Sample Procedure: VALIDATION OF CRYOPRESERVATION BAGS

STANDARD OPERATING PROCEDURE # XXX	Revision: A
Director of Quality Assurance:	Date:
Director of Cryopreservation:	Date:
Effective date:	
Next Review date:	

1.0 PURPOSE: This is a sample Standard Operating Procedure for validating cryopreservation bags and the process used for freezing, while frozen and during thawing. This procedure focuses on bag integrity and leakage assessment.

2.0 SCOPE: This Procedure includes selecting bags for validation, the validation process and the validation report. This procedure is used to determine whether the bag can survive extreme conditions of processing. This will validate the bag, ports, overwrap, label, and all "in process devices, procedures and components". Validation must challenge the limits of the procedure while using the same equipment, processes, and personnel that are used for routine processes. This procedure challenges the bag by subjecting it to the lowest temperature that might be achieved in a laboratory setting. And the procedure challenges the integrity of the bag by both over filling and under filling. This procedure challenges the durability of the bag by extreme temperature shock. This procedure challenges the entire process by subjecting the bags to ten sequential freeze thaw cycles. This procedure includes a form to document validation.

3.0 RESPONSIBILITY: Validation of cryopreservation bags is the responsibility of the Quality Assurance director who reports to the CEO of this institution. The Quality Assurance director must approve and sign this procedure. In the event that there is no Quality Assurance Director, a representative of management who reports to the chief executive officer or the chief executive officer may sign. The Cryopreservation Department Director also must approve and sign this procedure. It is the responsibility of the cryopreservation technical staff of this institution to carry out this procedure.

4.0 REFERENCES

4.1 This institution's SOPs related to freezing of products.

4.2 Cardwell, L and Sugrue MW (2009) Quality and Process Control. In Areman, EM and Loper K (Eds), Cellular Therapy: Principles, Methods, and Regulations (71-93)

5.0 MATERIALS AND EQUIPMENT:

5.1. Bags
5.2 Overwraps
5.3. Cryopreservation media
5.4. Red food dye
5.5. Sealer
5.6. Controlled Rate Freezer
5.7. Freezer
5.8. Thawing Water Bath, 40 degrees Celsius.

6.0 HEALTH AND SAFETY CONSIDERATIONS

6.1. Standard safety and personnel precautions should be followed

7.0. DOCUMENTATION REQUIREMENTS

(Insert your own facility-specific requirements here)

8.0. DEFINITIONS

8.0. "SOP" shall mean "Standard Operating Procedure".

8.1. "Procedure" and "Process" mean the same thing and are interchangeable.

8.2. “Critical equipment” shall mean any equipment that meets the following criteria: (a). Equipment that would make a defective product if it were not use properly. (b). Equipment that has adjustments or settings that control its operation. (c). Equipment that would create a defect that would not be detected by visual observation or subsequent procedures.
8.3. “Cryopreservation” shall mean freezing to some temperature below the solidification of the product.
8.4. “Filling” shall mean adding fluid to the bag to a volume indicated by this institution’s SOPs. If not otherwise specified filling will be to a thickness of 1.0 centimeters.
8.5. Temperature and volume measurements shall be made in International Metric units.
8.6. “Water Bath” shall mean a container of water in which the water is maintained at 40 degrees Celsius.
8.7. “Product” shall mean the bag, its contents, and any necessary accessories.
8.8. “Overwrap” shall mean a bag or other covering that is placed over the product to wrap the product bag, contain any leaks, and protect the product from contamination.
8.9. “This institution” shall mean the organization manufacturing the product and doing the validation.
8.10. “Cryopreservation media” shall mean the fluids that normally would be used to fill the bag, not necessarily including any biologics.

9.0. PROCESS – GENERAL

Records for Critical Equipment are examined to ensure that the equipment is installed in a quality manner (IQ). Records for critical equipment are examined to ensure that it operates in a quality manner (OQ). Records for critical equipment are examined to see that proper maintenance has been done. Each of these records: IQ, OQ, and maintenance are recorded. Obtain and reference any instructions from the bag manufacturer regarding use of the bag.

Nine bags are filled using this institution’s cryopreservation media following the SOPs of this institution. The fill solution is supplemented with red food dye to permit easy visualization of any leak. The bags are frozen in a controlled rate freezer following this institution’s SOPs. The bags are transferred into liquid nitrogen overnight or longer as noted in the validation report. The bags are removed from liquid nitrogen and placed directly into a 40 degree water bath. The bags are observed for leaks into the water bath (as evidenced by escape of red dye), readability of labels, and condition of ports and overwrap. Then the freeze thaw cycle is repeated nine more times with the same bags. The observations are recorded on the attached form.

10.0. PROCESS – DETAILS (INSERT YOUR OWN FACILITY’S DETAILS HERE)

10.1. Obtain and review the IQ, OQ, and maintenance records for all equipment.
10.2. Select nine bags to be tested: These are taken from the top, middle, and bottom of the next 3 cases of product bags that would normally be used if applicable.
10.3. Record the manufacturer and lot numbers of the bags.
10.4. Mark the bags with sequential numbers using the institution’s method.
10.5. Add red food dye to the cryopreservation media to develop a deep red color.
10.6. Fill bags 1, 4, and 7 with the volume of fluid generally used.
10.7. Fill bags 2, 5, and 8 with twice the volume of fluid generally used.
10.8. Fill bags 3, 6, and 9 with half the volume of fluid generally used.
10.9. Freeze the bags in the controlled rate freezer to -80 degrees Celsius according to facility SOP.
10.10. Transfer the bags to the liquid phase of a liquid nitrogen freezer.
10.11. Store overnight or longer.
10.12. Remove bags from the freezer and place directly into 40 degree Celsius water bath.
10.13. Observe for leakage of fluid. Report any leakage as “leak”.
10.14. Observe for loss of protective cover over port. Report cover loss as “cover lost”
10.15. Observe for ability to read bag identity information. Report inability to read as: “illegible label”.
10.16. Observe for breaks in the overwrap. Report as “overwrap failure”.
10.17. Sign and date each entry.
10.18. Remove any bags that leak or otherwise fail from the validation cycle.
10.19. Repeat the freeze and thaw process for 10 cycles.
10.20. Submit to the Quality Assurance Director or person responsible according to Quality Plan for review.
10.21. Any failure invalidates the process.

11.0. OTHER PERTINENT INFORMATION

11.1. In this section, include any information that relates to the validation process such as references that are not directly used. For example: literature on cryopreservation.

11.2. In this section, include previous or other pertinent validation studies or notes.

12.0. TRAINING REQUIREMENTS

12.1 Technicians responsible for validation work should read and be familiar with SOP's.

13.0 RECORDS:

Freezer IQ record number: _____
Freezer OQ record number: _____
Freezer Maintenance record number: _____
Controlled rate freezer IQ: _____
Controlled rate freezer OQ: _____
Controlled rate freezer Maintenance record number: _____
Water Bath IQ record number: _____
Water Bath OQ record number: _____
Water Bath Maintenance record number: _____
Bag Manufacturer: _____
Bag Lot Numbers: _____
Training record of person doing Validation procedure: _____

This is the data taken of 10 freeze/thaw cycles:

Cycle	results	Date	Signed
1.	_____	_____	_____
2.	_____	_____	_____
3.	_____	_____	_____
4.	_____	_____	_____
5.	_____	_____	_____
6.	_____	_____	_____
7.	_____	_____	_____
8.	_____	_____	_____
9.	_____	_____	_____
10.	_____	_____	_____

Review by Quality Assurance, Signed: _____ date: _____

Conclusion: _____

End of SOP # XXX rev A

Acknowledgement: This sample has been modified from one provided by Herb Cullis.