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New Tech for Bio

Sampling From a Bioreactor

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Sampling From a Bioreactor;
Important Factors to Look For When 'Shopping' for Sampling Systems

There are many types of systems and process equipment used in the upstream process of manufacturing biopharmaceuticals. Although the quality of each system and piece of equipment is highly important for medicines to be produced with their safety and efficacy intact, there is one system that cannot be emphasized enough; the importance of a proper sampling system. All other systems and equipment have to work but it is the system of sampling that leads to other decisions that may or may not be correct if the sampling system isn't reliable. Sampling tells us the story of what is going on in your bioreactor- faulty system; faulty story. Decisions following the sampling data can either save or cost the company thousands of dollars. In addition, an unreliable sampling system could lead to an opening in what is supposed to be a closed system. This could affect the health of the operators and the environment as well as risking contamination to the process.

Another problem with an unreliable sampling system; it could allow a product to move forward down the path of production with a potential problem that might have been overlooked if the sampling procedure did not catch the out of specification parameter, only to be realized in the clinical trials leading to the failures of clinical trials or potentially risking patients' lives or perhaps product recalls if the product managed to get to market. Sometimes when operators receive out of specification results, they keep sampling until they get the results they want. They don't realize that an unreliable sampling system could be the reason for out of specification results.

Besides being reliable, a sampling system needs to be cost-effective. Many companies based their equipment choice on costs. The fact that there are plenty of complaints about the prices of biopharmaceuticals, cutting costs seems to becoming a more necessary action when choosing new manufacturing equipment. Although it is not a sufficient to make a choice based on costs alone, it is often a critical part of the decision making when choosing which equipment to implement.

Also, easy to use equipment is becoming more and more a requirement; not just an option, especially with the complications being brought in by some of the new equipment coming into the market. Too many steps to a system, too many locations; too many pieces; too much tubing- all these could lead to mistakes, complications, contamination, and time between taking the sample and actually testing it. Time is critical for some of the various parameters being tested, like CO^2 and DO^2. If too much time passes, the sample is no longer a true

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representation of the process being tested.

What do you have to look for in a sampling device to ensure its reliability, cost-effectiveness and ease of use?
The most important factors to look for are its design, its materials, the documentation supplied in support of the system and the system's operation and procedures.

Design
The design of the sampling system can lead to good, effective sampling or could lead to a sample that does not resemble the process it came from. The first design parameter you can look at is the measurement and size of the inner volume of the sampling device which affects both the reliability and cost-effectiveness of the sampling system. The larger the inner volume, the more surface area that needs to be clean and the higher chance of contamination. The larger the inner volume, a larger thermal mass is created which could increase the vessel temperature unnecessarily. Also, the larger the inner volume, the larger amount of product loss, which can cost companies many unnecessary dollars. In addition, larger inner volume could mean larger condensation build-up which will be harder to clear. Larger volume could also risk the overflow of process fluid in the sampling receptacle.

Lengthy tubing, in addition to causing product loss and high process contact areas, may cause confusion. Also its dimension/size may be limited due weight and transportation issues.

Then you have to look at the amount of crevices and hard-to-reach areas in the interior design where product can get stuck and then will often be difficult to dislodge. Even a small amount of sitting water could lead to growth of microorganisms. How far back does the fluid go into the interior of the valve? In addition, crevices and hard-to-reach areas make steamability and cleanability all the more difficult. Also, the potential for product being trapped in places may require flushing before taking a new sample which again leads to product loss/extra costs.

Dead leg is another concern. The presence of dead volume can cause the need to flush the initial part of the sample which leads to product loss. Also, if there is no dead leg and no need to flush the initial part of the sample, the sample is more accurately representing the process.

How about the design of the sealing process? Is it a reliable seal? Is its functionality dependent on human operation? How many parts play a role in making the seal a success? Is each part reliable? Does the seal bring too much risk to the process?

Another question; does the design of the sampling device make it easy or hard to install. If installation is not done properly; it cannot function correctly during its lifetime. How it connects to the tank will often play a role in the installation. The design for installation also has to be aseptic. Easy installation does not necessarily mean sanitary.

It's also important to look for the design in relation to the sampling device's need for maintenance. How many parts are there to replace? How often is maintenance required? What parts needs to be replaced? What level of expertise is needed for maintenance? What is the cost of maintenance and what are the costs to pay the operators/employees to do the maintenance?

Finally, with regard to the design/construction of the sampling device, how is it machined? How are the fittings connected to the body? How close are the seals to the inlet of steam? Could this affect performance?

Obviously, its design is very important when choosing a sampling system, but it is equally important to look at the materials of the sampling device/system.

Materials
It is the material of the seal and the material of the sampling container that usually is the largest concern. What materials are the seals made from? How well can the seals withstand the steam/temperature? Will the seals wear down with time? What happens to the material if

heat is a concern? Do the materials require frequent maintenance? Where exactly are the process contact surfaces? What materials are the product contact surfaces? Regarding the sampling container, is it UV protected? How comprehensive is the supplier's extractable testing on the materials used, to avoid leachables in your process? Do they provide standard biocompatibility data? Will the material contribute particulates to your process?

Materials and their properties play a huge role in the success of a sampling system but operation of the sampling system, the various steps and procedures also play a role.

Operation/Procedures

The first thing to look at when analyzing the operation of the sampling system- Is it user-friendly? Is it a simple system or is it a complex one? You have to compare how many steps it takes to take a sample, between the different sampling systems out in the industry. Many steps often create more risk. Complicated steps also add risk. The amount of steps could delay the testing of the actual sample.

What about time-sensitive sampling? What about when checking for DO^2 and CO^2, when time does affect the sample? What happens when the sample no longer represents the process?

Another question to ask- does the sample stay in the same receptacle? Is flushing required before each new sample? This could lead to more product loss/excessive costs. How about the device configuration, e.g. the sample positions. How does that affect the operation? How might the configuration either protect or risk the process fluid? Do any of the sample positions affect the seal?

Also, how does the CIP procedure differ between sampling systems and could the procedures for maintenance affect the overall system?

It is clear that operation and the steps involved in sampling play a critical role. It is also highly important to look at documentation.

Documentation

Have the seals been tested? Has the device been tested for sterility? What information is there regarding the reliability of the fittings? Industry standards are also extremely critical when looking at the materials used; especially in regard to the material of the sample receptacles.

Also and most important, does the manufacturer/supplier stand behind their products 100% and will certify that each and every part of their system meets the specifications?

Documentation is a very important but the strength of the leak/failure potential of the sampling system is one of the most important factors to look at.

Leak Failure Potential

Does the sampling system put your process at risk? Does it put your tank at risk? Is there a possibility of leaking, from the seals, or other locations? Is there a possibility of steam and sample coming into contact with each other? Will your 'sample' be a true representation of the process?

In order to answer these you have to look at each factor, design, material and procedures of each sampling system. You need to do an in depth study of the engineering of the system, in order to make a great choice when choosing a sampling system for your bioreactors, to succeed in bringing safe and effective biopharmaceutical drug products to market.

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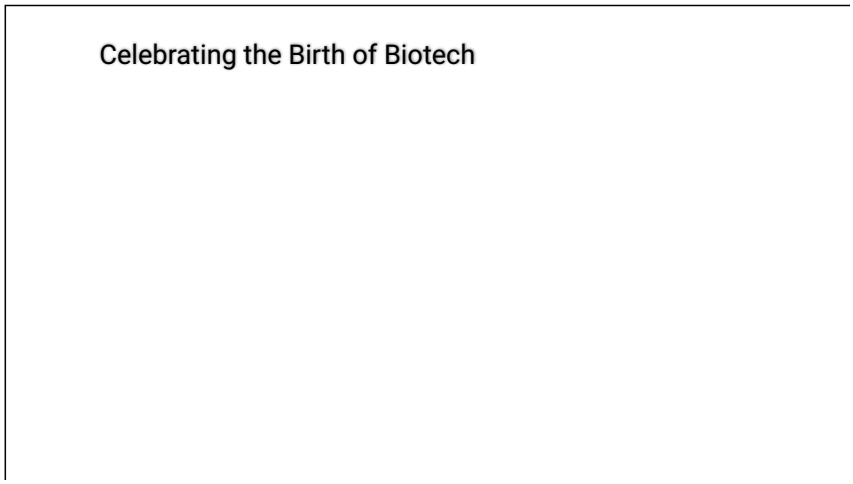

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