



BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Operation of the Thermo 7450 Controlled Rate Freezer
SOP Number: 12208
Revision: 07

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1. PURPOSE

This SOP outlines the operation of the Thermo 7450 Series Controlled Rate Freezer.

2. SCOPE

This SOP applies to Biopharmaceutical Development Program (BDP) personnel operating Thermo 7450 Series Controlled Rate Freezers at the Advanced Technology Research Facility (ATRF).

3. RESPONSIBILITIES

3.1 The Manufacturing Manager, Technical Operations, Biopharmaceutical Development Program (BDP).

- Defines the procedure.

3.2 BDP Personnel

- Trains on the procedure.
- Performs of this procedure.

3.3 Biopharmaceutical Quality Assurance (BQA).

- Provides quality oversight.

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4. SAFETY

- 4.1 Always be extremely cautious when working with or around liquid nitrogen. Be sure to use protective equipment (Cryo-protection gloves) when using this unit and avoid loose clothing and hair.
- 4.2 The nitrogen gas which evaporates from the unit will displace oxygen. Be sure appropriate ventilation and oxygen detection equipment is in place and functioning before using this unit.

5. LIQUID NITROGEN HOOKUP

Verify the liquid nitrogen line for the freezer is connected to a liquid nitrogen port and that the connection is tight. Open the valve, or valves, on the liquid nitrogen flow path.

6. UNIT STARTUP

- 6.1 Turn the power switch on the back of the unit to ON and wait for the display to show the profile list and turn on the associated PC. Ensure the printer on the top of the unit is set to "Online".
- 6.2 Prepare the calibrated Sample Thermocouple associated with the unit. (This step should be done in advance if using a vial)

6.2.1 Standard Thermocouple in a Vial

- 6.2.1.1 Fill a vial of the same type as those containing your samples with an equal volume of Water for Injection (WFI) or culture media (if directed per the Project Scientist) to the amount of liquid in your vials to be frozen. This will serve as the thermocouple vial.
- 6.2.1.2 Using a pointed object such as a pair of scissors or a pen, punch a small hole in the center of the cap of the thermocouple vial.

NOTE: Use extreme caution when puncturing the cap not to slip and injure yourself or others.

- 6.2.1.3 Insert the sample thermocouple through the hole in the vial. Keep the thermocouple in the center of the liquid. Then place the sample thermocouple vial in the center of the top rack.

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6.2.1.4 If your samples will not be at room temperature when you freeze them, cool the sample thermocouple vial to what will be the starting temperature for your samples to be frozen (4°C if in an ice bath) by either placing it in an ice bath or by following the next step.

6.2.1.5 Close the chamber door and begin the desired profile. The first step in most cycles is a 4°C hold. When the samples are ready, open the door and load them, then continue with the cycle.

NOTE: An initial temperature deviation is expected after loading material into the unit and resuming the cycle. This is normal.

6.2.2 Ribbon Thermocouple for Cell Therapy Bags

6.2.2.1 The ribbon thermocouple should be inserted in a cassette containing the cell therapy product, between the bag and the interior of the cassette. Alternatively, an identical bag containing WFI or culture media (if directed by the Project Scientist) of equal volume to the cell therapy product can be used for the thermocouple cassette.

6.2.2.2 Route the thermocouple wire through one of the openings in the corner of the cassette between the product and the label pouch so that the ribbon does not touch the cassette and close the cassette. Place the cassette in the center rack.

6.2.2.3 If you are not using a product bag for the thermocouple cassette and the product will not be at room temperature when delivered for the freeze, cool the sample thermocouple vial to what will be the starting temperature for your samples to be frozen (4°C if in an ice bath) by either placing it in an ice bath or by following the next step.

6.2.2.4 Close the chamber door and begin the desired profile. The first step in most cycles is a 4°C hold. When the samples are ready, open the door and load them, then continue with the cycle.

NOTE: An initial temperature deviation is expected after loading material into the unit and resuming the cycle. This is normal.

6.3 Freeze profiles can be controlled by the sample thermocouple or the chamber thermocouple. Six preset cycles are already programmed, along with several

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custom cycles to be used as needed. Custom cycles can be set per the Project Scientist.

7. OPERATION FROM UNIT

The unit can be operated from the control panel on the front of the freezer, but it is limited to the preset profiles listed in 8.4.1. This is not the preferred or suggested method for cGMP operation. For further details on operation from the unit, please see the equipment manual.

8. OPERATION FROM THE PC INTERFACE

8.1 Open the PC Interface Software and login on the opening screen.

8.2 Load the product to be frozen.

8.2.1 Product Vials

8.2.1.1 Load all vials into the freezing racks.

8.2.1.2 Place the racks onto the validated shelves 2, 3, and/or 4.

NOTE: Shelves 1 and 5 are not validated for vials and are therefore not used

8.2.1.3 The sample thermocouple vial must be placed in the center of the top rack with the thermocouple inserted (See Section 6.2.1), if not already performed.

8.2.2 Cell Therapy Bags

8.2.2.1 Load bags to be frozen into metal 250 mL cassettes. The ribbon thermocouple should be placed within the cassette (See Section 6.2.2) loaded onto shelf 5 with the shelf positioned in the middle to right side of the chamber.

8.2.2.2 Load remaining bags into the validated freezing rack locations working outwards from shelf 5 using adjacent shelves 3-7, (i.e. a two-bag run would use shelves 5 and 4; a three-bag run would use shelves 5, 4, and 6). Loaded bags must be of the same size and fill volume to be frozen in the same cycle.

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8.2.2.3 The maximum load is 5 bags placed on shelves 3 through 7 of the 10-shelf rack. Up to 50 cryovials may also be included in the same cycle, in their appropriate rack placed on the left side of the chamber. Use one rack as a base to elevate the second rack where the vials are placed.

8.3 Click the Open Profile button.

8.4 In the Open window, select the desired freezing profile then click Open.

8.4.1 For freezing of all bacterial cell banks, chose Preset 1 unless otherwise specified by batch record or Area Supervisor. A summary of all cycles typically used within the BDP is shown in the tables below. For full preset cycle details, see equipment manual.

Preset 1 (Bacterial Cell Banks)

Step Number	Rate (°C/min)	End Temperature (°C)	Trigger
1	Wait @ 4		
2	-1	-4	Sample
3	-25	-40	Chamber
4	10	-12	Chamber
5	-1	-40	Chamber
6	-10	-90	Chamber
7	End		

Cell Therapy Bags and Samples

Step Number	Rate (°C/min)	End Temperature (°C)	Trigger
1	Wait @ 4		
2	10min hold @ 4		
3	-1	-6	Sample
4	-25	-50	Chamber
5	10	-20	Chamber
6	-1	-45	Sample
7	-10	-120	Chamber
8	End		

8.5 Enter a descriptive title in the “Run File Name” box and enter the lot number in the “Data Tag” box to identify the run. Both fields should only contain alphanumeric characters.

8.6 Initiate the run by clicking the Start Run button.



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- 8.7 Select the appropriate COMPort, then click OK. Click OK to start profile download. Once the profile has downloaded, a popup will appear, click OK to acknowledge the profile has
- 8.8 Select the location to save the file. The default directory is C:\PC Interface\CRF_Programs\Run.
- 8.9 If the profile being run contains a wait step, you will need to click on the “Waiting for user” box which pops up at that time.
- 8.10 At the completion of the run, an alarm will sound and the Mode display box will say “End”. Click Ok to silence/clear the alarm and then the End Run button, then click OK to confirm. Enter your user password to end the run. Click OK to acknowledge the end of the run. Open the freezer and immediately remove the product to storage.
- 8.11 If required by Supervisor’s instructions or the MPR, print the required data from the run. The printout from the unit can be used or the run file from the computer can be printed to a PDF file and transferred to another computer for printing.

9. POST RUN ACTIVITIES

After each run, leave the door open to dry and then dry any remaining moisture from the door gasket and heat breaks. Inspect the interior and wipe down with any BDP-approved disinfectant if leaks or spills are noticed.

If no more runs are to be performed at this time, turn off the unit. Then close the valves on the LN2 line hooked up to the Controlled Rate Freezer.

10. DOCUMENTATION AND RECORDS

Document cleaning, maintenance, and use of the Thermo 7450 Liquid Nitrogen Freezer Log, Form 12208-01, in the appropriate logbook for the freezer used, being sure to include the following: Date, Time, Project and Lot numbers, Profile Run, and initials.

11. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
12208-01	Controlled Rate Freezer Activity Log

12. ATTACHMENTS

Attachment 1 PC Software Run Screen

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Attachment 1 PC Software Run Screen

