Keeping Pharmaceutical Processing Pure

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Pure water is as necessary to a pharmaceutical manufacturer's existence as oxygen is to the patients it serves. The trouble is, water doesn't want to be pure. It wants to dissolve things, and as a universal solvent, it's very good at that. In pharmaceutical manufacturing the dissolved oxygen and CO_2 in water can mean death to the manufacture of products designed to preserve the health of customers.

So to ensure purity in the manufacture of medicines, dissolved oxygen and CO_2 must be removed and prevented from contaminating the water supply. This is especially true of water stored in tanks. Oxygen in water can lead to microbial growth and CO_2 can affect water's pH.

One procedure to remove these impurities is called sparging. Typically, nitrogen is used not only to deaerate water, but to prevent oxygen and CO_2 reabsorption.

While nitrogen makes up 78 percent of the air we breathe, harnessing its properties for pharmaceutical manufacturing can be problematic and expensive. Nitrogen can be ordered from outside vendors but delivery, storage and handling high pressure cylinders in the working environment can be costly and hazardous. It also represents a finite supply that can be exhausted quickly when there's an unexpected rise in demand.

The costs to address these issues can be high and difficult to budget for, especially as the price of gas continue to increase. The environmental impact of truck-based deliveries is also gaining significance.

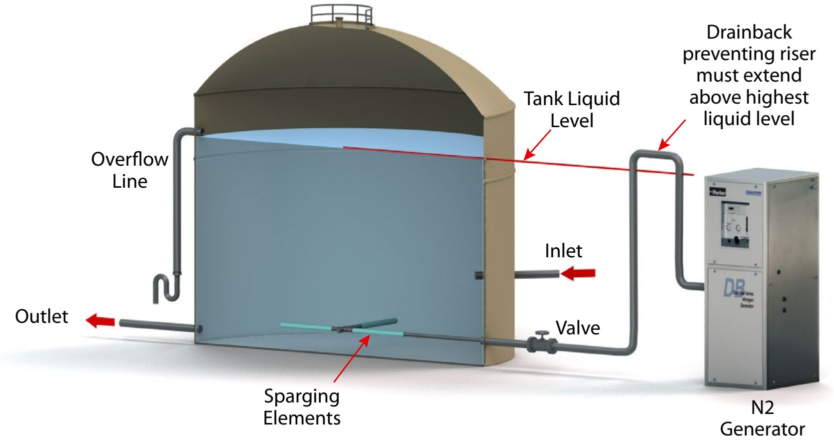
An alternative would be to generate the nitrogen needed on demand. In the pharmaceutical world, this investment is easily justified considering the value of the product, and the potential harm that introducing contaminated water can have on consumers.

Dynamic Duo

Nitrogen sparging and blanketing practices can prevent oxidation in the manufacturing process. Sparging and blanketing practices introduce near-pure nitrogen into the water tanks and maintain a protective layer of nitrogen. In other words, nitrogen sparges the water to remove any dissolved oxygen and CO_2. Humid air in the head space is replaced by pure, inert nitrogen.

This may be maintained by a precise valve-control system that automatically adjusts the nitrogen content to maintain the protective blanket as the tank is filled or emptied, or by simply having a continuous purge of low pressure nitrogen.

The nitrogen – when bubbled through water – agitates it and forces out oxygen and CO2 dissolved in it to prevent bacterial and algae growth. This can supplement the use of pumps that serve this purpose. However, a 500-gallon tank pumping at a gallon a minute can take up to 10 hours to churn



Installation to prevent back flow

Pharmaceutical manufacturers rely on a continuous supply of purified water for their operations. They must also ensure the purity of water stored for intermittent needs.

its contents. Sparging increases the rate of agitation in the tank, with sintered stainless steel plates or rods (called sparging elements) purging the water on a continuous basis.

In addition to preserving pH and eliminating microbial growth, deaerated water containing low concentrations of oxygen and carbon dioxide minimizes corrosion, as well as iron and copper oxide scale.

Supplied or Make Your Own?

There are two ways pharmaceutical plants may obtain nitrogen. The nitrogen can be received from a supplier as a gas in high-pressure cylinders or as a liquid in micro-bulk tanks (dewars) and bulk tanks. Relying on an outside supplier, however, is subject to price increases, rental agreements, hazmat fees, surcharges and taxes. Delivery of gas also requires access to the facility by a third party, and creates a security situation for the plant to manage.

An alternative to sourcing is to generate the nitrogen on-site via PSA (Pressure Swing Adsorption) nitrogen generators. Payback on such equipment can be two years or less. Nitrogen can be generated for eight to 12 cents per 100 cu. ft., while gas-utility companies charge 50 cents to a dollar or more per 100 cu. ft. The plant relies on an energy-intensive cryogenic process to cool air to extremely low temperatures to separate the nitrogen from air.

Nitrogen generators are also capable of producing up to 99.999% pure compressed nitrogen at dew points to –58 degrees F (–50 degrees C) from nearly any compressed air supply. The generators are designed to continually transform standard compressed air into nitrogen at safe, regulated pressures without operator attention.

Technical standards on water quality have also been established. The American Society for Testing and Materials (ASTM), the U.S. Clinical and Laboratory Standards Institute and the International Organization for Standardization (ISO 3696) classify purified water into Grade 1–3 or Types I–IV depending upon the level of purity. These organizations have similar, although not identical, parameters for highly purified water. Many laboratory, pharmaceutical, medical, research and dialysis applications require ultrapure water to meet one of these standards.

Nitrogen generators, such as those from Parker, use high-efficiency pre-filtration to remove all contaminants down to 0.01 micron from the compressed air stream. The filters are followed by dual pressure vessels filled with carbon molecular sieves (CMS). In one vessel at operating pressure, the CMS adsorb oxygen, carbon dioxide, and water vapor. The other vessel, operating at low pressure, releases the captured oxygen, carbon dioxide, and water.

Cycling the pressures in the CMS vessels causes contaminants to be captured and released while letting the nitrogen pass through. A final sterile-grade filter removes microbial contamination. Nitrogen purities can be set with a flow control valve. Reducing the flow increases purity while increasing flow decreases purity.

For example, a system that produces a flow of nitrogen as high as 1,530 std. ft^3/h at 99.9% purity can achieve higher flow rates if gas of lower purity is acceptable for that application. A built-in oxygen analyzer measures the oxygen concentration of the nitrogen stream. The system requires a minimum feed pressure of 110 psi and can operate at pressures up to 140 psi. The resulting nitrogen has a dew point as low as –58°F (–50°C).

On-site nitrogen generators are also compact, freeing up floor space. They're typically freestanding, housed in a

Parker DB Series Nitrogen Generator

cabinet, or skid-mounted. They come as packages with pre-filters, final filters and a buffer tank. The plant needs to connect a standard compressed air line to the inlet of the generator (after ensuring that a sufficient supply of compressed air is available) and attach the outlet to a nitrogen line.

When connecting a generator to a large tank of water, it is important to prevent back-flow of the water into the generator if compressed air is lost. A check valve may be used, but a more reliable method is to run a vertical leg above the level of the water overflow pipe (the highest water level in the tank) and then back down again into the nitrogen generator. With this plumbing configuration, if the compressor goes down, water in the line would only rise as high as the level of the water in the tank. Therefore, water would not back flow into the generator and cause damage. (See diagram.)

Pharmaceutical manufacturers rely on a continuous supply of purified water for their operations. They must also ensure the purity of water stored for intermittent needs. Therefore, these plants need to have FDA-compliant nitrogen sparging and blanketing practices to ensure high purity demineralized water. On-site nitrogen generation has several advantages.

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