CBMTG Laboratory Committee-Laboratory Guidance

Protocol for Validation of Cryopreservation Bags

Purpose:
To confirm, by examination and objective evidence, that a selected cryopreservation bag is compatible with institutional policies and standard operating procedures and functions adequately so as not to impact final product integrity.

Scope:
This protocol applies to the specific cryopreservation bags and institutional standard operating procedures identified in Table 1 below. Subsequent changes to the bag or revisions to standard procedures that significantly impact bag performance would require further validation.

References:

- FACT – JACIE International Standards Accreditation Manual, Fourth Edition, Version 4.2, 01/29/10
- Safety of Human Cells, Tissues and Organs for Transplantation Regulations, S... 2004, c. 23, s. 2, section 68
- CSA Standard Z 900.1-03, Cells, Tissues and Organs for Transplantation and Assisted Reproduction: General Requirements, 15.6.6
- Validation of Cryobags, Jo Lynn Proctor and Donna Regan, Telegraft Volume 13. No2, Summer 2006
- Validation of Cryopreservation Bags, Herb Cullis, SOP for ISCT

Table 1

	Processing	Infusion
Institution		
Standard Operating Procedures Title, version, effective date		
Bag Manufacturer		
Bag Manufacturer Part #		

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Compatibility Assessment

1. Carefully review the manufacturer's product insert/instructions for use, certificate of analysis and observe a bag.
2. Determine if the bag is compatible with current laboratory and infusion site policies, standard procedures and ancillary supplies (i.e. transfer sets, syringes, freezing cassettes, infusion sets etc.). Place a check mark in the appropriate column of Table 2 below. Record comments to explain incompatibilities.
3. Bags that are not compatible or adaptable will not proceed to the next section.
4. Deviations from Manufacturer's instructions are to be described at the end of Table 3.

Table 2

	Compatible	Incompatible	Comments
Intended Use			
Precautions, warnings or limitations			
Bag Configuration elements, (as required by the institution) such as: • Legible lot # and expiry on bag • Dimensions (cassette fit) • # of transfer lines • Transfer line connector type(s) • Transfer line clamps • Sampling/injection port • Label pocket dimension/location • Adequate space to adhere labels • Over wrap • Sterile packaging • Protected port access • Spiking guards			

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Functional Assessment

1. Data critical to this assessment is to be documented in Table 3 below. Review table prior to commencing validation.
2. Perform labelling, freezing, storage, thaw and infusion employing key applicable steps of the processing and/or infusion facility standard operating procedures recorded in Table 1 above. For example, use standard labels, freezing solution (at final product concentration), transfer methods, cassettes, freezing protocol, storage temperatures, thawing and spiking methods. The protocol must be executed by staff trained in the standard operating procedures.
3. 6 bags are to be tested, 3 with the manufacture's minimum fill minus 10 ml and 3 with the manufacturer's maximum fill volume plus 10 ml.
4. Calibration and maintenance of any equipment used in the execution of this protocol must be current.
5. All reagents and supplies used in the execution of this protocol must be in date.
6. Using the standard processing procedure, label bags: Min 1, Min 2, Min 3, Max 1, Max 2 and Max 3
7. Using the standard processing procedure, prepare a volume of freezing solution sufficient to accommodate the fill volumes described in #3 above.
8. Add red food colorant to the freezing solution to create a deep red color (unless the solution already has sufficient color). This will assist in identifying leaks.
9. Aliquot freezing solution into freezing bags using the standard processing procedure. NOTE: If leaks occur during transfer which are due to incompatibility between standard transfer equipment and bags, revise Table 2.
10. Freeze and store bags using the standard processing procedure.
11. Maintain bags in storage for a minimum, 24 hours.
12. Remove bags from storage, transport (can be simulated) and thaw using the standard processing/infusion procedures. Observe for the following:
    - Leaks
    - Loss of protective port covers
    - Legibility of pocket label
    - Integrity of over wrap.
13. Repeat steps 10 thru 12 twice for a total of 3 freeze/thaw cycles.
14. After the last thaw cycle, spike each bag using the standard infusion procedure and drain contents into a suitable receptacle for discard. Observe for the following:
    - bag damage
    - leaks
    - flow restriction at port.
15. Deviations from Manufacturer's Instructions are to be noted.
16. Complete Table 3.
17. Forward completed protocol for review and approval.

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Table 3

Bag Lot #		Bag Expiry Date	

Reagents and Supplies		
Description	Lot #	Expiry Date

Recorded by/date		Verified by/date	

Equipment		
Description	ID #	Next Calibration date or Current Calibration Expiry date

Recorded by/date		Verified by/date	

Key Procedures Summary	
Provide a brief description of the following:	
Freezing Solution Including concentrations of active ingredients	
Freezing Protocol (i.e. controlled rate, uncontrolled at -80, uncontrolled in LN2 vapour etc.) Attach freezing curves or freezer charts if available	
Storage conditions and allowable temperature range (i.e. liquid, vapour or mechanical and temperature range). Attach temperature charts for duration of validation storage if available	
Transport Conditions (i.e. dry shipper, dry ice, thawed with ice pack)	

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Freeze/Store/Thaw Test								
Cycle 1	Frozen by/date		Stored by/date		Thaw Temp°C		Thawed by/date	
	*Pass	Fail	Comments Provide details of failure. For leaks indicate location.					
Min 1								
Min 2								
Min 3								
Max 1								
Max 2								
Max 3								
*Pass = No leaks, Port protectors intact, Over wrap intact, labelling intact and legible								
Recorded by				Date				

Freeze/Store/Thaw Test								
Cycle 2	Frozen by/date		Stored by/date		Thaw Temp°C		Thawed by/date	
	*Pass	Fail	Comments Provide details of failure. For leaks indicate location.					
Min 1								
Min 2								
Min 3								
Max 1								
Max 2								
Max 3								
*Pass = No leaks, Port protectors intact, Over wrap intact, labelling intact and legible								
Recorded by				Date				

Freeze/Store/Thaw Test								
Cycle 3	Frozen by/date		Stored by/date		Thaw Temp°C		Thawed by/date	
	*Pass	Fail	Comments Provide details of failure. For leaks indicate location.					
Min 1								
Min 2								
Min 3								
Max 1								
Max 2								
Max 3								
*Pass = No leaks, Port protectors intact, Over wrap intact, labelling intact and legible								
Recorded by				Date				

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Infusion Test				
Performed by			Date	
	*Pass	Fail	Comments Provide details of failure.	
Min 1				
Min 2				
Min 3				
Max 1				
Max 2				
Max 3				
*Pass = No damage to bag from spiking, No leaks at port, Unobstructed flow of solution				
Recorded by			Date	

Deviations from Manufacturer's Instructions for Use

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Additional Comments

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Conclusion

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Reviewed and Completed by:_____
Sign and Date

Accepted by:

Lab Director/Designate _____
Sign and Date

Medical Director/Designate_____
Sign and Date

Quality Assurance_____
Sign and Date