

Cell Processing and Chain of Identity

Processing Apheresis Cell Product from Collection to Send Off
+
From Cell Return to Infusion

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Director, Cell and Gene Therapy Lab

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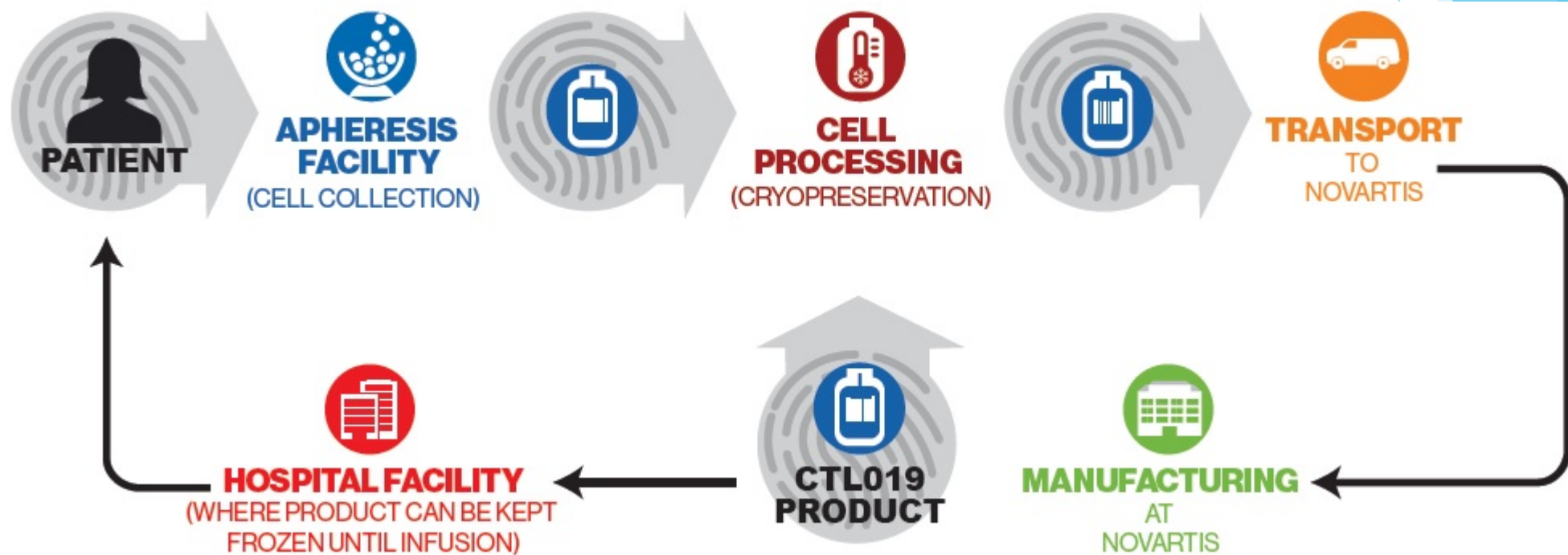
wangy2@email.chop.edu

CHOP Cell and Gene Therapy Lab




- ▶ No pertinent Conflict of Interest to declare
- ▶ A cGMP cell processing facility
- ▶ Performs a variety of **361** and **351** Human Cell and Tissue / Product (HCT/P) processing
Oversimplification: **simpler/safer** and **more complex/riskier** products (PHS Act Sec. 351, 361)
- ▶ Currently 6 FTE, 1 QA, 2 processing clean rooms (need more space !!)



Novartis CTL019 Workflow

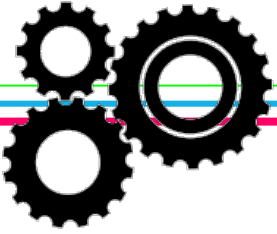


T-Cell Processing

- ▶ Pick up from apheresis 
- ▶ One product, one clean room 
- ▶ Pre-Processing Samples taken for cell count, sterility, Flow Cytometry (CD3, viability), manual diff
- ▶ Product Centrifuged to Remove Platelets and Plasma
- ▶ Product Concentrated/Diluted to Appropriate Concentration for Cryopreservation
5% Human serum albumin, 10% DMSO
- ▶ Divided into Minimum of 2 Bags + QC Vials
- ▶ ISBT labeling 



T-Cell Processing



- ▶ Samples from other institutions

- different processing

- different cryoprotectant

- fresh product, not ISBT

- ▶ Multi-day collections

- Low dose, can't freeze in 2 Bags

- ▶ ISBT label

- Sponsor needs Birthday (not req. ISBT)

Case by case discussion

Case by case discussion

Assign own DIN



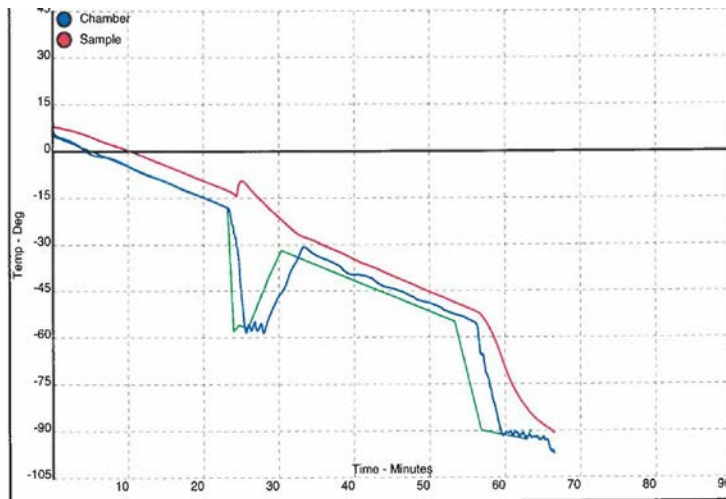
Case by case discussion

Add D.O.B

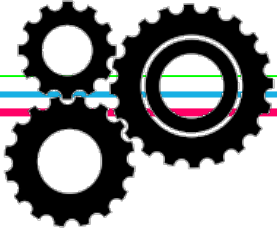


Cryopreservation

- ▶ Product Bags & Vials Placed in Controlled Rate Freezer (one product one freeze)
- ▶ Freeze to -90°C via Software-Based Freezing Program
- ▶ Transfer to Liquid Nitrogen Storage Tanks in vapor phase $<-150^{\circ}\text{C}$
- ▶ ISBT labeling



Cryopreservation



- ▶ Samples from other institutions
 - no expiration
 - different cassette size
 - already cold
 - not ISBT
- ▶ QC vials
 - low cell number (#, conc)

Assign CHOP exp date

Hopefully bag still fits in our/NVS cassette

Label verification under frost




Make CHOP label, tie on (not affixable)



Discussion with sponsor

Pre-Shipping

- ▶ Notified of Enrollment by Coordinator
- ▶ Product Information Provided to Novartis in Cell Chain (Coordinator) 
- ▶ CGTL is Notified Which Bags to Send
- ▶ Cell Pickup Scheduled with World Courier

Patient Details - Contact KYMRIAH Cares if patient identifiers do not exactly match your records

First Name Middle Initial
 Last Name Date of Birth
 Product Request Weight Weight Unit

Apheresis Collection Information (Please call KYMRIAH Cares if incorrect)



Cryopreserved Leukapheresis Pickup Location The Childrens Hospital of Philadelphia Stem Cell Lab
 Leukapheresis Collection Location Children's Hospital of Philadelphia
 Leukapheresis Expiry Date/Time/Time Zone

Notes/Additional Comments

Please Enter The Following Information About The Apheresis

Cryopreservation Date/Time/Time Zone : :
 Leukapheresis Collection Date/Time/Time Zone : :
 Please Describe Cryococktail Used

Please enter Leukapheresis Material Cryobag Information (enter up to 8 bags)

Del/Add	Apheresis ID	Cryobag Number	Cryobag ID	Total Nucleated Cell Count	UoM	Total Volume PerBag(mL)
	<input type="text"/>	1	<input type="text"/>	<input type="text"/> x10 ⁶	TNC	<input type="text"/>
						

Quality Assurance Details

Apheresis Batch



Apheresis Data Form Approval Details

Apheresis Data Form Last Approval Date Apheresis Data Form Last Approved By


By Clicking submit you indicate that you have verified that all information entered and displayed on the Apheresis Data Form is complete and accurate.

Shipping

CHOP → Novartis

- ▶ Courier Arrives with Cryoshipper the Morning of the Scheduled Delivery Date
- ▶ Complete Required Data and Release Forms for BOTH Novartis and CHOP, WayBill Order# match 
- ▶ Pack per Novartis Instructions
- ▶ Serialized zip tie to prevent tampering 
- ▶ Send via World Courier off to Morris Plains

Novartis → CHOP

- ▶ ~4 Weeks (manufacturing, QA testing for release)
- ▶ Unpack Cryoshipper, Return to LN2 Storage
- ▶ Complete Receipt Paperwork for CHOP 

Apheresis Data Form Part B

Both Section I and Section II of the Apheresis Data Form (ADF) Part B **must** be completed by the cell-processing facility prior to shipment of the leukapheresis material to Novartis. Please fill out all fields completely.

When all fields are complete, please sign under each section of the form. If completing the form electronically, please print the form and then sign. **Electronic signatures are not acceptable.** A second individual at your site will then need to independently verify the accuracy of the information and provide verification signatures.

The signed and verified form should be included in the dry vapor shipper for shipment with the leukapheresis material to Novartis. Please retain a copy of the form with your institutional records. If you should have any questions when completing the form, please call your Novartis Account Manager.

Section I: Required Information

This section of the ADF Part B contains information that is required for Novartis to release leukapheresis material for product manufacturing.

Patient Details	
Patient name (First, MI, Last):	
Date of birth (DD/MMM/YYYY):	
Donation Identification Number (DIN)/apheresis ID:	
Apheresis batch number:	

Cryobag Cell Content Information

CD3⁺ cell counts per cryobag are reported below. Total nucleated cell counts are reported on the ADF Part A. When entering cell counts, ensure that the cryobag numbering remains in the same order on each form (eg, cryobag 1 on Part B of the ADF corresponds to cryobag 1 on Part A of the ADF).

Cryobag Number	Cryobag ID	CD3 ⁺ Cell Count per Bag ^a
1		
2		
3		
4		
5		
6		
7		
8		
Total CD3 ⁺ Cell Count (include sum of all bags):		
Minimum Requirement ^b		1.0 x 10 ⁹ CD3 ⁺ Cells

^a Please note that cell counts in the table are reported per bag and are independent of patient weight.
^b Call Novartis Account Manager if minimum cell count requirements are not met.

Dewar Packaging ^a	
Date of Dewar packaging (DD/MMM/YYYY):	
Time of Dewar packaging (HH:MM):	

^a The date and time of Dewar packaging should be recorded as the point at which the cryopreserved leukapheresis material is loaded into the Dewar.

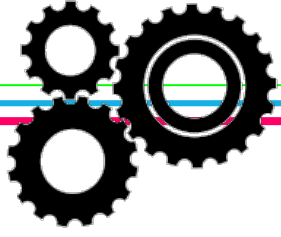
Signatures

By signing below, you indicate that you have verified the patient details and that all information entered in this section of the Apheresis Data Form Part B is complete and accurate.

This section completed by:	Date:
Verified by:	Date:

Please continue to complete Section II.

Shipping



- ▶ Two sets of paper work
 - similar info documented both internally and on sponsor paperwork
 - what about SOP (not just shipping)
- ▶ Multi-day collections
 - combined during manufacturing
- ▶ Watch out for weather





We do both


New SOP, to only show difference from
-- our institutional SOP
-- while referring to sponsor manuals

New DIN upon return (CMO not ISBT)



Thawing / Infusion


- ▶ 37°C Water Bath with secondary bag
- ▶ Transfer to Syringe(s)
- ▶ Deliver to Clinical Team at Bedside
- ▶ Confirm Patient and Product Identifiers
lab staff, MD, RN 
- ▶ Expires *30 minutes* from End of Thaw 

Coordination on infusion day is key
Multiple messages back/forth to ensure 

- pt is ready
- MD is ready
- lab is ready



 W2335 18 000... 

 7500 **B**
Rh POSITIVE

FOR AUTOLOGOUS
USE ONLY
Warning: Not Evaluated for Infectious Substances

Do Not Irradiate
Do Not Use Leukoreduction Filter
Rx Only

Donor:
Donor ID:

Expiration
Date/Time 
0182331221
21AUG2018 12:21 EDT
(21AUG2018 16:21 UTC)

Intended Recipient:
.....
Recipient MR#:
Recipient DOB:

 S2410100
T cells, Apheresis
7.5% DMSO
Other Additives Present
See Accompanying Documentation
Genetically Modified, Thawed, Non-
mobilized, Cultured

Total Volume: 34 mL
Store at 2-26 C

US License#: _____

v 1.0

THANK YOU!

