Frozen in Time

Manufacturers of Freeze Drying Machines and Vacuum Cold traps

Operating Manual **HSLS - 4**

Operating Manual

HSLS-4

Order Number:

Serial Number:

In case of enquiries please state the above

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Important Safety Instructions

This manual contains instructions which are intended to assist persons installing, operating and servicing the described equipment, machine parts or systems. These instructions have been prescribed to assure personal safety and to avoid personal injury and / or collateral damage. Care should be taken to read and carefully follow all safety instructions and operating procedures described herein.

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1. General Information

1.1. Introduction

What is freeze drying (lyophilization)?

Freeze drying is a process of dehydration where water or liquid is withdrawn from a material though sublimation. Sublimation is the conversion of a substance from a solid state to a gas. This conversion or *phase transition* is carried out in a freeze drying vessel. The material to be dried is frozen to less than -10°C and placed under a vacuum, heat is then introduced to the frozen product which causes the ice to sublime.

Freeze drying is typically used where the preservation of the material is important. It generally does not destroy the physical structure or chemical compounds of a product. Freeze drying is the gentlest process for preserving biological properties of sensitive tissues and tissue components. It is also commonly used for drying food, blood plasma, and pharmaceuticals.

The basic steps involved in freeze drying are the freezing of the product, primary drying and secondary drying.

Products such as wet material, aqueous solutions or suspensions are frozen. The final temperature being below the product’s eutectic, or collapse temperature so as to maintain its structural soundness. Once all water is converted to ice the condenser and vacuum systems are energized for the drying process.

Primary drying then removes unbound or easily removed ice by sublimation. The product is under vacuum to maintain a low pressure (of a few millibars) ensuring water vapour remains below its ‘triple point’ and is able to migrate into the system’s ice-collecting condenser. Primary drying removes up to 95% of the product’s moisture and is generally a slow, controlled process.

After the initial ice is sublimed, bound water may still be present which can limit the product’s stability and shelf life. Secondary drying is required to remove this sorbed water which is strongly bound to the product’s solids. Secondary drying usually begins during the primary drying phase but extends beyond it and normally at temperatures higher than during primary drying. Residual moisture is desorbed at this stage and the resulting moisture levels in the product are at 1 to 5% at the end of drying.

1.2. HSLS – 4 Technical data

HSLS - 4 Freeze Dryer Specifications	
Overall Dimensions W x D x H cm	**208 x170 x 210**
Specimen Chamber Diameter x Length cm	**100 x 100**
Specimen and Condenser Chamber Construction	**Polished 316L Stainless Steel**
Shelf Area m²	**2.6**
Number of shelves	**6 +1**
Shelf Size W x D in cm	**60 x 80**
Maximum Distance between shelves if they are all equally spaced in cm	**9.5**
Condenser Chamber Temperature	**-85 ºC**
Shelf Temperature Range ºC	**-70 to +70 ºC**
Stoppering Device	**Hydraulic**
Mobile Temperature Probes	**6**
Condenser chamber Defrost	**Electric**
Condenser Ice Capacity	**35 litre (20litres / 24hour)**
Refrigerant	**R-507 – R-23**
Vacuum Pump	**E2M40**
Refrigeration	**Two Stage Cascade Refrigeration**
Isolation Valve	**Ø 25cm**
Power Requirements	**3ph 415v**

1.3. Safety instructions

1.3.1. Removing panels

The freeze drier must be securely isolated or unplugged from the mains supply before any panels are removed and/or before any maintenance work is undertaken.

1.3.2. Solvents

Acidic or high concentration solvent products should not be dried because of risk of corrosion and damage to the vacuum pump.

1.3.3. Protective clothing/Danger of freezing skin

Operators should wear appropriate clothing and take precautions that would prevent bare skin from coming into contact with freezing surfaces i.e. gloves and long sleeves. Skin that does adhere to frozen surfaces can only be detached from the surface by applying heat. Do not use liquid.

1.3.4. Transporting the Freeze Dryer

The **HSLS-4** has lifting lugs and can be moved from one location to another if necessary by a crane or by forklift. The machine weighs 2300 Kg.

1.3.5. Steam exhaust

The freeze dryer has a pressure relief valve fitted for safety during steam sterilization. The steam exhaust pipe from this safety valve must be piped outside. This must lead to a safe venting area away from any obstacles or persons. The distance of the venting pipe should be kept to a minimum and upon exiting the building should be angled as to direct it in the safest possible manner. No valves or restrictions should be used on this pipework. Severe injury could result if exhaust gasses are not safely vented and directed.

1.4. When the HSLS-4 should not be used:

1. It is not properly installed by a qualified technician.
2. Panels are missing.
3. The operator is not authorized or trained.
4. Highly corrosive or solvent substances are present.
5. In hazardous or dangerous locations.
6. The products are explosive or highly flammable.
7. The products are infectious, toxic, pathogenic or radioactive unless in suitable vessels and in accordance with the relevant material safety data.

2. Installation and commissioning of the unit

2.1. Site of installation

The **HSLS-4** is designed to be placed in a clean room environment. The front, product chamber and controls all being accessible from the clean room and installed flush with it's surrounding. The rear of the machine shall be located in a separate room giving access to all serviceable parts and supply connections.

2.2. Mains power

The operating voltage indicated on the rear specification plate must correspond to the local supply voltage. Frozen in Time freeze dryers are units of safety class I. The **HSLS-4** requires a three-phase power supply of 380 to 415 Volts. The freeze dryer must be on a circuit protected by a fuse or circuit breaker with a maximum 63 Amp. A separate electrical supply will be required for the steam generator and the chiller. It is recommended that the steam generator is on a 125 amp supply and the chiller is on a 32 amp supply these must also be protected by their own sufficient fuse or circuit breaker.

2.3. Air/inert gas admittance

Filtered air can be admitted into the product chamber. If an inert gas is needed such as nitrogen then a supply of this is required usually as a stand alone gas cylinder. Vials can be sealed only with a vacuum or with partial inert gas fill, depending on the product. If *inert gas for stoppering* fill is selected on the freeze drier's *engineering* page of the automated screen, the valve (V007) will open, filling the main chamber with gas. Connect the desired gas type to this valve's feed.
During freeze drying the minimum vacuum level can be maintained by introducing filtered air or inert gas through bleed valve (V009) and control solenoid (V006). This supply hose can be connected to the appropriate gas bottle or air supply.

2.4. Dry Nitrogen supply

The **HSLS-4** will need a supply of dry nitrogen for its operation.

Thermal fluid circulates through the freeze drier shelves in a closed circuit. This circuit contains a refrigerated heat exchanger and immersion heaters which raise and lower the temperature of the thermal fluid. The fluid heats up to 135°C and cools down to -80°C during which time the volume of it will fluctuate. A header tank forms part of this closed fluid system and is adequately sized to keep the circuit full when the fluid level is at its lowest (-80°C) and to contain its maximum fluid level when the system is at its highest temperature (135°C).

During heating, the system will vent to avoid high pressure in the header tank. However, during cooling at -80°C a problem can occur where shelf fluid will attract moisture if there is any superfluous air in the system. This moisture will introduce unwanted water into the shelf circulating system.

When the system operates with shelf temperatures of between 0°C and 100°C this water will collect in low points as it is heavier than the fluid. The velocity of the fluid will carry small water droplets throughout the system. During the shelf freezing cycle these droplets turn to ice and block the fluid circulation. If a shelf's circulation becomes restricted its temperature will not equal that of the others. This temperature difference will cause one or more shelves to lag behind during the freezing or heating cycles. There would be no circulation of fluid at all before the shelf temperature rises to above 0°C (where the ice will melt). The potential introduction of water and ice into the system will severely disrupt a freeze drying cycle and needs to be avoided by the use of dry nitrogen.

To prevent ice from forming in the system, a 'blanket' of dry nitrogen needs to be maintained above the fluid in the header tank at all times. This nitrogen 'blanket' will not allow the fluid to come into contact with any moisture. The fluid is able to vent during heating but not pull in any moisture during cooling. As the fluid level drops in the header tank during cooling, the regulated nitrogen enters in through a one way valve (V037). As the fluid level rises with heating, excess nitrogen is pushed out through a second one way valve (V036) venting it into the surrounding air. As long as this nitrogen system is in place it will prevent moisture from entering the circulation system.

A side benefit of a steam sterilizing freeze drier such as the **HSLS-4** is that during sterilization the fluid temperature reaches 135°C and this would boil off any trapped moisture that might have entered the system. The vapor will rise out of the circulation system into the header tank and exhaust through the vent. Some vapour may condense and collect in the header tank (A059). Water in the header tank may be drained off through the valve (V038) using caution so as not to drain the system of any heat transfer fluid.

2.5. Drainage pipe for condensate

The condenser chamber drain valve will require a flexible pipe to be fitted and lead to a floor drain or collecting vessel. Water from the freeze drying cycle or the steam sterilizing cycle drains away from the condenser through this valve. Blow off drainage from the steam generator as described in section **4.2.** will also be directed through this pipe.

2.6. Venting vacuum pump exhaust gases

Exhaust gas from the vacuum pump contains oil mist. This oil mist is trapped by exhaust filter (N103). Remaining exhaust gases then pass through the filter and are piped outside or into a vent duct. If no exhaust filter is used it is essential that the exhaust is vented outside as it will be oil mist.

2.7. Steam Exhaust

The steam exhaust on the freeze drier leads from an internal manifold. The major component on the manifold is the overpressure relief valve from the main chamber. If the sterilization pressure accidently reaches 2.5barg then the relief valve will open and protect the vessels from over pressure.
Steam separators are also connected to the manifold and will give small bursts of hot water and possibly steam. The steam exhaust exits the freeze drier through the top panel. Any condensate in the exhaust manifold will drain away through the condenser chamber drainage pipe. Please see section 1.3.5. for important safety instructions.

3. The Freeze Drying Process

3.1. General Information on Freeze Drying with the HSLS-4

The freeze drier uses the process of sublimation for drying. Sublimation is the direct conversion from a solid to vapour state. Under vacuum, energy (heat) is supplied to the product via the heated shelves, this starts the sublimation process. The frozen product is dried under vacuum without thawing.
Primary drying removes the majority of liquid from the product. Secondary drying removes the last traces of moisture by means of deep vacuum. The vacuum pump is only intended to remove the air from the product chamber, not vapour. The condenser chamber works as a cryogenic pump as it takes large volumes of vapour from the product chamber and deposits it as a small amount of ice.

The main components of the freeze dryer are:

- Vacuum drying chamber (product chamber) with heated shelves and a vial closing device.
- Condenser chamber with temperatures of -85°C for deposition of vapour to ice.
- Vacuum pump to evacuate air.

Sublimation

The principle of sublimation is briefly explained using **Fig. 3.1a** Phase diagram for solid, liquid and vapour. If the pressure is higher than 6.1 mbar, water can exist in all three phases (solid, liquid, vapour) when the temperature is lowered or raised. At 6.1 mbar and 0ºC all three lines meet. This is called the triple point where all three phases can occur simultaneously. Below this point when the pressure is lower than 6.1 mbar, the ice is converted directly from a solid to a vapour on reaching the sublimation pressure curve.

The second diagram: sublimation curve **Fig. 3.1b** shows the vapour pressure of ice as affected by temperature and pressure.

Fig. 3.1a Phase diagram for solid, liquid and vapour

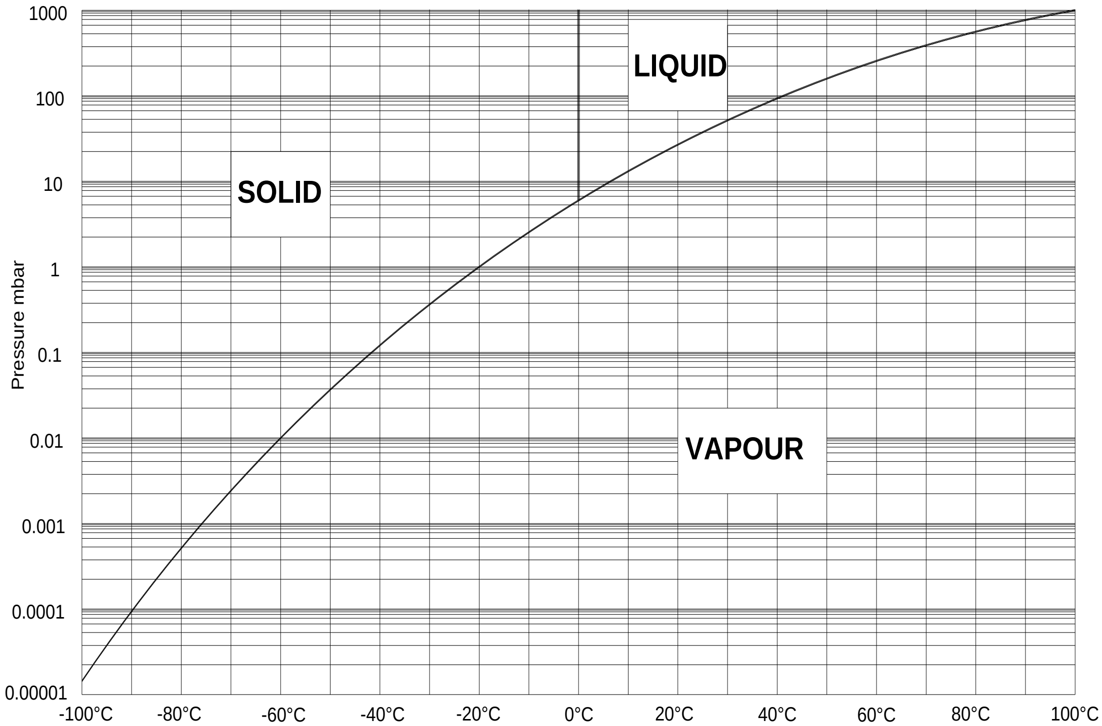


Fig. 3.1b Vapour pressure of ice

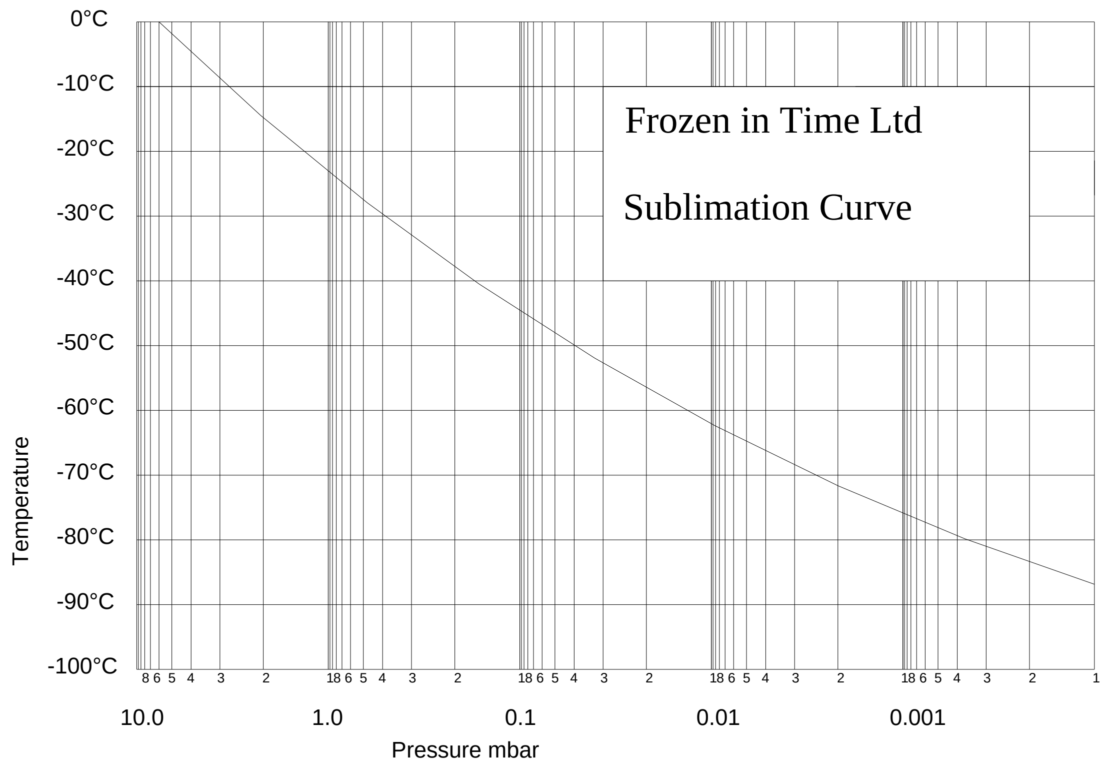
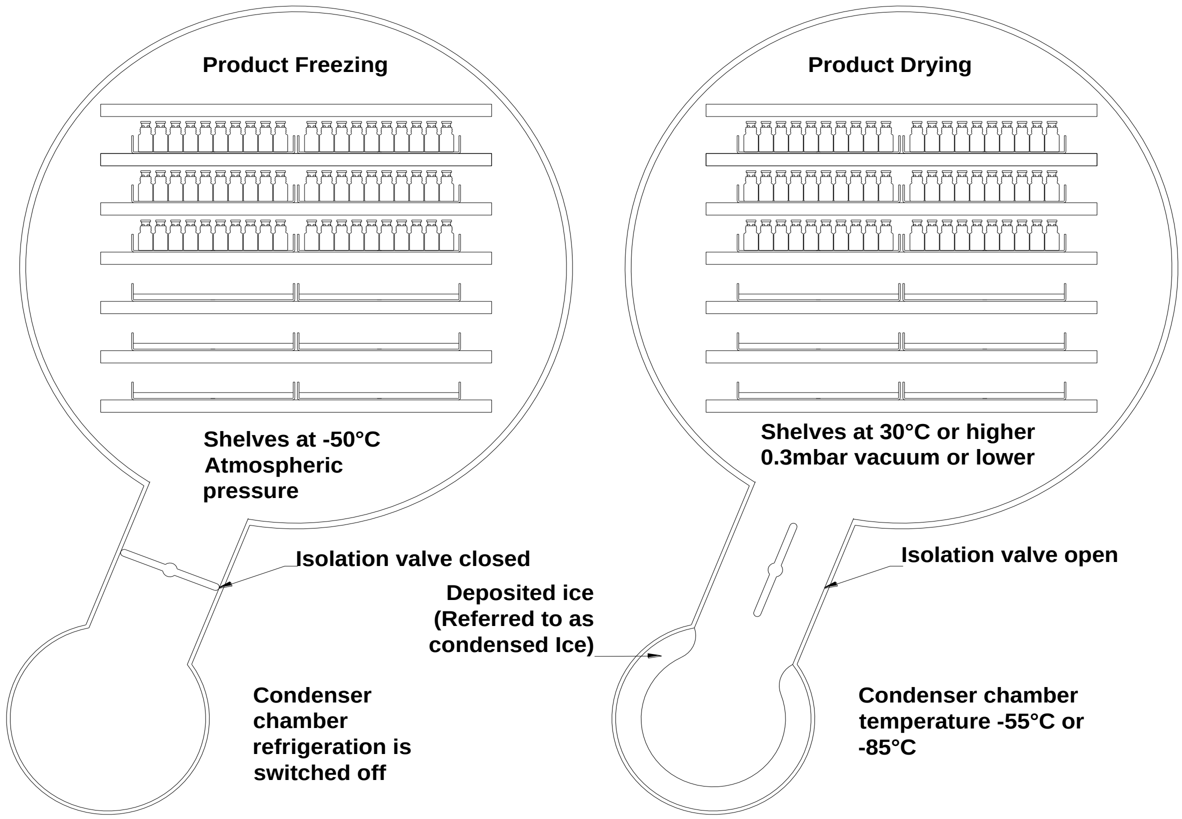


Fig. 3.1c Cross sectional diagram of the freeze drier chambers during Product freezing and Product drying.



Product Freezing

The Isolation valve is closed and the product is frozen by lowering the temperature of the shelves.

Product drying

The condenser chamber temperature is lowered to its minimum. When temperature goes below -30ºC approximately, the vacuum pump can be switched on. The isolation valve must be opened and a vacuum is created in both chambers. When the vacuum is sufficient, heating can be applied to the product shelves. Sublimation will take place, dehydrating the product. Deposition will occur in the condenser chamber where the vapour turns solid (ice).

3.2. Freezing the product.

Product can be frozen directly on the shelves of the **HSLS-4**. This is the usual option for product to be freeze dried in trays or vials. The product is placed on the shelves and the shelves are cooled down to the desired temperature. The freezing can be done in stages, at a controlled rate or as quickly as possible.

3.3. Primary and secondary drying

The condenser drops to its operating temperature.
The isolation valve is open
The vacuum pump is switched on.

The duration of the primary drying phase mainly depends on:

- The layer thickness of the product,
- The moisture content of the product,
- The heat supplied to the product during the drying process,
- The vacuum pressure inside the drying chamber during the drying process.

During primary drying the unbound moisture is removed by sublimation. Shelf temperatures can be raised in stages, at a controlled rate or set to maximum for fastest heat transfer. The heat input must of course not be enough to damage or melt the product. Too much heat will increase the amount of vapours to a point where the vacuum level diminishes to above the eutectic point of the product.

With increased pressure the rate of sublimation rises as long as it stays below the vapour pressure of the product. This is because at higher pressures the heat energy reaches the sublimation front of the ice core sooner. Therefore the drying period is shortened. The water vapour generated during the main drying phase is not intended to be removed by the vacuum pump. It is to be collected by the ice condenser. The purpose of the vacuum pump is to lower the partial pressure of the non-condensable gases so that the water vapour can be transported from the product to the ice condenser. However, small quantities of water vapor will be removed by the vacuum pump. The vacuum pump is equipped with a gas ballast valve that when open, removes traces of condensable vapors from the pump. For this reason, the gas ballast valve can be open during the main primary phase. The gas ballast valve is not required for secondary drying and closing it will help achieve a lower level of vacuum.

The end of the primary drying phase is reached when the product temperature is nearly the same as the shelf temperature (temperature difference between shelf and product being approximately 3 to 5ºC). Once the primary drying is completed the secondary drying will begin.

Secondary Drying

Secondary drying takes place enabling any remaining bound or sorbed water to be sublimed from the product. The last traces of water vapour are removed and the product becomes sufficiently dry and stable.

The residual moisture of the finished dried product depends mainly on:

- The temperature of the dried product during the final drying process,
- The final vacuum reached during the secondary drying process.

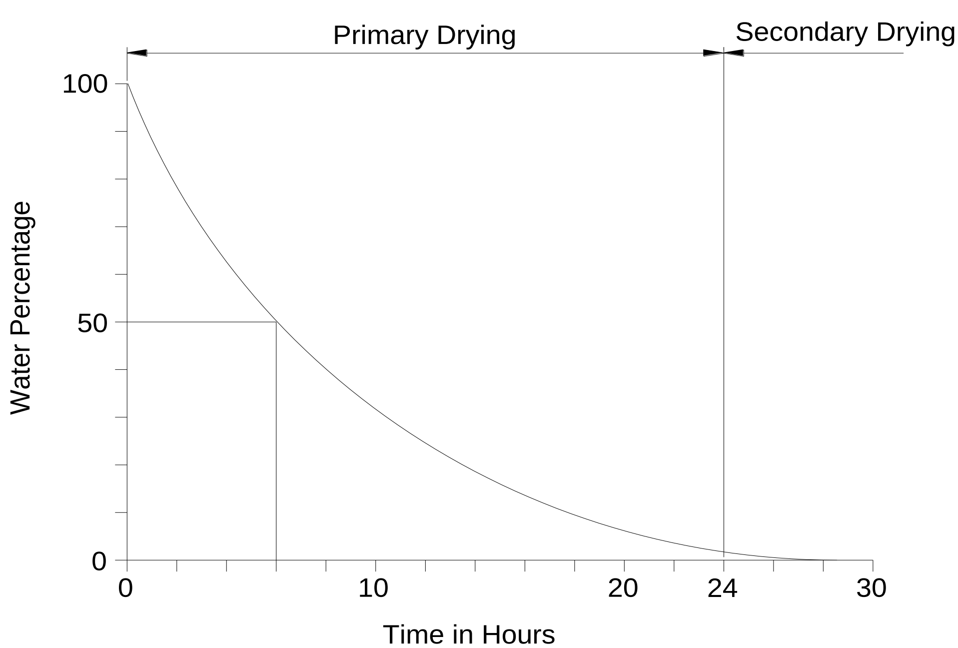
The final pressure in the drying chamber depends on the ice condenser temperature according to the vapour pressure curve above ice. **Fig. 3.1b**

e. g. 1.030 mbar corresponds to -20°C
0.370 mbar correspond to -30°C
0.120 mbar correspond to -40°C
0.040 mbar correspond to -50°C
0.01 mbar correspond to -60°C

The unit is in operating condition for secondary drying if the temperature of the ice condenser is lower than -50°C and the pressure is lower than 0.12 mbar. The final pressure measured when there is no product in the unit and its corresponding ice temperature is determined by the warmest ice surface in the condenser chamber.

The following diagram **Fig. 3.3b** shows the drying process for a product containing approximately 10% solid matter. During the first quarter of the primary drying phase approximately 50% of the water content is removed. During the next quarter of the primary drying phase approximately 50% of the remaining water content is removed. This continues until the drying curve approaches the time axis asymptotically. This typical drying curve is created due to the fact that the area of sublimation recedes into the product and the remaining water vapour must pass through the already dried layers. During the drying process the resistance increases. The drying curve is determined by the latent heat of sublimation and the amount of vapour transported. In order to increase the specific heat conduction properties of the product and to keep the water vapour volume as low as possible it is necessary that drying takes place as close as possible to the solidification point or eutectic point.

Fig. 3.3b Freeze Drying Curve



Facts regarding ice in a vacuum:

1.0 gram of ice at the following pressures will produce vapour in the quantities listed:

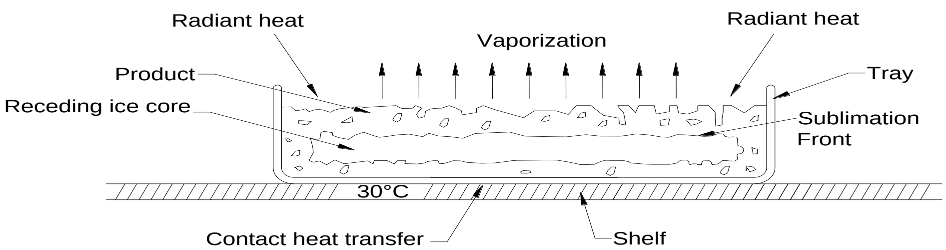
- 1.0 mbar assumes a volume of 1 m³ vapour
- 0.1 mbar assumes a volume of 10 m³ vapour
- 0.01 mbar assumes a volume of 100 m³ vapour

Heat supply during drying

The required heat for the product to be dried is supply to by:

- Conduction through contact with shelves in the drying chamber.
- Mild conduction through low pressure vapour.
- Radiant heat energy.

Effects of freeze drying of a product in a dish



Heat transfer takes place via the heated shelves by direct contact with the bottom of the tray. At the beginning of sublimation the transfer of heat is very effective from the wall of the tray to the frozen product. However, soon an area develops which is ice-free, porous, dried and has an insulating effect between the wall of the tray and the product. This slows down the heat energy transfer available to the ice core. The porous dried layer enables the passage of vapour from the ice core. If it is restricted, the temperature will increase and ice core will thaw rather than sublimate. This applies especially to inhomogeneous products and to greater layer thicknesses. During this drying phase it is important to regulate the heat supply and control temperature and pressure precisely.

3.4. Pressure rise test

The pressure rise test is a good way to confirm that there is no more vaporizing ice in the product. In the automatic cycle, parameters set on the engineering screen of the control system will be followed. When the secondary dying stage is considered to be finished, a pressure rise test will ensure it is. The shelf temperatures and the vacuum levels will still be in secondary drying conditions. The isolation valve is closed and the operator will watch to see the rate at which the vacuum level in the product chamber increases. The vacuum level will rise even with dry product, however the rate at which it rises when ice is still vaporizing is much greater. The operator must perform tests to become familiar with these rates of pressure rise. The pressure rise test can also be performed manually by the operator.

3.5. Inert gas vial filling

If the vials are to be charged with an inert gas such as Nitrogen, then this gas must be admitted before the vials are closed. If not then this step is skipped and vial closing is completed.

3.6. Vial closing

The vials are closed by raising the ram until all the shelves have stopped on the spacers. The ram activation buttons can be held for a few seconds after the shelves have closed to ensure the correct pressure has been exerted on the vial stoppers.

3.7. Air/inert gas admittance

After the vials have been closed the vacuum in the chamber must be released by admitting air.
Air will enter through the air admittance valve until the pressure is equalized and the door will release. This may take a several minutes.

3.8. Defrosting

Defrosting of the ice condenser can be carried out manually by pressing the defrost button on the manual screen. Defrost time and temperature is adjustable on the engineering screen of the control system. The drain valve must be opened to allow the water/condensate out.

In the automatic program, defrost must be selected from the post program list. Defrost will perform automatically at the end of the process. It will follow the conditions set on the engineering screen.

4. Steam sterilization processes

4.1. General Information on Steam Sterilization

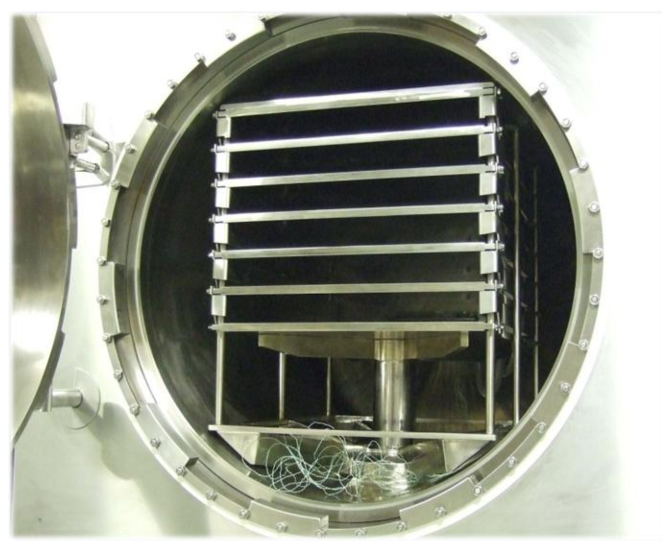
Steam sterilization is a very effective way to kill microbiological populations. Steam will ensure heat all surfaces are heated equally. The steam pressure will determine the temperature that the steam condenses at. All surfaces that are available to condense steam will reach the saturation temperature.
For complete sterilization a temperature of 121°C for 30 minutes or 132°C for 1 minute is required.
Steam pressure of up to 3.3bar absolute (2.3barg) is achievable in the freeze drier.
This relates to approximately 136°C

4.2. The steam generator

The steam generator will provide the steam necessary for sterilization. The unit provides 60kg/hr of steam. It uses 50kw and should be connected to a 125amp supply.
It is connected to a water supply which may need a softener.
Steam is connected from the generator to the freeze drier via a flexible steam hose. It is best situated as close as is conveniently possible. The drain is also connected in order for freeze drier to control the steam generator clean out operation. This will take place on the start up of every sterilization process.
As the pressure begins to rise during heating the drain will be opened for a few seconds (settable in the Steam Sterilization Engineering Page). This will flush out the lower portion of the boiler tank. The steam generator will stop heating when it reaches 4bar. It will also stop if the water level drops. However as long as there is constant water supply the water pump should keep it filled.
There is the option of using 1 or 2 heating elements depending on available power. It will use 25kw for one which is about 40amp or 50kw for two which is about 80amp.
The freeze drier controls the switching on and off of the steam generator. For more information please see the manual

4.3. Door locking and unlocking

In order for the steam sterilization process to take place the door must lock to make the freeze drier chambers a pressure tight system. The door locking mechanism is automatic. It uses a female castellated rotating ring that matches up with the interlocking ring on the door. Locking and unlocking can only take place when both chambers are under vacuum pressure. This is a safety mechanism to prevent unlocking while the system is under pressure. The rotation ring cannot mechanically rotate without the vacuum force applied.



4.4. The Automated Steam Sterilization Process

The steam sterilizing process is automated to prevent user error. Parameters can be changed in the engineering page to suit the sterilization method required. The door must be in the closed position before any automated program can start. The cycle will take the following pre-programmed steps 4.4.1 through 4.4.11.

4.4.1 Creating Vacuum

- The condenser chamber will cool down to its “Vacuum start set point” adjustable in the engineering page.
- The vacuum pump will start up and will create a vacuum in the initial vacuum manifold until the ”Initial Vacuum Test Pressure” is reached
- At this point the Vacuum valve will open and start to draw a vacuum on the condenser chamber will again need to reach the ”Initial Vacuum Test Pressure” before opening the isolation valve.
- As the isolation valve opens it will create a rapid pressure drop in the product chamber. This will ensure that the door is fully pressed upon the door seal.

4.4.2 Locking the door

- The pressure must now drop down low enough for the door to lock this level is determined by the set point “Min door pressure”. Upon reaching this level the door will lock.

4.4.3. Pressurizing

- The condenser chamber cooling and the vacuum pump will switch off
- The pressure from the steam generator will now fill the freeze drier vessels. Steam will condense on the internal surfaces and heat them up. The shelves have additional heating from the circulation fluid which is heated by separate heaters. They will heat up to 135°C.
- Condensed water will flow down into the condenser and out of the drain through a steam separator that allows only water out.
- When the steam pressure is achieved the sterilization will begin.

4.4.4. Sterilizing

- Pressure will be maintained for the sterilization time.

4.4.5. Depressurizing

- The condenser chamber will start cooling again and the steam will switch off.
- All the steam will condense creating a pressure drop in the system
- Condensed water will pass through the steam trap until the vessels reach 1100mbar at which point the drain valve will close.
- The vessel pressures will continue to drop as the condenser temperature drops.

4.4.6. Creating Vacuum

- When the condenser cools down to the “Vacuum start set point” the vacuum pump will start.

4.4.7. Unlocking the Door

- The pressure must now drop down low enough for the door to unlock this level is determined by the set point “Min door pressure”. Upon reaching this level the door will unlock.

4.4.8. Cooling the Shelves and Product Chamber

- The refrigeration will now be diverted to the shelves and product chamber cooling.
- The shelves will cool down to the “post sterilization shelf temperature”

4.4.9. Air/inert gas admittance

- The air admittance or inert gas valve will open at the same time as the shelves start to cool.

4.4.10. Defrosting

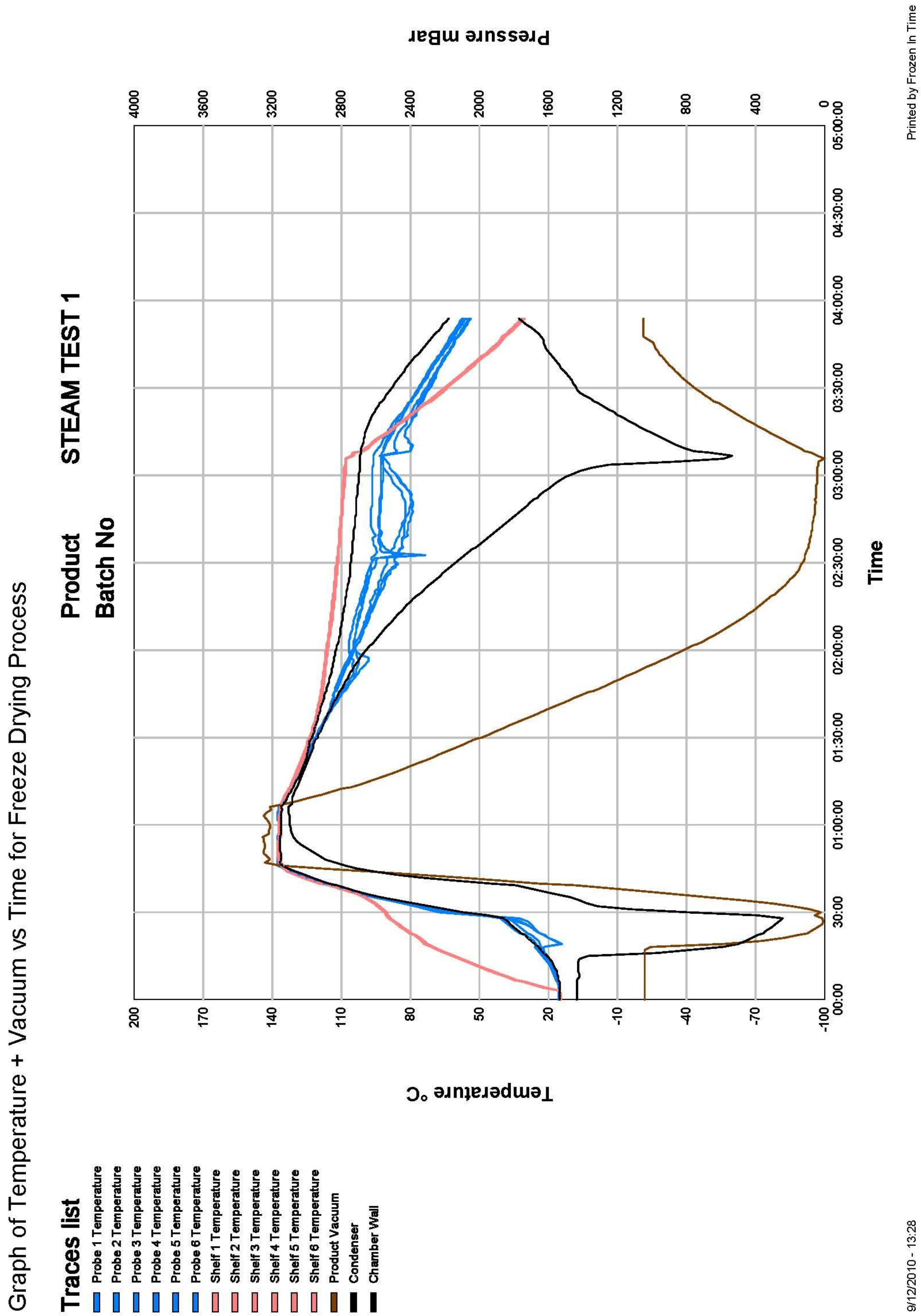
- As the shelves start to cool the, defrost will turn on and heat up to the defrost temperature for the set amount of time.

4.4.11. Drainage of condensate

- When the system pressure reaches atmospheric the drain valves will open and the defrost condensate will drain away.

4.5. Graph print out of the steam sterilization cycle

Below is an example of a cycle printout. On the left there is a key to identify graph lines. Product and Batch identification appear as the heading.



5. Operating the HSLS-4

5.1. Opening and Closing the door

The freeze drier has a lockable door to enable it to hold positive pressure during steam sterilization.

The door will swing open rotating on its hinge to allow access to the chamber. However to close completely against its seal it must pass through the castellated locking ring. This requires a linear movement of approximately 80mm. Once the door is swung closed parallel to its seal the close door button on the manual screen can be pressed and the door will travel inwards through the locking ring and come to a stop on the door seal.

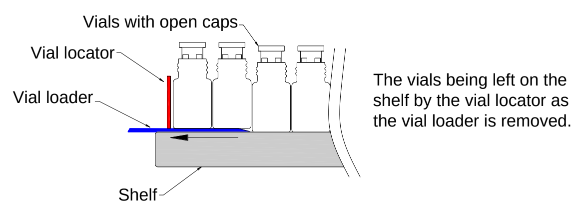
To open the door it must again travel past the locking ring and then it is released so it will swing open. The door can only be opened when the internal pressure is above 1000mbar. This will prevent the door trying to open when there is a vacuum force in the chamber.

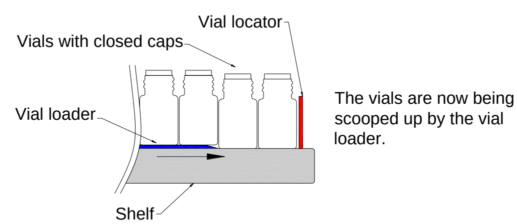
5.2. Loading Trays

5.2.1. Vial trays

The vial trays are bottomless to allow direct thermal contact between the vials and shelves. The vials are placed onto the shelf using a vial loader and vial locator. The vial loader is slid under the locator which contains all the vials to be kept in place on the shelf.

When the product is to be unloaded, the vial loader is slid back under the vial locater, supporting the vials. And the vials, vial locator and vial loader can be removed as one unit.





There are 6 usable shelves and each shelf holds 3 vial trays. The vial locators can hold various diameters of vials. Shelf spacers can be removed and replaced with the correct sized spacer to suit any vial height. Each of the shelves can be placed at differing heights in any combinations to suit.

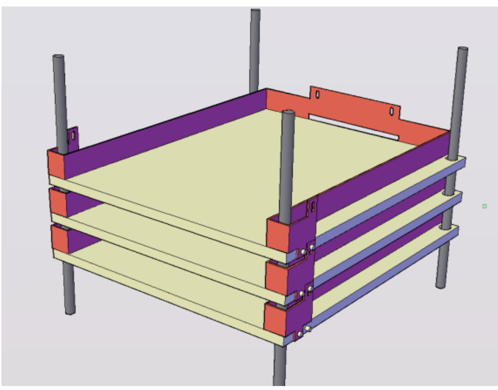
5.2.2. Bulk trays

Bulk trays can simply slide onto the shelves. Trays can be supplied in various sizes to suit the application.

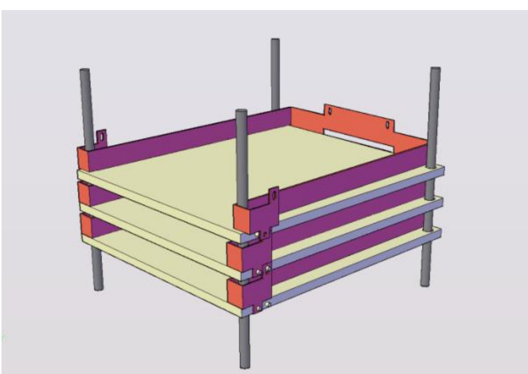
5.3. Changing shelf spacers

Shelf spacers are easily changed by the operator. It involves raising and lowering of the shelves. This can be done on the manual screen by first selecting the direction of the ram up or down. Then two hands pushbuttons located require pressing simultaneously to make the ram move. This ensures that the operator cannot trap an upper limb in the shelf mechanism. If the door is closed then the two buttons are not required to be pushed.

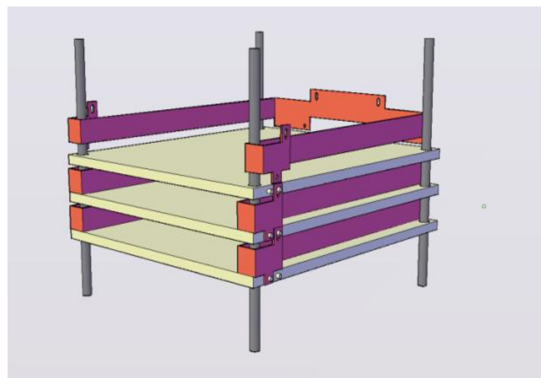
Each shelf is hung from the shelf above by a spacer. The spacer also determines the shelf closing distance. The travel distance between closed and open position is usually 10 to 15mm. Movement is possible due to slotted holes on each spacer.
When the ram is down, the shelves hang from studs on the right, left and rear of the shelves. When the ram is up each shelf is spaced apart by the uprights running from front to back. To take a spacer out:



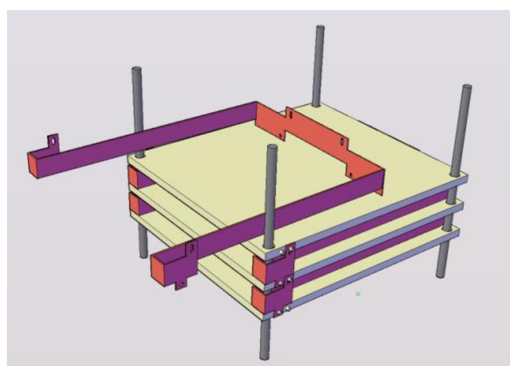
1. Raise the ram until the shelf weight is taken off the spacer but before the travel distance between shelf and spacer has closed.
2. Remove the domed headed nuts from each side.



3. Push the fronts of the spacer out sideways until they come clear of the studs
4. Push both sides backwards and this will take the spacer clear of the rear stud.



5. The ram can now be lowered, separating the upper shelf from the lower shelf.



6. The shelf should now be low enough that you can lift the spacer out.

To insert a spacer:

1. Lower the ram until the shelf is low enough to insert the spacer.
2. Push the fronts of the spacer out and back, this will allow it to sit over the edge at the rear and be clear of the studs.
3. Raise the ram until within 10 mm but before the gap between shelf and spacer has closed.
4. Pull the spacer forwards to locate on the rear studs
5. Push the fronts of the spacer inwards until they locate on the front studs.
6. Replace the domed headed nuts on each side.

This procedure is then repeated for every spacer. If all spacers are to be removed for cleaning or access then start removing from the bottom and work upwards. If large spacers are to be used that would space the shelves to a maximum distance then a slightly different loading sequence is required. First for the top 1 or 2 shelves install the smallest spacers that are available. Then work down installing the larger sized spacers on the lower 4 shelves. After this is done the top smaller spacers can be removed and be replaced with larger ones to match the other 4.

5.4. Raising and lowering the ram

The vial closing system is operated by raising the ram and closing the shelves when fitted with the appropriate spacers.

If an automatic program is running then the ram cannot be operated in manual mode. If the freeze drier is running in manual mode it is possible to raise and lower the shelves with the buttons on the manual screen. It is also possible to activate the ram when the door is open for positioning of the shelves. The procedure is as follows. First select the direction up or down and then hold in the two push buttons on the front panel.

The ram will operate in the direction that is selected. The two buttons require both hands to be used which prevents them from being trapped in between the shelves when the ram is activated.

5.5. Vacuum Pump

The vacuum pump fitted to the HSLS-4 has a 40 m^3/h displacement

The pump can be switched on using the controls on the Manual screen. There are several interlocks that prevent the vacuum pump from starting in ways that could cause problems.
These include not allowing the pump to start when:

- There is an insufficient temperature in the condenser chamber
- The drain valve is open
- The condenser chamber defrost is switched on
- Both the Product chamber air admittance and the Isolation valve are open.

In an automatic program the vacuum pump will be controlled completely by the PLC and no user operation is needed or allowed.

The vacuum pump oil should be changed when the pump is warm. The oil level should be visible in the sight glass. The intervals for changing the oil will depend upon the products being freeze dried. With the -80ºC condenser chamber version it will offer better pump protection than the -55 ºC The condenser chamber temperature must be lower than the temperature corresponding to the vapour pressure that the product is going to freeze dried at. In the case of water vapour the following is a good guide:

1.030 mbar correspond to -30°C
0.370 mbar correspond to -40°C
0.120 mbar correspond to -50°C
0.040 mbar correspond to -60°C
0.01 mbar correspond to -70°C
0.003 mbar correspond to -80°C

If the product contains large quantities of chemicals that are more volatile than water then lower temperatures in relation to vacuum levels are required.

An oil mist filter should be fitted to the exhaust port of the vacuum pump.

For extra information on the pump please see the separate operating manual.

5.6. Isolation valve

The Isolation valve can be operated by using the controls on the Manual screen. To avoid problems there are two interlocks that prevent the Isolation valve from being opened when:

- The defrost is on
- The vacuum pump is running and the Product air inlet is open.

In an automatic program the Isolation Valve will be controlled completely by the PLC and no user operation is needed or allowed

5.7. Air/inert gas admittance valve

Either filtered air or an inert gas can be admitted into the system.

5.8. Condenser drain valve

It also can be operated by the controls on the manual screen. To avoid problems there are two interlocks that prevent the condenser drain valve from being opened when:

- The condenser refrigeration is running
- The vacuum pump is running

5.9. Circuit breakers

The control box has circuit breakers that may trip out in the event of an electrical problem. If a function is not working, this is the first place to check. There are circuit breakers for the following items.

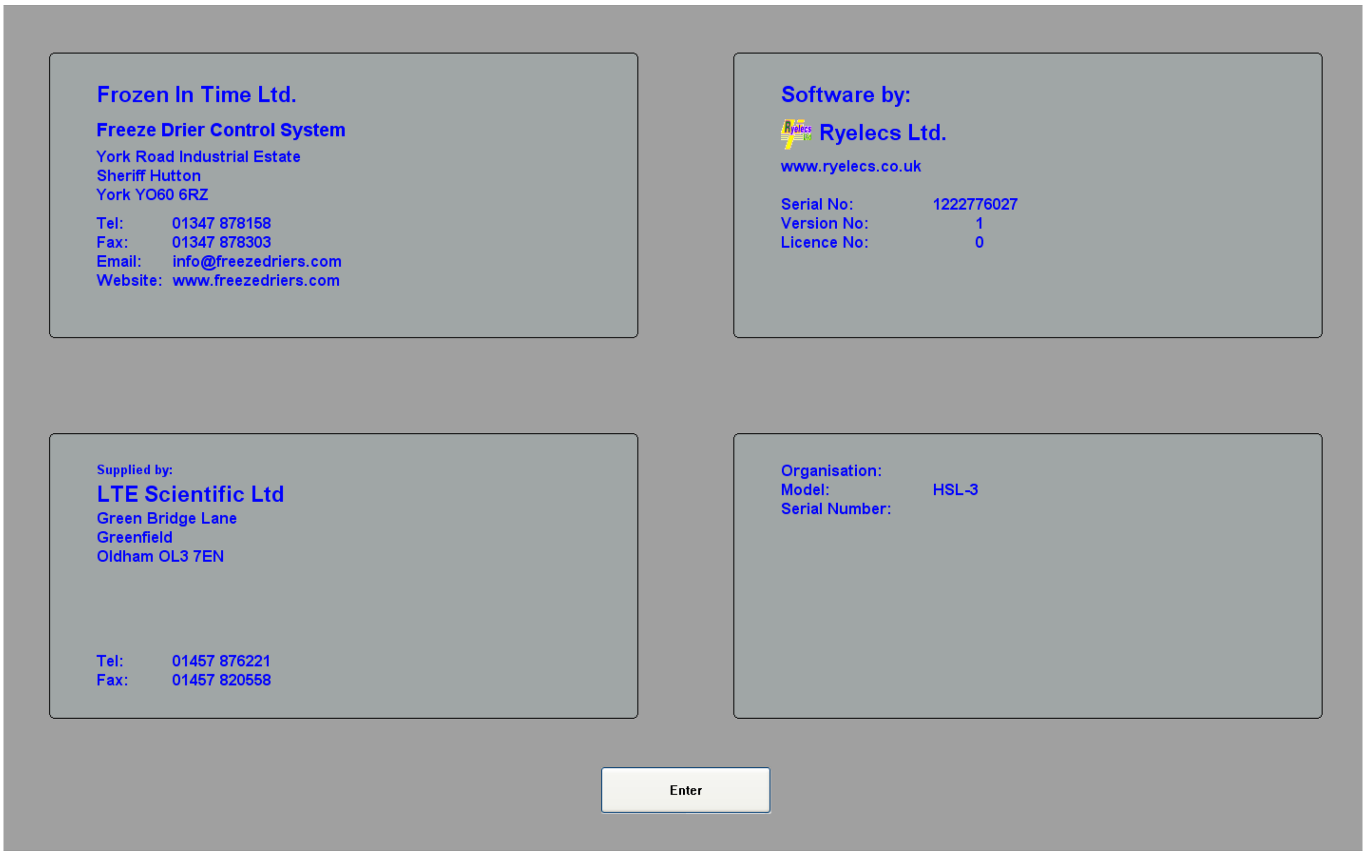
- 240V circuit
- 24Vdc circuit
- 24Vac circuit
- Hinge movement in
- Hinge movement out
- Circulation pump
- Refrigeration compressor 1
- Refrigeration compressor 2
- Immersion heaters 1,2 &3
- Defrost heaters
- Vacuum pump
- Hydraulic motor

Please see wiring diagrams for more detailed information.

6. The control system

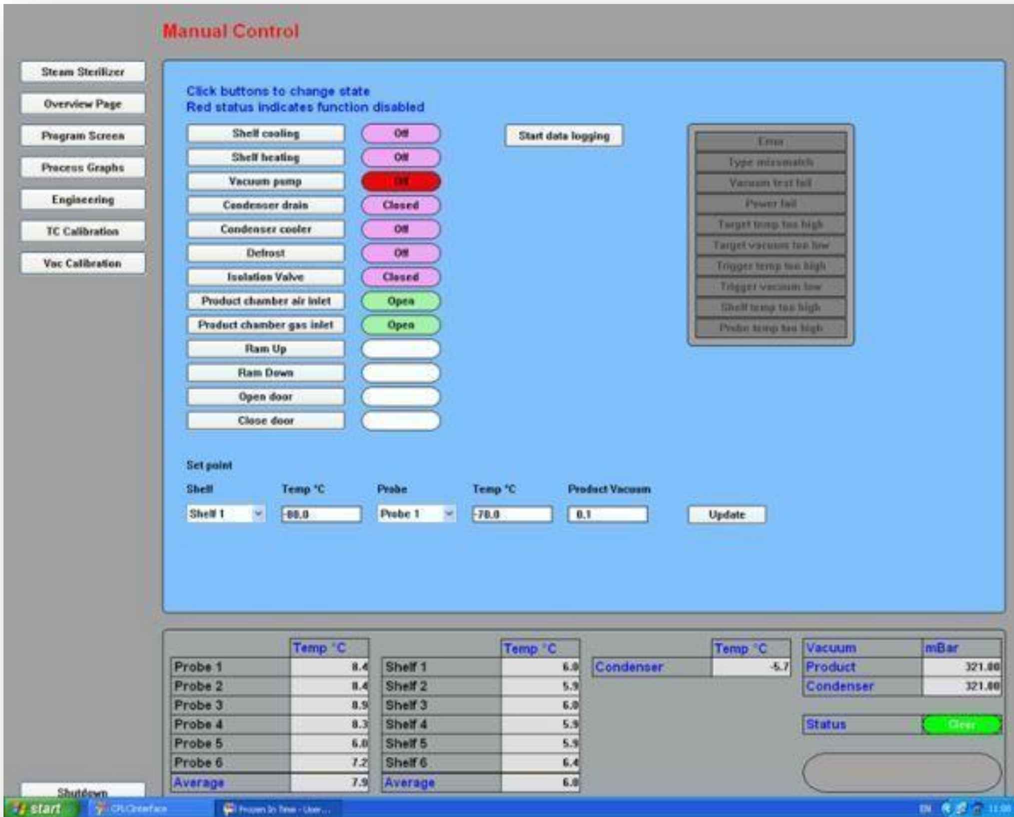
The control system for the freeze drier enables the operator to run the freeze drier fully automatically or manually. All data from the drying processes can be logged, saved and printed. The automatic cycles are easily programmed by the operator and can be saved or edited for later use. Programs can be changed while the cycle is running. There is a manual screen for complete manual control. This is often used when trying out a new product before a program is confirmed. The data logging and programming are done on the PC. The running of the program is looked after completely by the PLC. If there is a power failure the computer will safely shut down with the use of a built in uninterruptable power supply.

6.1. Start up Screen



This screen will appear on start up. Details of the machine Manufacturer, and any supply company. The model, serial number and owner details are also on display. Press Enter to start the program.

6.2. Manual Control Screen for Freeze Drying



This screen is for manual control. To change to another screen there are selection buttons down the left hand side:

- Steam Sterilizer
- Overview Page
- Program Screen
- Progress Graphs
- Engineering
- Thermocouple Calibration
- Vacuum Calibration

Next are the function buttons that are used to operate the freeze dryer. To the right of each button is the function indicator.

Pink means that the function is off but can be activated.

Green means that the function is active.

Red means that the function is off and cannot be activated due to a current lock on the function. During an automatic run all the manual function buttons are locked.

The function buttons include:

- Shelf Cooling
- Shelf heating
- Vacuum Pump
- Condenser Drain Valve
- Condenser Cooler
- Defrost
- Isolation Valve
- Product chamber air inlet
- Product chamber gas inlet
- Ram up
- Ram down
- Open door
- Close door

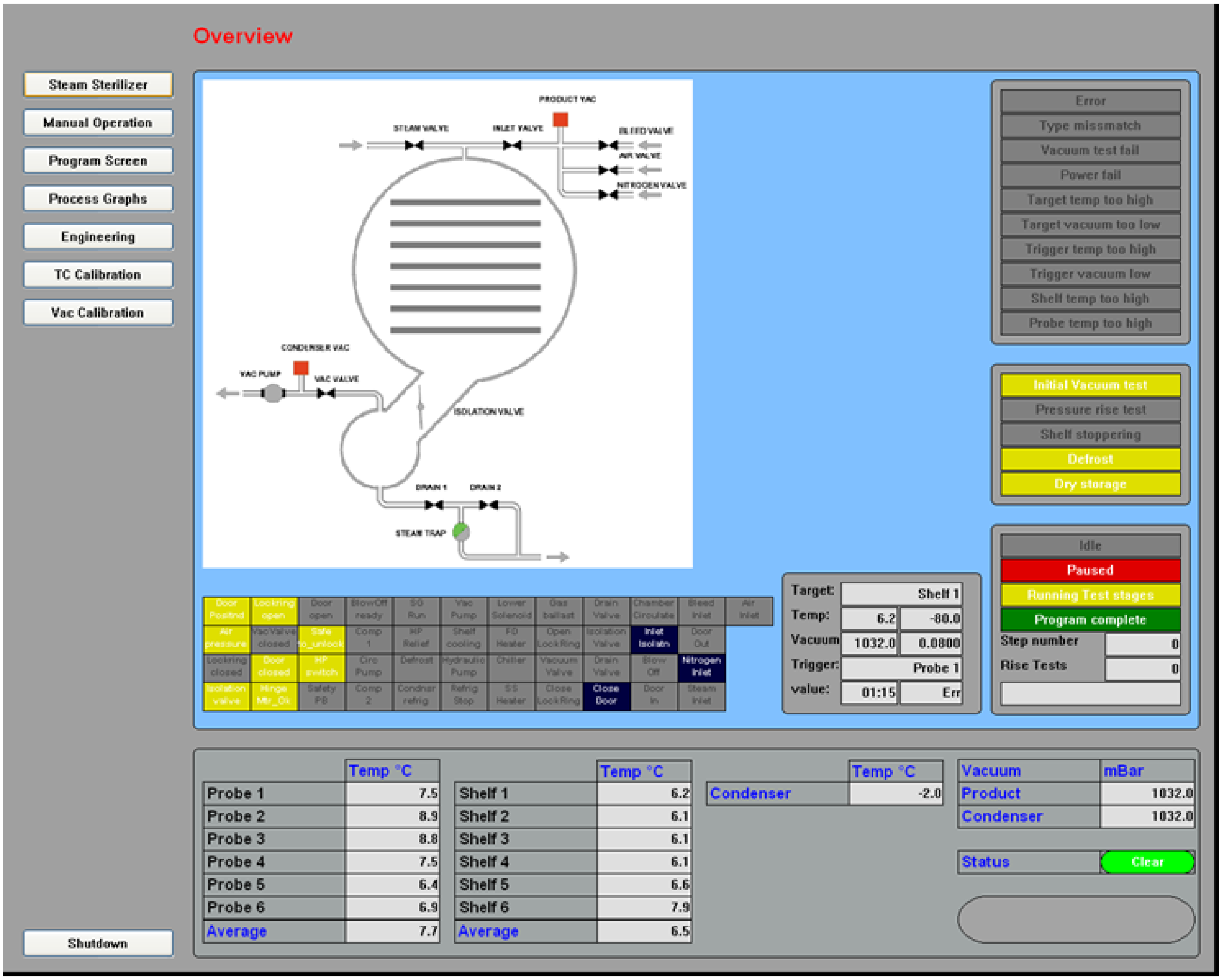
The ram function buttons need to be selected before operating the ram. Only one direction can be selected at a time up or down. To operate the ram both of the push buttons on the front panel need to be pressed simultaneously. This is to prevent the operator from trapping a hand in the closing device while the door is open.
On the right are the graph data logging start/stop buttons. These will activate the recording of temperatures, pressures and time on the graph page.
Further to the right are the error readings. Please see section 7.17. Computer error readings for further information. On the far right are the temperature readouts of the shelves, probes and condenser. Below that are the vacuum levels of each chamber indicated in millibars.

Set points are required to control temperatures and vacuum levels. If the product is to be lowered in temperature then it will be cooled by the shelf. There is a thermal lag between the shelves and the product due to the speed of thermal conduction. For fast cooling set the temperature of the shelf lower than the target temperature of the product probe. Once the product probe temperature has reached its set point or the shelf temperature reaches its set point then the cooling will stop.

For example:
The shelf temperature is set at -60ºC and the probe temperature is set at -40ºC. If the shelf reaches -60ºC before the product probe reaches -40ºC then the shelf will hold at -60ºC until the product probe reaches -40ºC. If the probe temperature reaches -40ºC before the shelf temperature reaches -60ºC the product probe will control the shelf temperature. The same principle applies when heating. The shelf can be set higher to allow the product to heat up quicker.

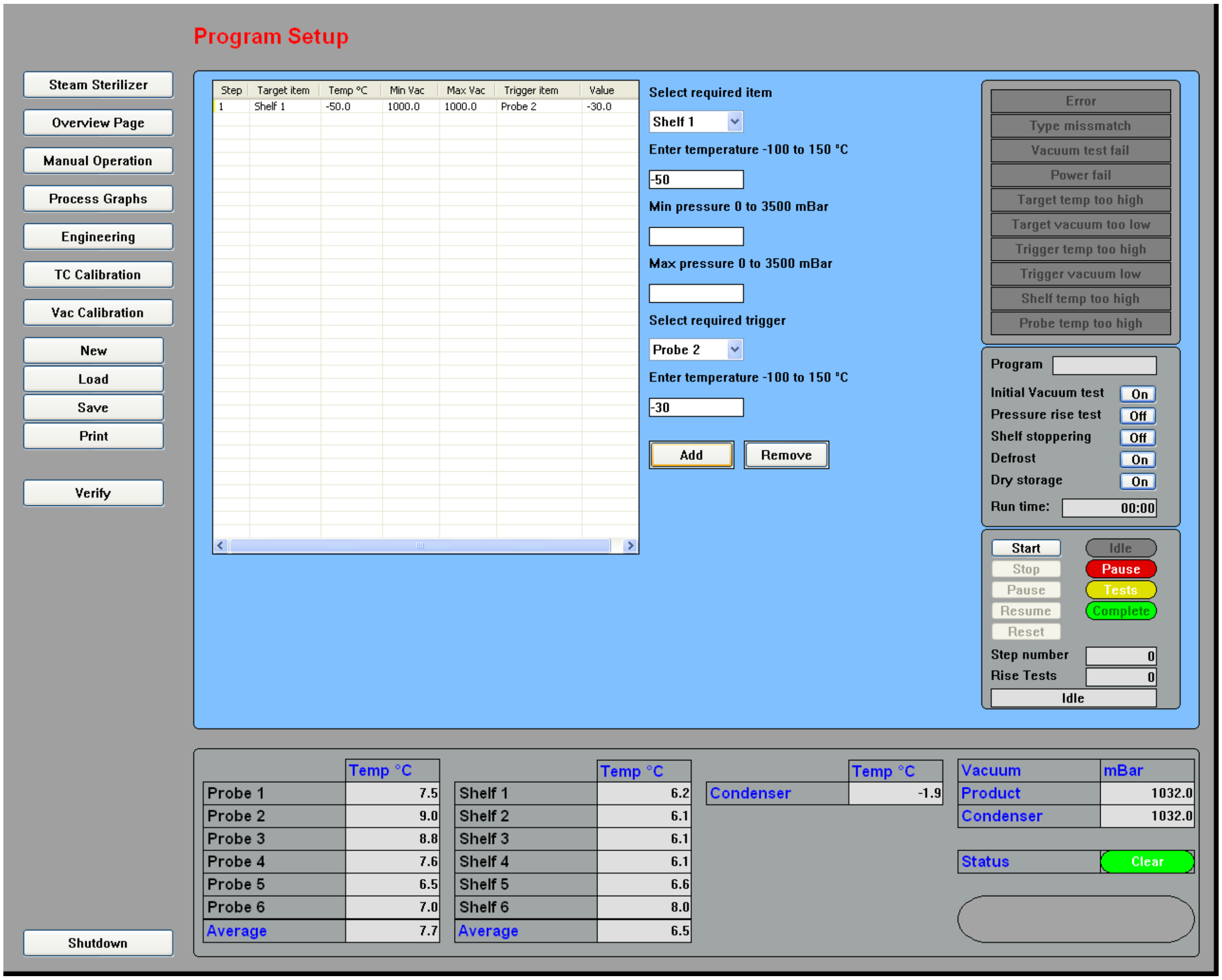
A further control on shelf heating is vacuum level. If vacuum pressure rises above its set point, heating is deactivated. As sublimation slows down the vacuum level will drop below the set point and heating switches back on.

6.3. Overview screen



This screen is for is an overview of the freeze drier it shows what parts of the freeze drier are running.
Vacuum and temperature set points, program step number and running status are also displayed.
PLC Inputs and outputs are shown in the grey boxes. Inputs turn yellow and outputs turn blue when they are active.
These are not intended for general use but more for fault finding.

6.4. Programming screen



The Program setup screen is for programming the automatic freeze drying cycle. To change to another screen there are selection buttons down the left side as on previous pages.

There are also options for:

- New - creating a new programs
- Load - load an existing program
- Save - save a program
- Print - the details of a program
- Verify – that program is within the capability of the freeze drier.

Next is the program step list. The automatic cycle is made up of programmable steps. The steps are entered using selection boxes directly to the right.

There are also 5 pre-programmed steps that can be included in the program.

- Initial vacuum test
- Pressure rise test
- Shelf stoppering
- Defrost
- Dry storage

The selection boxes enable steps to be added. These include:

- Select required item (which shelf or probe to use)
- Select target temperature
- Target vacuum (if a vacuum is to be maintained)
- Select required trigger (time, temp or vacuum)
- Select trigger value (a value time, temp or vacuum)

Steps can be copied, moved, edited or deleted.
The usual indications are given in the error code box. The right side shows the live temperatures and vacuum levels.
To start the program, press the start button. If it is to be stopped during the cycle, press the stop button or the pause button. At this point the cycle can be reset or resume.

Program setup

The program setup requires the input of a sequence of steps to complete a freeze drying cycle. The operator will define the running conditions within a step and an achievable value to prompt the next step. This value may be a temperature, a vacuum level or a time delay.
When a temperature is entered, the operator will need to specify which temperature probe is to be used.
Each shelf has a built in probe, these probes are listed: Shelf 1, Shelf 2………..
Each shelf has a mobile product probe, these are listed:
Probe 1, Probe 2…
When a vacuum is not required for initial freezing then this box can be left blank.
The following is a simplified example of programming a freeze drying cycle to explain the procedure.

Pre step

The operator may choose to activate the pre step listed as “**Initial Vacuum test**” this ensures that the chambers are going to be vacuum tight before the process is allowed to start.

Entering the first step

This is where a shelf or probe can be chosen for setting a target temperature. A triggering condition is set to initiate the next step.
To freeze the product to -40ºC the operator could do the following:

The first method
Select the required item as a shelf 1 temperature at -50ºC which would allow the shelves to cool down to this point. As the shelves cool down so will the product. The trigger Item would be a product probe 1 set at -40ºC. Upon reaching this the next step will be activated. Depending on the type or quantity of product, the thermal lag between the shelves may vary. In the time it takes the product to reach -40ºC the shelves may or may not reach -50ºC however they will not go below.
The disadvantage of this is:
Setting a minimum shelf temperature gives a constant temperature to absorb heat from the product. As the product temperature gets closer the temperature difference gets less. Therefore the rate of cooling is reduces. Freezing will take longer.
The advantages of this are:
The overall Product temperature will be much more even.
There is less chance of product temperature over shoot.

The second method
Select the required item as a probe 1 temperature at -40ºC. Set the trigger item probe 1 at -40ºC. This way the shelf will cool as cold as is possible for the refrigeration system.
The disadvantages of this are:
The overall Product temperature will be much less even.
There is more chance of product temperature over shoot.
The advantage of this is:
Fastest rate of cooling due to greater temperature differences between product and shelf

Entering the second step
A time step could be used to allow the product to stabilize in temperature. The temperature of the product probe can stay the same so probe 1 is set to -40ºC. If the time step was set to one hour, the next step would be triggered after this time.

Entering the third step
The third step could be to create a vacuum on the product.
The temperature of the product would not need further cooling so probe one would remain at -40ºC. A vacuum trigger would be selected next with a value of 0.1mbar. The condenser chamber would be automatically cooled to -30 ºC and the vacuum pump would start.
Once 0.1mbar has been reached the next step would trigger.
As this is the first step that the vacuum is used a value can be into the target vacuum box. This is the vacuum control setting. This setting will prevent the heater from activating while the vacuum level is above the value entered. As the probe 1 temperature is set at -40ºC the system would try and maintain this using heating or cooling. As the vacuum level improves the product will cool by sublimation so the heater would attempt to counter this.
Entering a value into the target vacuum box the same as the trigger value would prevent the heater from activating and allow natural vacuum cooling. The temperature will drop depending upon the level of vacuum created. If the box is left empty or a higher value is entered than the value in the target box then the heater would attempt to maintain probe 1 at the set temperature. Due to the heat input there will be more sublimation occurring while initial vacuum is being drawn. This will increase the length of time taken to achieve the initial vacuum level.

Entering the fourth step
The fourth step would be to heat the product up to 40ºC while maintaining a vacuum level below a set point. This set point is of most importance at the beginning of the primary drying stage when the sublimation rate is at its highest. If the vacuum level rises above a set value then the ice in the product will start to melt. The vacuum control level will ensure that the ice core of the product stays frozen. To achieve the maximum rate of sublimation the vacuum level must correspond to a vapour pressure of a temperature as close to the eutectic point as is safely possible.

With regards to setting the temperatures similar methods as in the first step can be applied. Set a maximum shelf 1 temperature, reducing the chances of over shoot, but expect heat transfer to take longer. Or allow the shelves to heat up to their maximum temperature allowed (settings are in the engineering page) increasing the heat transfer rate, but also increasing the chances of product temperature overshoot.

Entering the fifth step
The fifth step could be a time step to allow the product to stabilize in temperature.
The temperature of the product probe 1 can stay at 40ºC. If the time step was set to one hour, the next step would be triggered after this time.

Entering the sixth and final step

The sixth step in this example would be secondary drying. This can be considered as another vacuum step.

The temperature of the product does not need further cooling. Select a trigger item as vacuum, with a value of 0.05mbar. When 0.05mbar is achieved it is the end of the programmable steps. If selected there may be some post steps to complete.

Notes:

Usually programming an automated freeze drying process will involve many more steps detailed steps. As there are several shelves it is sometimes important to repeat each temperature step for each shelf or product probe. This will ensure that every probe reaches the set points required.

Post steps

These include;

- Pressure rise test
- Shelf stoppering
- Defrost
- Dry storage

The pressure rise test if selected will occur after the last of the programmed steps has ended. The isolation valve will close. An initial vacuum reading in the product chamber will be taken. After a preset timer has lapsed another vacuum reading will be taken. If the pressure rise is within an allowable range then the next post step will activate. If the pressure rise is too high then the valve will re open and drying will continue for a time span before retesting.

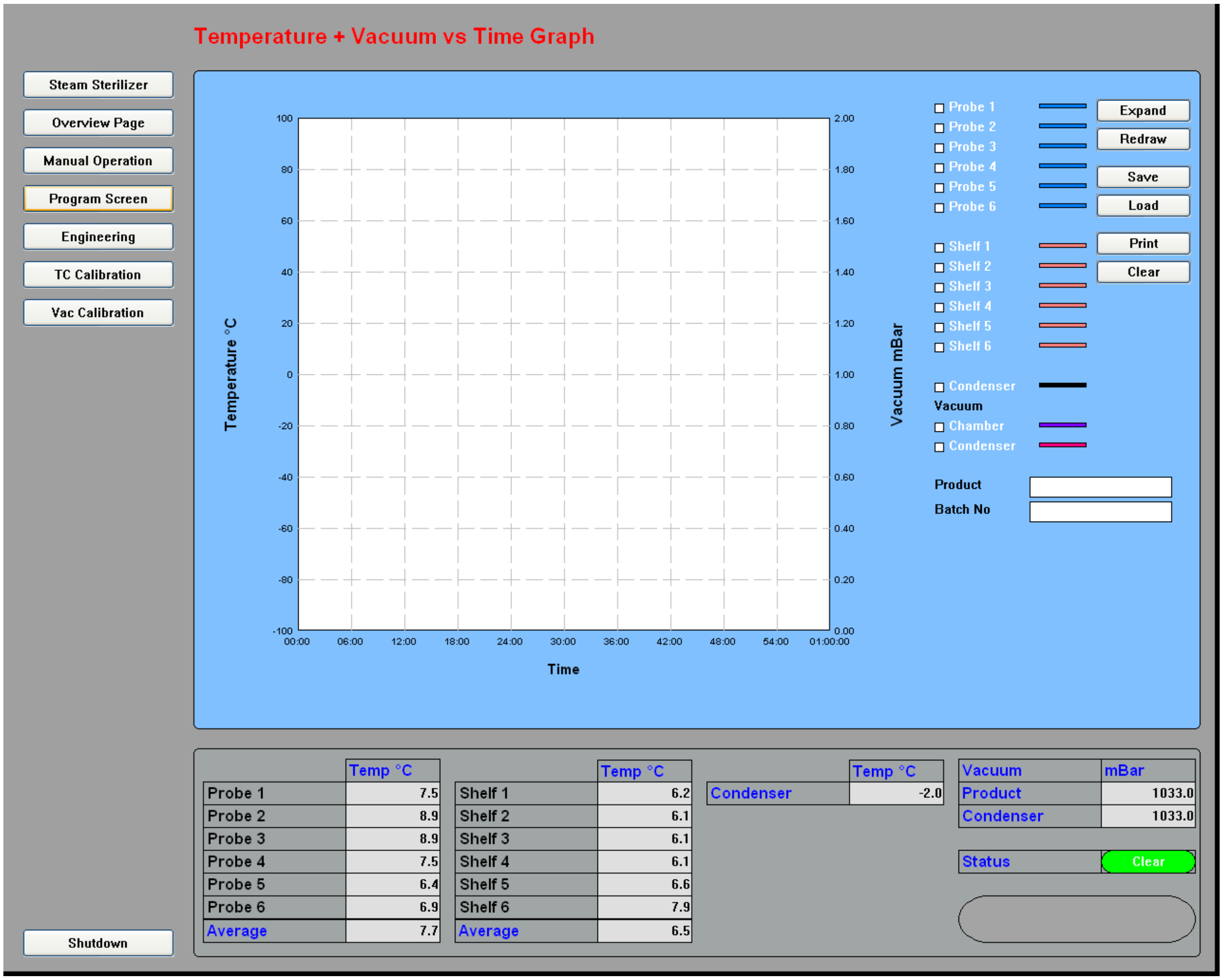
The shelf stoppering will follow if selected. This consists of three timed stages. The timers are adjustable on the engineering screen. Depending on the operators requirements, vials may be closed with a vacuum inside or with an inert gas fill. See engineering screen for settings.

If defrost is selected the condenser drain will open and defrost will activate. It will run for a preset length of time and not exceeding a preset temperature.

Dry storage is a means of storing the product within the freeze drier at a controlled temperature once the process has ended. This is useful if the product finishes its process in the middle of the night and there are no operators to unload it. If products are usually transferred to a fridge after drying then the freeze drier can match these conditions for ideal storage until unloading can take place.

The settings for the post and pre steps can be altered within the engineering screen.

6.5. Progress graph screen

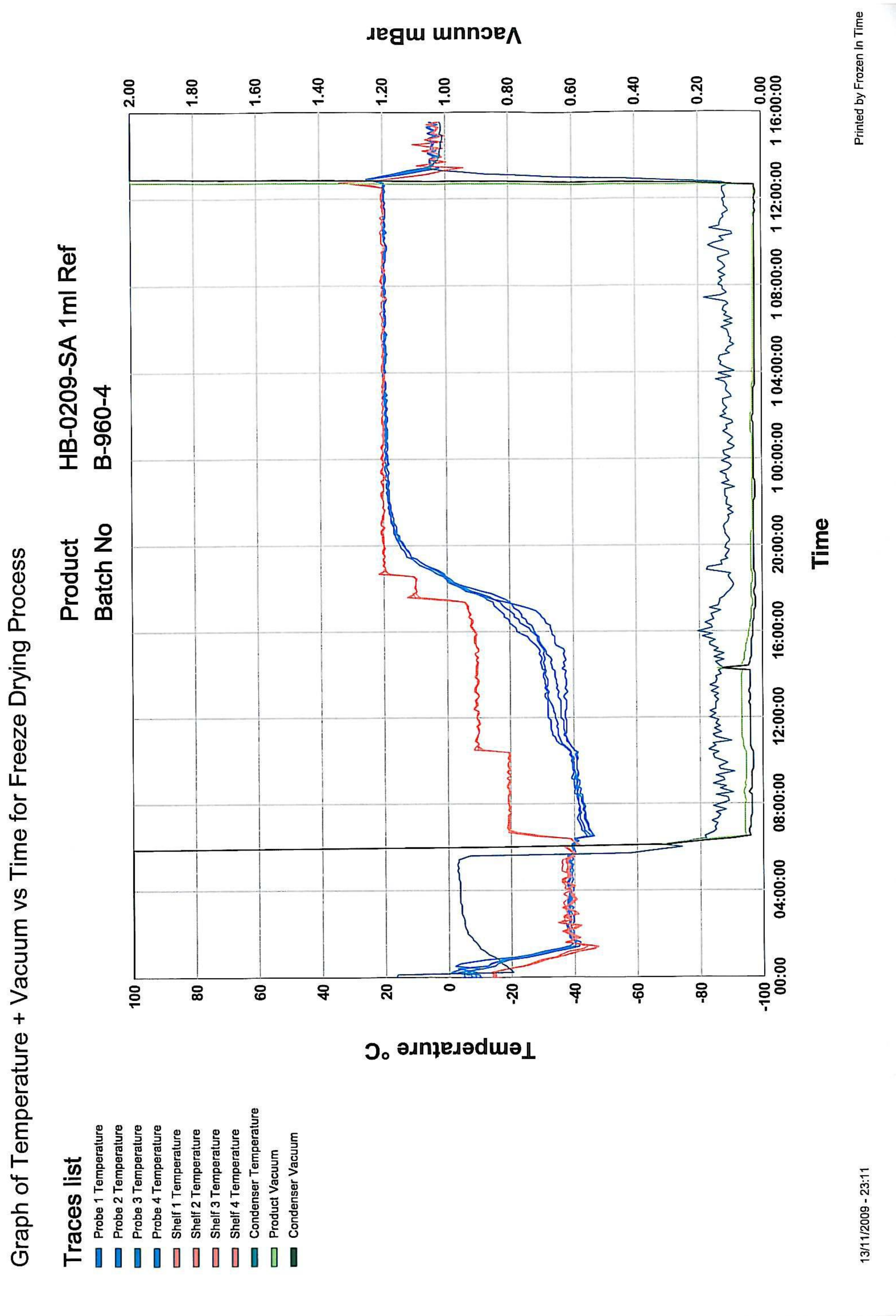


The data logging monitors temperatures of all mobile probes, shelves, condenser and vacuum levels. Information on temperature and vacuum changes becomes very easy to analyze on a line graph. Lines can be hidden to show the lines that are most important. Lines can be given separate colours for easy identification. Zoom and scale are available to pin point curves of most importance. The graph will auto scale as the cycle runs. The information can be saved or printed for records of products and individual batches. The graph will auto save as the program is running in case of a power failure.

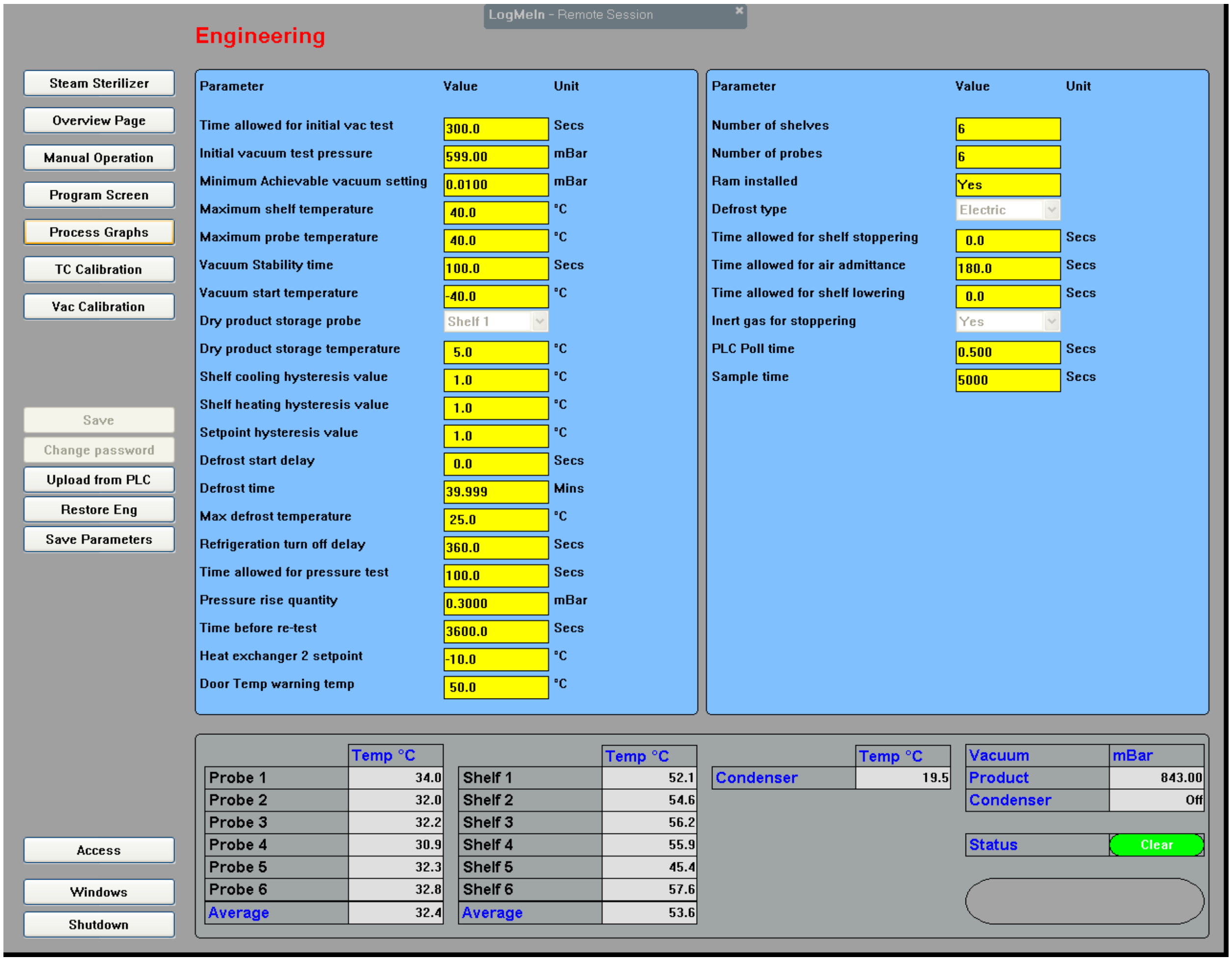
The Steam sterilization Graph page looks the same apart from the red background and the temperature and pressure scales are different.

6.6. Graph print out of the Freeze Drying Cycle

Below is an example of a cycle printout. On the left there is a key to identify graph lines. Product and Batch identification appear as the heading.



6.7. Engineering screen



The engineering screen is password protected to stop unauthorized alterations to running parameters.
There are two levels of password protection, the first is accessible by an authorized operator who would find it necessary to change settings between different products. The next level is only accessible for equipment setup.

Time allowed for initial vacuum test

This is the time that the vacuum pump will run during an initial vacuum test to confirm the chamber is leak tight before an automated program can start. A moderate vacuum level is set of approximately 600 mbar to confirm doors are closed and the vacuum pump is switched on at the motor. Depending on the volume of the chamber, a sensible time is allowed for this test. As soon as the vacuum level is achieved within the time frame, the test is complete. If the required vacuum is not achieved within the set time the program will not commence. The problem will require investigation.

Initial vacuum test pressure

This is the box were the vacuum level is entered. As mentioned above a sensible setting is 600 mbar, this is only achievable with a leak tight vacuum system. This vacuum level will not adversely affect unfrozen product.

Minimum achievable vacuum setting
This setting is to prevent an operator programming the automated cycle with unachievable vacuum level.

Maximum shelf temperature
This setting is to prevent the temperature of any shelf from exceeding a desired limit. It also prevents any values above this level being entered into the programming steps.

Vacuum stability time
The vacuum pump will only start when the condenser temperature is below a set level (Vacuum start temperature). As the temperature drops in the condenser temperature it may fluctuate around the temperature set point momentarily.
A time delay (vacuum stability time) will stop the pump switching on and off while the temperature hovers around the set point.

Vacuum maximum during drying
This is a vacuum set point that would indicate a failure in the system. If the vacuum level reaches this point then the cycle will go into a safe mode and the product will freeze down to -40ºC. As vacuum level is not being maintained it would indicate a vacuum failure, to prevent the product from melting it will be refrozen. This set point needs to be safely below the products eutectic point but not within normal running parameters. Reaching this set point will end the automatic cycle and keep the product frozen for the operator to investigate the vacuum failure.

Vacuum start temperature
This is the temperature set point that does not allow the vacuum pump to start until the condenser temperature is below it. Usually set at -30ºC. This will stop unfrozen water vapour being drawn into the vacuum pump.

Dry product storage probe
This is the product or shelf probe that is used to control the temperature when the freeze dryer is in dry storage mode. Dry storage can be selected to run after the automated freeze drying cycle has ended if the product is not unloaded straight away. If a cycle ends during the night and the operator cannot unload the freeze drier, preferred conditions such as fridge temperatures can be matched on the shelves. A product or shelf probe may be chosen for this control.

Dry product storage temperature
This is the temperature that dry product will be controlled to if dry product storage is selected.

Shelf cooling hysteresis
To achieve shelf temperature control and eliminate rapid switching between heating and cooling, hysteresis values can be entered. A typical value would be 1ºC would be set at the factory. This could be altered on the engineering screen by the operator.

Shelf heating hysteresis
To achieve shelf temperature control and eliminate rapid switching between heating and cooling, hysteresis values can be entered. A typical value would be 1ºC would be set at the factory. This could be altered on the engineering screen by the operator.

Set point hysteresis
This is a general set point for other thermal controls including defrost and condenser refrigeration.

Defrost start delay
Condenser chamber defrost. This a time delay before the defrost starts.
The defrost is electrical on the HSL-3 but on the HS-3 it is hot gas defrost.

Defrost time
This is the time that the condenser chamber will be heated for. A setting that will give enough time to melt all the condensed ice is required. This can be set by the operator to suit the application of the freeze drier.

Maximum defrost temperature
This is the maximum temperature that the condenser temperature is allowed to reach while defrosting.

Refrigeration turn off delay
The compressors of the refrigeration system will continue to run for a period of time after the refrigeration has been switched off. This will prevent liquid refrigerant being left in areas of pipe work that are exposed to high temperatures.

Time allowed for pressure rise test
The end of the automated cycle has the option a pressure rise test. This is where the product is sealed off in the product chamber to see if sublimation has finished. If the pressure rises above the set limit (pressure rise quantity) it can be considered to not be dry, as sublimation is still occurring. If the pressure rise is within limits the product is dry. For the pressure rise test there is a set time frame that the pressure rise can occur within.

Pressure rise quantity
The end of the automated cycle has the option a pressure rise test. This is where the product is sealed off in the product chamber to see if sublimation has finished. If the pressure rises above the set limit it can be considered to not be dry as sublimation is still occurring. If the pressure rise is within limits the product is dry. For the pressure rise test there is a set vacuum level that is allowable. A rise above this pressure indicates that the product is not dry and the test has failed.

Time before retest
A fail is if the pressure rises beyond the allowable **pressure rise quantity** within the **Time allowed for pressure rise test.** Time before retest is the time that the product will have back under drying conditions before the next test.

Heat Exchanger 2 set point
The R23 stage of the cascade refrigeration system will switch on and off around this temperature set point. This is the inter stage heat exchanger L066. It works as the condenser for the R23 refrigeration system and is cooled by the High stage refrigeration, the R507. This set point is adjustable but may only need changing if operating conditions have altered. Otherwise there is no need to adjust it. A value out of the normal range would stop the refrigeration from working. The normal range should be around -10°C. If it is set to high the R23 refrigeration system will cut out on its high pressure switch S050. If it is set to low it will not switch on at all.

Door Temperature Warning temp
The door will get hot during steam sterilization. There is an on screen display to warn the user if the door is hot. A suitable temperature level may be entered here. For example set it at 60°C and the warning light will come on when the door goes above 60°C It will switch off when the door cools down below 60°C.

Number of shelves
The number of shelves fitted to the machine. This will be set up in the factory. The right hand side live temperatures will rearrange on the screen to evenly fill the space available with the correct number of shelf temperature boxes.

Number of probes
The number of product probes fitted to the machine. This will be set up in the factory. The right hand side live temperatures will rearrange on the screen to evenly fill the space available with the correct number of product probe temperature boxes.

Ram installed
Some freeze driers do not have a vial closing device and therefore do not have a hydraulic ram. This will be set up in the factory. If there is no ram installed then NO will be selected. If a ram is installed, YES will be selected.
Screen function buttons will adjust appropriately.

Defrost type
This will have been selected at the factory.
This machine uses electrical heating elements

Time allowed for shelf stoppering
During automatic vial closing the ram will raise up to close the shelves together and seal the vials. This is the time allowed for this procedure and is set at the factory.

Time allowed for air admittance
Air or an inert gas can be admitted into the product chamber. If the product is to be sealed under vacuum then air should be adequate for back filling the chamber once the vials are sealed. If the vials are to be filled with a partial or full pressure of inert gas, nitrogen for example should enter before the vials are closed. The air or gas enters the chamber through solenoid valves. The valves are quite small and time taken for back filling the chamber can be several minutes. A value is entered that gives enough time for the chamber to reach an appropriate pressure, either partial or full. Tests can be made to help arrive at an ideal time frame. This will be set up initially in the factory.

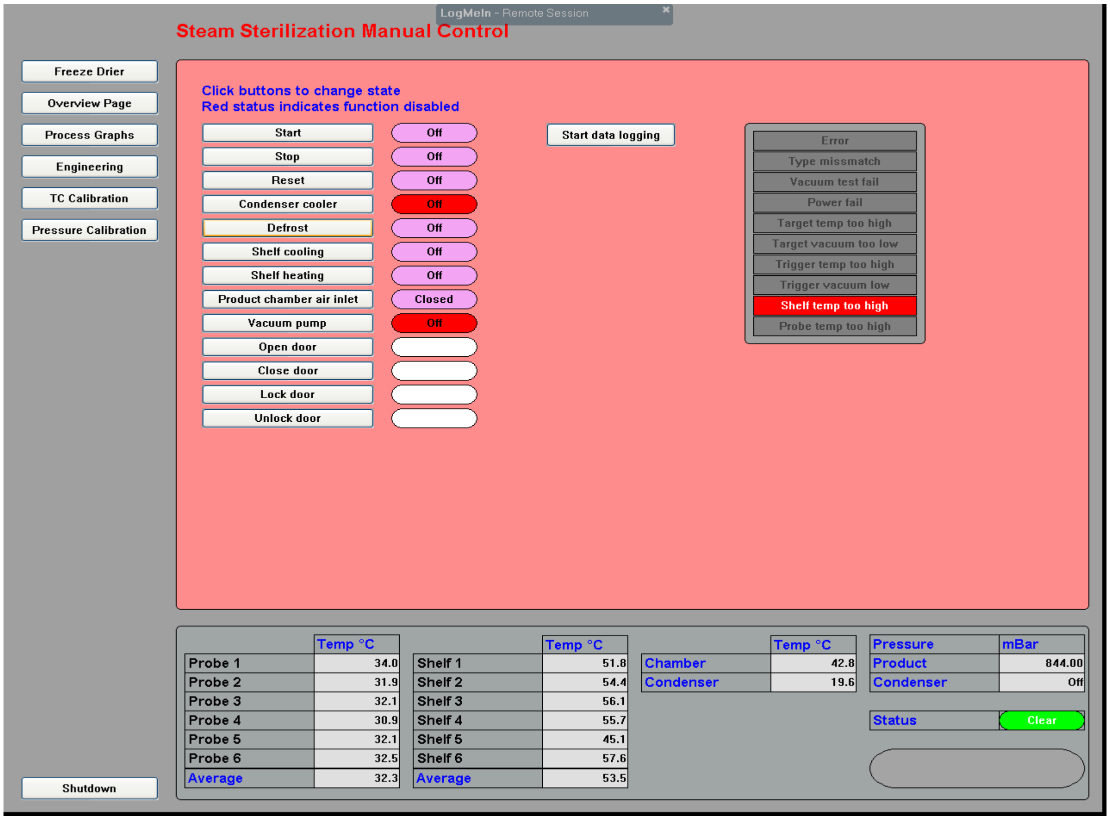
Time allowed for shelf lowering
Lowering of the shelves requires the opening of a release valve allowing the shelves to lower. This is the time allowed for this procedure and is initially set at the factory.
If it is preferred that the shelves are left closed at the end of the automated process, the value should be 0 seconds.

Inert gas fill
Air or an inert gas can be admitted into the product chamber. If the product is to be sealed under vacuum then air should be adequate for back filling the chamber once the vials are sealed. If the vials are to be filled with a partial or full pressure of inert gas, nitrogen for example should enter before the vials are closed. The air or gas enters the chamber through separate solenoid valves. Select YES for inert gas fill and NO for air fill.

PLC poll time
If displayed this will give the communication speed between the PC and the PLC

Sample time
If displayed this will show the sampling speed of the temperature and vacuum sensors

6.2. Manual Control Screen for Steam Sterilizer



This screen is for manual control. To change to another screen there are selection buttons down the left hand side:

- Freeze Drier
- Overview Page
- Progress Graphs
- Engineering
- Thermocouple Calibration
- Vacuum Calibration

Next are the function buttons that are used to operate the freeze dryer. To the right of each button is the function indicator.

Pink means that the function is off but can be activated.

Green means that the function is active.

Red means that the function is off and cannot be activated due to a current lock on the function. During a steam sterilize run all the manual function buttons are locked.

The function buttons include:

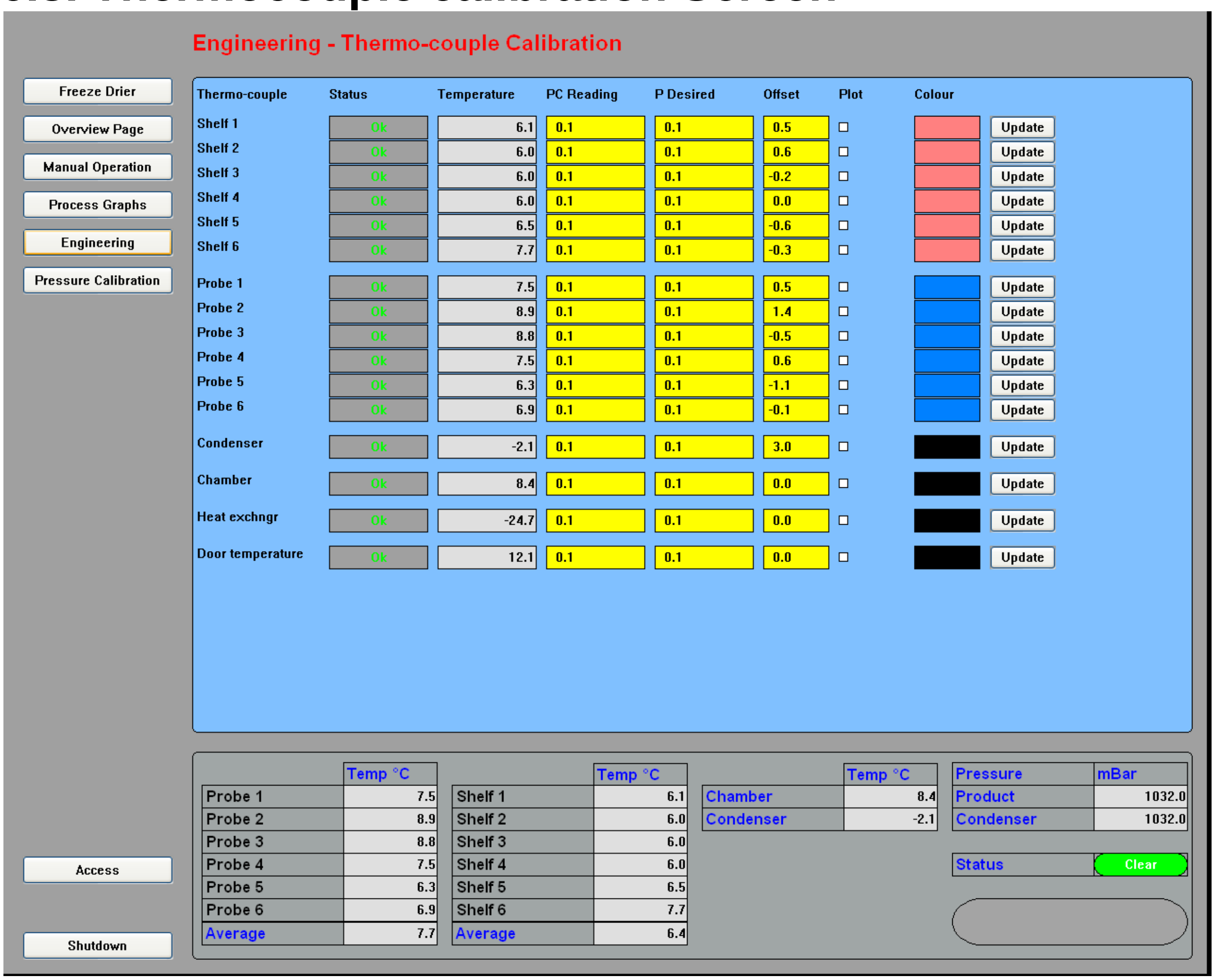
- Start
- Stop
- Reset
- Condenser Cooler
- Defrost
- Shelf Cooler
- Shelf heating
- Isolation Valve
- Product chamber air inlet
- Open door
- Close door
- lock door
- Unlock door

As on the Freeze drier manual page temperature and vacuum readings are given along the lower edge of the screen.

Start up of steam sterilize.

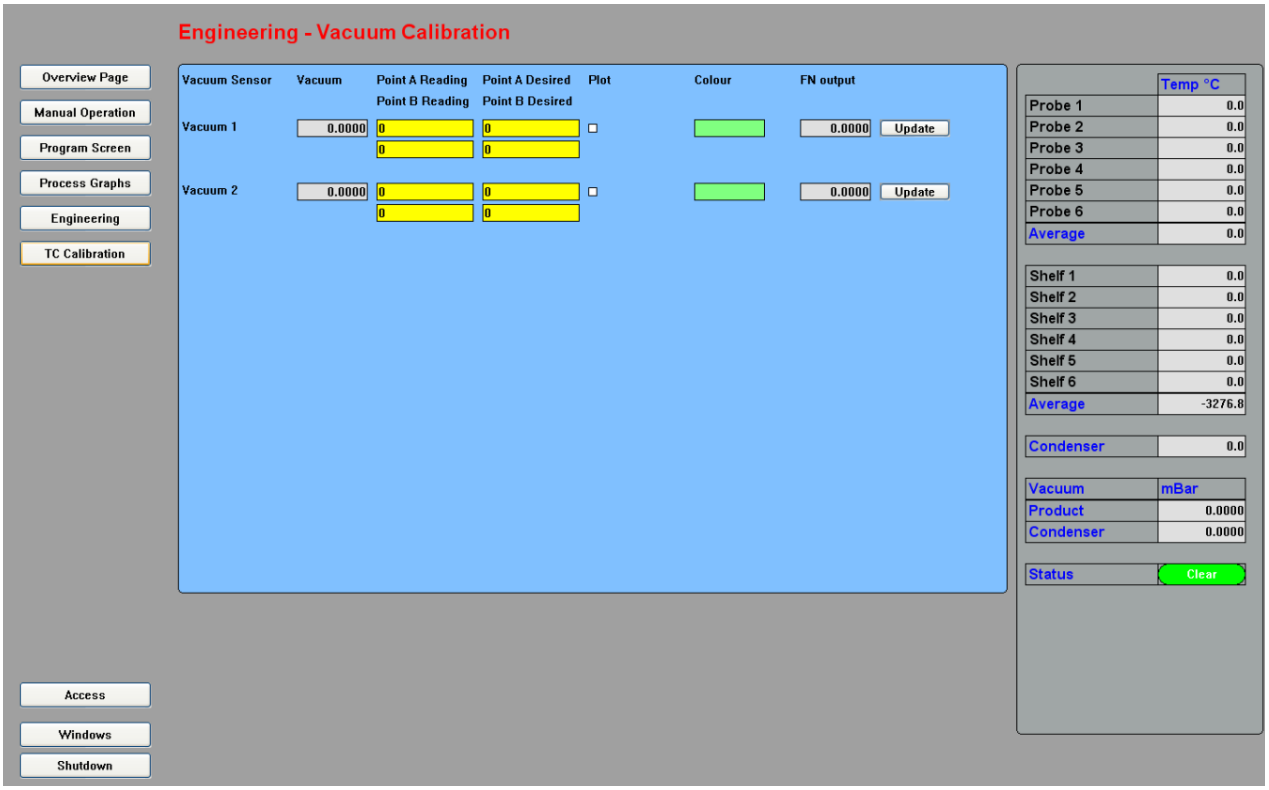
To start up a steam sterilize sequence process the door must be in the closed position. Then press the start button. The steam sterilization process will run using the parameters in the engineering page. The cycle can be left to run for its whole process on its own. If the cycle is to be stopped press the stop button. After pressing the stop button press the reset button. This will cancel the current steam sterilize process. If there is a power cut during the steam sterilize process then it must also be reset. Manual controls will allow the operator to cool the condenser to collapse the vacuum or open the drain valve to release the steam.
No freeze drying program can be run until the reset button has been pressed.
The door cannot be unlocked until there is a vacuum in the product chamber of less than 5mbar.
Once below 5mbar (or value set on the engineering page) the door can be unlocked. Note: The reset button must be pressed first if the cycle was stopped.
The chamber and shelves will now be dry due to the remaining high temperature and the vacuum level that they have been subjected to. The shelves and chamber will now begin to cool down further until they reach the Post Sterilize shelf temperature.

6.8. Thermocouple calibration Screen



This screen is for factory setup or periodic temperature calibration. Sensor connection status, PLC temperature reading, correction scaling and offset can be set to give the correct reading.

6.9. Vacuum calibration Screen



This screen is for factory setup or periodic vacuum calibration. Sensor connection status, PLC Vacuum reading, correction scaling and offset can be set to give the correct reading.

6.10. How to access the WINDOWS Screen

In order to exit the freeze drier software and access the Windows screen the operator must select the Access button on the engineering page. The daily access code must be entered. This gives access to all the adjustable value. Then select one of the other screens. On the lower left above the shutdown button there will appear a Windows button.
When this is pressed it will enable the operator to access windows, the freeze drier software will continue to run in the background.

7. Troubleshooting

7.1. Power failure

The freeze drier will resume its program or settings after a power failure. In the event of a power failure in the drying phase, the batch may become unusable. Whether the batch can be saved or not depends on the drying phase in which the product was in when the power failure occurred. If power returns within a few minutes then it is unlikely that any damage will have occurred. It is important to distinguish between the primary drying phase and the secondary drying phase. The product is in the secondary drying phase if the residual moisture has reached approximately 5 %. Below this value, the product is generally not damaged by a power failure.
If the product is in the primary drying phase, it is recommended that the product is refrozen.
It is also advisable to defrost the condenser chamber at this point.
If the product is considered to be still usable then freeze drying can restart.

7.2. Insufficient vacuum

Is the vacuum pump is running? If not:

- Check that the vacuum pump circuit breaker has not switched off.
- Check that the contactor is operating.
  If the vacuum is sufficient on the condenser chamber but significantly worse on the specimen chamber:
- Check that air admittance and inert gas valves are closed on the overview or manual screen.
- Check all vacuum connections on specimen chamber including door seal. Repair or replace.
- Check for oil leakages from the shelf thermal fluid. Oily residue may collect in the chamber.
- Check for water from cleaning or spilled product residue, this may vaporize preventing vacuum.
- Remove panels and listen for leaks after a vacuum evacuation has been tried.

If the vacuum cannot be achieved in the condenser chamber with the isolation valve closed:

- Check all vacuum connections on condenser chamber including door seal. Repair or replace.
- Check the condition of the isolation valve sealing surface. Glass pieces from broken vials can slit the rubber seal. If there is a doubt about this coat in vacuum pump oil or vacuum grease and test to see if there has been an improvement in the vacuum level.
- Check that there is no suction on the condenser drain hose. This would indicate a leaking valve.
- Check the vacuum pump is pulling an adequate vacuum, test with a separate vacuum sensor.
- Check that the isolation valve is sealing by opening it and pulling a vacuum on the product chamber as well, eliminating the seal of the valve.
  If the vacuum pump cannot achieve a sufficient vacuum then replace it or get it repaired.

7.3. The ram will not operate

If the ram is not raising

- Check that the Hydraulic pump circuit breaker has not switched off.
- Check that the contactor is operating.
- Check to see if the Hydraulic pump is running
- Check to see if the is any restriction to the shelf movement
  If the ram is not lowering
- Check that the shelves hangers are not restricting further lowering.
- Operate the release valve manually on the hydraulic pump to see if the ram lowers.
- Try to operate up and down using the external buttons on the electrical box.

7.4. Insufficient cooling of the condenser chamber

If the condenser chamber is not reaching the relevant temperature -85ºC
(Please allow 15% for high load conditions)

- Check to see if there is liquid flow in the refrigeration sight glass. Contact the manufacturer, supplier or a local refrigeration engineer.
- Check the circuit breakers for compressor 1, compressor 2 and fans.
- Check that the contactors are operating.
- Check the overview screen to ensure that refrigeration and condenser cooling are operating.

7.5. Insufficient defrosting of the condenser chamber

If defrost is not heating up.

- Check the circuit breaker for defrost
- Check that the contactor is operating.
- Ensure that defrost is activated on the overview screen
- Check that the settings in the Engineering screen are allowing its activation
- Check that temperature control is not controlled by a sensor that is malfunctioning and reading an incorrectly high temperature.

7.6. Insufficient cooling of the shelves

If the shelves are not reaching low set points or relevant temperature -70ºC

- Check the circuit breakers for compressor 1, compressor 2, fans and circulation pump
- Check to see if there is liquid flow in the refrigeration sight glass. Contact the manufacturer, supplier or a local refrigeration engineer
- Check that all the contactors are operating.
- Check the overview screen to ensure that refrigeration, shelf cooling and circulation pump are operating.
- Check that temperature control is not controlled by a sensor that is malfunctioning and reading an incorrectly low temperature.

7.7. Insufficient heating of the shelves

If the shelves are not reaching high set points or the relevant temperatures 60ºC or 135ºC .

- Check the circuit breaker for heater and circulation pump.
- Check that all the contactors are operating.
- Ensure that heater and circulation pump are activated on the overview screen.
- Check that shelf temperature control is not controlled by a sensor that is malfunctioning and reading an incorrectly high temperature.
- Check that there is not an unachievable vacuum set point entered preventing the heater from being activated.
- Check that the settings in the Engineering screen are allowing its activation

7.8. Fluctuations in shelf temperatures

If the shelf fluctuations are high it could be due low levels of thermal fluid in the system. Fluid levels should be topped up when the fluid is at its maximum operating temperature. This is when the level is at its highest it will ensure that no over flowing can occur later. Be sure to reconnect the nitrogen blanketing system after the fluid has been accessed.

Shelf fluctuations occurring when the fluid is below 0ºC. This can be caused when water vapour enters the thermal fluid and when it freezes it creates a flow restriction. Please contact the manufacturer, supplier or trained maintenance department. Maintaining a positive nitrogen blanket above the fluid prevents this situation from happening. See section **4.4 Nitrogen Supply**

Malfunctioning thermocouples can cause sporadic readings or solidly fixed irrelevant readings.

7.9. Defrost will not drain away

If the condenser chamber will not drain away after defrost it could be due to a blocked pipe. However first check that the drain valve is opening.

- Check the overview screen to see if the indicator shows that it is activated.
- Check to see if there is an air supply to both drain valves.

7.10. Air admittance will not open

If the vacuum cannot be broken in the product chamber the air admittance valve may not be operating. The air admittance is a slow operation. The sterile diaphragm will be opened for all operations apart from steam sterilization.

- Check that the overview screen valve labeled “Inlet Isolatn” is open.
- Check that the overview screen valve labeled “Air Inlet” or “Nitrogen Inlet” is open.
- Check that the sterile diaphragm inlet valve (V001) is open. If it is open the red marker will be visible on the top of the valve. If not check the air supply and solenoid electrical supply.
- Check that the solenoid coils on the inlet manifold are activating (V007) or (V008)

7.11. Isolation valve will not operate

If the Isolation valve does not operate:

- Check the overview screen to see if the indicator shows that it is activated.
- Check air supply to the valve. One supply will open it the other will close it. If neither supplies have pressure then there is a air supply problem. Check the solenoid electrical supply (V077) and (V078).
- If one supply has air and it is the wrong one then there is an electrical problem in the panel.

7.12. Doors will not seal under vacuum

If the doors will not seal under vacuum

- Check that the vacuum pump is running
- Close the isolation valve and check that the condenser can achieve a vacuum.
- Check to see if the door seal is installed correctly
- Close the product chamber door
- Open the isolation valve and see if the product chamber door pulls tight against the seal.
- Check to see if the vacuum level drops below atmospheric pressure.

7.13. Incorrect probe temperature

Incorrect probe temperatures can be due to

- Unplugged probes
- Broken thermocouples
- Thermocouples with loose connections
- Incorrectly calibrated thermocouples

7.14. Vials are breaking

Vials may break if:

- The wrong size of spacer has been used.
- The shelves are loaded unevenly
- Hydraulic relief valve has been adjusted too high.
- The vials remain on trays when the spacers do not allow for the extra thickness
- The vials have thicker stoppers when the spacers do not allow for the extra thickness
- The vials have been changed for a larger size when the spacers do not allow for the extra thickness

7.15. Vials are not closing

Vials may not close if:

- The wrong size of spacer has been used.
- The shelves are loaded unevenly
- Hydraulic relief valve has been adjusted too low.
- The vials have thinner stoppers when the spacers do not allow for the lower height.
- The vials have been changed for a smaller size when the spacers do not allow for the lower height
-

7.16. Trays are distorting

Large trays can have a tendency to distort with high and low temperature. Avoid using large trays where possible. When they are cold they tend to twist and when they are warm they tend to bow. The shelf to tray contact becomes less and freeze drying rates are reduced. If they must be used it is a good idea to clamp the sides down using the shelf closing device. Be careful not to restrict the flow of vapours from the trays to the condenser.

7.17. Computer error readings

On the lower right side of all screens there is a box giving the status of the connection between the PC and the PLC. If it is green and reading clear the connection is good. If it is red and the reading is PLC error the connection is bad or the PLC is switched off.

There is also a box of eight error messages that display on the programming and overview screens.

8. Maintenance

8.1. Condenser chamber

Before each start-up, ensure that condenser chamber is drained.

8.2. Heat exchangers

If the unit is water cooled it uses a chiller and these points will apply to the chiller.
The refrigeration heat exchanger is used to cool the refrigerant compressed by the refrigeration unit. The heat exchangers are located on each side of the unit and should be kept free of dust or dirt residues. The heat exchanger can be cleaned by brushing, using a vacuum cleaner from the outside or by using compressed air from inside of the unit. Excessive build up on the heat exchanger leads to a decrease in performance and may cause a failure of the unit.

8.4. Rubber seals

Special attention must be paid to the rubber seals. If the seals are dirty, they must be removed, cleaned and slightly greased with vacuum grease. If they show signs of cracking they must be replaced. Do not clean seals using solvents.

8.5. Vacuum pump

Clean up any oil spills on or around the freeze drier from oil changes.
For the maintenance of the vacuum pump, please refer to the separate operating manual.
Additionally:
The oil level of the vacuum pump must be regularly checked at the sight glass (in case of continuous operation at least once a day). Top up oil to the required level via the oil inlet. Due to possible operation with gas ballast, oil consumption cannot be avoided. For topping-up see the operating manual of the pump. The oil change should always be carried out with warm pump.

8.6. Exhaust filter

The exhaust filter should be replaced if it becomes saturated. Where possible there should still be a pipe after the exhaust filter leading into open air. Take care that the condensate in the filter does not rise too high.

8.7. Cleaning

Use soapy water or other water-soluble, mild cleaning agents to clean the freeze dryer. Avoid corrosive and aggressive substances. Do not use alkaline solutions, solvents or agents with abrasive particles. Remove product residues from the ice condenser chamber using a cloth. It is recommended to open the doors of the freeze drier when it is not in use so that moisture can evaporate.
If there is the risk of toxic, radioactive or pathogenic contamination, special safety measures must be considered and adhered to.

8.8. Checks by the operator

The operator has to ensure the important parts of the freeze dryer and those necessary for safety are not damaged. This especially refers to:

- Doors and hinges
- Seals
- Oil level of vacuum pump
- Heat exchangers
- Exhaust filter
- Thermocouples
- Shelf spacers
- Water coolant pipes
- Steam pipes