

## Optimal conditions in bioreactors



## Industry Situation

**Background**

Biopharma combines the principles of biology, biotechnology, and pharmaceuticals to develop therapeutic products that harness the power of living organisms and their molecules to diagnose, treat, and prevent diseases. These products are typically large and complex molecules used for medical purposes, such as proteins, peptides, antibodies, nucleic acids, or living cells.

The Biopharma industry has experienced rapid growth in recent years, driven by advancements in biotechnology, an increased understanding of diseases at the molecular level, and the growing demand for targeted and personalized therapies. It is a highly competitive and dynamic sector critical in advancing medical science and improving patient outcomes.

The biopharmaceuticals market is valued at 651 Billion USD in 2027. Asia Pacific is growing at the highest CAGR over 2019-2027. Amgen Inc., Abbvie Inc., Bristol-Myers Squibb Company, Eli Lilly and Company, Johnson & Johnson are the major companies operating in biopharmaceuticals.

## Application Challenges

Biopharmaceutical processes involve cell cultures, fermentation, and purification steps. Effective process monitoring requires a comprehensive understanding of the underlying biology and chemistry, as well as the ability to capture and interpret data from multiple sources. Obtaining real-time data can be challenging, as biopharmaceutical processes are susceptible to inherent variability, both within and between batches. Ensuring batch-to-batch consistency is crucial for product quality and regulatory compliance.

In-line sensors provide instant feedback on measurement changes, enabling timely adjustments and facilitating process optimization. Monitoring pH and oxygen in real-time is a critical aspect of biopharma processes to ensure optimal conditions for cell culture, fermentation, and downstream processing. pH and oxygen sensors can experience stability issues and drift over time, requiring frequent calibration to maintain accuracy. Complex biopharma media can lead to sensor fouling or contamination, affecting sensor performance and accuracy. pH and oxygen sensors must withstand harsh conditions encountered in biopharma processes (including SIP), such as extreme temperatures, pH ranges, and aggressive chemicals. Our robust solutions are designed for challenging biopharma processes.

## Reference Application

The biopharmaceutical industry is highly regulated, and regulatory agencies, such as the U.S. Food and Drug Administration (FDA), impose stringent guidelines and requirements for manufacturing processes. Accurate control of cell culture fermentation ensures compliance with regulatory standards and guidelines, enabling smooth product development, clinical trials, and commercialization.

The METTLER TOLEDO solutions were developed in accordance with the industry and process requirements.

The applications covered in this document are:

- pH and oxygen control during fermentation/cell culture
- Conductivity & pH in media and buffer preparation

## SBU Contact

Ehsan Mahdinia – Industry Manager  
Pharma



# Fermentation/Cell Culture

## Door Opener Solution

### Door Opener/Value Offering

Maintaining accurate pH and oxygen levels in bioreactors.

### Solutions:

Accurate control of cell growth conditions, including pH and oxygen supply, ensures optimal cellular metabolism, resulting in higher productivity and better product yields.

### Product/Solution to be presented:

InPro 3253i, InPro 6860i HD, InTrac 797

### Advantage over competition

- Similar pH and DO sensor type from bench to large-scale manufacturing.
- We offer pH and DO sensors that withstand multiple harsh SIP conditions.
- A pH sensor range that is designed for fermentation and cell culture and resists clogging. This will minimize drift and process variability.

- Our optical DO sensor with aerophobic anti-bubble OptoCap eliminates signal noise leading to higher process reliability

- Unique retractable sensor housing with dual flushing chambers for CIP, SIP, and calibration.

### ISM offers:

- Diagnostics that indicate when maintenance or replacement will be necessary
- Full traceability, audit trail, and easy maintenance

## Contact Job Titles

- Bioprocessing engineers
- Fermentation and cell culture scientists
- MSAT or MTECH team members

## Value Selling Approach

### Pre-Visit

Check Pharma Application Spotters Guide with details of this application and supporting material listed under sales tools.

### During Visit

Check whether they utilize inline sensors for fermentation; use the FOCA technique to discover their needs and concerns related to the upcoming project. Ask about the sensors' cleaning routine and time spent on maintenance and the impact of possible fouling/improper pH readings. Show them the benefits of ISM and retractable housings (simplified maintenance). Mention the importance of service coverage in extending the pH sensors' lifetime.

### After Visit

Send the selected value content.

## Sales Insights

Accurate cell culture fermentation is crucial for biopharmaceutical companies to optimize productivity, maintain consistent product quality, comply with regulatory standards, achieve process scalability and accelerate time-to-market.

- A drift of the pH measurement caused by clogging of the sensor diaphragm and SIP cycles leads to incorrect process control, which adversely affects the biology in the bioreactor. This impacts the yield and quality of the desired proteins.

- Insufficient oxygen levels negatively affect cell health and output. Excess oxygen causes unwanted oxidative stress to the cells. The drift of the measurement caused by SIP cycles and measurement noise due to air bubbles complicates process control.

## Sales Tools

### **Recommended Content – Review Before**

- VSG: C00190EN, C00189EN
- Conversation: Eliminating DO Fluctuation in Cell Cultures and Fermentation
- Application Spotters Guide Pharma: PA9736EN
- Detailed Application Overview: PA9667EN
- FOCA Questions PA9668EN
- Process Analytics in Biopharma: PA9214EN
- Competitive Comparison: InPro 3253i PA9199EN
- Virtual Biopharma Factory: IND30552268

### **Recommended Content – To Show**

- Application Presentation: PA9690EN
- Soution presentation: Excellent Measurement stability with high-performance optical DO Sensors

### **Recommended Content – To Share**

- Application Note: Easier Sensor Sterility and Fewer Batch Losses PA0162EN
- Datasheet: InPro 3253i PA2049EN
- Datasheet: InPro 6860i HD PA2033EN
- Guide: pH & DO Accuracy Guide for the Pharmaceutical Industry PA0016EN

Web: [Sensors for bioreactors](#)

LMS: [pH measurement](#)

## Service DO Opportunities

Full preventive maintenance covering calibration, inspection, cleaning and operational testing will help maximize sensor lifetime and catch any out-of-specification performance issues.

- For more details, check service datasheets: Recommended Services for pH Sensors (PA2051EN) and DO Sensors (PA2053EN)

# Media and Buffer Preparation

## Door Opener Solution

### **Door Opener/Value Offering**

Conductivity and pH control in media and buffer preparation.

### **Solutions:**

Control blending and mixing in media preparations and buffer solutions

### **Product/Solution to be presented:**

InPro 7100i, InPro 3250i, Intrac 797

### **Advantage over competition**

- We can offer sensors that will withstand multiple SIP and CIP conditions
- Digital communication ensures signal integrity.
- Same sensors from R&D to commercial volumes
- Conductivity sensors factory calibrated and certified valid for one year from installation
- ISM offers:
  - Plug and Measure
  - Full traceability, audit trail, and easy maintenance
  - Continuous performance diagnostics (on pH sensors)

## Contact Job Titles

- Bioprocessing engineers
- Manufacturing team
- MSAT or MTECH team members



## Value Selling Approach

### **Pre-Visit**

Check Pharma Application Spotters Guide with details of this application and supporting material listed under sales tools.

### **During Visit**

Find out what is the typical process conductivity range and how they control pH value. Ask the customer about cleaning and calibration routines which is usually cumbersome. Inquire about what tools they use for audit trails and how they ensure compliance with sensor maintenance regulations. Ask if they suffer from measurement fluctuations and sensor fouling and what challenges they currently face. Show selected presentation.

### **After Visit**

Send the selected value content.

## Sales Insights

Application: The control of blending and mixing in media preparations and buffer solutions.

Conductivity can indicate excess salt formation as a result of inadequate pH control. Temperature is usually increased to optimize the dissolution rate and reduce mixing time.

Customers always do these measurements. pH and conductivity are major control variables and quality attributes that help ensure the consistency of both media preparations and buffer solutions. The drift of the pH measurement caused by SIP cycles leads to off-spec preparations. Analog conductivity measurements can suffer from interference from (rotating) process equipment.

## Sales Tools

### **Recommended Content – Review Before**

- VSG: C00190EN, C00189EN
- Process Analytics in Biopharma: PA9214EN
- Virtual Biopharma Factory: IND30552268
- Application Spotters Guide: Pharma PA9736EN
- Detailed Application Overview PA9688EN
- FOCA Questions: PA9689EN
- Comparison of InPro 3250i and CPS77D in CIP Cycles Test: PA8170EN

### **Recommended Content – To Show**

- Application Presentation: PA9690EN

### **Recommended Content – To Share**

- Datasheet: InTrac 797 / 799 Housing PA2060EN
- Datasheet: InPro 3250i PA2097EN

**Web:** [Sensors for bioreactors](#)

**LMS:** [pH measurement](#), [conductivity](#)

## Service DO Opportunities

Full preventive maintenance covering calibration, inspection, cleaning and operational testing will help maximize sensor lifetime and catch any out-of-specification performance issues.

- For more details check service datasheets: Recommended Services for pH Sensors (PA2051EN).