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Freeze Dryers
Lyophilizers from Laboratory to Production

MAGNUM® CIP Pilot Freeze Dryer

Clean-In-Place in Freeze Drying

How It Works…

- **Photos and Description of The Magnum CIP Pilot Freeze Dryer**
- **CIP Cycle Design Considerations**
- **Single Tank and Multi-Tank Descriptions**
- **Post CIP Drying Methods**

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MAGNUM® Clean In Place Freeze Dryer

Expanded Capacity for R&D and Small-Scale Production

Offering **up to 20 sq ft of shelf area** and a **condensing capacity of 30 liters,** the MAGNUM® CIP Pilot Freeze Dryer stands out amongst the competition. This lyophilizer offers 30% more shelf area than most other units in its class. While the MAGNUM® is commonly used for R&D purposes in the lab, it is the perfect lyophilizer for small scale production. This unit is designed for lower moisture content products such as Tissue, Diagnostics, Medical Devices, and more.

Our **easy-to-use software** provides automatic freeze-drying, defrost, system and leak rate testing. Data can be printed either numerically or graphically. This same control system is used on industrial dryers, allowing scaling to production. An interactive maintenance screen simplifies component servicing. All systems are **remotely accessible**, with customer approval, for troubleshooting process issues.

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SYSTEM PERFORMANCE

- 10 shelf pull down from +20 to –40C in less than 40 minutes
- Vacuum pull down to 100 mT in less than 20 minutes
- Vacuum leak rate less than 30 mT per hour
- Vacuum level 10 mT in clean dry system (-85)

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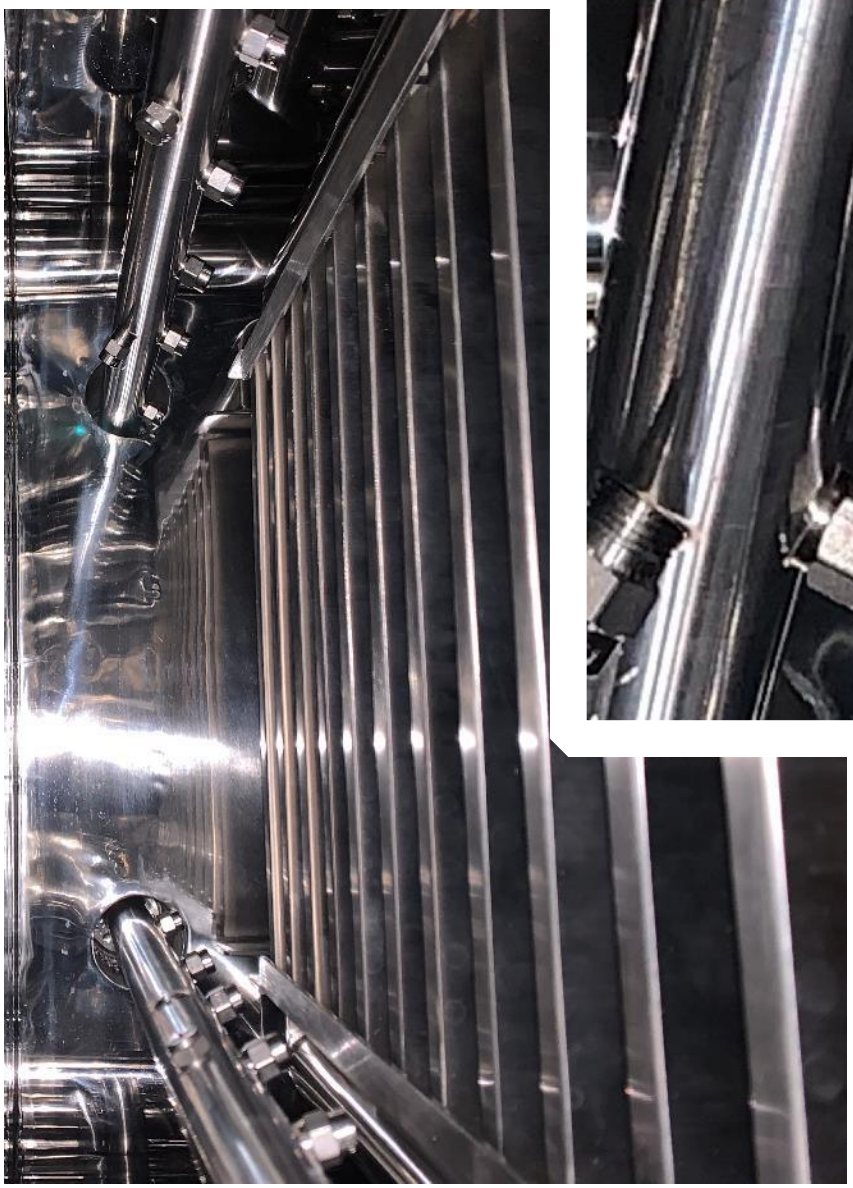
Millrock Technology offers Optional Clean In Place (CIP) systems to ensure against cross contamination and meeting FDA cGMP compliancy.

We will help you with professional consultation to design a Freeze Dryer that will meet your unique requirements.



Freeze Dryers that are CIP-able Include:

- Chambers Sloped To Drain
- Diaphragm Valving on CIP Sources and Drain Plumbing
- Manifolds and Nozzles
- Water Ring Pump
- And Software for Programming and Drying Cycles

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CIP in Freeze Drying

During the freeze-drying process particulates can be spread onto the freeze dryer's internal surfaces. The internal surfaces can be manually cleaned by hand wiping surfaces with water and/or alcohol which also provides some sanitation while cleaning. The validation of manual cleaning can be difficult, so a method of Clean In Place may be requested which is more repeatable and can be more easily validated.

As a concept, Clean In Place is the ability to rinse the inside of the freeze dryer via spray of liquid. CIP systems are designed for the specific application and vary greatly in complexity. The intent of the process can range from simply rinsing surfaces with filtered water to remove residual material through the spray action to performing a scrub and sanitization using detergents and multiple rinse cycles.

Clean In Place is performed by spray nozzles mounted on manifolds inside the chamber. A typical spray nozzle provides 0.5 to 1 GPM with a 40 PSI water source. To keep the flow requirements to reasonable levels, a zone will typically contain no more than 40 nozzles, for a CIP skid flow requirement of 40 GPM. Small systems may use 20 nozzles, while large systems may use over 200 nozzles. Multiple manifolds that are independently operated are required to reach different areas of the freeze-dryer; each is called a "Zone."

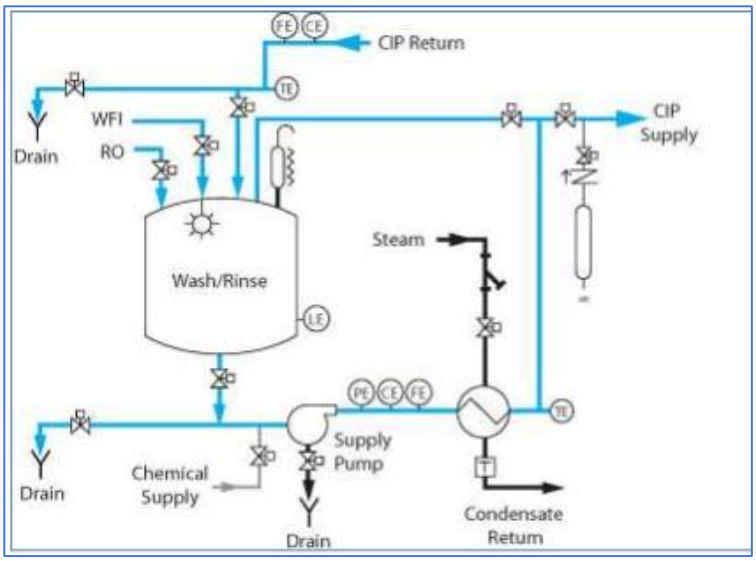
CIP cycle designs take the following into consideration:

- ✓ Type of material for the rinse
  - De-I, RO, or WFI Water
  - Detergent
  - Caustic and Acid
- ✓ Rinse time
- ✓ Temperature of rinse
  - Steam or electric heat
- ✓ Single pass or recirculation
- ✓ Sensing and monitoring
- ✓ Manual vs. Automation

The simplest CIP system uses filtered water to rinse the internal surfaces, washing the materials toward the drain. The amount of water used depends on the number of nozzles required to cover all the surfaces inside the chamber(s). Filtered water is preferred, such as RO, De-I or WFI for a clean rinse. The CIP skid system or CIP storage tank is sized based on the flow rate and time required to cover all the surfaces. Tank sizing is based on the flow per zone and time required to rinse all surfaces. For example, a CIP cycle that requires 20 GPM for 10 minutes would require a 200-gallon tank. In some cases, when only water is used the condenser chamber may be used for storage and the CIP water can be recirculated to reduce the need for larger storage tanks.

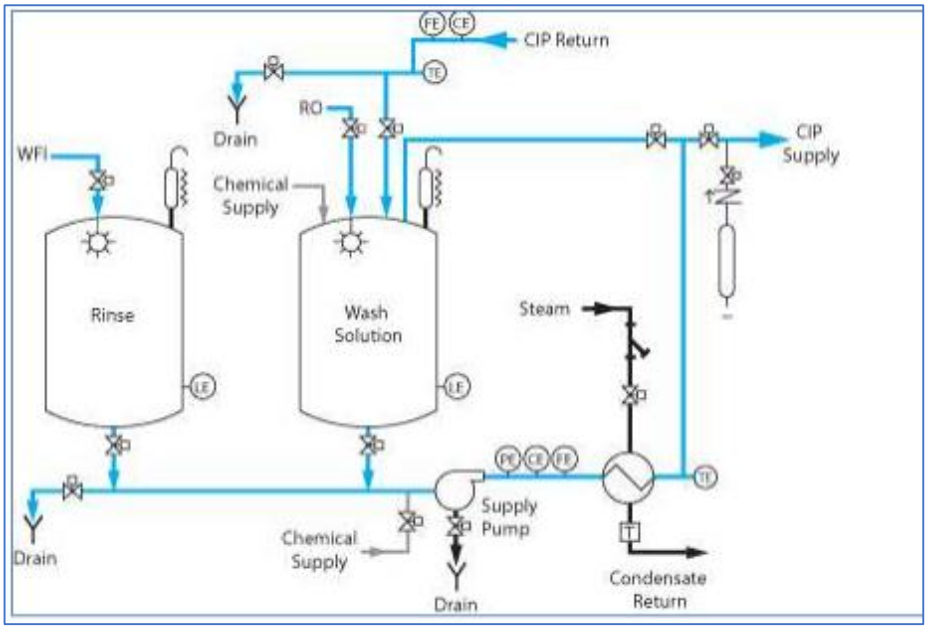
CIP in Freeze Drying

The majority of CIP cycles used in freeze-dryers are performed with room temperature water. In some cases a higher temperature water (hot water) may be needed. Using a storage tank offers the opportunity to heat the water. Note: The hot water may cause proteins and biologics to stick to the freeze-dryer surfaces.



Single Tank CIP Skid with optional steam heating – Courtesy of Sani-Matic

A 2 stage CIP system will provide filtered water pre-rinse (70-145 F), warm detergent wash (70-145F), filtered water post rinse, hot De-I or WFI (85 C) post rinse and a system blow-down. The temperature of each step is controlled, and the conductivity of the water can be monitored. A complex control system will include full PLC automation with 21 CFR Part 11 compliant operation.



Multi-Tank CIP Skid with optional steam heating – Courtesy of Sani-Matic

CIP systems are very effective in covering the majority of surfaces, but only reasonably cover 95-98% of the internal surfaces. Larger chambers are more difficult to cover, and 95% coverage may be a reasonable expectation. Validation of coverage is performed by spraying the internal surfaces with riboflavin, cycling the CIP system, then inspecting the system using an ultraviolet black light to see if there is any residual material visible.

When CIP is installed on non-Steam sterilizable freeze-dryers a post-CIP freeze-drying run needs to be performed to dry out the product chamber before product is placed inside.

For steam sterilizable systems, the CIP process is executed prior to the steam cycle. The steam cycle raises the temperature of the chamber to a point that allows drying to take place.