

Process Analytical Technology for downstream process

UV sensor OUSAF44 and conductivity sensor CLS82D, focus on chromatography.



The fermentation is performed in the upstream process. The product is then ready for the downstream process which includes a number of steps. The first step is the primary recovery, followed by initial purification, polishing, and finally the formulation.



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In the primary process centrifugation and /or filtration may take place according to the product that needs to be isolated which can come directly from the culture medium extracellularly or intracellularly released after cell disruption. After the initial purification step any major process and product impurities are removed.

The chromatography technology is used in the initial purification as well in the polishing steps. There are several types of chromatography and they work on the basis of separation methods including size exclusion, ion exchange or hydrophobic interaction chromatography.

In the chromatography columns the target products are retained or released according to their affinity with the separation material the column is made of. Buffers are pumped in the column in order to stabilize the product. Purification and polishing are highly important, it is in these steps that quality of the

final product is established and guaranteed. The accuracy is given by the use of inline Process Analytical Technologies (PAT).

With regards to tight control of the chromatography process, Endress+Hauser has developed a specific PATs fitting the Life Science industry requirements. These sensors are used to measure UV, pH and conductivity. The conductivity sensor Memosens CLS82D is mounted at the inlet and outlet of the column to determine with precision the moment in which the new buffer has completely replaced the previous one. The same control function is applicable to the pH sensor Memosens CPS171D which is mounted at the column's outlet. The photometer is also mounted at the outlet. The photometer OUSAF44 detects the protein concentration based on the light absorption and provides a signal to the automation system. The most used wavelength for protein detection is 280nm, because of the presence of the aromatic amino acids structures.

The OUSAF44 is available with standard wavelengths ranging from 254nm to 365nm, however specific desired wavelengths are also possible. The process is controlled based on the concentration set point. The product which concentration is above the threshold is directed in the collector vessel for finished products, otherwise redirected to the waste.

Because three sensors have to be mounted in the outlet of the column, we have developed a very compact flow assembly where pH and conductivity sensors can be installed. The CYA680 flow assembly can be directly mounted on the top of the OUSAF44 flow assembly. Both assemblies are available also for small size lines from 1/4" and certified conform to the Food and Drug Administration (FDA) certification and biocompatibility according to United States Pharmacopeia USP (USP class VI).

Emphasis on technology

Memosens CLS82D is a 4-pool conductivity sensor suitable for measurement in low range as well as high range from 1µS/cm to 500 mS/cm. The wide measuring range has to do with the operative environment in which the sensor is used: during the production process the conductivity is high while during the rinse process is very low.

Leaking sensors is a problem of the past! The new ceramic sensor element holds the platinum measuring electrodes without use of seals. The components have the same thermal expansion behavior therefore the sudden temperature variations during




Cleaning In Place (CIP) and Sterilization In Place (SIP) do not have any impact. The 4-pole conductivity sensor is easy to calibrate in the lab or in the workshop, thanks to the Memosens technology combined with the use of Memo-base Plus CYZ7 1D-software. The software is suitable for use in GLP/ GMP- work environments.

UV sensor OUSAF44 is provided with patented low-pressure mercury vapor gas discharge UV light source which provides long life and stable operation. The patented EasyCal™ system option allows for quick and simple on-line NIST traceable calibration. The highest accuracy is guaranteed by use of the precision optical path length (POPL) adjuster which enables exact adjustment of short path lengths (<5mm). The POPL is advisable where the highest data consistency between online protein concentration measurement and lab measurement is required. The OUSAF44 sensor offers a wide

range of FDA and United States Pharmacopoeia (USP) compliant materials and process connections that provide extreme flexibility to process development and scale-up.

In addition, the 4 sensors (conductivity at the inlet of the column and pH, UV and conductivity at the column's outlet) can be connected to a single Liquiline CM44P transmitter at the same time. The **Liquiline CM44P** is the universal transmitter and can work with conductivity, pH and oxygen Memosens sensors as well as with the traditional analogical sensor technologies.

 www.nl.endress.com/cm44p
www.nl.endress.com/cls82d

 Watch the movie with the title: EasyCal calibration with the Liquiline CM44P or use the following link: youtu.be/5aPHzQnLEoY

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