



Standard Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures¹

This standard is issued under the fixed designation E1565; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

INTRODUCTION

The stability of biological material stored at low temperatures is dependent on proper handling procedures and the development of adequate safeguards. Because of the sensitivity of many biological materials, care must be taken that critical temperatures are not compromised during retrieval and other activities involving handling of the material. Safeguards must also be established to ensure both adequate temperatures at all times during storage and that inventory control provides a mechanism for ease of retrieval.

1. Scope

1.1 This guide covers recommended procedures for handling material stored at low temperatures in mechanical freezers and liquid nitrogen freezers.

1.2 This guide covers recommendations for implementing procedures for ensuring adequate inventory control.

1.3 This guide covers recommendations for implementing procedures for safeguarding material stored at low temperatures.

1.4 This guide does not cover the development or maintenance of equipment and facilities for low-temperature storage which are covered in Guide [E1564](#).

1.5 This guide does not cover practices for preservation by freezing which are covered in Practice [E1342](#).

1.6 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.7 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

¹ This guide is under the jurisdiction of ASTM Committee [E55](#) on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee [E55.04](#) on General Biopharmaceutical Standards.

Current edition approved Dec. 1, 2014. Published January 2015. Originally approved in 1993. Last previous edition approved in 2006 as E1565 – 00 (2006). DOI: 10.1520/E1565-00R14.

2. Referenced Documents

2.1 *ASTM Standards*:²

[E1342 Practice for Preservation by Freezing, Freeze-Drying, and Low Temperature Maintenance of Bacteria, Fungi, Protista, Viruses, Genetic Elements, and Animal and Plant Tissues \(Withdrawn 2011\)](#)³

[E1564 Guide for Design and Maintenance of Low-Temperature Storage Facilities for Maintaining Cryopreserved Biological Materials](#)

[E1566 Guide for Handling Hazardous Biological Materials in Liquid Nitrogen](#)

3. Terminology

3.1 *Definitions*:

3.1.1 *cryogenic temperatures*—temperatures below or equal to -100°C .

3.1.2 *liquid nitrogen freezers*—freezers that operate by a refrigeration system in which cooling is provided by a refrigerant such as liquid nitrogen.

3.1.3 *mechanical freezers*—freezers that operate by a refrigeration system in which cooling is provided by mechanical means such as a compressor.

² For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

³ The last approved version of this historical standard is referenced on www.astm.org.

4. Significance and Use

4.1 The proper handling of material stored at low temperatures ensures that the stability of sensitive biological materials is not compromised.

4.2 Properly designed inventory control systems ensure the maximum use of freezer space, that all material can be located easily, and that any item is retrieved easily without compromising the stability of other items in the freezer.

4.3 Properly designed safety and security procedures ensure that material stored at low temperatures is not compromised during storage, and that if material is lost due to freezer failure or operational problems, replacement material is available (see Guide [E1566](#)).

5. Procedures

5.1 *Inventory Control and Handling:*

5.1.1 Prior to storing frozen material, set up a system of labeling and tracking vials that ensures proper identification, location, and date of preparation of the vials. The label should include at least an identification code and lot number for the material.

5.1.2 Set aside a portion of the initial lot of the material designated as seed or master stock. The seed stock should be segregated from the working stocks, to be used for replenishing working stocks. A seed stock system ensures that future working stocks are close in passage to the original material.

5.1.3 Design an inventory system that allows easy access with simple locator codes. The best inventory system for large liquid nitrogen units is one in which vials are attached to metal canes in a vertical array. Boxes can be used for smaller units. Designate each freezer, box or cane, and location within a box, using a unique combination of letters and numbers, and then assign each lot of material a location code.

5.1.4 Maintaining inventory records on a computer simplifies access and allows cross referencing locations and vial label information. The inventory system should be designed to allow vacated locations to be re-stocked with new material in order to maximize storage space.

5.1.5 The inventory system should be designed to minimize handling during stocking and retrieval operations. This will not only reduce worker exposure to cold temperatures, but it will also minimize the exposure of other materials when retrieving a particular item.

5.1.6 The storage of vials on canes ensures that only the vial being retrieved is exposed to warmer temperatures. Canes also provide an inventory system that allows easy access to all material.

5.1.7 When boxes are used for storage in liquid nitrogen, place a small number of working vials in an easily accessible location, leaving the majority of vials untouched in the colder portion of the freezer.

5.1.8 Store seed material in a separate freezer to ensure that it is not compromised by repeated handling during the retrieval of working stocks.

5.2 *Safekeeping:*

5.2.1 Store some vials of working stock or seed material, or both, separate from the main lot of material for safekeeping.

5.2.2 Maintain safekeeping material in a separate freezer and in a remote location, if possible.

5.2.3 Do not rely on seed material alone for safekeeping, as it is irreplaceable. Material designated for safekeeping should be replaceable and should not be considered any less vulnerable than the working stock it is backing up.

5.3 *Safety:*

5.3.1 Precautions shall be taken to provide personnel protection from the extreme cold encountered at cryogenic temperatures. Extremities shall be protected at all times using gloves. Thin nylon gloves provide some protection when handling ampules, but insulated gloves designed for working at cryogenic temperatures should be used when possible.

5.3.2 When vials are stored directly in the liquid, they should be filled to a point that minimizes the air space in the vial, and they shall be sealed completely. Vials may be examined for leaks by immersing them in an aqueous methylene blue (0.05 %) solution at 4°C.

5.3.2.1 Because of the potential for exploding vials when retrieving from liquid nitrogen, precautions shall be taken to protect the operator from glass shards. Heavy gloves, laboratory coat, and face shield should be mandatory whenever retrieving vials from liquid nitrogen. In addition, glass vials should be placed inside a metal canister before removing the vial to warmer temperatures.

5.3.3 Nitrogen will displace oxygen in confined areas with poor ventilation, especially during fill operations. Care shall be taken to ensure the proper ventilation of all areas housing liquid nitrogen freezers, and an oxygen monitor with alarm should be installed in the area.

5.3.4 Hazardous biological materials should not be maintained directly in liquid nitrogen, because of the potential for leaking and exploding vials (see Guide [E1566](#)).

5.3.5 When freezers are no longer used, they should be decontaminated after warming before removal or reuse.

6. Keywords

6.1 biological material; inventory control; low temperatures

 **E1565 – 00 (2014)**

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