

Frequently Asked Questions: Effectively Transition to the 7th Edition FACT-JACIE Hematopoietic Cellular Therapy Standards

The questions below were submitted after the webinar presented by Dr. Paul Eldridge, FACT Standards Chair, on March 14, 2018:

1. Can you explain an electronic record keeping system for reporting to CIBMTR that requires validation?

There are programs that develop in-house databases completely independent of their institutional electronic medical record system. These databases serve as repositories of data required to be reported to the CIBMTR. Reports are pulled directly from these databases and transmitted to the CIBMTR. In this situation, the “source data” is electronic and managed by the transplant program. These database systems require validation as an electronic record system under FACT Standards.

2. Does FACT have specific expectations regarding submission of data to CIBMTR from centers outside the U.S.? Previous inspections show that our center has excellent accuracy but a poor level of quantitative completion due to inadequate staff.

While accuracy is an essential criterion, incomplete data collection does not meet the intent of the Standards, nor does the presence of inadequate staff. FACT encourages accredited centers to submit data to CIBMTR, and requires that, at a minimum, programs collect all data necessary to complete the Transplant Essential Data Forms (CIBMTR) or Minimum Essential Data-A forms (EBMT) [B9.1]. Further, programs are required to define staff responsible for collection and reporting of data [B9.3] and to have sufficient staff to comply with B9.1 [B3.1.11.5].

3. Our law and regulation request review of agreements every three years. Is this acceptable or do we have to follow the two years?

Standards B/C/D4.6.3 state, “agreements must be dated, reviewed, revised and approved by both parties, and legal counsel if necessary, on a regular basis as defined by the program, and at least every two years.” If the FACT standard is more stringent than your local regulation, you must follow the FACT standard. If your local regulation specifically forbids a more frequent review cycle, then FACT would not require you to go against your regulations. This would need to be demonstrated to the inspector.

4. Are establishment and maintenance requirements for written agreements applicable to research, or only for FDA approved cellular therapy products?

For third-party manufactured products, written agreements are expected for both research and licensed products. The scope and specific items covered in those agreements may be very different, but agreements outlining expectations and responsibilities for all parties should be in place. For licensed products in the US, FDA assumes responsibility for product manufacturing. Facilities participating in collection of initial cellular products or in administration of such cellular therapy products would only be required to verify the licensure status of the product. Agreements could be limited to issues of service.

5. If the BM product is always in the hands of someone (qualified courier), is it stored?

There is a difference in requirements for transport and for storage; however, technically, a product is being stored while it is being transported (i.e., in the hands of someone, such as a qualified courier). There are standards concerning management of products during both storage and transport/shipping. Products that are in storage must be in a qualified storage container (e.g., refrigerator with alarmed monitor) but are not under the immediate control of qualified personnel. Products during transport/shipping must be in a container qualified to maintain appropriate temperature and integrity and be under the control of a qualified courier.

6. Are there ISBT 128 standards for labeling research products?

The ISBT 128 standard is flexible enough to accommodate research products, but in the US, labeling of products under Investigational New Drug (IND) applications is described and specified in the IND document and approved by the FDA. That is the labeling that should be followed for research products. Facilities should request this information from the IND holder and follow requirements. If no labeling is specified and the IND holder does not provide instructions, then following established labeling procedures for your facilities would be expected. FACT encourages use of ISBT 128 terminology, coding, and labeling early in product development.

7. The ISBT 128 label example on the webinar is different than the current Digi-Trax CT label version 3.4. Is this another format of an ISBT 128 label?

The ISBT 128 standard has specifications for size and layout of labels. Multiple vendor (and in-house) systems are ISBT 128 compliant and produce acceptable labels that vary in small details but the overall format is the same as specified in the standard. The example presented during the webinar was used to demonstrate specific points in a compliant label. There are many approaches to produce compliant labels.

8. What is expected if our label company does not currently have approximate volume, name, and quantity of anticoagulant on the partial label?

The requirement is for the elements to be affixed. It does not mean that all elements must be on the same affixed label. One option is to create a secondary label with elements not available on the first label.

9. Is it required to have both a partial and a full label at distribution for administration?

If a full label is used, a partial label is not required. If a partial label is used, then a full label must at least accompany the product that is labelled with the partial label.

10. Please clarify what labeling is required during all stages of processing. D7.4.1 states, "At all stages of processing, the CT product shall be labeled with the proper name of the product and the unique numeric or alphanumeric identifier, at a minimum".

As the standard states, those two minimum elements should be on product containers during processing (i.e. in-process labels). At the completion of processing, additional elements are required on labels and are described in Appendix II. Please note that labels at completion of processing (and possibly used during storage) have different requirements from final labels at distribution. Many programs elect to skip the label at completion of processing and store the product using the distribution label.

11. Are Cytokine Release Syndrome (CRS) and neurologic toxicities adverse events specific for Immune Effector Cellular (IEC) therapy? Would staff in an autologous program be expected to have training and knowledge for these?

While CRS and neurologic toxicities are well-known in regard to IEC therapy, they are not solely confined to that therapy. These toxicities have been seen in recipients of haploidentical donor transplants and after some check-point inhibitor therapies. Further, many immune effector products currently available are autologous products. Staff at any program should have training and knowledge of those toxicities as they may relate to the product/procedures that are in use in the program

12. For discharge prior to engraftment (day 1 discharge to another center) does the program have to verify ongoing FACT compliance of those institutions?

The program is expected to have an audit/review process in place to verify ongoing compliance with relevant standards sufficient to meet the needs of the specific recipient or type of recipient. Verification of compliance at each discharge is not necessarily required, but may be needed if different types of patients are discharged at different time points and have different needs. The audit/review process should be included in written agreements with the receiving center. There are requirements concerning communication about each discharged patient. It is not the intent of this standard that the receiving institution be FACT or JACIE-accredited or necessarily meet all clinical standards.

13. What qualification is expected from other facilities that ship patients' products to our program if the patients were collected elsewhere but will be transplanted in our institution? Is FACT/AABB accreditation or state license sufficient for qualifying?

In instances where your routine activity is to use products collected elsewhere, those collection facilities should meet FACT Standards. For situations when you occasionally have to receive products collected elsewhere, review the information in the [FACT-JACIE Accreditation Manual, Seventh Edition](#) for Standard B1.2.

14. The intent of confirmatory HLA typing is to ensure that there was not a sample mix-up in the initial typing. Please clarify whether the confirmatory typing must be at high resolution.

Per information provided in the Accreditation Manual for Standard B6.4.12.3, verification typing does not have to be at the same resolution as the initial typing. For complete information, please review Standard B6.4.12 and accompanying tables, explanations, and examples.

15. For long-term follow-up, are we expected to apply this to past patients or patients transplanted moving forward?

Generally, compliance with a new standard is expected from the date that standard became effective. For this specific instance, the standard requires "...an infrastructure and policies or Standard Operating Procedures in place for provision of appropriate long-term follow-up, treatment, and plans of care." It is up to your facility to determine and describe the effective date of these policies and to what extent patients who have previously been treated will be included. At a minimum, the standard applies to patients transplanted on or after the effective date of the standard and to patients currently under the active care of the transplant team.