ClorDiSys

Application Note #14:

Lyophilizer Sterilization

Uses:

A lyophilizer (lyo) is typically decontaminated on a periodic basis and usually after each production batch. The typical process is to decontaminate by using steam to raise the temperature and hold it there until 6-log kill is attained. After the proper sterilization time is reached, the lyophilizer is then left to cool before product is brought in for another cycle. Because of the large thermal mass, this can take many hours. Lyophilizers also need to pull deep vacuums to perform the drying function. Heating and cooling with steam causes thermal expansion and contraction which compromises the tight tolerances required to keep the lyo sealed enough to reach deep vacuum levels. To mitigate these concerns, and to provider a faster sterilization cycle, decontaminating the inside components of the lyo can be accomplished using gaseous chlorine dioxide.

Benefits:

CD vs Steam

Quicker Cycles with Chlorine Dioxide (CD) Gas than Steam

1.5 to 3 hours depending on desired level of kill and sensitivity of components vs. 24 hours for steam.

Less Stress on the Lyophilizer with Chlorine Dioxide (CD) Gas than Steam

No thermal stresses with CD as there are with steam as there are no heating and cooling requirements.

CD vs VPHP

Quicker Cycles with Chlorine Dioxide (CD) Gas than Vapor Phase Hydrogen Peroxide (VPHP)

1.5 to 3 hours depending on desired level of kill and sensitivity of components vs. 8 to 12 hours for VPHP.

No Cycle Development Required for CD gas

CD: 1 mg/liter for 2 hours or 5 mg/liter for 30 minutes of Exposure.

VPHP: Cycle parameters must be developed for every specific application. If ambient temperatures change, the cycle parameters most likely need to be changed.

Better Distribution with a True Gas like CD gas

CD gas is a true gas which naturally fills the space it is contained within, no matter the shape or amount of items inside the space.

VPHP is a liquid at room temperature and as such has limited natural diffusion. Small internal diameters and hard to reach areas in the lyo are not large enough for vapors to flow and decontaminate these critical internal components.

CD Gas Features:

- Sterilization at ambient temperatures
- short cycle times
- precise concentration monitoring
- Uses a true gas
- excellent distribution into hard to reach areas
- simple to validate
- detailed cycle reporting
- no liquids in process
- does not require tight control of dew point
- quick aeration (can literally be minutes)
- non-carcinogenic
- non-flammable
- no measurable residuals
- does not condense out or breakdown during the process

Equipment Required:

The equipment required to decontaminate the inside of a lyophilizer consists of:

- Minidox-M/Cloridox-GMP Portable CD Generator
- ClorDiSys SCT with Carbon Scrubber System (optional)
- Lyophilizer with proper ports

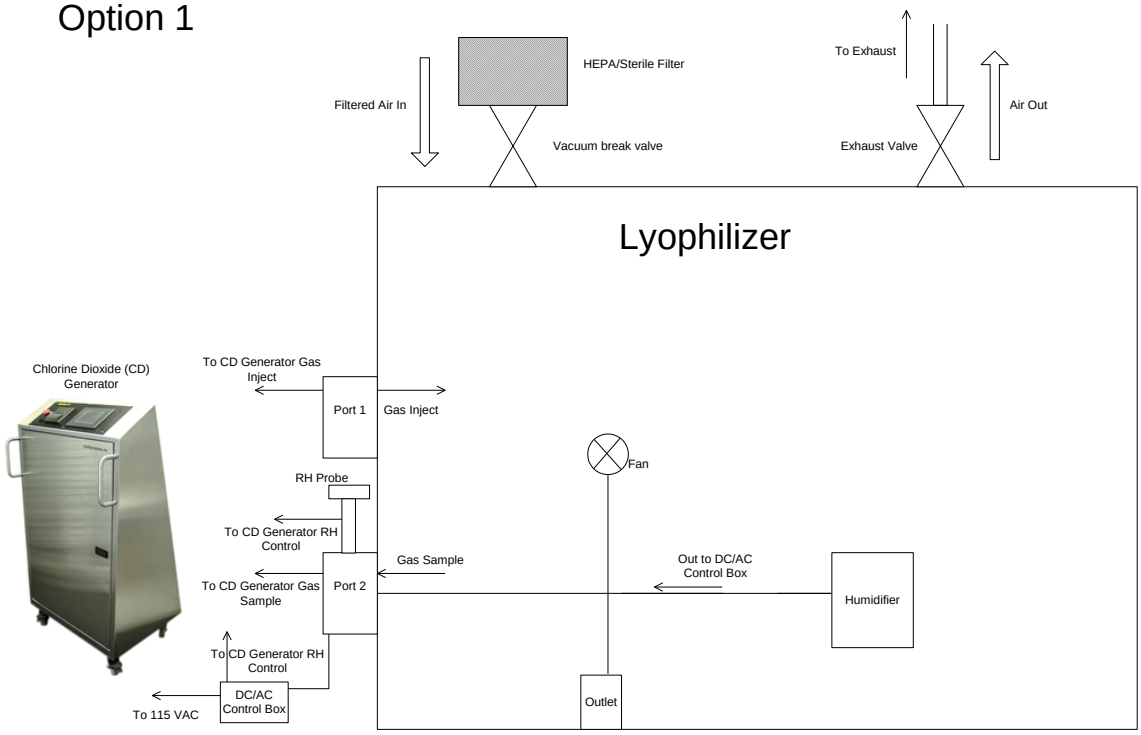
Equipment Setup:

The setup of the equipment can be accomplished in a few ways per the below diagrams and instructions:

The chosen method depends mostly on connections available at the lyophillizer.

Option 1:

The first setup shows a ClorDiSys CD gas generator directly connected to the lyophilizer. In this set-up chlorine dioxide gas will be directly injected into and sampled from the lyophilizer with attached ports. Similarly, RH would be raised and monitored through another port directly connected to the lyo. In this direct connect method, gas would normally be removed using the lyo's vacuum pump system.



Option 1A:

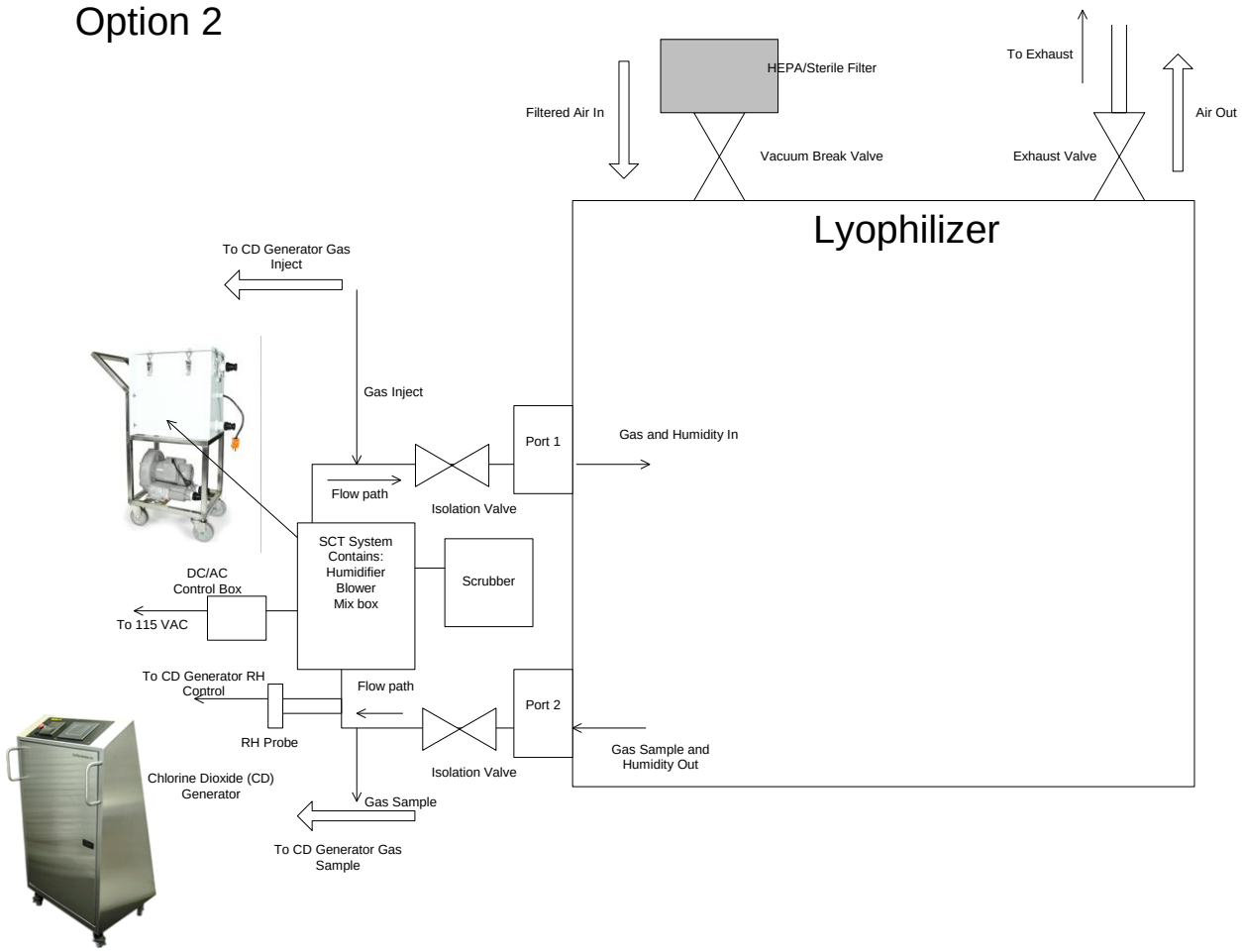
An optional humidifier and RH control box can be temporarily placed within the lyo with the door ajar for the power cord to extend outside the chamber for power. The lyo interior can then be humidified and the RH equipment pulled out. The door can then be sealed and a cycle started.

Option 1B:

If no power is available inside of the lyo to power a small humidifier, wet paper towels or a spray bottle could be used to increase humidity.

Option 2:

The second setup shows a ClorDiSys CD gas generator connected to a ClorDiSys SCT system which interfaces to the lyophilizer. In this setup, gas is injected and sampled within a small recirculation loop. This is used in applications where there is limited or no power, no enough ports or possible recirculation problems inside the lyo. Again, the method chosen method depends mostly on connections available on the lyophillizer.



Field Configurables:

The Minidox-M or Cloridox-GMP can also be configured to control the vacuum pulll sequence of the lyophilizer. The setup of the CD Generator is as follows:

Minidox-M Optional Configurable Settings
FC-1
Vacuum Pump
This FC is connected to the vacuum valve to turn it on and off when needed.

FC-2
Vacuum Valve
This is a signal that is sent to the vacuum valve when vacuum needs to be pulled.

Equipment Operation:

Option 1: *The operation of the equipment for a ClorDiSys CD gas generator directly connected to the Lyophilizer is as follows:*
The normal sterilization process is automated and consists of 5 steps:

1. Precondition: Raising of humidity to make spores susceptible to gas.
   This is achieved by using the RH probe in the lyo to read humidity and then turning on the steam generator located in the lyo as needed to adjust the RH.
2. Condition: Holding of raised humidity level for spore softening.
3. Charge: Injection of gas into chamber
   This is achieved by injecting CD gas into the lyo until the photometer measures that the concentration set-point is reached.
4. Exposure: Holding of gas concentration for the set amount of time.
5. Aeration: Expulsion of gas and humidity. This can be done by sucking sterile air into the lyo and pulling the gas via the vacuum pump

Option 2: *The operation of the equipment for a ClorDiSys CD gas generator connected to a ClorDiSys SCT system which interfaces to the lyophilizer is as follows:*

The normal sterilization process is automated and consists of 5 steps:

1. Precondition: Raising of humidity to make spores susceptible to gas.
   This is achieved by using the RH probe in the loop to read humidity and then turning on the steam generator located in the mix box as needed to adjust the RH.
2. Condition: Holding of raised humidity level for spore softening.
3. Charge: Injection of gas into chamber
   This is achieved by injecting CD gas into the CD Gas Inject Tee until the photometer measures that the concentration is reached.
4. Exposure: Holding of gas concentration for the set amount of time.
5. Aeration: Expulsion of gas and humidity. This can be done by sucking sterile air into the lyo and pulling the gas out via a ClorDiSys Scrubber. A ClorDiSys supplied sealed blower or diaphragm pump is utilized to circulate and remove the CD gas.