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Managing Foam Level in Bioreactor Vessels

The pharmaceutical industry uses fermentation process in Bioreactor vessels to grow microorganisms that are used in antibiotics, vaccines, steroids, etc…

Typically, cell cultures and raw materials (called "broth") are mixed by an agitator and then allowed to settle. As the broth settles, the fermentation process begins and the cells start to grow. CO^2 gases, produced by the fermentation process, are drawn through filters by a vacuum pump in the top of the fermentation vessel. The filters keep outside contaminants from getting into the vessel, and prevent the microorganisms from getting out.

In many fermentation processes foam, or froth, is generated on top of the broth. As the foam layer expands and rises in the vessel, de-foaming agent is added to reduce it before it reaches the outlet to the vacuum pump. If the foam gets into the outlet the filters will become fouled, blocking the exchange of gases. This forces the process to be shut down and the batch in progress will be ruined.

A ruined batch can often represent hundreds of thousands of pounds in lost product. Filters must then be cleaned or replaced prior to the next batch. If foam gets into the vacuum pump, the pump must be taken apart and sterilized. In some cases the foam will short circuit the pump necessitating its replacement.

The de-foaming agent is sometimes sprayed in on a pre-scheduled basis to ensure the foam does not get too high. This method typically results in excessive use of the de-foaming agent. To prevent this, a point level switch is often used to activate the de-foaming spray at a fixed foam level. This can be a conductance, ultrasonic, or RF admittance type switch.

The de-foaming agent is typically a silicone-based oil that breaks down the foam. The de-foaming agent is very expensive so fermentation operators strive to use as little as possible, thus reducing cost. Additionally, excessive use of the agent can upset the fermentation process, affecting mass and oxygen transfer. Anything added to the broth must eventually be processed out, so less is better.

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Foam Level Measurement Technologies

The following is a review of the most common point level measurement devices used for foam detection in fermentation vessels.

Conductivity Switch

Conductivity switches are often used for foam detection in fermentation vessels. Unfortunately, conductivity switches are notorious for false level indication due to material bridging between the active electrode and ground. This condition will cause the de-foaming agent to be dispensed continuously until the false alarm is recognized. In an automated process this will be extremely expensive and the excessive use of de-foaming agent is likely to upset the fermentation process resulting in a lost batch.

Also, the foam will often leave a hard, insulating coating on the electrode as it dries, insulating the conductivity switch and causing it to not "see" a high-level condition. This would result in fouling of the filters and possible damage to the vacuum pump.

Ultrasonic Gap Switch

Ultrasonic gap switches operate by sending an acoustic signal from a transmitting crystal across an opening (gap) to a receiving crystal. The acoustic signal is driven at a magnitude that is too low to travel across the gap when in air or gas. When a liquid fills the gap, the acoustic signal travels through the liquid to the receiving crystal and indicates the presence of material.

The 'IntelliPoint' Point Level RF Switch is the best and most versatile point level switch for liquids, slurries, granulars, and interface applications

Foam, being mostly gas, is not a good medium for conducting acoustic signals. The bubbles will attenuate the signal to a point where it will no longer traverse the gap. Also, coatings, left by the foam, will dry into a hard crust in the gap, which will further attenuate the acoustic signal. Either of these conditions will cause the foam level to pass the high-level control point, fouling the filters, and possibly damaging the vacuum pump.

RF Admittance

RF Admittance level switches provide the best possible solution to high-level foam detection. ABLE Instruments' Drexelbrook RF level switches will easily detect any water based (conductive) foam. Products such as the **Intellipoint** have driven shield circuitry which allows the sensor to ignore even heavy, crusty coatings left by the foam.

Sensors are available with sanitary, electropolished surfaces. RF Admittance level sensors can be used in applications from cryogenic to 2000 degrees Fahrenheit & Vacuum to 10,000 psi. The Intellipoint provides a continuous AutoVerify self-check circuit that ensures the operational integrity of the switch at all times. The Intellipoint is also self-calibrating. Simply install the sensor into the vessel and apply power.

The microprocessor based electronic unit calibrates the switch for the optimum set point. Using the Intellipoint to automate the de-foaming process will ensure that foam does not reach the vent line preventing a lost batch due to clogged filters. Dispensing de-foaming agent only when necessary reduces cost and eliminates process upset condition due to excessive use.

ABLE also offers the 401-700-035 Flash Programmer/ interface Validation kit. The Flash Programmer allows an operator to read and store the capacitance values and alarm set point of the Intellipoint using a laptop computer. These recorded values are very important to plant personnel responsible for periodic validation procedures. This information allows the operator to compare current values to stored values since the last validation period.

Particle Size, Shape and Distribution with Real Time Analysis

ABLE also offer the CANTY process camera based dynamic image processing systems for monitoring critical functions in the **fermentation process**. A microscopic camera, in conjunction with Canty's **sight** and **light** products, captures images for cells down to .7 micron (.3 micron with phase contrast) and identifies the cell size distribution and culture count for process control. Typically cell viability can be determined since a count of the ratio of live to dead cells is calculated by way of the cell structure revealed by the image.

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