

To The Point

Protecting Perishable Property

A malfunction or loss of power to refrigerators, bioreactors or freezers can be devastating to life science organizations such as biotech firms. Drug discovery companies as well as contract manufacturing or research organizations are no less immune from spoilage risk. Incidents arising from a Change in Controlled Environment (CICE) can be very costly beyond just the monetary value. CICE losses can result in missed R&D project milestones or adverse customer relationships. A successful risk management program integrates a planned approach to minimize the impact of losing critical cell lines or other sensitive property.

Quantify the Risk

The first step is to understand the significance of perishable property and the risks associated with the controlled environments. Values may range from a few hundred dollars to millions of dollars, often requiring months of replacement lead time. This can negatively impact revenue and relationships.

The initial risk assessment should include the following steps:

- Itemize the perishable property stored and/or work in process for each bioreactor and in each refrigeration, freezer or cryo storage unit.
- Identify critical temperature thresholds.
- Determine how long it will take the unit to reach the critical temperature or excursion in the event of power loss or other failure (refer to the manufacturer guidelines).
- Calculate property replacement cost, including reconstitution.
- Estimate the impact on operations, business relationships, contractual responsibilities, and ensuing revenue implications if the temperature range is not maintained.
- Evaluate current control methods, including maintenance programs.

Manage the Risk

There are a number of solutions available to manage CICE. Duplication and separation of critical sensitive materials and process equipment is a key to minimizing the impact of the loss of a bioreactor, refrigeration, freezer or cryo unit. The level of robustness in terms of needed countermeasures depends on the risk assessment outcome.

- Duplicate refrigerated contents in multiple refrigeration units.
- Consider storing duplicate biologic material in separate refrigeration or freezer units.

- Ensure that additional freezers and coolers have sufficient capacity to store all of the contents of a failed unit.
- Place additional refrigeration units on separate circuit breakers.
- Depending on the critical nature of the material stored and the likelihood of a widespread power failure, consider the duplication of critical stock in a separate fire area, a separate building, or at a separate distinct location.
- Duplicate processing equipment such as bioreactors possible smaller size units should be on separate circuit breakers.

Reliability of Power Supplies and Human Errors

Spoilage incidents can result from power supply issues or human error. Examples include contractors turning off the electrical power without realizing the consequences, personnel mistakenly leaving a freezer door open, or individuals forgetting to plug a unit back in after relocation. Each of these actions can lead to the loss of controlled environmental conditions.

Consider the following best practices to avoid these common mistakes:

- Hardwire CICE storage and process units into the electrical system rather than using a plug and socket.
- Good contractor selection and close supervision is essential for any business. Highlight critical considerations as part of the contractor orientation process. Unless told, a contractor may not differentiate between a refrigerator full of cell lines and a refrigerator containing food. To minimize this exposure, consider a process specific permit system.
- Use infrared thermography to scan for abnormal operating temperatures in electrical and mechanical systems. This inspection technique is conducted on energized equipment to identify hot spots. Early detection of problems provides the

opportunity to address hazards with an inexpensive correction that can prevent equipment failure.

- Where the preservation of sensitive stock is essential, employ reliable backup power supplies and refrigeration commensurate with the risk. Generators need an auto-start mechanism and must have sufficient fuel to last until either power can be restored or alternative arrangements made for the storage of the refrigerated or heated materials. In addition, it is imperative that scheduled maintenance and regular load-testing take place on the generators.
- Voltage surge protection should be considered for the building as a whole or for critical refrigeration units. This is also key to protecting a property against the effects of a lightning storm.
- While it may seem obvious, it is considered a best practice to label cold storage and bioreactor units with:
 - **Unique Identifier** (e.g., "Freezer A," "Bioreactor 1")
 - **Temperature Range or Operating Parameters** (e.g., "-80°C Freezer," pH range for bioreactor)
 - **Contents Description** (e.g., "Biological Samples," "CHO Cell Culture" for bioreactor)
 - **Hazard Warnings** (if applicable) (e.g., "Contains Biohazardous Materials")
 - **Owner/Contact Information:** responsible person, department, and contact details
 - **Calibration/Inspection Status:** last inspection date and next due date
 - **Power Supply Warnings** (if applicable) (e.g., "Warning: Critical Power Supply — This unit requires continuous power to maintain storage temperature.")
 - **Cryogen Warnings** (for cryogenic storage): warnings regarding liquid nitrogen or other cryogenics present

Alarms and Emergency Response Mechanisms

In the event of a refrigeration, freezer or bioreactor unit failure, it is important that early detection of a temperature excursion is achieved so that corrective action can be taken.

Here are some important factors to consider:

- Bioreactors may have other critical operating parameters in addition to temperature that require monitoring: pH, Dissolved Oxygen Levels, Stirring/Agitation, Dissolved Solids, Cell Density, Pressure, etc.
- Automatic bioreactor equipment and monitor systems should be checked to ensure any critical spare parts such as a system control chip is kept on hand
- Manual monitoring at scheduled times for cold storage is only as reliable as the individual taking the measurement. An automatic alarm and monitoring system connected to a central monitoring station is generally more reliable for monitoring all types of temperature and other parameter excursions.
- If an automatic dialer type alarm system is used, it is imperative that the dialer does not stop calling the responder list until a person is reached. It is not enough for the dialer to accept a voicemail or answering machine and stop dialing. Most dialer systems require the responder to put in an access code to ensure that a person actually received the alarm.
- It is recommended that consideration be given to updating older automatic dialer type alarms with more modern

technology. Cloud-Based Monitoring System can provide real-time monitoring, data logging and alerts via email, SMS or mobile apps. Wireless sensors can integrate with centralized platforms for advanced monitoring/control. Integrated Building Management Systems (BMS) can monitor and control multiple aspects of a facility including cold storage.

- Another key factor to consider is who will respond to temperature excursion alarm signals. The emergency response plan should ensure that an engineering response coordinated with the CICE product owner and solution can be achieved within the critical hold time. Ensure there is a written Standard Operating Procedure (SOP). Then communicate and rehearse the SOP with all relevant parties.

Fire Department Pre-planning

Fire personnel are trained to shut down power on arrival at a site. Pre-planning with the fire department could avoid this. By letting them know there is temperature-sensitive property on site, responders can be trained to maintain electricity to critical areas, thus minimizing damage.

Liquid Nitrogen Dewars

Liquid nitrogen dewars provide different exposures than refrigerators and freezers and require some different solutions. They are not always reliant on the electrical supply and are portable and flexible, which is why they often contain critical stocks and raw materials. However, the very low temperatures involved often give a false sense of security. Although temperatures may be low, the critical thaw temperature is also likely to be low.

Consider the following controls to help reduce exposure to risk:

- Ensure the high and low temperature alarms are set with early warning notifications to ensure an emergency response in an appropriate time frame.
- Include low liquid level alarms to ensure that manual refilling liquid nitrogen operations are completed, especially as human error often plays a large part in any loss.
- It is worthwhile having a liquid nitrogen auto-fill system to support manual procedures in place.
- Liquid nitrogen back-up tanks should be available that are large enough to store all stock when needed.
- As with conventional refrigeration appliances, duplication between units and sites should be strongly considered.

Focusing on risk management can significantly reduce exposures and help prevent or minimize business disruptions. It can also strengthen shareholder confidence.

Resources

[Change in Controlled Environment Emergency Planning Worksheet](#)

Learn More & Connect

For more information on protecting your business, contact your local risk engineer, visit the [Chubb Risk Consulting Library](#), or check out www.chubb.com/riskconsulting.