

Solutions for Life Science



Faster, More Consistent pH Results

Tools and Techniques to Speed Your Workflow

METTLER TOLEDO

Accelerating Life Science Research

Controlling Variability Is the Key

Controlling pH in your samples and reagents is essential to achieve accurate, reproducible results.

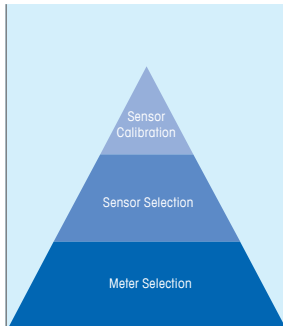
Biological systems are so sensitive that even seemingly insignificant changes in their environment can significantly alter their behavior and change your results. At METTLER TOLEDO we understand the importance of controlling variability in your experiments and have set the standard for precision measurement for more than 60 years.

For high throughput assays, micro-volumes, challenging chemistry and regulatory compliance, with a quality meter, the right sensor and good technique, your measuring system can deliver extraordinary accuracy and precision. METTLER TOLEDO offers a wide range of quality pH meters and superior sensor technology, so whatever your measurement challenge, we have the tools to meet your need.

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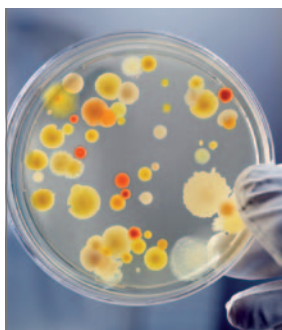
METTLER TOLEDO pH solutions – Simply reliable



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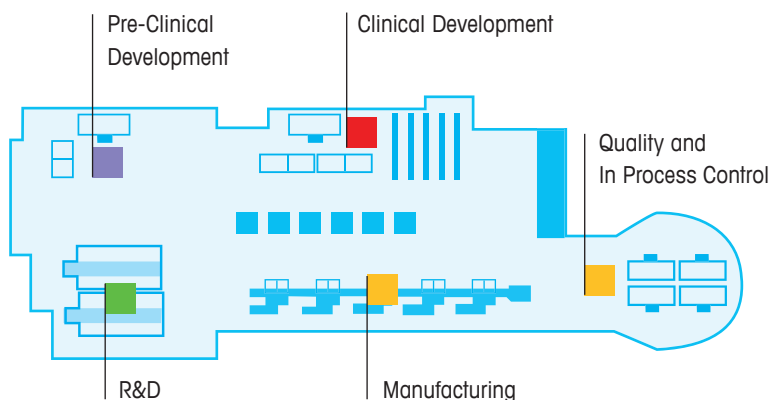
Quality throughout the Lifecycle

Precision from R&D to Product Delivery

At every step of the drug development process, measurement-related risks abound, each with a unique ability to negatively affect your product's time-to-market and overall quality. From your buffers for chromatography, electrophoresis and enzymology, to the composition of your culture media and stains, everything must be exactly right.

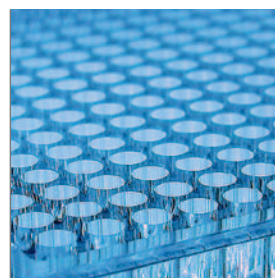
Renowned for accuracy and precision, METTLER TOLEDO offers a broad range of high quality instruments to reduce measurement risk at every step in your production process.

Life Sciences Virtual Tour



R&D

1 Million Compounds
Targets ID, Target Validation,
Lead Discovery, Lead Optimization



Key pH Requirements

Accuracy & Precision
Easy to use pH equipment
High-throughput solution
Increased Productivity

Risks and Cost of Failure

False positive/negative results
– Missed opportunities
– Candidates failing in clinicals
Complicated equipment:
– low efficiency
– long staff training time
– risk of mistakes
Poor pH measurements
– Waste of samples



Pre-Clinical Development

100 Compounds
Pharma- and Toxicology



Key pH Requirements

Accuracy & Precision
Competence & Efficiency
Traceability & Repeatability
Easy to use pH equipment

Risks and Cost of Failure

False positive/negatives results
– Jeopardizing clinical trials
– Efficiency loss
– Time loss detecting failures
Poor pH management & documentation
– Non-compliance of regulations

Clinical Development

3 Compounds
Phase I–III: Studies on efficacy
of drug



Key pH Requirements:

Accuracy & Precision
Traceability & Repeatability
User excellence
Regulatory compliance

Risks and Cost of Failure:

Undetected side effects
– Delayed Time-to-market
– Repetition of entire test series
Missing statistical evidence
– Delayed time-to-market
– Failed drug approval
– Scrutiny of entire process

Manufacturing

1 Compound
Quality and In Process Control



Key pH Requirements:

Utmost Accuracy & Precision
Strict quality control
Regulatory compliance
No downtime

Risks and Cost of Failure:

Production errors not detected
– Batch recalls from market
Unreliable test results in QC
– Production stop or batch recalls
– Image loss

Reliability and Reproducibility

Precise Measurements Require Planning

Proper Care and Technique

Problems in electrochemical measurement usually result from sensor mishandling in calibration, storage, maintenance and day-to-day operation. The freshness of your buffers, pH temperature and filling/storage technique can also affect results.

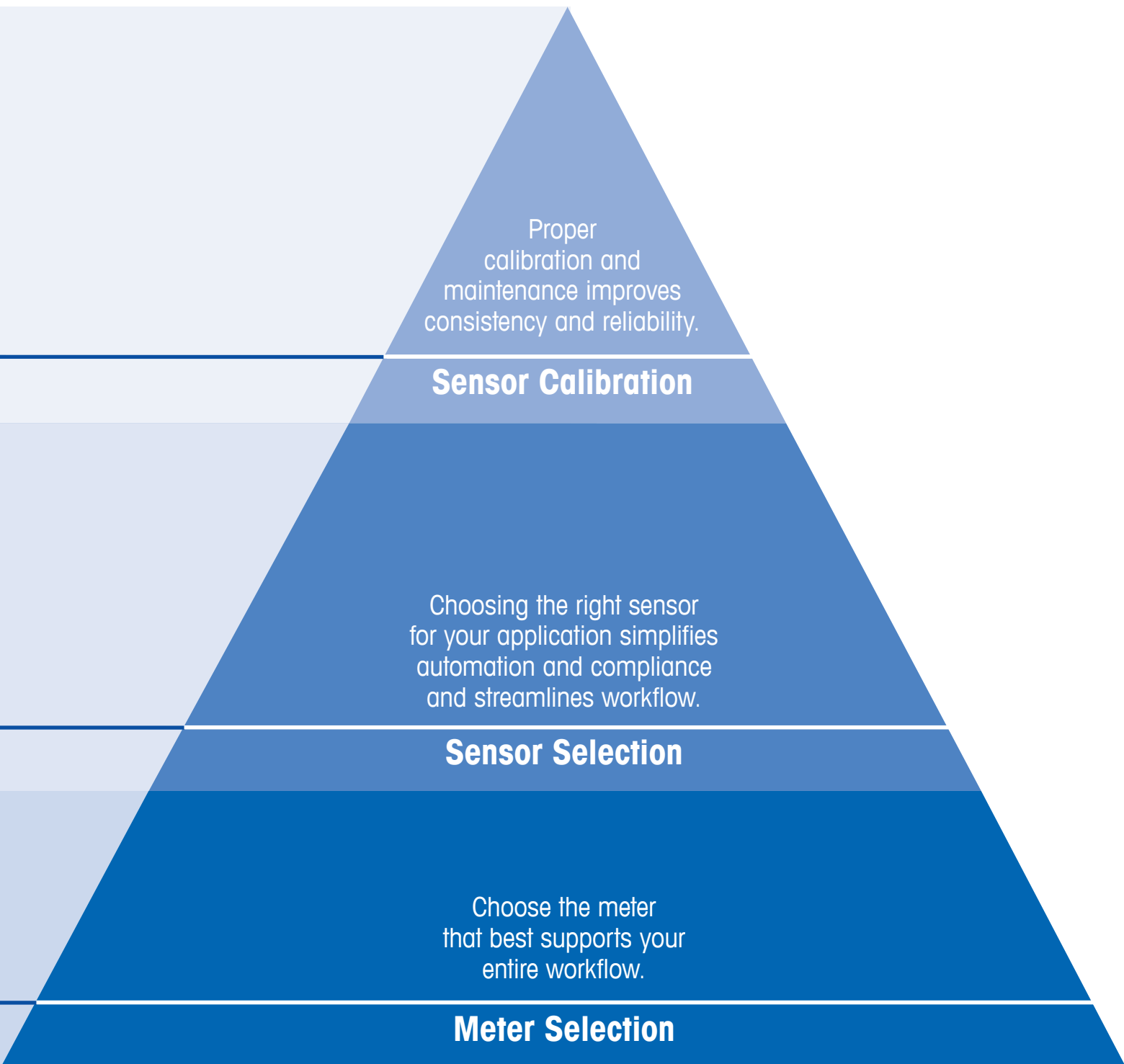
The Right Sensor

With so many types of sensors available, choosing the one best suited to your application will speed your response time and deliver more accurate results. Having the right sensor also minimizes maintenance time, lowers lab operation costs and even enhances ergonomics.

A Quality Meter

The quality of your electrochemical meter directly affects the reproducibility of your results. When choosing a meter, you must factor in its accuracy and settable, ease of use, water resistance, level of automation and its data management capability.

By using the right equipment for your application and following a few basic rules for sensor handling and calibration, your electrochemical measuring system can deliver the highest-possible accuracy and precision.








Plan for Success

Solutions for Every Application

- Do these buffers have the correct pH value?
- Does this culture media contain the proper composition?
- Which of these functional areas support or impede workflow?

Answers to questions like these require accurate measurement of electrochemical parameters.

	Challenge	Parameter	Solution
	Precise calibration	pH, conductivity, ISE, ORP	Page 10
	Avoiding or compensating for temperature effects	pH, conductivity, ISE	Page 12
	Micro-volume containers, such as 96-well plates or NMR tubes	pH, conductivity	Page 14
	Tall containers, such as test tubes and centrifuge tubes	pH, conductivity, ORP	Page 16
	Avoiding contamination of electrolyte sample	pH	Page 18



Large volumes

Volumes larger than 50 mL are generally easiest to measure, whereas very large volumes, 1 L or more require more mixing while adjusting pH. Moving a liquid too quickly with a stir bar can lead to pH value fluctuations, stir at a low but constant speed. Large volume buffers and applications include:

- Citrate buffer in immunohistochemistry
- PBS phosphate buffer in cell biology
- Tris HCl pH8.8 for acrylamide gels
- TBE buffer for electrophoresis

Small samples

Many electrodes are large, so measuring pH in small volumes can be tricky – the electrode can displace a relatively large amount of volume or simply will not fit inside the tube. METTLER TOLEDO offers a range of micro and semi-micro sensors to avoid these problems (see pages 14–17).

Some small-volume applications:

- RNA sample analysis using microarrays
- DNA sample analysis using PCR
- Protein sample analysis using immunoprecipitation

Sample analysis can also be affected by the pH of the sample. For example, many protein samples are prepared at very low pH, and neutralization buffer is added to raise the pH to 7 before further analysis. The volumes of these samples are often <500 μL . If pH is checked after an experiment, there may only be 20–100 μL or less.

Calibration Is Key

Does Your Meter Meet Your Need?

Calibration mistakes are easy to make, but by following a few simple rules and, of course, having the right equipment, you can achieve highly accurate results.



SevenEasy™
Ideal for routine lab work



SevenMulti™
For regulated labs and those that require more advanced automation

The right meter

Maximize accuracy and precision by choosing a meter that:

- Has the appropriate error limits and measuring range for your applications
- Allows a broad enough range of calibration points and calibration algorithm

- Offers the correct level of security regarding user management, password protection etc.
- Supports your compliance and automation needs

Find the most suitable meter for your needs at ► www.mt.com/pH

The right service solutions

Regular service will increase your meter's accuracy and extend its life. METTLER TOLEDO offers many service options – tailored to your needs – to ensure that your meter perform reliably.



For perfect calibration results

- Use fresh buffers
- Apply the same stirring conditions as for the measurement itself
- Choose the calibration standards that bracket the expected measuring range
- Calibrate and measure at the same temperature



Specific to conductivity

- Use low conductivity standards like 10 or 84 $\mu\text{S}/\text{cm}$ as quickly as possible – they react with CO_2 , which changes the value
- Avoid electrostatic charges from the measurement vessel
- Avoid bubbles in the probe

Specific to ISE (ion-selective electrodes)

- Always use the correct ionic strength adjustment (ISA) solution – in the right concentration
- Condition the ISE according to the operating instructions

Measuring pH

Temperature is a Critical Component

pH results are only correct if the sample temperature is taken into account. With these simple but effective rules for avoiding negative temperature effects, it's easy to obtain accurate, reproducible results.

Automatic Temperature Compensation



ATC works best with normal-size samples.

- Use a sensor with integrated temperature probe and wait for a stable signal. The meter automatically corrects the pH signal. ATC works best in samples larger than 10 mL.
- Any "Pro" type InLab® sensor – InLab® Micro Pro, Science Pro, Expert Pro – has integrated temperature probes, eliminating worries over wrong temperature settings or not capturing temperature.
- For sensors without an integrated temperature probe, use a separate probe.

Manual Temperature Compensation



MTC is extremely accurate, but can be time-consuming.

- If the temperature of your sample is known (you're working in a climate-controlled room or the samples just came out of the refrigerator) enter this known temperature in the measuring settings of your instrument to correct the pH (or conductivity) signal.
- When measuring samples with different temperatures, MTC can be time consuming, because the setting must be changed with every temperature change.



Keep your sensor with your sample.

Make sure temperatures match by storing the sensor with samples in the refrigerator or incubator, or at room temperature. This guarantees the highest accuracy because the pH membrane, reference system and sample are at the same temperature.

**Measure the sample,
not your sensor.**

With very small samples, the sensor can take so long to reach equilibrium that the sensor temperature is wrongly interpreted as the sample temperature. The sample mass is negligible compared with the sensor mass, so take the time necessary to ensure that you actually measure the sample temperature.

METTLER TOLEDO sensor technology –
Always with your application in mind

Measuring Small Samples?

Micro pH Sensors Meet the Need

The more precious or rare the sample, the greater the challenge to use it for analysis. METTLER TOLEDO's new micro pH sensors fit any size of sample container – particularly handy for precious or rare samples because they eliminate the need for larger volumes in electrochemical analysis.

InLab® Micro family – mini technological marvels

The newly developed InLab® Ultra-Micro enables pH measurement of samples as small as 15 µL.

Rigorously tried and tested, InLab®

Micro reliably meets all standard micro applications.

These micro pH sensors are too small to use an integrated temperature probe for automatic temperature compensation.

Container type	Typical sample size	Minimum sample volume in this specific container type			
		pH diameter 3mm			Conductivity diameter 4mm
		InLab® Ultra-Micro	InLab® Micro	U402-M3-S7/200	InLab® 751-4mm
Small test tubes	> 2 mL	100 µL	200 µL	200 µL	500 µL
LiteTouch Tubes reaction vials	1.5 – 1.7 mL	25 µL	65 µL	65 µL	300 µL
Sample tubes	0.5 mL	25 µL	65 µL	65 µL	300 µL
NMR tubes	400 – 800 µL	20 µL	45 µL	45 µL	300 µL
96 well plates	200 – 300 µL	20 µL	45 µL	45 µL	150 µL
PCR plates	200 – 300 µL	20 µL	45 µL	45 µL	150 µL
Sequencing vials	5 – 15 µL	15 µL	45 µL	45 µL	150 µL



InLab® 751-4mm – micro-conductivity made easy

- With a measuring range of 1 $\mu\text{S}/\text{cm}$ to 200 mS/cm , the InLab® 751-4mm covers the conductivity range typically used in the life sciences.
- The InLab® 751-4mm features an integrated temperature probe that automatically captures the sample temperature and corrects results to a defined reference temperature. For correct results, immerse the sensor to the minimum immersion level marked on the probe.
- Learn more about temperature effects on page 12.

Small, Robust and Versatile Efficient Semi-micro Sensors

Semi-micro sensors are significantly easier to use than micro sensors with test tubes and other small containers. Sample volume is still relatively low and 5–6 mm diameter semi-micro sensors promote efficient workflow.

InLab® Micro Pro Temperature corrected pH



The InLab® Micro Pro with integrated temperature sensor supports automatic temperature compensation (see page 12). With a shaft diameter of only 5 mm, it's a technological masterpiece.

InLab® Semi-Micro Maintenance and contamination free pH measurements



The InLab® Semi-Micro contains the latest in polymer electrolytes: XEROLYT® EXTRA. Service and operation could not be simpler thanks to the polymer electrolyte and the open reference connection. With no junction, there is no possibility of contamination or blockage.

InLab® Redox Micro Easy oxidation-reduction potential



ORP (oxidation reduction potential), also known as redox potential, is important in biology and easily determined with the InLab® Redox Micro. This traditional InGold product is based on the tried and true platinum ring design.



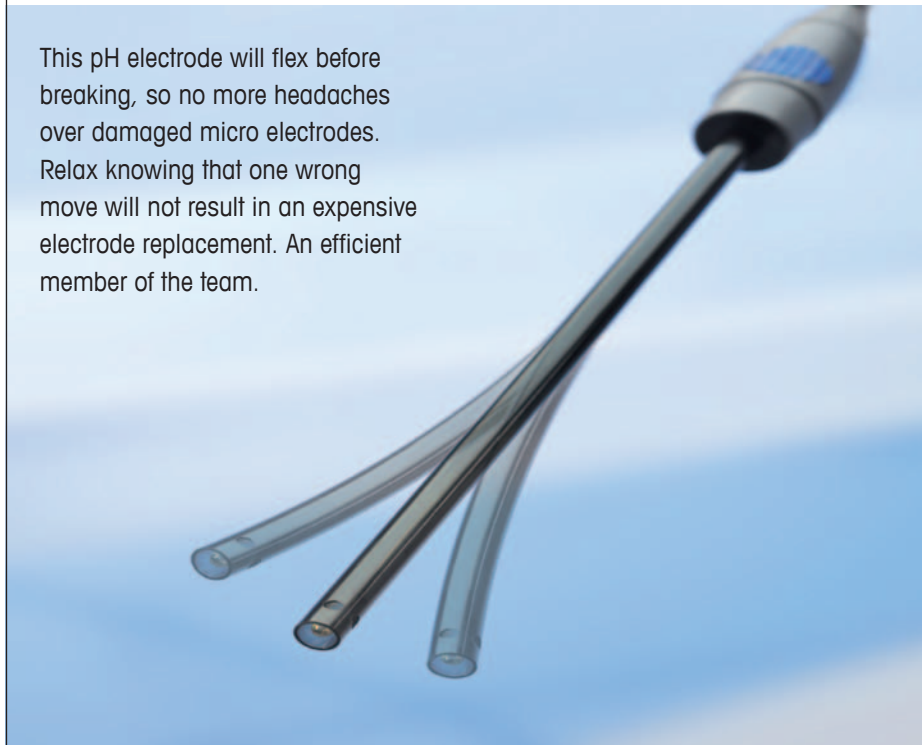
InLab® 752-6mm
Versatile semi-micro
conductivity



With a measuring range of 1 $\mu\text{S}/\text{cm}$ to 200 mS/cm this unique semi-micro conductivity sensor is a real generalist – ideal for direct measurements in test tubes or micro titrations. Its 6 mm diameter allows for a minimum immersion depth of only 15 mm.

InLab® Flex-Micro
Pliable pH precision

This pH electrode will flex before breaking, so no more headaches over damaged micro electrodes. Relax knowing that one wrong move will not result in an expensive electrode replacement. An efficient member of the team.



Contamination Control For Secure Results

When measuring samples there is always the risk of contamination, either by sample carry-over or by microbiological or genetic contamination. Conventional pH electrodes can also be damaged by electrolyte out-flow when measuring TRIS-based buffers or proteinaceous samples. This is not the case when working with InLab® electrodes!

Avoid Sensor Contamination with TRIS Buffers

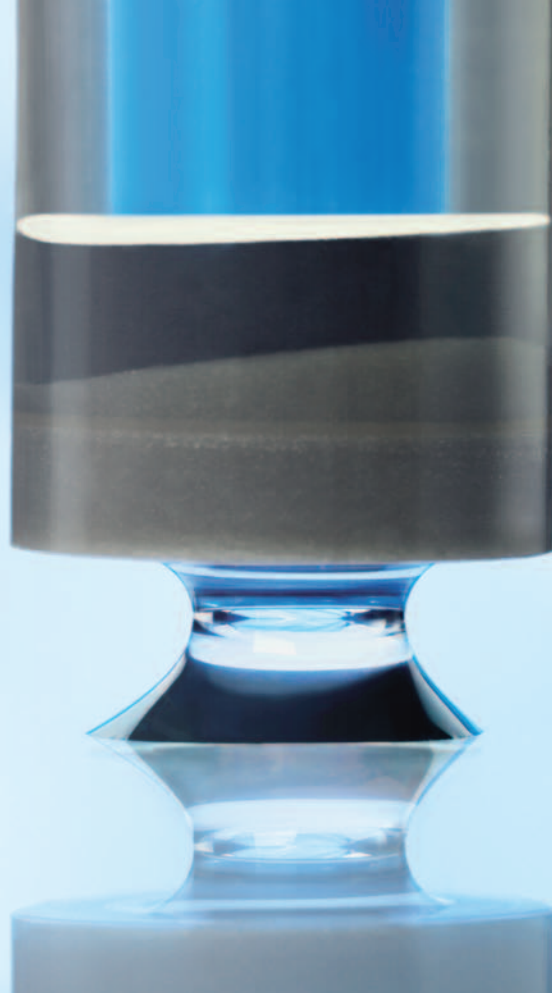
Accurate pH measurement is a key factor in buffer quality. TRIS-based buffers – widely used in biological research ranging from molecular biology to histology – can damage standard pH equipment.

How does TRIS do its damage?

When measuring pH during TRIS buffer preparation, the reference junction on conventional pH electrodes can clog when TRIS reacts with silver ions in the fill solution. This reaction can also occur with protein in the buffer, such as BSA. The eventual result is slow or fluctuating readings, or even entirely wrong results.

InLab® electrodes by METTLER TOLEDO are specifically designed for compatibility with TRIS-based buffers, assuring reliable results and accurate buffer values. The electrolyte in InLab® electrodes is guaranteed to be free of silver ions, eliminating the possibility of contamination of the junction in TRIS or protein-containing buffers.





Avoid sample contamination with surface measurements of drop-size samples

To avoid sample contamination altogether (such as KCl in sample), pipette a drop-size sample (minimum 10 μ L) from your main sample and measure it with a flat membrane surface electrode. This works best on a microscope slide and only 10 μ L of sample is needed!

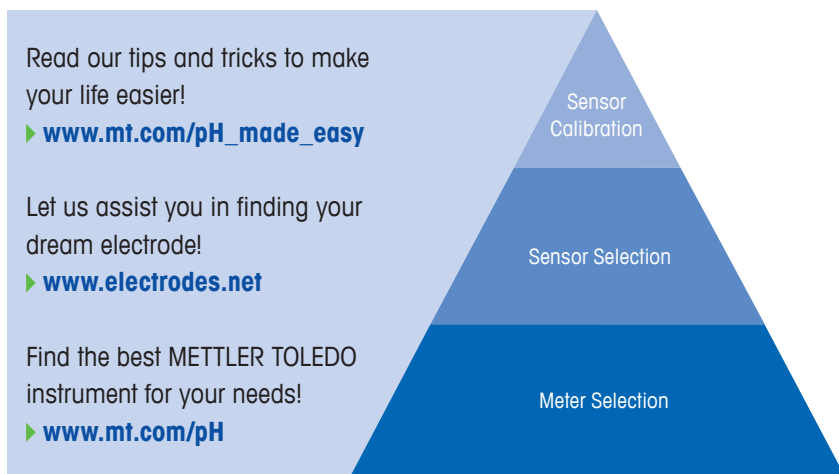


Clean with RNase and DNase cleansers and autoclave to eliminate biohazard

The pH electrode models InLab® Power, Power Pro, Viscous and Viscous Pro can be sterilized by autoclaving. By cleaning the sensor with RNase and DNase decontamination solutions first, the potential for biological contamination is significantly reduced.

The Importance of Correct pH Results in Life Sciences

To achieve the most accurate and reproducible results in electrochemistry, simply follow the three levels of the pyramid!



www.mt.com/pH

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