FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY
AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER

FREQUENTLY ASKED QUESTIONS: FACT and COVID-19

Updated October 29, 2020

1. **Is FACT going to conduct virtual inspections during the pandemic?**
   FACT plans to begin virtual inspections by the end of 2020. There are details to be finalized, but initial plans have been made and approved by the FACT Board of Directors.

2. **Is my program eligible for a virtual inspection?**
   Programs eligible for a virtual inspection include:
   - Renewal accreditation inspections of clinical, apheresis, or cell processing programs applying independently or together as a hematopoietic cell transplant program, including immune effector cells.
   - Add-on services involving an existing accredited program (such as immune effector cells [IECs] or more than minimal manipulation processing).
   - Reinspections, provided at least one member of the original inspection team participates, and there were no citations related to the physical integrity of the location itself.

   Situations not currently eligible for a virtual inspection, and for which an on-site inspection will be required, include:
   - Initial accreditation inspections.
   - Addition of an entirely new service in a new space, such as a pediatric program at a Children's Hospital being added to an existing adult program in another facility or a separate current Good Manufacturing Practices (cGMP)-compliant processing facility added to an accredited program.

   In general, inspections will be either virtual or on-site, not a mixture. There may be exceptions. For example, an add-on to an existing program that is in the renewal process could have a virtual inspection for the renewal portion and an on-site visit of only the add-on portion (e.g., a cGMP facility for IECs added onto an accredited transplant program).

   FACT is working toward resuming some prioritized on-site inspections where these can be done in compliance with state, local, and CDC guidance and inspector and facility restrictions. This applies primarily to new applicants.

3. **When can my program expect to undergo a virtual inspection?**
   Priority for virtual inspections will be given to cellular therapy programs whose on-site inspections were canceled, then to those who were in the process of scheduling when the on-site inspections were suspended in March 2020. Cord Blood Banks will begin virtual inspections slightly later.

   All programs have been given an additional six-month extension of their accreditation expiration date as we resume inspections in this new way. This represents a permanent change, making this a total extension of twelve months for all programs.

4. **What does my program need to do to prepare for a virtual inspection?**
   Programs will receive direct, individual communications regarding additional documentation that will be required either as an extra annual report or additional pre-inspection updates, depending on where they are in the accreditation cycle.

   Please watch for communication from your FACT Accreditation Coordinator and share this information with appropriate individuals within your program, including apheresis and cell process facility personnel. You may contact your FACT Accreditation Coordinator if there are any questions (http://www.factwebsite.org/About_FACT/FACT_Staff.aspx). If you do not know who your accreditation coordinator is, contact Suzanne Birnley, Manager of Accreditation Services at suzanne.birnley@unmc.edu.

5. **How will virtual inspections be conducted?**
   The platform for FACT's interactive virtual inspections will be a FACT HIPAA-compliant ZOOM Healthcare account. Additional information and a recorded video tour of facilities will be submitted in advance through the FACT Accreditation Portal.

   Cellular therapy inspections will most likely occur over two days to allow both inspectors and program staff additional time to review and prepare additional documentation.

   The Virtual Inspection Task Force is finalizing:
   - The list of the additional documents that will be submitted in advance.
   - A list of documents that the program must be prepared to show to the inspector via ZOOM shared screen, which may include electronic documents such as SOPs, a portion of the EMR, or other scanned documents. Paper records may be shared via scanning, a document camera, or a cell phone camera.
   - A list of items that will be demonstrated via a video tour of each site.
   - A proposed inspection agenda, including additional persons to be interviewed during the inspection, such as a staff nurse, pharmacist, ICU / ER physician or staff.

6. **How will confidentiality be protected during virtual inspections?**
   FACT will conduct the inspections on a HIPAA-compliant Zoom Healthcare Account.
   Additional safeguards in place include:
   - FACT has a Business Associate Agreement in place with each applicant and accredited facility to cover confidentiality issues, including protected health information (PHI) that may be viewed but not retained by FACT or its volunteers. Our FACT Attorney has approved the Business Associate Agreement; however, FACT will work with organizations individually if there are concerns.
   - FACT requires staff and volunteers to sign a confidentiality and conflict of interest agreement annually.
   - Virtual inspection processes will be implemented to protect confidentiality, including, but not limited to:
     - Inspectors will conduct the inspection from a private space.
     - Virtual backgrounds in ZOOM will not be allowed.
     - Inspections will not be recorded.

7. **Since our accreditation timeline has changed, when will our Annual and Renewal Reports be due? How much data is expected for these reports – 12, 18, or 24 months?**
   The due dates for your Program's reports depends upon where you are in the accreditation cycle.

   If you have been awarded accreditation in the last six months, your Annual Report will be due 18 months from the date of the awarded accreditation. In this case, your Annual Report should include 18 months of data, i.e., since your accreditation date.

   If you are currently between the awarded accreditation and your Annual Report and were not awarded accreditation in the last six months, your Annual Report will be due 24 months from the date of the awarded accreditation. In this case, your Annual Report should include 24 months of data, i.e., since your awarded accreditation date.

   If your program has already submitted the Annual Report, your next Report is the Renewal Report which will be due 24 months after your Annual Report. In this case, your Renewal Report should contain 24 months of data, i.e., all data since your Annual Report.

   As inspections resume, whether virtual or on-site, monitor the due dates assigned to your program via the online Accreditation Portal. Your FACT Accreditation Coordinator will update these due dates as appropriate.

   If you have questions at any time regarding the length of time between applications or reports, or if you want to clarify the time frame for data inclusion, please contact your Accreditation Coordinator.

8. **Are we required to wait the entire 18 months to complete these reports or can we submit the information early?**
   FACT staff are currently working remotely and are able to receive and review your reports. FACT encourages you to submit the reports along your new timelines.

   As time permits, FACT Accreditation Coordinators may offer individual Programs the option to submit information ahead of usual due dates. If you want to start on your reports early, contact your FACT Coordinator to open your application in the FACT Accreditation Portal.

9. **So that we can prepare now and keep appropriate records, are there details available about the information to be required on our Annual Report related to COVID-19?**
   An additional report in the portal will be required regarding information related to COVID-19 regardless where you are in your accreditation cycle. This report will be independent of the Compliance Application, Annual Report, or Renewal Report. The template for this report is currently under development. When finalized, your Accreditation Coordinator will create the report and assign your organization a due date. Organizations will be given 30 days to complete this information. Information to be requested will include at a minimum:
   - Was there any relocation of services for inpatient or outpatient care? If yes, submit your risk assessment of the move, including ensuring adequate space and protection from airborne microbial contamination and provision of adequate medications, blood products, and other critical services.

- Did your program make changes in the number of types of transplants performed during the pandemic?
- Were there staff changes or shortages experienced on your transplant service?
- How did your program manage COVID-19 infection in your transplant patients – were patients managed on the transplant unit or transferred to other appropriate quarantine space? Did you provide physician or nurse support or training in the event of patient transfer?
- Were COVID-19 issues incorporated into your quality management meetings?
- Was there a relocation of the apheresis collection service, a need to change apheresis providers, or disruption in service?
- Was your apheresis service involved in the collection of convalescent plasma? Did this affect your ability to collect apheresis products for your transplant patients?
- Was there relocation of the processing facility or disruption in its ability to meet the needs of the clinical program?
- Was there a disruption in your ability to provide marrow collection services? If yes, what alternatives were employed to meet patient needs?
- Are any of the relocations expected to be permanent?
- Describe any telemedicine initiatives in your BMT program.

10. **When will we get an updated Accreditation Certificate listing the new expiration date?**
    FACT will provide a new Accreditation Certificate listing the new, extended accreditation expiration date to each Organization that is not currently in the renewal process. We expect to mail these before the end of 2020.

    For programs in the renewal process, FACT will send new Accreditation Certificates to all accredited organizations at the time of accreditation. If circumstances necessitate further delays, adjustments will be made to timelines. If a certificate is needed sooner, you may request one from your Accreditation Coordinator.

    The official list of FACT-accredited organizations and the services for which each is accredited is available at www.factwebsite.org.

11. **When our inspection is rescheduled, will we have the same inspection team?**
    The choice of the inspection team will be determined by applicant and inspector availability and whether the inspection is virtual or in-person. In-person inspections, when possible to schedule, will continue to have some travel and quarantine limitations that will impact the selection of a team. Some additional training will be required for the virtual inspections. Prior review and preparation by inspectors will be a consideration when relevant.

Updated May 22, 2020

1. **What are the updated recommendations for cryopreservation of bone marrow and peripheral blood grafts for transplantation?**
    NMDP/Be The Match announced in its May 19, 2020 Network News that the requirement to cryopreserve products in response to the COVID-19 pandemic had been adjusted based on results from their research recently posted on line in Biology of Blood and Marrow Transplantation.

Using data from the CIBMTR observational database, Mary Eapen et. al. found that patients transplanted for severe aplastic anemia had a higher rate of graft failure at one year and an inferior overall survival rate at one year when the graft had been cryopreserved than if it had been administered fresh. These findings differ from results of prior studies of patients receiving cryopreserved grafts for hematologic malignancies. These data support the use of non-cryopreserved grafts for patients with severe aplastic anemia whenever possible.

Updated April 21, 2020

1. **HPC products destined for our clinical program are being cryopreserved at the collection center or occasionally by a third-party facility due to COVID-19 travel restrictions and other concerns. Is our program expected to have written agreements in place to be in compliance with standards B4.6.1 and D12.1.1?**
   Presumably, these products are unrelated donor products facilitated by a donor registry. Most likely, any single program will receive only one such product from a specific collection site or cryopreservation facility. This makes it impractical to have an individual written agreement in place with each collection or cryopreservation facility. FACT would consider these services of cryopreservation and shipment to be an extension of the program's written agreement with the Donor Registry.

2. **When our laboratory cryopreserves an unrelated donor product for another transplant center, what records should we include with the shipment?**
   FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration, Seventh Edition, require [D13.5.2] the Processing Facility to provide "a copy of all records relating to the collection, processing, and storage procedures performed related to the safety, purity, or potency of the cellular therapy product". This would include at a minimum, the volume, total nucleated cell count, cell viability, CD34+ and CD3+ cell counts if performed, microbial culture results, testing, processing, and cryopreservation methods, identification and quantification of additives and cryoprotectants, and the freezing curve. The Processing Facility records should also identify any other facility participating in the collection or processing, and the extent of its responsibility [D13.5.3].

   In addition, the Donor Registry will provide registry-specific product analysis forms and potentially, additional data forms related to collection, processing, or storage that should be included with the product shipment. Data required will include identifiers for the donor and recipient, collection date, and product characteristics, including anticoagulants, additives, and the results of all testing performed.

   If the Collection Center or Laboratory providing products to an accredited Clinical Program is not FACT or JACIE accredited, the Clinical Program may have to specifically request processing information, including the data listed above.

Laboratories undertaking cryopreservation for another transplant program should obtain recipient information necessary to perform the optimal pre-cryopreservation processing. Particularly in the case of bone marrow products, documentation of the donor and recipient ABO group is critical to ensure red cell reduction strategies are used prior to cryopreservation in the case of incompatibility.

Updated April 8, 2020 and October 29, 2020

1. **Our BMT Program is accredited for Immune Effector Cells. An Infectious Disease physician in our institution is considering opening a trial to treat patients with COVID-19 using an investigational cellular therapy product. The product is manufactured as an "off the shelf" product by a third-party manufacturer. The patients will not be transplant patients and will not be treated on the transplant unit. Does this trial fall under our HCT accreditation?**
   In this scenario, the accredited program has no responsibility for procurement of the starting material or for manufacturing or administering the product. Among the many models of immune effector cell program structure, this would be considered to be a cellular therapy trial within the same institution, but not a part of the accredited program. The trial does not affect the BMT Program accreditation, even though the program is accredited for immune effector cells.

   However, the FACT Standards for Immune Effector Cells are relevant to this sort of clinical trial. FACT recommends that physicians utilizing cellular therapies outside of the BMT unit consult and follow these Standards to the extent possible. In particular, aspects of quality management such as SOPs, training, appropriate facilities for the population being treated, good documentation practices, management of occurrences and adverse events, data management, and follow - up of clinical outcomes could contribute to the safe administration of these products. Transplant physicians with expertise in immune effector cells and their toxicities could offer valuable consultation.
   - Data management: CIBMTR through its Cellular Immunotherapy Data Resource may be interested in capturing these cellular therapy product infusions.
   - Some patients with severe COVID-19 have been reported to have a cytokine release syndrome, a disorder with which physicians utilizing immune effector cells have familiarity.

2. **Our Apheresis Department is developing workflows and protocols to facilitate virtual visits. Does FACT have any position on telemedicine in Apheresis?**
   Telemedicine is being implemented in many areas of medicine. Due to the COVID-19 pandemic, interest has grown rapidly to minimize the risk of transmission of infectious diseases between patients and medical staff, to reduce the need to travel for care, to preserve supplies of personal protective equipment, and to increase flexibility of the workforce. Telemedicine could also facilitate specialty care to patients who otherwise lack access due to geographic isolation or limited mobility. There are many HIPAA-compliant and suitable platforms and formats available to facilitate these visits. Many institutions have secure platforms for telemedicine embedded into the EMR. Laws, regulations, and institutional policies are variable across state and national boundaries. Although concerns related to reimbursement have been limiting, the Centers for Medicare & Medicaid Services (CMS) has recently expanded telehealth coverage and access by waiving certain requirements during this public health emergency.

   While FACT has no standard that explicitly cites telemedicine, many Standards would apply to the application of these technologies in an accredited apheresis facility. These would include, but not be limited to, the responsibility to abide by applicable laws and regulations (C1.3), maintenance of a comprehensive system of document control (C4.5), policies and standard operating procedures to manage occurrences (errors, accidents, deviations, adverse events, adverse reactions, and complaints) (C4.10), qualification of critical vendors and equipment (C4.13), electronic records (C11.7), policies and standard operating procedures addressing critical aspects of operations and management (C5.1), and staff training (C5.5). Standards related to donor and recipient confidentiality and issues of consent require particular attention when these actions occur in the telemedicine environment.

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1. **We are in the middle of the renewal process. What should we do?**
   To the extent possible, you should continue to submit documents and respond to Requests for Information (RFI) sent to you from your Accreditation Coordinator. FACT Accreditation Coordinators are available by phone or email to assist you. FACT understands that staff shortages and other demands during this COVID-19 pandemic may limit your ability to follow the usual timeline. Extensions of deadlines for response will be granted by your coordinator as needed on a case-by case basis.

2. **What will happen to our accreditation if our allogeneic transplant numbers fall below the minimum requirement in 2020 because our resources were stretched to accommodate COVID-19 issues?**
   Clinical treatment decisions, the availability of medications, donors, cellular therapy products, and clinical trials may each affect the number of stem cell transplant patients during the COVID-19 pandemic. FACT will make every effort to work with your program and make accreditation decisions on a case-by-case basis, in a reasoned and fair manner.

3. **We may need to temporarily relocate our transplant patients due to COVID-19. What will FACT require us to submit related to relocation?**
   FACT is aware that health care facilities may face significant challenges in meeting the needs of all patients during this pandemic. Both inpatient and outpatient settings may be affected. Temporary relocations of cellular therapy patients based on institutional needs related to COVID-19 do not require immediate reporting to FACT. A description of the activities and the facilities utilized will be requested at the time of the Program's Annual Report to FACT.

   FACT expects that any temporary relocation of cellular therapy recipients or shifts in models of delivery of care should be undertaken to the extent possible using your Quality Plan and Clinical Standards as a guide. Considerations include a risk assessment of the alternate location, ensuring the facility is in an appropriate location with adequate space and protection from airborne microbial contamination, and that there is availability of appropriate medications, blood products, trained health care professionals, and additional care as required by these patients.

4. **What are the expectations of FACT related to deviations?**
   To the extent possible, management of deviations should follow usual quality management processes. Planned deviations from standard processes should be approved by the appropriate director or medical director, reviewed by the quality manager, and performed and documented in the usual manner. Unplanned deviations should be documented, investigated, reported, and a corrective action plan developed if appropriate, using the mechanisms described in your Quality Management Plan.

5. **How will FACT be treating care adjustments related to COVID-19?**
   Specific patient care recommendations are outside of the scope of FACT Standards. However, our parent society, the American Society for Transplantation and Cellular Therapy (ASTCT) and its Infectious Disease Special Interest Group have developed interim guidelines for COVID-19 management of HCT and cellular therapy patients. These will be updated as new information becomes available related to epidemiology, clinical outcomes, and efficacy of drug therapies: https://www.astct.org/connect/astct-response-to-covid-19

   EBMT has also published guidelines:
   https://www.ebmt.org/ebmt/news/coronavirus-disease-covid-19-updated-ebmt-recommendations-8th-march-2020

   The American Society of Clinical Oncology (ASCO) has also developed useful clinical guidelines related to caring for cancer patients in the context of the coronavirus pandemic:
   https://www.asco.org/asco-coronavirus-information?cid=DM4750&bid=39975269

   In addition, FACT's global partner The World Marrow Donor Association (WMDA) has provided blood and donor guidelines and resources for cord blood banking:
   - Cord Blood Support Service
   - Information specified per country (on restrictions on import/export)
   - Donor suitability criteria
   - European Centre for Disease Prevention and Control

Numerous other resources are available, including the World Health Organization and the Centers for Disease Control and Prevention.

6. **How should we screen donors for allogeneic transplant?**
The potential risk of transmission of COVID-19 by blood or cellular therapy product infusion is unknown; however, respiratory viruses are not generally known to be transmitted by blood transfusion. Programs considering enhanced screening of potential donors should consult FDA guidance to provide donor education, encourage self-deferral as appropriate, and manage post-donation information about COVID-19. As updated on July 2, 2020, this may include considering whether donor in the 28 days prior to collection cared for, lived with, or had close contact with individuals diagnosed with or suspected of having COVID-19 infection; had been diagnosed with or suspected of having COVID-19 infection; or had a positive diagnostic test for SARS-CoV-2 but never developed symptoms. FDA will update these recommendations as more information becomes available.
    - https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/updated-information-human-cell-tissue-or-cellular-or-tissue-based-product-hctp-establishments

Due to the uncertainty of the situation and the potential for additional travel bans, NMDP/Be The Match continues to recommend cryopreservation of donor products collected by apheresis and some marrow products (those not intended for patients with bone marrow failure syndromes) to allow for delivery of the product to the transplant facility prior to starting a recipient's preparative regimen. When requesting a fresh product infusion, transplant centers must identify a backup donor. NMDP recommends typing several donors at one time.

Neither testing of donor products nor quarantine is currently recommended by NMDP or FDA. The most current information from NMDP, updated on October 22, 2020 at the time of this writing, is available at:
https://network.bethematchclinical.org/news/nmdp/be-the-match-response-to-covid-19/

7. **What can we do if an allogeneic donor is suddenly unavailable for an urgent transplant?**
The National Marrow Donor Program/Be The Match recommends that unrelated donor products, with the exception of marrow products for patients with bone marrow failure syndromes, be cryopreserved and shipped to the Transplant Center prior to initiating the recipient's preparative regimen. Many transplant centers have begun this practice for related donors also. At least two experts have volunteered to assist if a facility is unfamiliar with cryopreservation of allogeneic marrow products. Their contact information is available at:
http://www.aabb.org/advocacy/regulatorygovernment/Documents/Cryopreservation-of-Allogeneic-HPC-Marrow-Products.pdf. Additionally, FACT Consulting is available. FACT-accredited facilities must follow all relevant standards related to change control for a new procedure, process validation, and personnel training.

If an alternative donor is not readily available, some programs are considering the use of cord blood grafts. Cord blood units are readily available for use, do not raise infectious disease questions related to coronavirus, and can be shipped without travel restrictions. NMDP/Be The Match has a Cord Blood Consultative Service for CB unit selection and is offering cord blood units from network banks for practice to programs unfamiliar with thawing and washing procedures.

In addition, a presentation on thawing practices is available from NMDP/Be The Match: Cord Blood Thawing Methods.

8. **Is there any specific guidance for autologous transplant patients, specifically about screening for COVID-19, documentation of screening, sedation, and other issues?**
   For documentation of screening of autologous transplant patients prior to transplant, prior to collection of the hematopoietic cellular therapy product, or prior to a clinic or apheresis visit, FACT recommends this documentation follow routine medical record documentation practices. There may be specific institutional screening policies that should also be followed. Programs that want to implement enhanced screening for COVID-19 prior to collection of autologous HCT/Ps should follow FDA recommendation to include questions whether in the previous 28 days, the patient/donor has:
   - Cared for, lived with, or otherwise had close contact with individuals diagnosed with or suspected of having COVID-19 infection;
   - Been diagnosed with or suspected of having COVID19 infection; or
   - Had a positive diagnostic test for SARS-CoV-2 but never developed symptoms.

   For specific guidance about sedation, medications, consideration for delay of transplant, or other clinical issues, refer to the recently updated ASTCT Interim Guidelines for COVID-19 Management in Hematopoietic Cell Transplant and Cellular Therapy Patients at http://astct.informz.net/z/cjUucD9taT0yMTQzNjc4JnA9MSZ1PTUxNTU4MzAzMCZsaT0xOTc3OTg5Nw/index.html ;!!JkUDQA!bcHjooAv-726AebrD0ocS0THJGL8EfNT4y5OmrBHlOD-H0mqf4e3OjEBrjrsb5n0$.