

# TOP 5 Biotech Applications

**optek**<sup>®</sup>  
inline control

**english**

deutsch

español

portuguese

русский язык

中国

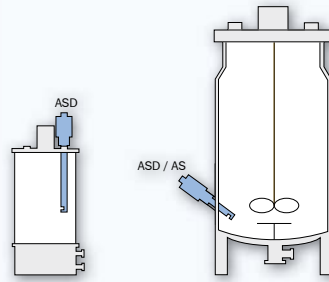
日本語

français

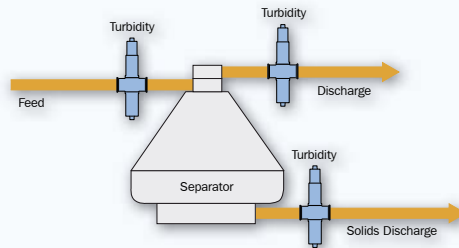
italiano



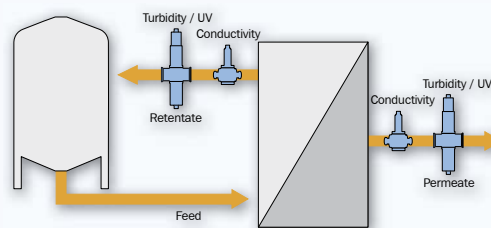
## TOP 1 Fermentation



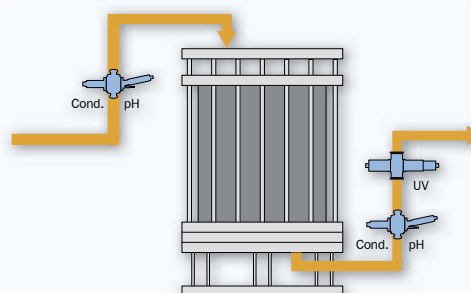
## TOP 2 Centrifuge Control



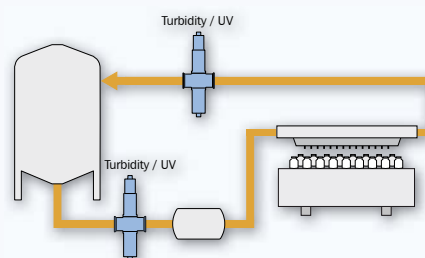
## TOP 3 Ultrafiltration



## TOP 4 Chromatography



## TOP 5 Formulation and Filling



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### TOP 5 Biotech Applications

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**In many stages of biotech processes, optek instruments help to ensure optimum system performance.**

optek is the world's leading manufacturer of inline photometric and electro-chemical process instrumentation.

With more than 30,000 installations in various applications and industries, our team provides the best in quality, consulting, support and long term performance, worldwide.

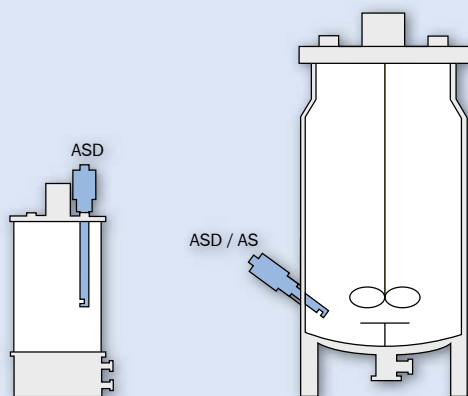
High quality materials withstand the toughest process conditions, including aggressive media, high temperature and high pressure applications. Cleanability is ensured using high quality polished wetted materials, superior design, as well as sapphire optical windows.

As a global partner to the biotech industry, optek offers the most advanced technologies including superior signal amplification, inline calibration support, PROFIBUS® PA, and multilingual user interfaces for easy onsite operations. Our support ensures long term satisfaction with programs like "SpeedParts" and "SwapRepair" to provide our customers sustainable operations and minimized downtime at the lowest cost of ownership.

**Optimize your process with optek.**

**optek®**  
inline control

## 04 | Fermentation



The optek probe series of bioprocess analyzers were designed specifically to integrate easily into bioreactors and fermenters. These precise systems provide the user with a powerful tool to characterize cell growth in the laboratory and large scale cell culture and fermentation. The real-time biomass concentration is measured as a function of light absorption, which is less sensitive to air bubbles and coating than back-scattering instruments.

Reliable inprocess measurements greatly reduce sampling time and risk of contamination during offline analysis.

### Lab/Process Development

ASD series probes were developed for smaller scale bioreactors used in R&D and process development areas. They are extremely repeatable and easy to use. Probes come in a variety of insertion depths and optical path lengths to give the best resolution possible.

optek ASD sensors are suitable for CIP/SIP runs and ASD19 type probes are autoclavable. Superior sapphire optics with no seals, gaps or crevices ensure that no contamination occurs.

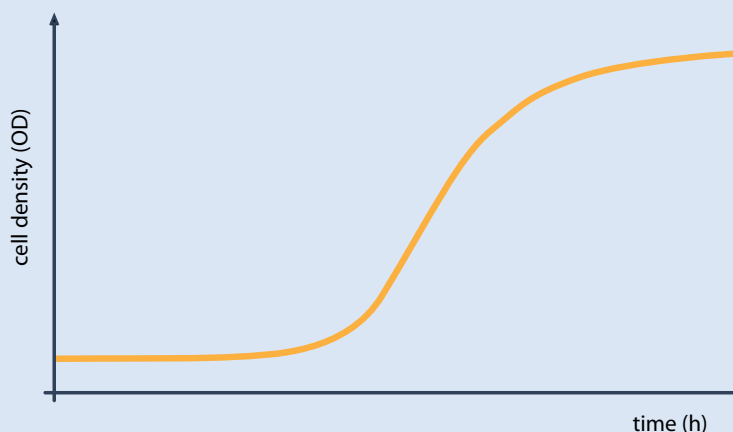
The Fermenter Control converter is specifically designed to integrate easily into existing bioreactors and fermenters. Using input from one or two optek ASD series probes, the Fermenter Control precisely measures cell growth/biomass as a function of Near Infra-red (NIR) absorption. The results are displayed in any laboratory unit, such as OD, AU, TCD, cell count, wet or dry weight. Due to the superior principle of NIR absorption, stability and measurement reliability are provided even in systems with a high degree of aeration and agitation.



optek Fermenter Control Converter



optek ASD19-N Single Channel Absorption Probe

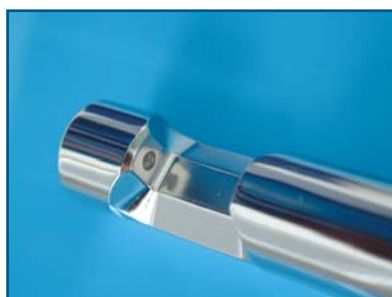


## Production/Manufacturing

AS series probes were developed for large scale reactors. This offering gives the user the same type of probe used in process development for the manufacturing scale.

Depending on point of installation, AS series probes are available with different shaft lengths for installation flexibility. Optional calibration accessories are available for quality control checks before each process run.

One optek C4000 converter can operate up to two AS series probes and can be panel mounted or installed in a stainless steel or plastic housing to ensure IP ratings up to IP66. Results are displayed in any unit, such as OD, AU, TCD, cell count, wet or dry weight. optek probes are available with a wide selection of optical path lengths, from 1 to 40 mm. Shorter optical paths are typically used for dense fermentations such as bacterial and yeast cultures. Longer paths are used for mammalian cell cultures. This flexibility allows optimal resolution.



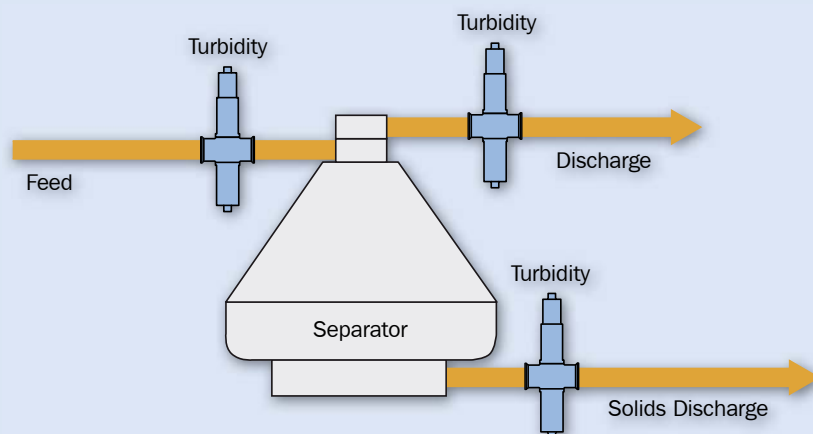
optek AS16-N Single Channel Absorption Probe



optek AS16-VB-N Single Channel Absorption Probe with calibration option



## 06 | Centrifuge Control



Installing optek sensors at the inlet and at the outlet of a centrifuge, optek in-line photometers have proven to greatly improve separation performance, reduce losses and improve product consistency.

### Feed/Inlet

The feed often has high variable solids loading. Separation efficiency can be greatly improved by installing an optek AF16-N or AS16-N NIR-sensor prior to the separator. The separator feed rate can then be optimized, based on real-time solids concentration measurements.

Flow may be adjusted to meet system requirements for optimized performance and prevent overloading of the separator.

### Discharge/Outlet

The separator outlet (discharge) is the most common point of installation for process photometers. Monitoring at this point can help manufacturing maximize the efficiency of the system. Some systems control discharge based on time parameters set from the previous run, which is only valid with average constant feed load.

A more efficient approach is to control the discharge based on need, which can be monitored by an optek inline sensor. Most installations can reduce frequency of bowl shoots significantly over the run. This increases yield, ensures consistency downstream, reduces mechanical wear, and helps avoid "blinding" of downstream filters.

Typically for cell culture processing, an optek TF16-N scattered light sensor is installed to ensure immediate detection of lowest concentrations. An optek AF16-N absorption sensor is commonly used for higher density fermentation processing.

### Solids Discharge/Outlet

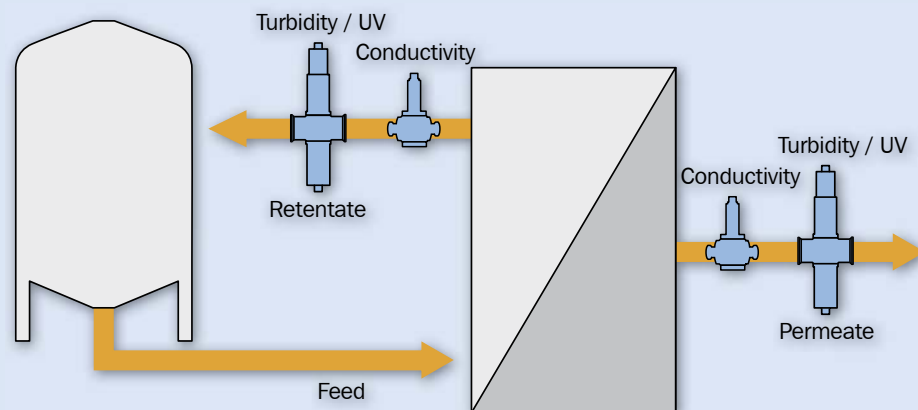
When measuring the absorption in the solids discharge stream of the separator, an optek sensor equipped with a small optical path length will accurately correlate absorption measurements directly to weight-percent. This enables accurate yield measurement and control of product quality.



optek C4000 Photometric Converter



optek AF16-VB-N Single Channel Absorption Sensor with calibration option



In a typical UF process, two installation points are usually considered.

## Permeate

Using an optek AF45 UV sensor on the permeate stream allows the user to ensure filter integrity, increase throughput and minimize product losses. Identification of trace contaminants in low ppm ranges and detection of filter breakthrough in real-time ensures process consistency, while eliminating sample collection for laboratory analysis.

## Retentate

An optek AF45 or AF46 UV sensor is an ideal way to monitor the concentration of proteins during the filtration process. The sensor is installed in the return line to the recirculation tank. Real-time concentration readings up to high OD levels can be measured and trended without violating the integrity of the system and without wasting product through sampling.

## Conductivity

optek CF60 or ACF60 conductivity sensors can be installed in the permeate or retentate line to ensure proper process control.

This conductivity sensor features a superior six-electrode, four-pole design. The patented arrangement of the four current electrodes around the two potential electrodes results in a reliable and precise measurement of a broad conductivity range:  
CF60: 0 - 100  $\mu$ S/cm up to 850 mS/cm  
ACF60: 0 - 10  $\mu$ S/cm up to 850 mS/cm

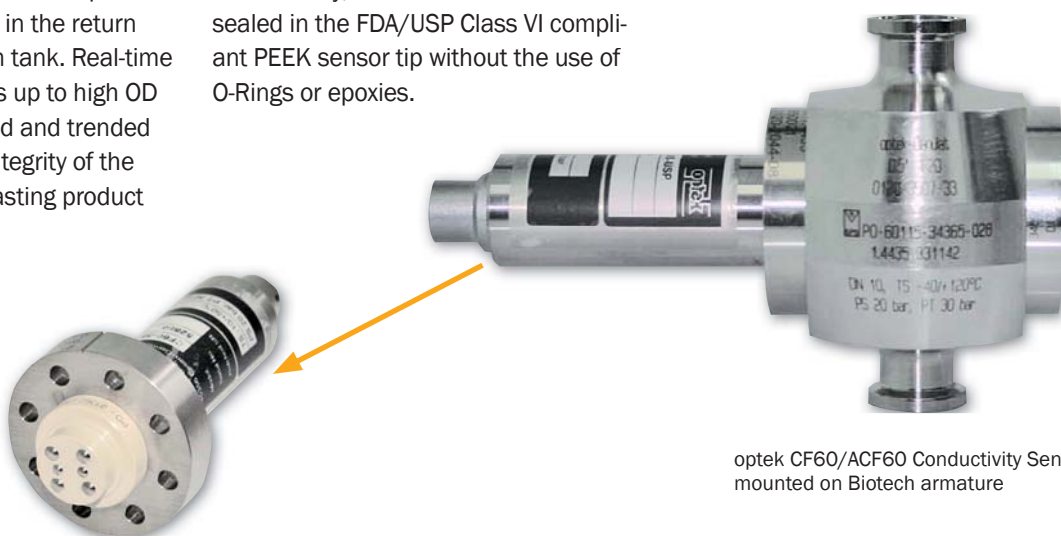
This unique design also provides greatly reduced sensitivity to sensor fouling and polarization. Designed for ultra-sterility, the six electrodes are sealed in the FDA/USP Class VI compliant PEEK sensor tip without the use of O-Rings or epoxies.

## Converters C4000/C8000

optek converters allow the operation of multiple sensors.

The C4000 is typically used if only optical instruments are required and is able to operate two turbidity or UV measurements for permeate and retentate control simultaneously.

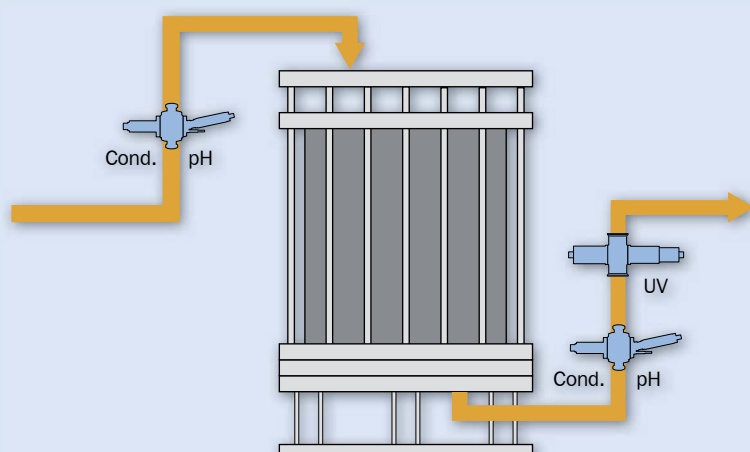
The C8000 is installed if turbidity/UV sensors are required along with electro-chemical measurements such as pH and/or conductivity.



optek CF60/ACF60 Conductivity Sensor mounted on Biotech armature

Patented six-electrode four-pole conductivity sensor

## 08 | Chromatography



Protein purification in biotechnology usually requires one or more liquid chromatography steps during downstream processing.

optek inline photometric and electrochemical sensors are designed specifically for real-time measurement and control. This improves chromatographic separations, generating consistent and repeatable data to allow more discrete pooling criteria for maximizing yields and improving quality.

### Pre-Column

An inline ACF60 conductivity sensor which includes a temperature sensor and the PF12 pH sensor give real-time measurements of conductivity, temperature and pH.

### Post-Column Chromatography Monitoring

During purification, accurate, reliable and repeatable post-column measurement is necessary to ensure accurate pooling to maximize yields and protein/DNA fraction purity.

Mounted directly inline in the column outlet stream, an optek single wavelength AF45 or dual wavelength AF46 UV sensor can improve the efficiency of the separation process. This ensures product purity and greatly reduces offline testing and manual analysis.

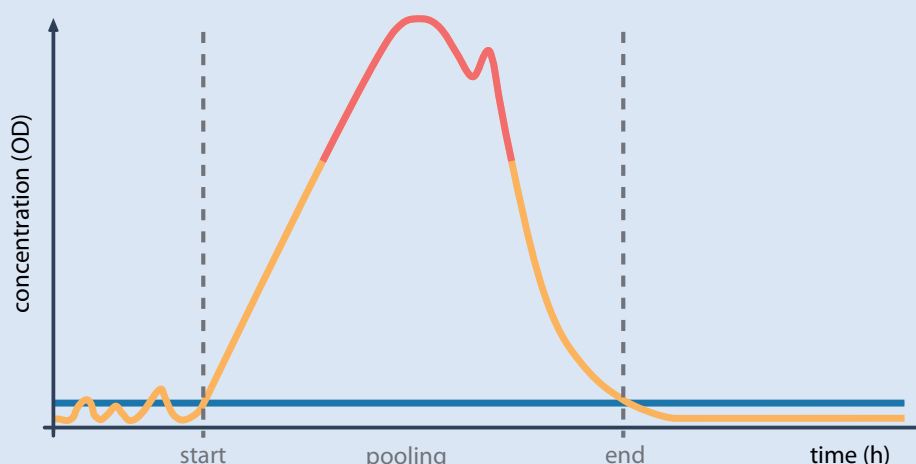
A NIST-traceable filter package allows users to calibrate the sensors inline in a quick, repeatable manner. (See page 12 for further details.)

Additionally, the patented six-electrode four-pole conductivity sensor ACF60 and pH sensor PF12, both mounted in one optimized flow cell with low holdup volume monitor the process. A wide measuring range of 0-10  $\mu\text{S}/\text{cm}$  to 0-850  $\text{mS}/\text{cm}$  allows monitoring transitions between buffers and control of the cleaning process, while a PF12 sensor is used for adjustment of the gel packing by means of the pH value. Additionally, equilibration methods are monitored and column integrity is ensured.



optek AF46 Dual Channel UV Absorption Sensor





## Dual Wavelength

The primary wavelength measures concentration of protein at i.e. 280 nm for pooling purposes. Using the secondary wavelength measuring i.e. at 300 nm simultaneously, this signal is used to achieve readings even at the highest concentration ranges.

Dual-wavelength provides precise resolution at low OD to start or stop collection of the fraction using 280 nm, and also a high-range secondary wavelength to monitor elution at the highest OD ranges.

Measurements at wavelengths 254/280 nm assess purity level and nucleic acid (DNA/RNA) contamination of protein.

Due to modularity of optek inline sensors, different optical path lengths (OPL) are possible. Depending on concentration range required, the OPL and the wavelength combination are specified to achieve the highest repeatability and linearity.

## C8000 - 8 measurements taken from 5 sensors with only 1 high precision converter

In a chromatographic separation skid the following measurements are required:

PRE-column:

combined in one sensor body for low hold-up volume

- conductivity (optek ACF60)
- temperature (optek ACF60)
- pH (optek PF12)

POST-column:

combined in two sensor bodies for low holdup volume

- Dual channel UV (optek AF46)
- conductivity (optek ACF60)
- temperature (optek ACF60)
- pH (optek PF12)

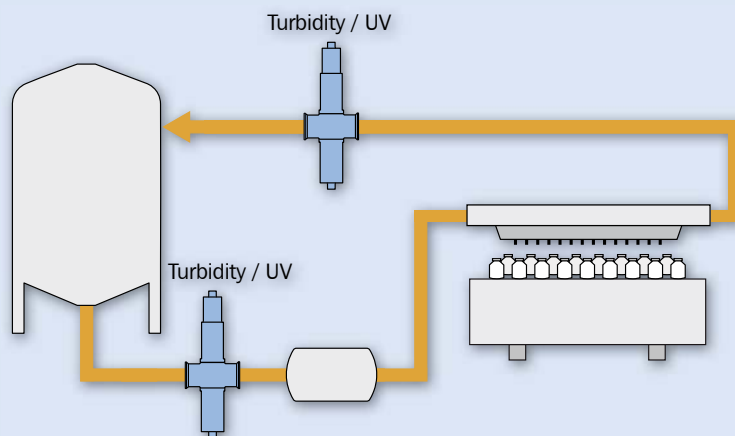


optek ACF60 Conductivity Sensor and PF12 pH Electrode Adapter mounted on Biotech armature



optek C8000 Universal Converter

## 10 | Formulation and Filling



Formulation and filling areas can see inconsistencies due to mixers, tank levels, pump cycling, pH and temperature variations, and even lab variances. optek sensors can help operators and quality areas get a live view of inconsistencies, and either make changes to help meet acceptance windows, or stop a non-conforming product lot from going forward.

This will help in avoiding additional costs with process knowledge to prevent lot failures.

Installing optek sensors inline can help to improve consistency, conformity and productivity. An optek TF16-N monitors the product concentration of suspensions ensuring stable levels during the filling process. Sensors are either installed directly in tanks or in feed or outlet process streams, as well as at the filling stations for verification.

Depending on the product, optek inline sensors can monitor for turbidity, color, dilution target, or even opalescence in biologics.

Providing quality with a live data record for the entire batch leads to optimal QA/QC for documentation and process understanding.

### Turbidity

Many products have a base turbidity that relates to the product concentration. optek turbidity sensors are extremely accurate in low concentration ranges, while also having a wide dynamic range accommodated for high concentration ranges.



optek Stainless Steel Housing with C4000 Converter



optek TF16-N Scattered Light Dual Channel Turbidity Sensor

## Dilutions

Certain products that contain turbidity will be diluted to attain the proper target dosage. optek inline sensors monitor the transition and verify that the target dosage is being met before going to the fill stations.

## Opalescence/Haze

Certain biologics that are stored in a vessel prior to going to filling stations acquire a phenomenon called “opalescence.” This usually is a non-desired effect caused by temperature drift. It is mostly aesthetic in nature, and usually does not affect potency of the drug. However, certain companies will disqualify production lots due to the undesired effect. optek UV or scattered light sensors are able to monitor opalescence occurring on a small scale. This alerts the operators immediately preventing product losses while ensuring product quality.

All of the sensors listed come complete with all certifications for manufacturing areas.



optek C4000 Photometric Converter



optek AF45-VB Single Channel UV Absorption Sensor with calibration option

## 12 | Calibration



optek calibration accessories have been specially designed for non-intrusive calibration and verification of optek UV sensors AF45 and AF46. The unique Calibration Cuvette enables product calibration without need to interfere with the process line. It allows users to create a correlation of absorption signals to the concentration of product or an equivalent substance, creating an easy link from lab to process.

Three series of solid filters are available to ensure confidence in your measurements. The UV-L filter series is used to calibrate photometric accuracy and linearity. The UV-B filter series verifies integral blocking and the UV-S filter series tests for long term stability of the sensor.

All optek filters ship with NIST-traceable certification (National Institute of Standards and Technology). optek is equipped with an extremely high quality NIST-traceable calibrated spectrophotometer assuring quality and quick turn around time for recertification of filters.

The main advantages of the optek calibration concept include:

- only 1 filter (set) for multiple sensors ensures identical calibration
- only the filter needs to be sent back for recertification, while the sensor remains operating.



optek calibration accessories



High-end spectrophotometer in optek calibration laboratory





## UV Sensors

### Calibration Cuvette

Non-intrusive product calibration, establish calibration curves (linearization functions) for product or model substance

### Calibration Filters UV-L

Nominal Absorption:

0.45, 0.9, 1.8 and 2.4 CU

Purpose: verify photometric accuracy and linearity

### Calibration Filter UV-B

Nominal Absorption: > 3 CU

Purpose: verify integral blocking

### Calibration Filters UV-S

Nominal Absorption:

Application specific

Purpose: test for long term spectral stability



### Calibration Case

Holds up to 7 calibration filters

## NIR-Absorption Sensors

Calibration filters are available with different nominal absorption values for both inline and probe versions of NIR-Absorption Sensors.

NIST-traceable standards can be used to test performance prior to production runs.

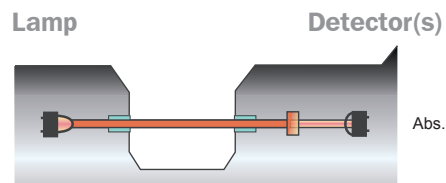




# 14 | Principles of Measurement

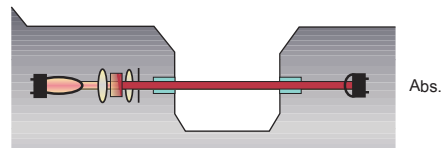
## Sensor ASD19/ASD25

NIR-Absorption,  
single channel concentration  
measurement



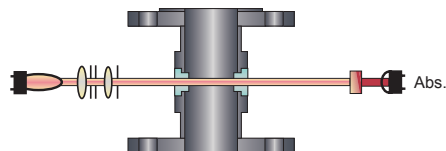
## Sensor AS16

VIS- and NIR-Absorption,  
single channel concentration and  
color measurement



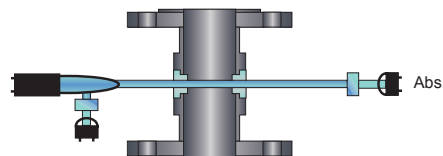
## Sensor AF16

VIS- and NIR-Absorption,  
single channel concentration and  
color measurement



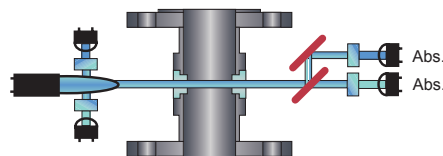
## Sensor AF45

UV-Absorption, single channel concentration  
measurement with compensation of lamp  
intensity



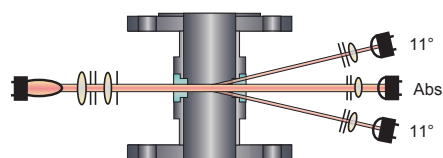
## Sensor AF46

UV-Absorption, dual channel concentration  
measurement with compensation of  
lamp intensity



## Sensor TF16

11° Scattered Light and NIR-Absorption  
dual channel turbidity measurement





## Additional Benefits | 15



optek offers superior sanitary sensor bodies for inline applications.

### Process Connections:

- Clamp TC L14 AM7
- Clamp / Flange / Thread DIN 11864
- Tube-end ISO 1127, DIN 11850, BS 4825
- other aseptic connections on request

### Line Sizes:

- 0.25 - 3.0 inches (DN06 - DN80)
- others on request

### Materials:

- 1.4435 (316L) stainless steel (BN2)
- 1.4539 (904L) stainless steel
- Gaskets: EPDM (FDA, USP class VI, 3-A)
- Windows: Sapphire
- Conductivity: PEEK (FDA, USP class VI)

### Design:

- minimized holdup volume
- electro-polished  $R_a < 0.4 \mu\text{m}$
- minimal gap, minimal tolerance
- optimized flow
- wide OPL variations (1 - 200 mm)
- $dF < 0.5 \%$  with solid block sensor bodies (316L)
- $dF < 1.0 \%$  with welded sensor bodies (316L)
- pressure tested according to PED
- certified materials



optek systems are also available with Explosion proof and PROFIBUS® PA.

Interested in Foundation Fieldbus Applications?

Just ask optek!



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