Author(s): MARK MELUSO, KEY SCIENTIFIC & DON PAWELKO, SP INDUSTRIES

BACKGROUND INFORMATION ON VACUUM GAUGES AND ISOLATION VALVES:

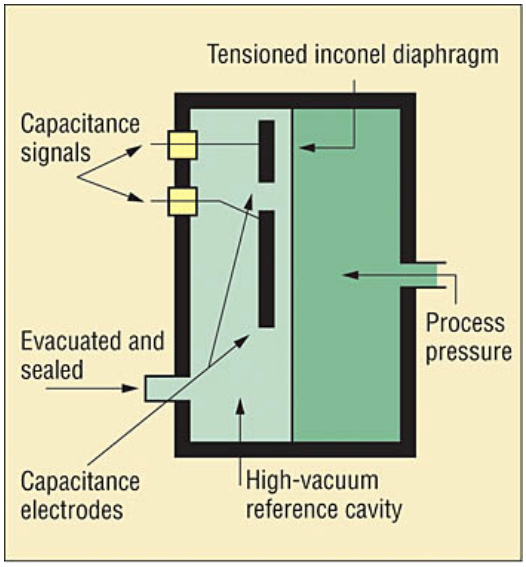
Vacuum Gauges / Pirani & Capacitance Manometer:

There are two types of vacuum gauges/sensors that are routinely used in well-equipped pilot scale and production lyophilizers:

- ***Capacitance Manometers*** (Give true vacuum readings and are not erroneously influenced by water vapor)
- ***Pirani Gauges*** (Give artificially high readings proportional to the amount of water vapor present in the lyophilizer chamber)

Here's how they work:

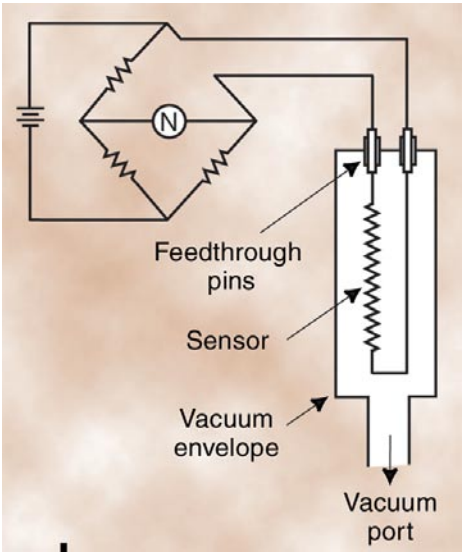
Capacitance Manometer



As system (process) pressure changes, there will be a change in pressure on the diaphragm causing the diaphragm to move. There will be a direct correspondence between pressure input and voltage output as the distance between the diaphragm and the electrodes changes. A typical capacitance manometer's signal conditioning electronics will provide an output varying from 0 to 10 volts with a linear relationship between output voltage and pressure.

Capacitance manometer pressure measurements are independent of the composition of the vapor or gas mixture in the vacuum space.

Pirani Gauge



A Pirani gauge works on the principle that when a heated metal filament is suspended in a gas, it will lose heat to the gas molecules as they collide with the wire. If the gas pressure is reduced, the number of molecules present will fall proportionately and the wire will rise in temperature due to the reduced cooling effect.

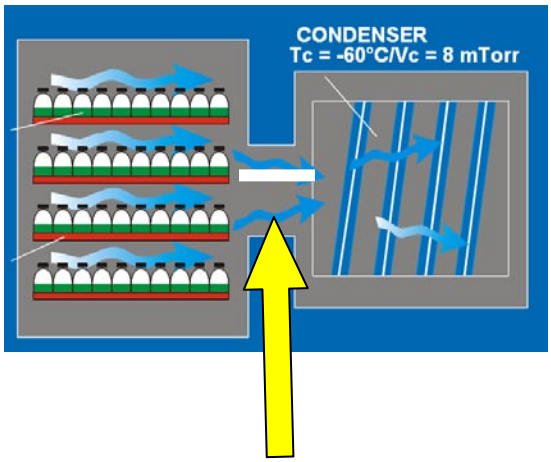
The electrical resistance of a wire varies with its temperature. This resistance, and hence the pressure of the gas, can be used to measure the vacuum surrounding the wire. In many systems, the wire is maintained at a constant temperature and the current required to achieve this is therefore a measure of the vacuum being studied.

The important part to note here is that these gauges are calibrated in pure nitrogen and they will read erroneously in the presence of other gases. During freeze drying, when there is water vapor present in the lyophilizer, the Pirani gauge actually gives an erroneously high pressure reading. The more water vapor we have in the vacuum space, the more “off actual value” the Pirani gauge will read. This will be a valuable asset to us later when discussing the capacitance manometer & the Pirani pressure differential.

Generally, Pirani gauges cannot be steam sterilized. They have to be valved out of a steam-sterilizable system when steam is in use and a hence are not the preferred gauge in a freeze dryer that will be sterilized with steam.

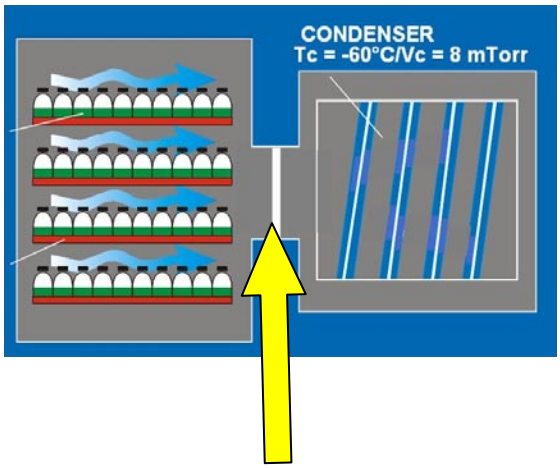
Isolation valves

The isolation valve is generally a butterfly type valve that sits in the spool (throat or vapor port) of a freeze-dryer, located between the product chamber and the condensing chamber.



Isolation Valve in open position

Allowing vapor flow to condenser



Isolation Valve in closed position

Preventing vapor flow to condenser

The isolation valve has several functions, but for our discussion, only one is important: Barometric endpoint determination, otherwise known as a pressure rise test for primary drying endpoint determination.

BAROMETRIC PRESSURE RISE AND PIRANI VS CAPACITANCE MANOMETER END POINT DETERMINATION

We are now ready to discuss the merits of both methods:

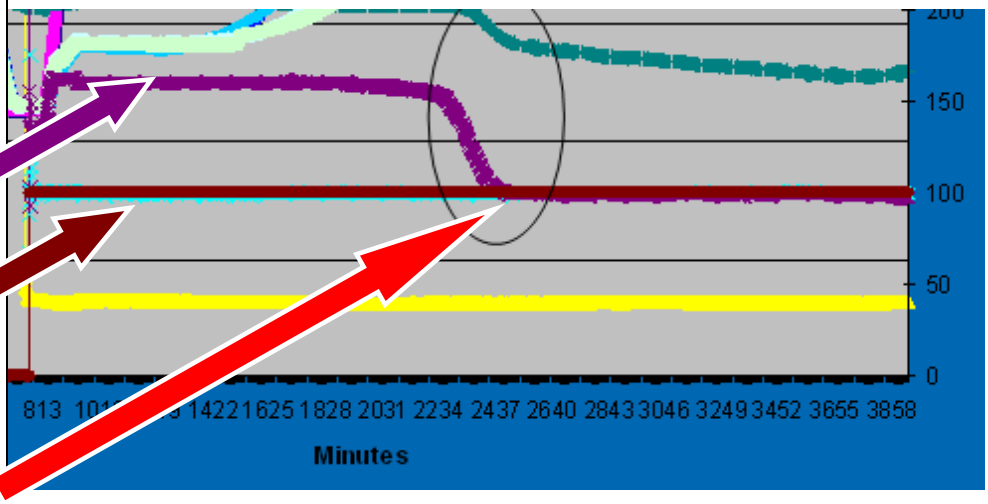
Pirani vs. Capacitance Manometer Measurement:

When water vapor is present, the Pirani gauge readout will be skewed to an erroneously high pressure level. As the amount of water vapor begins to recede, the erroneously high pressure reading, at the Pirani gauge, due to water vapor in the chamber will decrease concomitantly with the decrease in water vapor until there is little or no more water vapor leaving the sample. At this point the capacitance manometer and Pirani gauges will indicate vacuum/pressure values will read the same (or close to the same) pressure.

This is the Pirani measurement. Remember this is an erroneously high reading because of the water vapor in the chamber

This is the Capacitance Manometer measurement

The circled area where they come together marks the end of primary drying



The advantage of this method is that it is non intrusive and it can be utilized on any freeze dryer that is equipped with both a Pirani gauge and a capacitance manometer pressure gauge. The disadvantage is that it becomes harder to see a differential when very low water vapor flows are present. Another disadvantage is that the Pirani adds a heated element to the inside of the freeze dryer which may be an issue if the product being freeze dried has a high flammable solvent content.

Barometric Endpoint Determination

By closing the isolation valve for a short period of time the vapor liberated from the vials has no where to go except to fill the product chamber weakening the vacuum level slightly. One can then open the isolation valve and continue the process. The process has the isolation valve open the majority of the time and then closed for a short period at regular intervals. As the process moves toward completion, the pressure rise in the chamber when the valve is closed will decrease in size until it is below approximately 5 mTorr. It is generally assumed that at this point there is so little vapor being generated that the primary drying phase is essentially complete. The interval between valve closings and also the amount of time the valve is closed can be modified to match the formulation. The advantage of this is that is can be used with small vapor flow as well as high vapor flow conditions. By adjusting (increasing) the valve closing time, it can also be used to observe the progress of secondary drying. The disadvantage of this method is that it creates a slight disruption of the cycle while the valve is closed and it can only be utilized in freeze dryers equipped with an isolation valve and an external condenser.