Process Analytics Solutions for Biotechnology and Pharmaceutical Applications
Our industrial solutions cover the diverse steps in a host of manufacturing processes. Solutions range from receiving raw materials through various manufacturing processes, in-line process control and end-of-line packaging control, to logistics and shipping. These solutions are integrated into the customer’s IT environment, helping automate their workflows.

METTLER TOLEDO instruments are used in research, scientific, drug discovery, and quality control labs, amongst many others in the pharmaceutical, chemical, food&beverage and cosmetics industries.

METTLER TOLEDO invests between USD 60 and 70 million per year in R&D, having increased the R&D spending by an average of more than 10% each year for the past five years. METTLER TOLEDO has an outstanding reputation as a global innovator. It also has highly specialized know-how in the field of automation and robotics, miniaturization, software development, as well as optical- and laser-based applications. METTLER TOLEDO is committed to total quality management and ISO standards and compliance with industry regulations.

Within the METTLER TOLEDO group, the Process Analytics division focuses on analytical measurement solutions for industrial production processes. The division is comprised of two long-standing business units – INGOLD and THORNTON – which are recognized as leaders in the markets they serve.

THORNTON – Leading Pure Water Analytics.

Thornton Inc. was acquired in 2001 and is now the second member of the Process Analytics division. THORNTON continues to focus on pure and ultrapure water measurement systems, complementing INGOLD’s in-process measurement solutions.

Dr. Richard D. Thornton, a professor at the Massachusetts Institute of Technology (MIT), founded Thornton Inc. in 1964. THORNTON develops, manufactures, markets and services innovative analytical instruments and sensors for measurements in pure and ultrapure water applications with such parameters as resistivity/conductivity, DO, flow, pressure, pH / ORP, temperature and TOC (Total Organic Carbon).

For nearly forty years THORNTON has been recognized as the technology leader by defining the most accurate resistivity measurement of ultrapure water. THORNTON works closely with customers and international organizations, such as USP, EP, JP, FDA, ASTM in establishing industry standards for the pharmaceutical, semiconductor and power industries.

Premier international pharmaceutical manufacturers and global water system fabricators prefer innovative products from THORNTON.
INGOLD – Leading Process Analytics.

Founded in 1948, Ingold AG became part of Mettler AG in 1986, forming the cornerstone of the Mettler-Toledo Process Analytics division.

INGOLD has a long history of innovations, starting with Dr.Ingold’s invention of the pH combination electrode, the first sterilizable pH electrode produced for the pharmaceutical industry. The INGOLD pH, DO, CO2, conductivity and turbidity product lines firmly establish Mettler-Toledo GmbH as a worldwide leader for process analytical measuring systems in chemical, food & beverage, biotechnology and pharmaceutical industries meeting the challenging requirements of modern industrial liquid processes, INGOLD introduced hygienic sterilizable pH, oxygen, CO2 and turbidity sensors, and set industry standards with its famous INGOLD socket for fermentation vessels and the IP 68 VP connector for watertight installations. Our latest innovation was the industry sterilizable dissolved CO2 measuring system which now helps customers to optimize their cell cultures.

INGOLD is well known for its long experience in offering reliable quality measurement solutions for biotechnology and pharmaceutical applications which ensure an optimal yield and low overall costs for our customers.

**Fermentation control with pH, CO2 and DO**, see p.6

pH is the most important quality parameter for cell and bacterial growth, metabolic activity and final products in bacterial fermentation or cell culture processes. DO and CO2 control, on the other hand, is critical for an optimized growth environment and hence for yield. Proven hygienic design, withstanding repeated sterilization / autoclave treatment is indispensable for protection of valuable fermentation batch contents. INGOLD’s long-life sensors with minimum drift provide highly accurate and reproducible measurements and offer an ideal tool to optimize yield and overall cost-of-ownership.

**Cell growth monitoring with turbidity sensors**, see p.7

One of the most important parameters when monitoring mammalian cell processes in bioreactors, is cell density. INGOLD’s sterilizable turbidity sensors offer reliable and accurate inline monitoring of cell growth, thus providing the basis for achieving higher viable cell densities at reduced medium consumption.

In addition to our measurement equipment we help our customers to comply with regulations and integrate into process control systems:

- FDA compliant services, see p. 13
- Compliance with regulations, see p. 14
METTLER TOLEDO products ensure safety and reliable top performance throughout a plant.
Synthesis Reactor

Fermentation

Downstream processes, p. 10

pH
Conductivity
Turbidity

Separation
Drying
Crystallization
Filtration

Effluent Treatment, p. 12

pH
DO
Conductivity
Turbidity

Waste Water Tank

Final Products
High product yield with INGOLD quality products.

For more than 50 years Mettler-Toledo Ingold has actively engineered new products to meet the demands of our customers to improve their process efficiency and to comply with FDA and GMP regulations. A wide range of hygienic measurement solutions with sterilizable / autoclavable pH, DO and turbidity sensors helps our customers controlling and optimizing fermentation and cell culture processes.

**pH measurements**

A complete range of sterilizable and autoclavable pH electrodes with low drift and long serviceable life

**Combined pH/temperature electrodes**

The highly versatile solution provider, InPro 2000 Series, is particularly suitable for high accuracy requirements due to a flowing liquid junction.

The low-maintenance pH electrodes InPro 3100 with high pressure resistance and InPro 3253 with unmatched stability performance.

**Non-glass pH electrode**

The highly robust non-glass electrode InPro 3300 based on ISFET technology offers fast response time and EHEDG certified hygienic design.

**CO₂ measurements**

CO₂ In-situ monitoring

The new InPro 5000 CO₂ sensor features hygienic design and accurate in-situ monitoring, specially required for optimized fermentation with mammalian cells. The transmitter CO₂ 5100 e offers diagnostic information, two current outputs and integrated PID controller.

**DO measurements**

Enhanced performance and unmatched hygienic design

The InPro 6800 DO sensor for use in biotechnology applications is available complete with EHEDG, 3-A and 3.1B material certificates. The service-friendly design of the inner body guarantees an optimal cost of ownership.

**Advanced line** transmitters for pH, DO and CO₂

The pH 2100 e and O₂ 4100 e are advanced performance transmitters with two current outputs and PID controller. A unique sample calibration routine secures a highly accurate measurement, particularly in long lasting batches. Two wire units in Ex and non-Ex versions are both available with HART®, PROFIBUS® and FOUNDATION Fieldbus interface in Ex.

**Sterilizable retractable housings**

The enhanced retractable housings InTrac 796 e/797 e/799 e are designed for sterilization of gel- and liquid-electrolyte pH electrodes as well as for DO and turbidity sensors and turbidity sensors and other in-situ sterilization of electrodes/sensors.

The TriLock™ system guarantees:
- safe insertion into process
- safe withdrawal of sensors
- sensor exchange during ongoing process

The InTrac 798 is suitable for 120 mm pH electrodes, with enhanced safety and cleanability features (EHEDG tested).
A unique cell growth monitoring system

The easy-to-handle turbidity transmitter Trb 8300 is equipped with application-specific parameter sets, offers linearity over a wide range of concentration, and an easy-to-use calibration routine, ProCal.

The sterilizable turbidity sensor family InPro 8100/8200 functions on the principle of backward scattering of light. These sensors cover a wide measuring range with an extraordinary linearity up to high concentrations.

Hygienic housings

InFit 761/764-50 CIP is a static housing family for the safe mounting of gel- and liquid-electrolyte pH electrodes as well as of DO sensors. These housings feature a unique hygienic design with the use of FDA approved materials and EHEDG certificates.

Versatile static housing family

InFit 761/764-50 CIP is a static housing family for the safe mounting of gel- and liquid-electrolyte pH electrodes as well as of DO sensors. These housings feature a unique hygienic design with the use of FDA approved materials and EHEDG certificates.
Accurate and reliable measurements under harsh conditions.

Mettler-Toledo Ingold solutions cover a wide range of difficult operational conditions, such as those commonly found in chemical synthesis processes, e.g. in vitamin or hormone production. Our measurement systems are able to master the most demanding process environments operating at high temperatures and pressures – the industrially proven equipment designs ensure long serviceable life and reliability for critical processes. Many products are available with international Ex and pressure certificates to comply with plant safety requirements.

pH measurements

pH electrodes – the right solution for every application

For the most demanding processes

Substantially prolonged operational life reduces maintenance and replacement costs. The pH electrode InPro 4800 is designed for toughest applications and is resistant to particularly high operational pressures.

The versatile proven industry leader

InPro 4250 is a high-performance, industrial pH electrode with enhanced Xerolyt® Plus polymer electrolyte. Direct contact of sample media with the polymer electrolyte ensures freedom from clogging. High resistance to solvents and acids. The InPro 3250 is particularly suitable for high accuracy requirements.

The selection is completed by

the liquid filled electrode type InPro 2000 (see p.6), a versatile solution provider with high accuracy measurement, long life and double diaphragm option for applications with high contamination potential.

«Advanced Line» pH transmitters

The two-wire transmitter pH 2100 e is suitable for highly reliable and accurate pH measurements in many industrial applications. The package offers HART® or PROFIBUS® and FONDATION Fieldbus communication in Ex and non Ex versions.

Temperature-compensated pH electrodes – InPro 2000, 3000 and 4000 families.

The integrated temperature sensor provides you with the following benefits:

- elimination of calibration errors.
- more precise pH measurements.
- measurement of process temperature directly at the location of pH measurement.

The result:
More accurate and reliable measurements with INGOLD technology!
Cleaning and calibration systems

EasyClean – a fully automated pH measuring solution

Our range of automated sensor cleaning and calibration systems offer unique solutions for chemical processes. This system is particularly suitable for measurement points with frequent calibration cycles and ensures more reliable measurements, and a longer sensor life, leading to an improved cost-of-ownership. EasyClean is perfectly complemented by the InTrac SL housing family, and is available in either Ex or non-Ex versions.

Retractable housings

The versatile retractable housing

The enhanced InTrac7XX e housing family has been designed to meet the highest standards of safety during online process measurement tasks. They provide a straightforward means for the insertion and withdrawal of sensors without any need to interrupt the ongoing process plus TriLock™ for safety. These housings come complete with 3.1B and ATEX/FM certificates.
High quality products for cost-saving process efficiency.

High process efficiency is a critical factor in separation, filtration, crystallization or drying in order to save costs and to improve yield. Compliance with FDA standards and CIP/SIP conditions are mandatory. Beyond that, low maintenance, rugged and versatile design as well as long serviceable life are other important requirements to optimize overall cost-of-ownership.

**pH measurements**

**Accurate and versatile low-maintenance electrode**

The InPro 3250 is an enhanced pH electrode for a wide range of applications, and fully autoclavable or in-situ sterilizable featuring high pressure specifications. A solution ground option with enhanced diagnostics features is also available.

**M 700 the versatile multichannel solution.**

The M 700 transmitter is a versatile multi channel system and freely configurable even on-site. It is available in hygienic design and comes with a wide variety in Ex and non-Ex versions and with a wide variety of software options (21 CFR part 11, logbooks).

**Conductivity measurements**

**CIP-applicable conductivity sensor**

The InPro 7108 VP sensor is used for medium to high conductivity measurements. All sensors of this family are equipped with a built-in Pt1000 temperature sensor (RTD), and come with 3.1B certificate.

**Unique diagnostic features**

The transmitter Cond 7100 e covers a wide range of applications, with enhanced safety features such as unique USP 23 set points. The SensoCheck™ feature allows polarization to be detected early and reliably. Digital communication versions with integrated HART®, PROFIBUS® or FOUNDATION Fieldbus protocols in Ex and non-Ex are also available.

**IP 68 VarioPin connector – the new industrial standard for all METTLER TOLEDO sensors**

The rugged construction of the VarioPin connector provides users the watertight connection of a fixed cable with the convenience of a detachable cable. The Vario Pin connector is tested to IP 68, ensuring that the connection is dust and submersion proof.
Crystallization onset/filter break-through monitoring

The new easy-to-handle transmitter Trb 8300 is equipped with application-specific parameter sets, and offers an unmatched wide linearity, as well as an easy-to-use calibration routine. Together with the high turbidity sensors InPro 8100/8200 the system provides a highly accurate crystallization onset monitoring system. For low turbidity monitoring e.g. for filter breakthrough control the forward/sideward sensors are the first choice.

Static state-of-the-art housing

InFit 761-25CIP, the modern static housing for safe, quick and simple mounting of pH electrodes, DO and conductivity sensors with PG 13.5 thread. InFit 761 meets the latest European pressure directives and provides full process safety with 3-A and EHEDG certificates.
Accurate pH measurement is important for determining the state of the raw effluent, for controlling the dosage of chemicals in neutralization and other necessary chemical treatment steps, as well as for monitoring the quality of the final discharge.

An efficient control of DO transfer into the treatment basins is required in order to enable aerobic microorganisms to decompose the organic compounds. Our rugged measuring systems provide a reliable solution to these demands.

Value Line transmitters

**Cost effective solutions for standard applications**

These transmitters for pH, DO and conductivity are characterized by their straightforward installation, set-up and operation. They offer two current outputs and are available in panel- and wall-mount versions.

**pH measurements**

**The low-maintenance electrode**

The InPro 3250 offers self-cleaning of the diaphragm, effected by the partly flowing liquid junction, hence, long operational life in effluent applications.

**The cost-effective polymer body electrode**

The InPro 4010 with PSO body and polymer reference electrolyte ensures reliable measurements in contaminated effluents. The InPro 4500 as a 1" thread-in PVDF version is equipped with a flat membrane, a solution ground and offers a robust and easy-to-handle alternative.

**DO measurements**

**Unique price/performance ratio**

Designed for simultaneous measurement of DO and temperature values in the field of effluent treatment applications, the InPro 6050 offers high and reliable performance.

**Turbidity measurements**

**The new low-cost polymer body sensor**

InPro 8050 for high turbidity together with the transmitter Trb 8300 are ideal for highly contaminated effluent applications and offer easy and reliable measurement at reasonable costs.

**Conductivity measurements**

**The robust 4-electrode sensors**

The InPro 7108/CPVC is used for reliable measurement from medium to high conductivity.
FDA-compliant quality and services – making the difference.

High product quality in pharmaceutical applications can only be achieved if all the relevant steps of a process are carefully defined and measuring results are precise and reproducible. Complete documentation of each single step is of highest priority. METTLER TOLEDO has the knowledge to assist in equipment qualification (EQ) to meet the most stringent legal regulations.

Design qualification (DQ)
In this very first step, the functional, operational and technical specification for a measuring point have to be defined. METTLER TOLEDO offers the requested certificates to prove product quality.

Installation qualification (IQ)
Following basic installation and initial calibration, the measuring loop is ready for testing. All relevant data will be recorded in the EQ document provided by METTLER TOLEDO service personnel.

Operational qualification (OQ)
Before used in the process, the guaranteed performance has to be checked and recorded in the EQ document. A detailed operational qualification is the final touchstone for successful system functionality.

Performance qualification (PQ)
Periodically performed system tests guarantee proper functionality of a measuring loop. Results are protocolled in the logbook and are key information for a traceable validation.

Maintenance qualification (MQ)
METTLER TOLEDO will train personnel to set up a preventive maintenance plan, indispensable for ensuring trouble-free process operation.

Compliance tools and services are available as individual modules or comprehensive packages.

With this package METTLER TOLEDO is able to provide customized validation services.

Global services
- Conductivity sensor calibration (NIST traceable)
- NIST traceable buffers
- Validation support/consulting
- Equipment qualification according to the latest QM standards as defined by the responsible authority
- Sensor performance qualification

METTLER TOLEDO meets the latest standards of GMP and FDA guidelines.
Compliance and enhanced safety – hygienic design by INGOLD including USP class VI.

It all started with the INGOLD socket and the 465 sterilizable pH electrode some decades ago. Today, METTLER TOLEDO has unrivalled in-depth experience in hygienic equipment design and a proven track record in meeting the most stringent FDA and GMP regulations.

Housings and sterilizable/autoclavable sensors suitable for CIP and SIP procedures in pharmaceutical applications are core products of the INGOLD program.

INGOLD process adaptions
The INGOLD safety weld-in socket is the optimized process adaption and offers the highest possible level of safety. The optimal positioning of O-rings, makes them ideal for use in combination with CIP/SIP approved housings.

Compliant with EHEDG, FDA, USP class VI and 3-A guidelines
Hygienic CIP-housings are based on stringent design principles, are fully sterilizable and fulfill the requirements of 3-A and EHEDG standards. They are available with 3.1B certificates for the housing material and FDA 21 CFR 177 compliant sealing/O-ring material as standard supply, on request even with USP class VI.

Smooth surfaces
The smooth surfaces of Mettler-Toledo Ingold CIP-housings prevent the adherence of microorganisms. CIP approved housings are produced either from one single workpiece or have smooth, crevice-free welded seams. The materials fulfill the requirements of AISI 316L.

Electrodes and sensors for CIP/SIP procedures complying with USP class VI
Most INGOLD pH electrodes and DO sensors are designed to be sterilizable and autoclavable up to 140 °C (284 °F). Conductivity and turbidity sensors are also sterilizable. O-rings exposed to wetted parts of DO and CO2 sensors comply with USP class VI as a standard.

Documentation and certificates
All applicable sensors and housings fulfill the new European pressure directive and are supplied with 3.1B certificate. A comprehensive selection of our instruments is 3-A and EHEDG certified and in compliance with GMP guidelines.
A worldwide network of experts at service.

METTLER TOLEDO provides full sales and service coverage worldwide. Wherever our customers are, we are the competent partner. Many global industrial manufacturers rely on our longstanding experience.

Distribution network
Based on its several global production sites, more than 20 market organizations, and numerous sales representatives, METTLER TOLEDO maintains a wide distribution network all over the world. Satisfaction of our customers is based on three pillars:

- **Consulting:** With the knowledge of our experts, we support you in finding the best solution, including planning, product selection, and installation of our measurement solution.
- **Top products:** A complete range of products and systems to meet measurement requirements
- **After-sales service:** With our customized, lifelong service management, we are able to assist in managing measurement loops throughout their whole life-cycle.

Mettler-Toledo Process Analytics’ four producing organizations are close to our customers all over the world and provide:

- Faster logistics
- Fast response time to market demands