant facilities, or as a processing facility, will AABB expect me to verify that the transplanter has done this evaluation before I ship product? 5.24.2, 5) - Which infectious disease markers are required for the patient and for what purpose? **Outcome:** This standard is the responsibility of clinical facilities, but this is something that should be specified in agreements between facilities. For item #5, the ID markers that are those that are relevant to the protocol, therefore, the committee added "as indicated by the clinical protocol."
5.29.6 #5 (5.25.5)	No	**Comment:** Clarify #5 to state "if applicable" since infectious disease testing is not required for types of donations (autologous). **Outcome:** The committee noted this comment but did not feel a change was necessary at this time. Infectious disease testing is still required for autologous donors, though the testing depends on what the type of therapy/clinical protocol.
5.29.6 #6 (5.25.5)	Yes	**Comment:** What does assessment of red cell compatibility with the intended donor mean? For unrelated, it is impossible; most places do not do it even for related. If keeping it, suggest adding "if applicable" at the end of the sentence. **Outcome:** In response to this comment, the committee edited item b clarify the nature of red cell compatibility: b) Assessment of **blood grouping** ~~red cell~~ compatibility **between** ~~with~~ the intended donor **and recipient**.
5.31.4.1	Yes	**Comment:** The committee received several comments regarding this standard: • I think the most relevant change you might make moving forward is to have something that ties reporting to CIBMTR to be consistent with federal regulations and agreements related to cooperative group participation (BMT CTN), participation in the NMDP, etc. This is distinct from whatever data collection and analysis center wish to have for their own quality improvement systems. I would suggest that you have a section about compliance with US Federal regulations regarding data reporting, and perhaps something similar for other countries. These may be distinct from what AABB requires centers do for their own internal quality, etc. Suggested revision of standard 5.31.4.1: "The clinical program shall submit data regarding administration procedures and outcomes to the Competent Authority as required by national and local regulations. For example, hematopoietic transplants in the United States would report data to **the contract holder for the Stem Cell Therapeutic Outcomes Database of the CW Bill Young ...Program** (Center for International Blood and Marrow Transplant Research (CIBMTR) **outcomes** ~~collection~~ registry. For cellular therapies under investigational use, outcomes data shall be reported to the agency overseeing the protocol." • Please revise to omit the words collection registry:" ….to the Center for International Blood and Marrow Transplant Research (CIBMTR) ~~collection registry~~." **Outcome:** Ultimately, the committee decided to delete this standard because they believe the requirements are adequately covered by the general requirement that centers must always adhere to relevant local and national regulations.
Reference Standard 5.7.1A	No	**Comment:** In general, there are requirements for labeling in the BBTS Standards that are not in the CT Standards. For example, a requirement of the BB/TS Standards is to have the following statements on the label: "Rx Only" "This product may transmit infectious agents" "See Circular of Information--" Should CT Standards also require as A^5 (accompanying label)? Especially "Rx Only". Also, I suggest that Line 16 "Do Not Irradiate" label should be required at Completion of Procurement as well.

		Outcome: The FDA does not require these additional items so the committee did not feel a change was necessary at this time.
Reference Standard 5.7.1A	Yes	**Comment:** Row #1, "Completion of procurement[1]" column: there is no footnote below the table that is applicable to this column header. Row #14: Suggest revising to: "Name and address of the facility that determines the product has met the release criteria and makes the product available for distribution." **Outcome:** The committee noted that there is in fact an applicable footnote for "Completion of Procurement". Item #14 was revised to state: "Name and address of the facility **that determines the product has met release criteria and makes the** ~~making the~~ product available for distribution." Also, the labeling requirement for accompanying records was removed for this item at completion of processing because products have not been made available for distribution at that time.
Reference Standard 5.8.5A	Yes	**Comment:** 1st footnote: 21 CFR 1271.60(d)(2), 21 CFR 1271.370(c) should be included. **Outcome:** The committee added both CFR references to the footnote.
Reference Standard 5.11A	No	**Comment:** There does not appear to be a requirement that the donor qualification process be private and confidential (for example, see BB/TS Standard 5.3.1.) This is of concern because some cord blood banks will use a health history questionnaire which is completed by the father as well as the mother (of the cord blood donor). Appropriate wording regarding confidentiality could be added to Reference Standard 5.11A **Outcome:** The committee felt that no change was necessary at this time. Other parts of the standards, including chapter 6, address confidentiality issues.
Reference Standard 5.11B	Yes	**Comment:** Sepsis is a relevant communicable disease but it is not listed in the tables. Donor screening measures (medical history, clinical and physical evidence) must include risk factors for sepsis. In the footnote regarding WNV, note that FDA has issued draft guidance for WNV testing. The guidance has not been finalized yet. http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ Also, there is a draft guidance on *T. cruzi*: Draft Guidance for Industry: Use of Serological Tests to Reduce the Risk of Transmission of Trypanosoma cruzi Infection in Whole Blood and Blood Components for Transfusion and Human Cells, Tissues, and Cellular and Tissue-Based Products. This guidance was finalized in 2010 and is only applicable to blood and blood products. http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM213415.pdf **Outcome:** The committee added a line item to the reference standard to capture health history risks for Bacteremia. They elected not to link to draft guidance because they did not want to confuse the membership with a draft that may change over the next year. Finally, while the finalized guidance pertains to *T. Cruzi* for blood and blood products, it does not apply to HCTPs. Since there is no finalized guidance on *T. Cruzi* for HCT/Ps, the committee chose not to include this suggested reference.
Reference Standard 5.16A (Reference Standard 5.16A, 5.16C)	Yes	**Comment:** "5) Potency assay specific to the cellular therapy product. a) For HPCs, CD34 analysis or comparable assay (except for marrow)." Is the word "viable" still needed before CD34, i.e. viable CD34? **Outcome:** The committee added a new requirement for a viability test that is applicable to all products. It now reads as such: 5) Potency assay specific to the cellular therapy product. **a) A test for viability**

Reference Standard 5.16A (Reference Standard 5.16A, 5.16C)	No	**Comment:** Reference standard 5.16.A (1) (c): Change donor lymphocyte infusion to MNC or T Cell to be compliant with ISBT128 nomenclature. Reference standard: Add 5.16A (1) **(e) "For Investigational and IND Products, relevant cell population in conformance with the IND protocol or expected outcome"** or move 5.16.A (7) to 5.16.A (1) (e) **Outcome:** The committee noted this comment but did not feel a change was necessary at this time. The testing required by IND may not be just about cell count, and the testing required by #7 is broader than #1.
Reference Standard 5.16A (Reference Standard 5.16A, 5.16C)	Yes	**Comment:** #4 and #7 might be better combined and I don't think we define sterility testing. Also, I believe the recipient's physician always needs to be contacted if a product is contaminated. Perhaps remove #7 and add to #4 as: "4) Microbial contamination (culture for aerobic and anaerobic and fungal elements) at the completion of processing. a) Notify the recipient physician of positive culture results. If the results may affect the donor's health, also notify the donor's physician. **b)** Testing of the cellular therapy product shall conform to the IND protocol, or, if not covered by an IND protocol, shall include, at a minimum, culture for aerobic and anaerobic and fungal elements." **Outcome:** The committee felt that #7 did not belong under #4 because that would remove the elements related to "sterility, identity, and viability." However, they agreed that notification to the recipient must always occur, so the requirement was edited as such: 4) Microbial contamination (culture for aerobic and anaerobic bacterial and fungal elements) at the completion of processing. **a) Notify the recipient physician of positive culture results.** b) If results affect the donor's health, ~~or the therapeutic value of the product,~~ notify the donor's physician ~~and recipient's physician of positive culture results~~.
Reference Standard 5.16A (Reference Standard 5.16A, 5.16C)	Yes	**Comment:** Please note that for any investigational product, the testing must be performed in accordance with the criteria defined in the IND application. Therefore, we suggest deleting the reference to "cultured cells" in 5.16.A(7). Also, for licensed products, the testing must be performed in accordance with the criteria defined in the approved license application. **Outcome:** The committee added the bolded item below in response to this comment: 7) Testing of cultured cells shall conform to the IND protocol, or, if not covered by an IND protocol **or approved license application**, shall include sterility, identity, and viability testing.
Reference Standard 5.16B	Yes	**Comment:** "If the final product contains red cells" appears in 5.17B and not in 5.17A in the 6th edition of *CT Standards*. ABO/Rh is an important processing test of any product which originates from peripheral blood, cord blood, or bone marrow, at collection regardless of use and so should be included in all the processing tests (5.16A, 5.16B, 5.16C). This may of course not be applicable for cells procured from other sources for example pancreatic islet cells so 5.16C could state 'if applicable' or similar. The wording "If the final product contains red cells" in 5.16A & 5.16B is an issue because if a product is for hematopoietic reconstitution the ABO/Rh type of the collected product is essential information whether the final product contains RBC or not. Conversely, ABO/Rh of the final product is relevant if the product contains RBC regardless of intended use. My main concern is that 5.16A does not require ABO/Rh of collected product as a processing test and 5.16B only requires ABO/Rh if the final product contains RBC. If the product in 5.16C is derived from blood or bone marrow, then ABO/Rh is an important product processing test.

		Also suggest including "viable" in #5a): "**Viable** CD34 or comparable assay (except for marrow)" **Outcome:** The committee agreed that ABO/Rh should be required if the product contains RBCs or if it is intended for hematopoietic reconstitution. "If the final product contains red blood cells" was deleted from Item #1 of Reference standard 5.16B.
Reference Standard 5.16B	Yes	**Comment:** As explained above, for licensed cord blood products, testing must be performed in accordance with the criteria defined in the approved license application. **Outcome:** The committee noted the comment and added a new #7 which reads as follows: **7) These tests shall be performed in addition to any testing required to conform to the criteria defined in a US FDA license application.**
Reference Standard 5.16B	Yes	**Comment:** #1 states "If the product contains red blood cells ---" I am not aware of any HPC, Cord Blood products which do not contain red cells and that is probably a moot point because by definition the ABO/Rh type of an HPC product is a critical characteristic. Also, #3) c) States "CD34 analysis " but it would be helpful if this stated, as in #5) c), "Viable CD34 assay" **Outcome:** The committee deleted the phrase "if the product contains red blood cells" from item #1. #5 c) was edited to clarify that the test required is "viable CD 34 (direct measurement)."
6.1.2	Yes	**Comment:** I can imagine there are times when the writing is done by a technical writer who is familiar with the subject area, but not trained and/or qualified. They may just be good at writing. Maybe the trained/qualified person only needs to review and verify content for accuracy and effectiveness, and does not need to be the one to write. **Outcome:** In response to the comment, the committee edited the standard as such: **6.1.2 Document Review, Approval, and Distribution** The facility shall review and approve all controlled documents before use. The document control process shall ensure that policies, processes, and procedures: 1) Are ~~written and~~ reviewed by personnel trained and/or qualified in the subject area.
6.1.2	Yes	**Comment:** Since CT now falls under CMS and CLIA, please add that new and changed procedures have to be performed by an authorized individual, i.e. the laboratory director on the CLIA license. **Outcome:** The committee reviewed this comment and added a new item #2 to address this concern when testing is performed whether or not the facility is subject to CMS/CLIA: **2) Are approved by an authorized individual.**
Reference Standard 6.2.1A	Yes	**Comment:** Please revise this standard to state: "Quarterly ~~and annual~~ reports by quality representative to executive management" This change would assist with an issue of consistency where annual reports are not mentioned in the referenced standard 1.2.4.1 and 1.2.4.2. **Outcome:** The committee agreed with this change and made the change for consistency.
8.5 (8.3)	Yes	**Comment:** Should this standard include "Adverse events as described in section…" **Outcome:** The committee agreed with this comment and added in a new #6 that reads as follows: **C 8.5Monitoring Clinical Activities**

		Facilities performing clinical activities shall have a program that monitors and addresses patient care practices for all cellular therapies. The following shall be monitored: 6) Adverse events
10.2.1 #1	Yes	**Comment:** Should donors be included in subnumber 1? **Outcome:** The committee agreed with this comment and the standard now reads: **10.2.1 Environmental Controls** The facility shall design, approve, and implement an environmental control system that monitors the following conditions: 1) Optimizes **donor**, patient and employee safety.
Glossary - Authorization	Yes	**Comment:** I believe you have now added some detail for this but should the Standards define "authorization" in the glossary (also relevant for reference standard 4.6A) **Outcome:** The committee agreed with this comment added the following definition: **Authorization (in relation to procurement from cadaveric donors): A legal record providing permission for postmortem recovery of cells/tissues and subsequent use.**
Glossary - Competence	Yes	**Comment:** Please revise the definition of "Competence" to state: "...task according to procedures **are** evaluated on an on-going basis." This would provide clarity to the definition. The wording as it currently sits makes it unclear if the procedures are evaluated on an on-going basis or the ability to perform the task is evaluated on an on-going basis. **Outcome:** The committee chose to include "shall be" instead of "are" in the definition which now reads as follows: **Competence:** Ability of an individual to perform a specific task according to procedures **shall** be evaluated on an ongoing basis.
Glossary – Critical Elements	Yes	**Comment:** Why are there three separate definitions of the term critical, as opposed to keeping as something like "Critical steps/tasks"? **Outcome:** The committee agreed with this comment and the definitions were combined so that the phrase "Critical Tasks" was broadened to address "critical" in general and the word "steps" was added an example of a critical element for completeness. **Critical ~~Tasks~~:** Elements (such as materials, equipment, **steps, or** tasks) that directly affect the quality of the product or service.
Glossary – Databases (not included)	No	**Comment:** We suggest adding a definition for *databases* to the Glossary. **Outcome:** The committee noted the question but did not feel a definition is necessary.
Glossary - Eligibility	Yes	**Comment:** In limited cases, the regulations allow the use of an HCT/P from a donor for whom the donor eligibility (DE) determination has not been completed only in cases of urgent medical need and in accordance with 21 CFR 1271.60. Including the "eligibility determination not completed" in the definition of "Eligibility" does not correctly describe the regulatory requirements and the committee may wish to add a separate definition for donors for whom donor eligibility determination has not been completed. Therefore, we suggest revising the last sentence to of eligibility to read as follows: "A donor may be found eligible or ineligible (see "ineligible donors")." Please note that products (i.e. unrelated allogeneic cord blood) from ineligible donors or from donors for whom DE determination has not been completed are not qualified for licensure.

		We also suggest that you include a definition for "Eligible" donors. The committee may wish to consider the following: Eligible Donor: A donor who is found to be free from risk factors for communicable disease agents or diseases based on all the required donor screening and tests that have been completed in accordance with the applicable regulations. **Outcome:** The committee did not feel a definition for eligible donor was necessary at this time, however, they did restructure the definition of "eligibility" into a list for clarity. It now reads as follows: **Eligibility:** With respect to donors, the evaluation of cellular therapy donors for risk factors and clinical evidence of relevant infectious disease agents or diseases for the purpose of preventing the introduction, transmission, and spread of infectious disease. A donor may be found to be a) eligible, b) ineligible (see "ineligible donors") or c) the determination may be incomplete (e.g., screening is incomplete or donor testing is not performed in a timeframe specified by the test kit manufacturer's instructions).
Glossary - Hematopoietic Progenitor Cells	Yes	**Comment:** We suggest deleting the clause, "regardless of tissue source" from the definition. **Outcome:** The committee noted this comment and removed the term "tissue" to clarify the definition.
Glossary - Ineligible	No	**Comment:** We suggest revising the definition to read as follows: "A donor who has identified risk factor(s) for communicable disease agents or diseases based on all the required donor screening and tests that have been completed in accordance with the applicable regulations." **Outcome:** The committee noted the comment but did not feel a change was necessary at this time.
Glossary – IRB, IND, INV (not included)	No	**Comment:** Should there be a definition for IRB, IND, INV. **Outcome:** The committee did not feel that definitions were needed for these terms as they are spelled out and described in the standards.
Glossary - Label	Yes	**Comment:** It appears that product information that may be attached to a container (i.e. tie-tag) is excluded from this definition. **Outcome:** The committee included "attached" for completeness. The definition now reads as such: Label: An inscription affixed or **attached** to a product for identification.
Glossary - Labeling	No	**Comment:** The listed definition of labeling does not correspond to FDA definition and requirements for labeling. You may refer to 21 CFR parts 600.3(dd), 312.6, 201, 610 subpart G and 1271.370. **Outcome:** The committee noted this comment but did not feel that a change was necessary at this time.
Glossary - Leukocyte rich products	No	**Comment:** Why is there a definition of leukocyte rich products? **Outcome:** The committee noted the acronym is spelled out in the standards and it is needed.
Glossary – Leukocyte	No	**Comment:** Please remove leukocyte rich products from the glossary. **Outcome:** The committee felt that it was important to keep this definition and chose to make no change.
Glossary - Mononuclear Cells	No	**Comment:** Please add a definition for Mononuclear Cells. **Outcome:** The committee agreed and crafted a definition. **Mononuclear Cells (MNC):** Lymphocytes and monocytes in the collected product.
Glossary – Offsite Location	Yes	**Comment:** The definition for Offsite Location only addresses the definition of a location with an example of one permitted location, i.e., the cloud which misses the concept of offsite. "Offsite" is a concept which we see frequently missed by

		facilities during assessments. We suggest adding the words “remotely located” to the definition A "remotely located" physical storage facility or electronically supported storage medium, including the “cloud” maintained by a third party. **Outcome:** The committee noted the comment and edited the definition as follows: **Off-site Location:** A physical storage facility or electronically supported storage medium, ~~including the “cloud” maintained by a third party~~ **that provides reliable redundancy of data**.
Glossary - Processing	Yes	**Comment:** Please revise to the definition of “Processing” to state "Any activity performed on a cellular therapy product, ~~other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution,~~ such as testing for microorganisms, preparation, sterilization, steps to inactivate or remove adventitious agents, preservation for storage and removal from storage. **Excludes recovery, donor screening, donor testing, storage, labelling, packaging or distribution**." Rationale: provide clarity of definition. **Outcome:** The committee noted this comment but did not feel a change was necessary at this time.
Glossary - Quarantine	No	**Comment:** Please remove "cross” as it relates to contamination so that the definition is consistent with the standards **Outcome:** The committee noted this comment, but felt that quarantine is meant to ensure that cross contamination does not occur, so in this case they felt that maintaining the term as a part of the definition was appropriate.
Glossary – Urgent Medical Need	No	**Comment:** We suggest revising the definition of Urgent Medical Need to read as follows, “means that no comparable product is available and the recipient is likely to suffer death or serious morbidity without the product.” **Outcome:** The committee noted this comment but did not feel a change was necessary at this time.
Glossary – T Cell (not added)	No	**Comment:** The Glossary appears to be missing the definition of the term T Cell. **Outcome:** The committee noted this comment but did not feel the addition was necessary at this time.