



Getting the Product to the Patient

Adrian P. Gee
Center for Cell & Gene Therapy



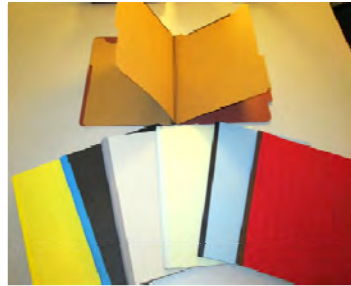
Overview

- Folder Assembly & Review
- Certificates of Analysis
- Labeling
- Fresh versus Cryopreserved Products
- Release procedure
(additional manipulation & testing?)
- Transportation
- Documentation of Administration (additional testing?)
- Procedure Review



Folder Assembly & Review

- A standardized format helps techs, QC and QA
- Helps in location of information
- Essential elements:
 - Standardized component numbering
 - Manufacturing flowchart
 - Detailed worksheets
 - Standardized filing order for information
e.g. old to new



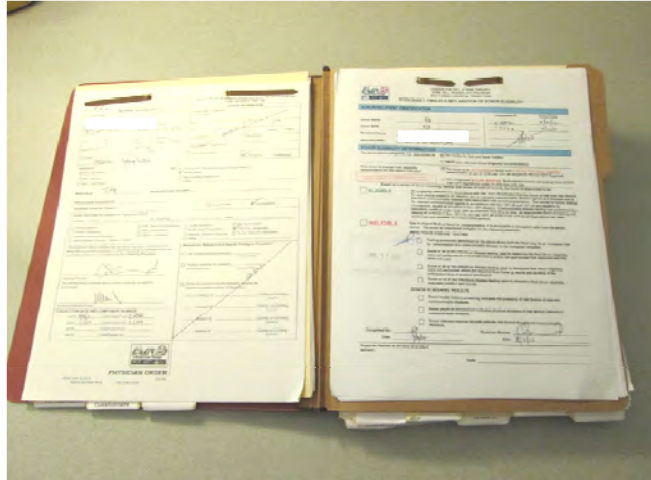
Folder Assembly & Review

Standard review process

- Laboratory manager review
- Folder to QA
- Results requested from QC
- Final review by QA
- Generation of Certificate of Analysis by QA
- C of A sign-off by QA and Lab. Medical Directors
(not IND holder)



Folder Assembly

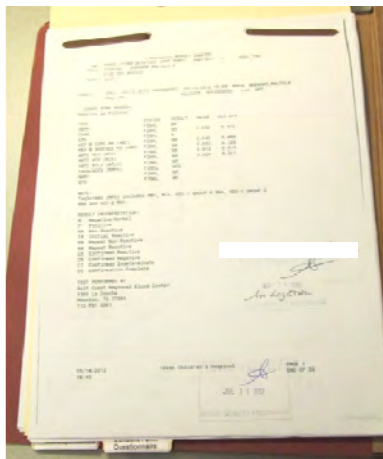


Prescription

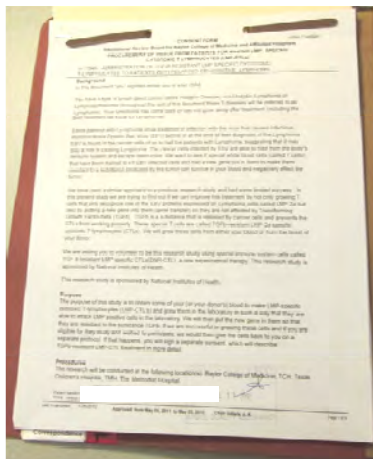
Donor Eligibility



Folder Assembly



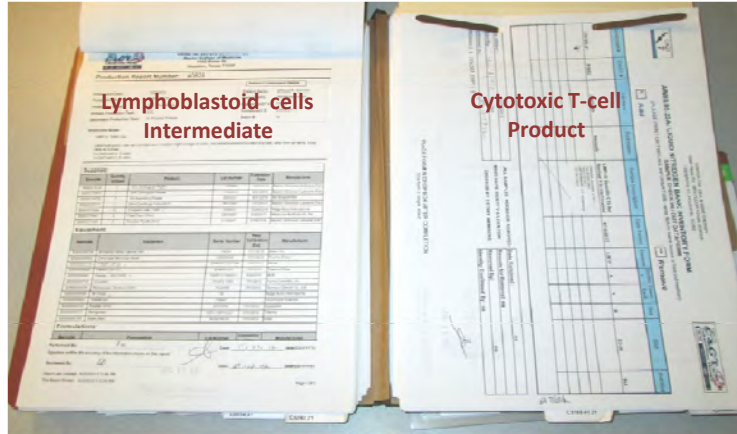
ID Testing & Questionnaire



Consent(s)



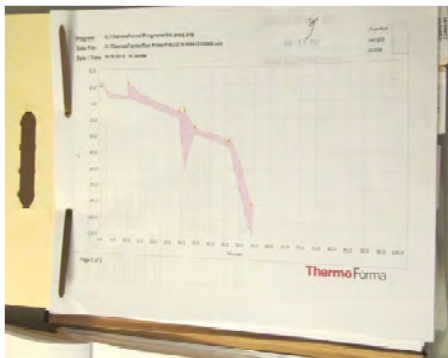
Folder Assembly



Each tab contains information on one intermediate or component



Folder Assembly



Freeze Curve

Test	Assay	Date	Result
Cell Count
Viability
Cytotoxicity

QC Test Results



Release Tests

Guidance for Reviewers

Instructions and Template for Chemistry, Manufacturing, and Control (CMC) Reviewers of Human Somatic Cell Therapy Investigational New Drug Applications (INDs)

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Submit comments and suggestions regarding this draft document by the date provided to the Federal Register notice announcing the availability of the draft guidance. Submit comments to Division of Drug Management (HFA-303), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. You should identify all comments with the draft number listed in the notice of availability that published in the Federal Register.

Additional copies of this draft guidance are available from the Office of Communications, Training, and Manufacturers Assistance (OTMA-09), 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-435-4799 or 301-427-1800, or from the Internet at <http://www.fda.gov/cder/guidances.htm>.

For questions on the content of this draft document contact Dawn Weber, Ph.D., at 301-427-5112.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
August 20

- Discuss specific tests and specifications with FDA at pre-IND meeting
- Some flexibility from official CFR methods
- Some standard expectations
e.g. >70% viability, <5.0EU/ml endotoxin

Test	Method	Specification	Sensitivity	Specificity
Sterility				
Mycoplasma				
Purity (endotoxin)	Endotoxin			
Purity (other contaminants)	Additives, other cells etc.			
Identity	Cell surface markers - phenotype			
Potency	Function – by end of Phase 2			
Others (cell dose,)	Dose			
Others (cell viability)	Viability			



C of A for Fresh versus Frozen

- Specified in CMC
- Fresh products – different release criteria (rapid turnaround assays)
 - Gram stain
 - Endotoxin
 - Phenotype
 - Other test results reported retrospectively with contingency plans
- Performed after any additional manipulation e.g. washing



Certificates of Analysis

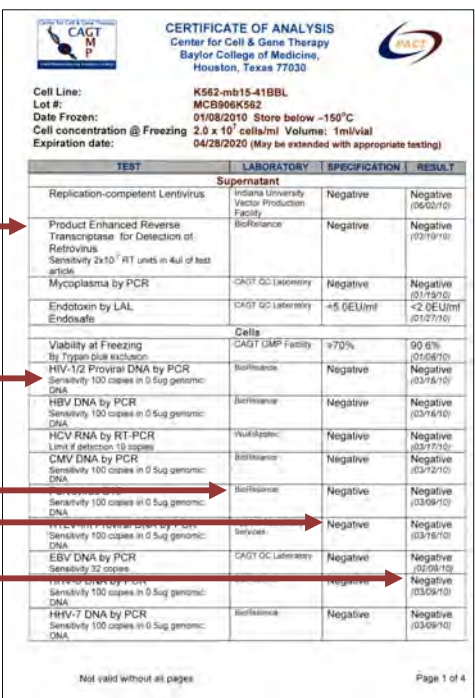
Test →

Sensitivity →

Performed by →

Specification →

Result →



CERTIFICATE OF ANALYSIS
Center for Cell & Gene Therapy
Baylor College of Medicine,
Houston, Texas 77030

Cell Line: K562-mb15-41BBL
Lot #: MCB006K52
Date Frozen: 01/08/2010 Store below -150°C
Cell concentration @ Freezing: 2.0 x 10⁶ cells/ml Volume: 1ml/vial
Expiration date: 04/28/2020 (May be extended with appropriate testing)

TEST	LABORATORY	SPECIFICATION	RESULT
Supernatant			
Replication-competent Lentivirus	Indiana University Vector Production Facility	Negative	Negative (06/02/10)
Product Enhanced Reverse Transcriptase for Detection of Retrovirus Sensitivity 2x10 ⁷ RT units in 4ul of test article	BioReliance	Negative	Negative (02/19/10)
Mycoplasma by PCR	CACT GC Laboratory	Negative	Negative (01/19/10)
Endotoxin by LAL Endosafe	CACT GC Laboratory	<5 OEU/ml	<2 OEU/ml (01/27/10)
Cells			
Viability at Freezing by Trypan blue exclusion	CACT GMP Facility	≥70%	90.6% (01/08/10)
HIV-1/2 Proviral DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/16/10)
HBV DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/16/10)
HCV RNA by RT-PCR Limit of detection 10 copies	WuXiApatec	Negative	Negative (03/17/10)
CMV DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/12/10)
Adenovirus DNA Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/09/10)
HSV-1/2 Proviral DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/16/10)
EBV DNA by PCR Sensitivity 32 copies	CACT GC Laboratory	Negative	Negative (02/09/10)
HHV-8 DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/09/10)
HHV-7 DNA by PCR Sensitivity 100 copies in 0.5ug genomic DNA	BioReliance	Negative	Negative (03/09/10)

Not valid without all pages Page 1 of 4

Labeling

- Copy submitted in CMC
- Include required language
- ISBT 28 terminology OK
- Include partial label if used
- System for label control
- Review before use
- Version control system



Labeling

Product name
ISBT 128-based

Required
language

Label
Version #

Label
Review

TG-T CELLS - CAR CD30 Transduced ATC, Ex-Vivo Expanded, Cryopreserved		
Component # C5290.61.30	Collection Date and Time 9/11/12 8:00 AM	Transfusion ABO Group by ABO Group by Rh Group by Kell Group by HLA Group by Graft Group by Other
Expiry Date and Time 9/11/12 4:00 PM	Rh n/a	Product Contains Viral Units DMBO 10% --S.4. 50% HBSG 40% 0.533 2.665 2.132
Net Vol (mL) 5.23 mL	DO NOT IRRADIATE DO NOT USE LEUKO-REDUCTION FILTER	Recipient Wt (kg) 85A 262
Recipient Name DOE, John	Recipient MRN 11819021221	Recipient CAQTR P3788
VOLUNTEER DONOR This product may harbor infectious agents.		Donor Name DOE, John
AUTOLOGOUS		Donor ABO O Rh D
Approved by: CAST (M) Facility, Baystate College of Medicine		Donor CMR P3788



Medical Consultation Report

- Medical approval
- Recipient details
- Component #
- Component Type
- Vector if Transduced
- Component Volume & Composition
- Visual Inspection on delivery
- Administration details
- Adverse reactions

<p>Fill this form in the patient medical record following infusion of the component. Use one form per infusion. For a copy of the completed form in the indicated number and format the patient copy to the CAST Cell Processing Laboratory. Adverse reactions associated with the infusion must be reported. Lab # volume Number (322) 63-1000 Lab Contact Number (322) 831-4214</p>																			
<p>MEDICAL DIRECTOR'S CONSULTATION REPORT</p> <p>Physician Name: [Signature] Date: 9/11/12</p>																			
<p>PATIENT INFORMATION</p> <p>Recipient Name: DOE, John Recipient MRN: 02144 Medical History: <input type="checkbox"/> DM <input type="checkbox"/> DM2 <input type="checkbox"/> DM3 <input type="checkbox"/> DM4 <input type="checkbox"/> DM5 <input type="checkbox"/> DM6 <input type="checkbox"/> DM7 <input type="checkbox"/> DM8 <input type="checkbox"/> DM9 <input type="checkbox"/> DM10 <input type="checkbox"/> DM11 <input type="checkbox"/> DM12 <input type="checkbox"/> DM13 <input type="checkbox"/> DM14 <input type="checkbox"/> DM15 <input type="checkbox"/> DM16 <input type="checkbox"/> DM17 <input type="checkbox"/> DM18 <input type="checkbox"/> DM19 <input type="checkbox"/> DM20 <input type="checkbox"/> DM21 <input type="checkbox"/> DM22 <input type="checkbox"/> DM23 <input type="checkbox"/> DM24 <input type="checkbox"/> DM25 <input type="checkbox"/> DM26 <input type="checkbox"/> DM27 <input type="checkbox"/> DM28 <input type="checkbox"/> DM29 <input type="checkbox"/> DM30 <input type="checkbox"/> DM31 <input type="checkbox"/> DM32 <input type="checkbox"/> DM33 <input type="checkbox"/> DM34 <input type="checkbox"/> DM35 <input type="checkbox"/> DM36 <input type="checkbox"/> DM37 <input type="checkbox"/> DM38 <input type="checkbox"/> DM39 <input type="checkbox"/> DM40 <input type="checkbox"/> DM41 <input type="checkbox"/> DM42 <input type="checkbox"/> DM43 <input type="checkbox"/> DM44 <input type="checkbox"/> DM45 <input type="checkbox"/> DM46 <input type="checkbox"/> DM47 <input type="checkbox"/> DM48 <input type="checkbox"/> DM49 <input type="checkbox"/> DM50 <input type="checkbox"/> DM51 <input type="checkbox"/> DM52 <input type="checkbox"/> DM53 <input type="checkbox"/> DM54 <input type="checkbox"/> DM55 <input type="checkbox"/> DM56 <input type="checkbox"/> DM57 <input type="checkbox"/> DM58 <input type="checkbox"/> DM59 <input type="checkbox"/> DM60 <input type="checkbox"/> DM61 <input type="checkbox"/> DM62 <input type="checkbox"/> DM63 <input type="checkbox"/> DM64 <input type="checkbox"/> DM65 <input type="checkbox"/> DM66 <input type="checkbox"/> DM67 <input type="checkbox"/> DM68 <input type="checkbox"/> DM69 <input type="checkbox"/> DM70 <input type="checkbox"/> DM71 <input type="checkbox"/> DM72 <input type="checkbox"/> DM73 <input type="checkbox"/> DM74 <input type="checkbox"/> DM75 <input type="checkbox"/> DM76 <input type="checkbox"/> DM77 <input type="checkbox"/> DM78 <input type="checkbox"/> DM79 <input type="checkbox"/> DM80 <input type="checkbox"/> DM81 <input type="checkbox"/> DM82 <input type="checkbox"/> DM83 <input type="checkbox"/> DM84 <input type="checkbox"/> DM85 <input type="checkbox"/> DM86 <input type="checkbox"/> DM87 <input type="checkbox"/> DM88 <input type="checkbox"/> DM89 <input type="checkbox"/> DM90 <input type="checkbox"/> DM91 <input type="checkbox"/> DM92 <input type="checkbox"/> DM93 <input type="checkbox"/> DM94 <input type="checkbox"/> DM95 <input type="checkbox"/> DM96 <input type="checkbox"/> DM97 <input type="checkbox"/> DM98 <input type="checkbox"/> DM99 <input type="checkbox"/> DM100</p> <p>Recipient CAQTR: P3788 Donor MRN: 02144 Recipient ABO: O Rh D Recipient Rh: D Recipient CMR: P3788</p>																			
<p>Component Number(s): C5169.41.21</p>																			
<p>COMPONENT DESCRIPTION</p> <p>Please check all that apply:</p> <table border="0"> <tr> <td><input type="checkbox"/> ABO: A</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> <tr> <td><input type="checkbox"/> ABO: B</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> <tr> <td><input type="checkbox"/> ABO: AB</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> <tr> <td><input type="checkbox"/> ABO: O</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> <tr> <td><input type="checkbox"/> ABO: Other</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> <tr> <td><input type="checkbox"/> ABO: Other</td> <td><input type="checkbox"/> Rh: Rh D</td> </tr> </table> <p>Product Modifications (check all that apply):</p> <table border="0"> <tr> <td><input type="checkbox"/> Irradiated</td> <td><input type="checkbox"/> Filtered</td> </tr> <tr> <td><input type="checkbox"/> Leukoreduced</td> <td><input type="checkbox"/> Cryopreserved</td> </tr> <tr> <td><input type="checkbox"/> Other</td> <td><input type="checkbox"/> Other</td> </tr> </table> <p>Special Instructions/Comments: 30°C TSP 2.11 G/M (BINK)</p>		<input type="checkbox"/> ABO: A	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> ABO: B	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> ABO: AB	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> ABO: O	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> ABO: Other	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> ABO: Other	<input type="checkbox"/> Rh: Rh D	<input type="checkbox"/> Irradiated	<input type="checkbox"/> Filtered	<input type="checkbox"/> Leukoreduced	<input type="checkbox"/> Cryopreserved	<input type="checkbox"/> Other	<input type="checkbox"/> Other
<input type="checkbox"/> ABO: A	<input type="checkbox"/> Rh: Rh D																		
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<input type="checkbox"/> Irradiated	<input type="checkbox"/> Filtered																		
<input type="checkbox"/> Leukoreduced	<input type="checkbox"/> Cryopreserved																		
<input type="checkbox"/> Other	<input type="checkbox"/> Other																		
<p>Volume and Cellular Composition of Component</p> <p>Total Volume: 5.8 mL in 1 container</p> <p>Component Contains:</p> <table border="0"> <tr> <td>DMO 10%: n/a</td> <td>DMO 50%: n/a</td> <td>DMO 40%: n/a</td> <td>DMO 30%: n/a</td> <td>DMO 20%: n/a</td> <td>DMO 10%: n/a</td> </tr> </table> <p>Date completed by: [Signature] Signature (CAST Tech): [Signature] Date verified by: [Signature]</p>		DMO 10%: n/a	DMO 50%: n/a	DMO 40%: n/a	DMO 30%: n/a	DMO 20%: n/a	DMO 10%: n/a												
DMO 10%: n/a	DMO 50%: n/a	DMO 40%: n/a	DMO 30%: n/a	DMO 20%: n/a	DMO 10%: n/a														
<p>VISUAL INSPECTION Delivery Date and Time:</p> <p>Component has been visually inspected for color, clarity, and volume. Patient and component identity have been confirmed and found to agree with the final infusion label. Inspection will be noted on any problems before infusion. Signature here signifies the component's understanding that the laboratory identified in the component has a history system in place for the tracing of the component from the donor to the recipient and that the final disposition of the component is in the donor as required by 21 CFR Part 127.100.</p> <p>Reviewed By: CAST Cell Processing Lab Tech</p>																			
<p>PROCEDURE NOTE</p> <p>Final Disposition: <input type="checkbox"/> Infused <input type="checkbox"/> Discarded <input type="checkbox"/> Other</p> <p>Procedure: <input type="checkbox"/> Standard <input type="checkbox"/> Special <input type="checkbox"/> Other</p> <p>Adverse Reactions: <input type="checkbox"/> None <input type="checkbox"/> Adverse Reactions</p> <p>Adverse reactions associated with the infusion must be reported. Lab # volume Number (322) 63-1000 Lab Contact Number (322) 831-4214</p> <p>Attending Physician Signature: _____ Date: _____</p>																			
<p>COMPONENT INFUSION FORM</p> <p>HISTORY: PHYSICAL, PROGRAM NOTES AND CONSULTATIONS</p> <p>WHITE - MEDICAL RECORD TELLOW - CAST LAB PINK/GEL - PROCESSING</p>																			

WORKSHEET DW03.07.21: PHYSICIAN ORDER FOR CTLX THAW AND INFUSION

Return the signed form with the processing request to CACT. Electronic signatures accepted with the return form by request (availability).

Contract Number for QA Details: Dr. Gale (852) 694-0214

Recipient Name: DOE, John Recipient CMY Number: PTFB
 Recipient BSA (m²): 2.00 Date BSA Calculated: 8/16/2012 Facility: Yonkers DART (SSN):
 Recipient MRN Number: 8021381422 Inpatient TCH Other
 Donor: na Donor MRN: na MASP Number: na

Product Available for Infusion: Transfused ATC

Date Frozen	Component/Bag#	Location	Yp (ml)	CTI (bag or tube)	CTLM ² (bag or tube)	Running Total (CTLM ² / m ²)	Final Product Size (ml)
8/20/2012	C2004.01.30	110319-1	3.0	3.00E+07	1.50E+07	1.50E+07	1.50E+07
8/20/2012	C2004.01.30	110319-2	3.0	3.00E+07	1.50E+07	3.00E+07	3.00E+07
8/20/2012	C2004.01.30	110319-3	3.0	3.00E+07	1.50E+07	4.50E+07	4.50E+07
8/20/2012	C2004.01.30	110319-4	3.0	3.00E+07	1.50E+07	6.00E+07	6.00E+07
8/20/2012	C2004.01.30	110319-5	3.0	3.00E+07	1.50E+07	7.50E+07	7.50E+07
8/20/2012	C2004.01.30	110319-6	3.0	3.00E+07	1.50E+07	9.00E+07	9.00E+07
8/20/2012	C2004.01.30	110319-7	3.0	3.00E+07	1.50E+07	1.05E+08	1.05E+08
8/20/2012	C2004.01.30	110319-8	3.0	3.00E+07	1.50E+07	1.20E+08	1.20E+08
8/20/2012	C2004.01.30	110319-9	3.0	3.00E+07	1.50E+07	1.35E+08	1.35E+08
8/20/2012	C2004.01.30	110319-10	3.0	3.00E+07	1.50E+07	1.50E+08	1.50E+08
8/20/2012	C2004.01.30	110319-11	3.0	3.00E+07	1.50E+07	1.65E+08	1.65E+08
8/20/2012	C2004.01.30	110319-12	3.0	3.00E+07	1.50E+07	1.80E+08	1.80E+08
8/20/2012	C2004.01.30	110319-13	3.0	3.00E+07	1.50E+07	1.95E+08	1.95E+08
8/20/2012	C2004.01.30	110319-14	3.0	3.00E+07	1.50E+07	2.10E+08	2.10E+08
8/20/2012	C2004.01.30	110319-15	3.0	3.00E+07	1.50E+07	2.25E+08	2.25E+08
8/20/2012	C2004.01.30	110319-16	3.0	3.00E+07	1.50E+07	2.40E+08	2.40E+08
8/20/2012	C2004.01.30	110319-17	3.0	3.00E+07	1.50E+07	2.55E+08	2.55E+08
8/20/2012	C2004.01.30	110319-18	3.0	3.00E+07	1.50E+07	2.70E+08	2.70E+08
8/20/2012	C2004.01.30	110319-19	3.0	3.00E+07	1.50E+07	2.85E+08	2.85E+08
8/20/2012	C2004.01.30	110319-20	3.0	3.00E+07	1.50E+07	3.00E+08	3.00E+08
8/20/2012	C2004.01.30	110319-21	3.0	3.00E+07	1.50E+07	3.15E+08	3.15E+08
8/20/2012	C2004.01.30	110319-22	3.0	3.00E+07	1.50E+07	3.30E+08	3.30E+08
8/20/2012	C2004.01.30	110319-23	3.0	3.00E+07	1.50E+07	3.45E+08	3.45E+08
8/20/2012	C2004.01.30	110319-24	3.0	3.00E+07	1.50E+07	3.60E+08	3.60E+08
8/20/2012	C2004.01.30	110319-25	3.0	3.00E+07	1.50E+07	3.75E+08	3.75E+08
8/20/2012	C2004.01.30	110319-26	3.0	3.00E+07	1.50E+07	3.90E+08	3.90E+08
8/20/2012	C2004.01.30	110319-27	3.0	3.00E+07	1.50E+07	4.05E+08	4.05E+08
8/20/2012	C2004.01.30	110319-28	3.0	3.00E+07	1.50E+07	4.20E+08	4.20E+08
8/20/2012	C2004.01.30	110319-29	3.0	3.00E+07	1.50E+07	4.35E+08	4.35E+08
8/20/2012	C2004.01.30	110319-30	3.0	3.00E+07	1.50E+07	4.50E+08	4.50E+08
8/20/2012	C2004.01.30	110319-31	3.0	3.00E+07	1.50E+07	4.65E+08	4.65E+08
8/20/2012	C2004.01.30	110319-32	3.0	3.00E+07	1.50E+07	4.80E+08	4.80E+08
8/20/2012	C2004.01.30	110319-33	3.0	3.00E+07	1.50E+07	4.95E+08	4.95E+08
8/20/2012	C2004.01.30	110319-34	3.0	3.00E+07	1.50E+07	5.10E+08	5.10E+08
8/20/2012	C2004.01.30	110319-35	3.0	3.00E+07	1.50E+07	5.25E+08	5.25E+08
8/20/2012	C2004.01.30	110319-36	3.0	3.00E+07	1.50E+07	5.40E+08	5.40E+08
8/20/2012	C2004.01.30	110319-37	3.0	3.00E+07	1.50E+07	5.55E+08	5.55E+08
8/20/2012	C2004.01.30	110319-38	3.0	3.00E+07	1.50E+07	5.70E+08	5.70E+08
8/20/2012	C2004.01.30	110319-39	3.0	3.00E+07	1.50E+07	5.85E+08	5.85E+08
8/20/2012	C2004.01.30	110319-40	3.0	3.00E+07	1.50E+07	6.00E+08	6.00E+08
8/20/2012	C2004.01.30	110319-41	3.0	3.00E+07	1.50E+07	6.15E+08	6.15E+08
8/20/2012	C2004.01.30	110319-42	3.0	3.00E+07	1.50E+07	6.30E+08	6.30E+08
8/20/2012	C2004.01.30	110319-43	3.0	3.00E+07	1.50E+07	6.45E+08	6.45E+08
8/20/2012	C2004.01.30	110319-44	3.0	3.00E+07	1.50E+07	6.60E+08	6.60E+08
8/20/2012	C2004.01.30	110319-45	3.0	3.00E+07	1.50E+07	6.75E+08	6.75E+08
8/20/2012	C2004.01.30	110319-46	3.0	3.00E+07	1.50E+07	6.90E+08	6.90E+08
8/20/2012	C2004.01.30	110319-47	3.0	3.00E+07	1.50E+07	7.05E+08	7.05E+08
8/20/2012	C2004.01.30	110319-48	3.0	3.00E+07	1.50E+07	7.20E+08	7.20E+08
8/20/2012	C2004.01.30	110319-49	3.0	3.00E+07	1.50E+07	7.35E+08	7.35E+08
8/20/2012	C2004.01.30	110319-50	3.0	3.00E+07	1.50E+07	7.50E+08	7.50E+08
8/20/2012	C2004.01.30	110319-51	3.0	3.00E+07	1.50E+07	7.65E+08	7.65E+08
8/20/2012	C2004.01.30	110319-52	3.0	3.00E+07	1.50E+07	7.80E+08	7.80E+08
8/20/2012	C2004.01.30	110319-53	3.0	3.00E+07	1.50E+07	7.95E+08	7.95E+08
8/20/2012	C2004.01.30	110319-54	3.0	3.00E+07	1.50E+07	8.10E+08	8.10E+08
8/20/2012	C2004.01.30	110319-55	3.0	3.00E+07	1.50E+07	8.25E+08	8.25E+08
8/20/2012	C2004.01.30	110319-56	3.0	3.00E+07	1.50E+07	8.40E+08	8.40E+08
8/20/2012	C2004.01.30	110319-57	3.0	3.00E+07	1.50E+07	8.55E+08	8.55E+08
8/20/2012	C2004.01.30	110319-58	3.0	3.00E+07	1.50E+07	8.70E+08	8.70E+08
8/20/2012	C2004.01.30	110319-59	3.0	3.00E+07	1.50E+07	8.85E+08	8.85E+08
8/20/2012	C2004.01.30	110319-60	3.0	3.00E+07	1.50E+07	9.00E+08	9.00E+08
8/20/2012	C2004.01.30	110319-61	3.0	3.00E+07	1.50E+07	9.15E+08	9.15E+08
8/20/2012	C2004.01.30	110319-62	3.0	3.00E+07	1.50E+07	9.30E+08	9.30E+08
8/20/2012	C2004.01.30	110319-63	3.0	3.00E+07	1.50E+07	9.45E+08	9.45E+08
8/20/2012	C2004.01.30	110319-64	3.0	3.00E+07	1.50E+07	9.60E+08	9.60E+08
8/20/2012	C2004.01.30	110319-65	3.0	3.00E+07	1.50E+07	9.75E+08	9.75E+08
8/20/2012	C2004.01.30	110319-66	3.0	3.00E+07	1.50E+07	9.90E+08	9.90E+08
8/20/2012	C2004.01.30	110319-67	3.0	3.00E+07	1.50E+07	1.00E+09	1.00E+09
8/20/2012	C2004.01.30	110319-68	3.0	3.00E+07	1.50E+07	1.01E+09	1.01E+09
8/20/2012	C2004.01.30	110319-69	3.0	3.00E+07	1.50E+07	1.02E+09	1.02E+09
8/20/2012	C2004.01.30	110319-70	3.0	3.00E+07	1.50E+07	1.03E+09	1.03E+09
8/20/2012	C2004.01.30	110319-71	3.0	3.00E+07	1.50E+07	1.04E+09	1.04E+09
8/20/2012	C2004.01.30	110319-72	3.0	3.00E+07	1.50E+07	1.05E+09	1.05E+09
8/20/2012	C2004.01.30	110319-73	3.0	3.00E+07	1.50E+07	1.06E+09	1.06E+09
8/20/2012	C2004.01.30	110319-74	3.0	3.00E+07	1.50E+07	1.07E+09	1.07E+09
8/20/2012	C2004.01.30	110319-75	3.0	3.00E+07	1.50E+07	1.08E+09	1.08E+09
8/20/2012	C2004.01.30	110319-76	3.0	3.00E+07	1.50E+07	1.09E+09	1.09E+09
8/20/2012	C2004.01.30	110319-77	3.0	3.00E+07	1.50E+07	1.10E+09	1.10E+09
8/20/2012	C2004.01.30	110319-78	3.0	3.00E+07	1.50E+07	1.11E+09	1.11E+09
8/20/2012	C2004.01.30	110319-79	3.0	3.00E+07	1.50E+07	1.12E+09	1.12E+09
8/20/2012	C2004.01.30	110319-80	3.0	3.00E+07	1.50E+07	1.13E+09	1.13E+09
8/20/2012	C2004.01.30	110319-81	3.0	3.00E+07	1.50E+07	1.14E+09	1.14E+09
8/20/2012	C2004.01.30	110319-82	3.0	3.00E+07	1.50E+07	1.15E+09	1.15E+09
8/20/2012	C2004.01.30	110319-83	3.0	3.00E+07	1.50E+07	1.16E+09	1.16E+09
8/20/2012	C2004.01.30	110319-84	3.0	3.00E+07	1.50E+07	1.17E+09	1.17E+09
8/20/2012	C2004.01.30	110319-85	3.0	3.00E+07	1.50E+07	1.18E+09	1.18E+09
8/20/2012	C2004.01.30	110319-86	3.0	3.00E+07	1.50E+07	1.19E+09	1.19E+09
8/20/2012	C2004.01.30	110319-87	3.0	3.00E+07	1.50E+07	1.20E+09	1.20E+09
8/20/2012	C2004.01.30	110319-88	3.0	3.00E+07	1.50E+07	1.21E+09	1.21E+09
8/20/2012	C2004.01.30	110319-89	3.0	3.00E+07	1.50E+07	1.22E+09	1.22E+09
8/20/2012	C2004.01.30	110319-90	3.0	3.00E+07	1.50E+07	1.23E+09	1.23E+09
8/20/2012	C2004.01.30	110319-91	3.0	3.00E+07	1.50E+07	1.24E+09	1.24E+09
8/20/2012	C2004.01.30	110319-92	3.0	3.00E+07	1.50E+07	1.25E+09	1.25E+09
8/20/2012	C2004.01.30	110319-93	3.0	3.00E+07	1.50E+07	1.26E+09	1.26E+09
8/20/2012	C2004.01.30	110319-94	3.0	3.00E+07	1.50E+07	1.27E+09	1.27E+09
8/20/2012	C2004.01.30	110319-95	3.0	3.00E+07	1.50E+07	1.28E+09	1.28E+09
8/20/2012	C2004.01.30	110319-96	3.0	3.00E+07	1.50E+07	1.29E+09	1.29E+09
8/20/2012	C2004.01.30	110319-97	3.0	3.00E+07	1.50E+07	1.30E+09	1.30E+09
8/20/2012	C2004.01.30	110319-98	3.0	3.00E+07	1.50E+07	1.31E+09	1.31E+09
8/20/2012	C2004.01.30	110319-99	3.0	3.00E+07	1.50E+07	1.32E+09	1.32E+09
8/20/2012	C2004.01.30	110319-100	3.0	3.00E+07	1.50E+07	1.33E+09	1.33E+09
8/20/2012	C2004.01.30	110319-101	3.0	3.00E+07	1.50E+07	1.34E+09	1.34E+09
8/20/2012	C2004.01.30	110319-102	3.0	3.00E+07	1.50E+07	1.35E+09	1.35E+09
8/20/2012	C2004.01.30	110319-103	3.0	3.00E+07	1.50E+07	1.36E+09	1.36E+09
8/20/2012	C2004.01.30	110319-104	3.0	3.00E+07	1.50E+07	1.37E+09	1.37E+09
8/20/2012	C2004.01.30	110319-105	3.0	3.00E+07	1.50E+07	1.38E+09	1.38E+09
8/20/2012	C2004.01.30	110319-106	3.0	3.00E+07	1.50E+07	1.39E+09	1.39E+09
8/20/2012	C2004.01.30	110319-107	3.0	3.00E+07	1.50E+07	1.40E+09	1.40E+09
8/20/2012	C2004.01.30	110319-108	3.0	3.00E+07	1.50E+07	1.41E+09	1.41E+09
8/20/2012	C2004.01.30	110319-109	3.0	3.00E+07	1.50E+07	1.42E+09	1.42E+09
8/20/2012	C2004.01.30	110319-110	3.0	3.00E+07	1.		

Thaw Preparation Checklist



 CENTER FOR CELL & GENE THERAPY
 UPMC FACILITY, 18TH FLOOR PERI CENTER
 1100 EAST KENNEDY AVENUE, HOUSTON, TEXAS 77030

WORKSHEET: CW03.11.21 THAW PREPARATION CHECKLIST

Patient Name: C5244 H/T ; C5306 -9-D

Component(s): C5244 H/T ; C5306 -9-D

Hospital Involved: TCH TMI Type of Container: Cryobags Cryovials

GENERAL PREPARATION

Date & Time of Thaw Scheduled: 01/10/12 10:00 AM KIME

Component Infusion Form - prepared

Liquid Nitrogen Blank - Sample Check In/Out (Delatium) - completed

Microbiology Test Order forms - completed & processed

These vials - inspected & information verified

Documentation Report Form (if necessary)

Professional Rating Form - completed and signed (if applicable)

THAW CART PREPARATION

Water bath covered

Microbiology Sample Inflow attached

Thaw Medium Subst returned (if applicable)

Syringes with saline - on cart

Cooler filled with LN2

Bags for Infusion placed in cooler

5 x 1 Liter of Saline - filled and on cart

Personal O₂ Monitor

Check / Restock Supplies

Cryobags

LN2 Cooler

Gloves

Needles - 18-gauge

Syringes - 50cc, 30cc, 10cc, 5cc

Alcohol swabs

Biohazard bags

Plastic bags

Cryovial rack

Fresh tube rack

Sampling site tags

Female Lined containers

Red tape

Cryovial Box (if cryovials) A&A

POST INFUSION DOCUMENTATION / PROCESS

Component Infusion Form - completed & signed

Saline discarded / Water bath Cleaned & Dried

Documented use of water bath on water bath log

Waste materials discarded into appropriate waste containers

Liquid Nitrogen Blank - Sample Check In/Out (Delatium) - infusion label(s) attached

Activity Production report generated

Thaw cart organized and placed outside room C1950 09

Documented use of Personal O₂ Monitor on log Charge Form generated & given to Flow Tech (Initials & Date) LL 01/10/12

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Frozen Products

- Allows completion of traditional release testing
- Stability during storage
- Thawing technique \pm wash
- Testing on thawed products
- Stability after thawing
- Thaw & transport or vice versa?



Product Stability

- Information on product stability if administration is delayed
- Data on viability & functionality under defined conditions
- Return to storage
 - Allowed?
 - Under what conditions?
 - Additional testing required?

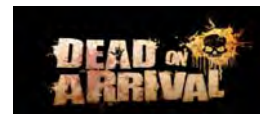
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Transportation & Shipping

- Transportation – within facility
- Shipping – to another facility
 - Easiest method – frozen in dry shipper
 - Viability on arrival – usually good
 - Depends on method of measurement
 - Functionality on arrival – sometimes poor
 - Need optimization studies for non-hematopoietic transplant products



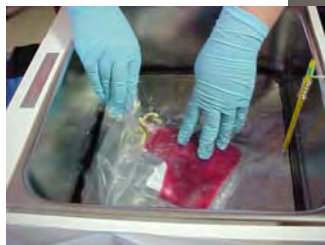
Transportation Frozen

- LN₂ transport container?
- Oxygen monitors
- Route to be used?
- Risk to others?



Transportation & Thawing

- Thaw & transport?
 - Product stability
- Transport & thaw?
- Waterbath vs. mechanical heater



Testing at Administration?

- Not usually specified by FDA
- May be used to develop stability profile
- Time delay between bedside & testing laboratory
 - Viability: Dye exclusion versus 7-AAD
 - Functionality
 - Sterility
 - Phenotype?



Adverse Reactions

- Captured on Medical Consultation Report that travels with the product.
- Triggers a Cell Processing Incident Report
- Investigated by GMP and Clinical QA
- Reported at Quality Meetings



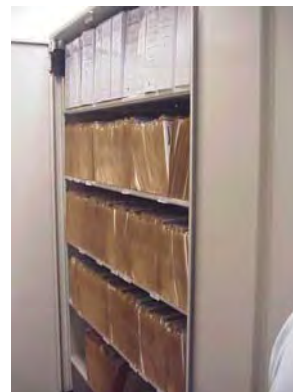
Positive Sterilities after Infusion

- Negative Gram stain
- Later receive positive Bactec sterility
- Possibility should be addressed in CMC Section 4 – SOP available
- Actions:
 - Immediately inform recipient's physician
 - Request organism ID and sensitivities
 - Resubmit reference vial
 - Convey ID and sensitivities to physician asap
 - Initiate Incident Report
 - Investigate possible causes
 - Include in IND report if product related



Post-Administration Review by QA

- Completed administration forms
- Completed donor eligibility form
- Inventory removal form
- Reagents/materials used for administration
- Copies of labels used for samples & sample submission forms
- Any Incident Reports or Variances
- Updated product inventory form
- Re-file folder



Summary

We recommend a standardized system for

- Documentation (flexible enough for all protocols)
- Manufacturing records
- Record review
- Release testing in CMC

Develop stability testing program (frozen and thawed)

Understanding of cryopreservation effects (viability versus function)

Better functionality/potency testing

