



thermo scientific

pH Measurement in the Lab

pH Measurement per USP <791>
Preparing your Lab

ThermoFisher
SCIENTIFIC

Why you should read this ebook

The purity of pharmaceutical products depends on the quality of raw materials. The United States Pharmacopeial Convention (USP) is a non-profit organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements manufactured, distributed and consumed worldwide. USP <791> refers to the standardized test method for pH measurements used in the pharmaceutical, food and beverage, patient care, and dietary supplement industry.

In December 2014, USP <791> officially went into effect. This version of <791> is part of the Second Supplement to USP 37-NF 32.

pH measurements within the pharmaceutical industry often reference USP<791>. Thermo Scientific™ Orion™ pH meter kits are part of a high-quality pH test method designed to assist with compliance to USP <791> pH requirements.

A growing number of foods and beverages are sweetened with plant-based stevia (Rebaudioside A). In 2009, USP released standards that manufacturers can use to help ensure the quality and purity of the stevia ingredients they put in their products.

When you take a medicine or supplement, you won't get the therapeutic benefit unless the pill or capsule dissolves properly in your body. A medication or supplement that meets USP standards is able to pass tests that ensure it dissolves so your body can absorb it.

All prescription and over-the-counter drugs sold in the United States, no matter where in the world they are made, must meet the USP quality standards that exist for that product.



Visit usp.org for more information

Measurement system and instrument requirements

As of December 1, 2014, the requirements per USP <791> for pH measurement were revised. For details and exact language, see USP <791> pH General Chapter, The United States Pharmacopeial Convention. usp.org

pH Measurement system requirements

Component	
Electrode	<ul style="list-style-type: none">• ph sensor (H⁺) and suitable reference• Choice of combined or half-cells
Meter*	<ul style="list-style-type: none">• Voltage measurement• Handles high-input impedance
Temperature device	<ul style="list-style-type: none">• Embedded in electrode• Alternatively, use an external temperture device

*If no meter, then embedded inside the pH sensor

Instrument requirements

Measurement	
pH	<ul style="list-style-type: none">• 2-point calibaration capable• Resolution 0.01 pH or better• Temperature compensating
Temperature	<ul style="list-style-type: none">• Accuracy $\pm 1^{\circ}\text{C}$• Resolution 0.1°C

Typical acceptable parameters and requirements¹

Per USP <791> pH, purchased buffers traceable to NIST and having a stated pH value accurate to 0.02 pH may be used. Thermo Scientific Orion pH buffers meet these criteria. For each lot, a Certificate of Analysis is issued which documents the NIST traceability and the pH value accuracy to 0.02 pH or better. Alternately, the analyst may prepare buffers in compliance with Table 2 in the USP <791> method.

pH Measurement system calibration requirements

pH Measurement system calibration requirements	
Component	
Buffers	Three buffers minimum: at least 2 buffers for calibration and 1 buffer for verification
Verification	<ul style="list-style-type: none">• The verification buffer value should be between the calibration buffers• +/- 0.05 pH of the expected value at that temperature
Typical acceptable parameters	
Typical Slope	90 – 105%*
Typical Offset	+/- 30 mV (0.5 pH units at 25°C)*

*Typical Offset and Slope values suggested by USP <791> should be used unless otherwise defined by the pH measurement system manufacturer.³

Slope 92-102% and Offset ±59 mV are defined by Thermo Scientific Orion specifications.



Measuring pH per USP <791>

Thermo Scientific Orion pH meters, electrodes and solutions are part of a high-quality pH test method designed to assist with compliance to USP <791> pH requirements. Orion pH meters, electrodes and buffers offer features commonly desired by highly-regulated labs.

USP <791> Element	General Recommendation	Implementation
Temperature Device	$\pm 1^{\circ}\text{C}$	Verify against a NIST-traceable thermometer
Calibration Buffers	2 (minimum)	(USA Buffer Set) 3-point calibration with pH 4.01, 7.00, and 10.01 buffers, or 5-point calibration with pH 1.68, 4.01, 7.00, 10.01, and 12.46 buffers
Slope Value	92 - 102%*	Slope is displayed on the meter screen when calibration is complete Slope is also displayed in the meter calibration log
Offset	$\pm 59\text{ mV}$ *	Offset can be calculated by the meter, or Offset can be measured in pH 7 buffer ² , or Offset can be calculated by the analyst
Verification	$\pm 0.05\text{ pH}$	Analyze pH 6.86 buffer. Compare results to a table of buffer values at temperature See table on page 10 of eBook

* Slope 92-102% and Offset $\pm 59\text{ mV}$ are defined by Thermo Scientific Orion specifications.

Remember to consult with the SOP prepared by your internal quality or regulatory group when performing your testing per USP <791>.

Calibration buffers

For DIN Buffer Sets	Consider a 3-point calibration at pH 4.01, 6.86, and 9.18 buffers, or a 4-point calibration at pH 1.68, 4.01, 6.86, and 9.18 buffers.
	Verify in pH 7.00 buffer.
	Obtain the offset from the meter calculation, or from the mV value reading during the pH 7.00 buffer verification, or by analyst calculation.

Choosing Calibration Points:

USP <791> specifies a minimum of two calibration points. Other multipoint calibrations are acceptable, if the calibration accuracy and pH sensor slope and offset criteria are met.²

For Optimal Accuracy	Consider choosing buffers that are not more than 3 or 4 pH units apart. For wide-range pH testing, a 3-point calibration at pH 4.01, 7.00, and 10.01 is an option. A 2-point calibration at pH 4 and pH 10 may impact your accuracy.
For Full-Range pH Testing	Consider a 5-point calibration at pH 1.68, 4.01, 7.00, 10.01 and 12.46.
For Short-Range pH Testing	A 2-point calibration is the minimum requirement (for example, at pH 4 and 7 OR at pH 7 and 10).

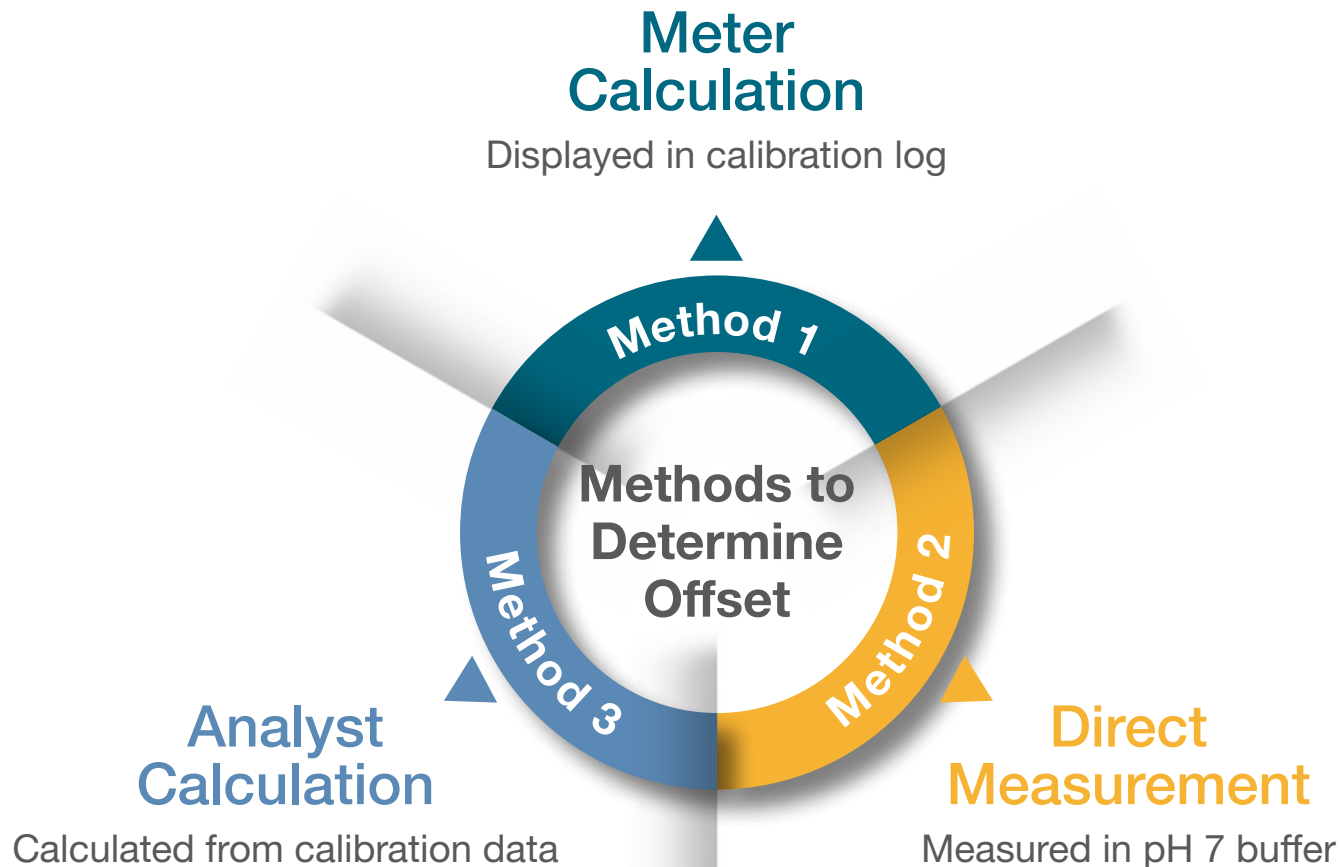
Slope Value

The slope value is always displayed by the meter after the calibration and in the meter's calibration log. Compare the displayed value to the defined parameters of 92-102% per Thermo Scientific Orion specifications.³



Offset

There are different valid methods to determine the offset of the electrode, including by calculation or by direct measurement in pH 7.00 buffer². Choose the option that best fits your requirements and always consult with the SOP prepared by your internal quality or regulatory group.



Method 1 – Meter calculation

Displayed in calibration log

Thermo Scientific Orion meters will calculate offset during the calibration. When using the Thermo Scientific™ Orion™ Versa Star Pro™ pH meter, the calculated offset (sometimes noted as E_0) can be found in the calibration log display and in the computer/printer capture of the pH calibration log. When using the Thermo Scientific™ Orion Star™ A200 series or Orion Star A300 series pH meters, the calculated offset can be found in the computer/printer capture of the pH calibration log.

- The meter will calculate an offset for each segment of the calibration. For a 2-point calibration, one offset (E1) will be calculated. For a 3-point calibration, two offsets (E1, E2) will be calculated, and so on.
- When more than one offset is calculated, each offset should meet the +/- 59 mV criteria per Thermo Scientific Orion specifications.³ The calculated offsets should be similar, but may not be identical values.

Method 2 – Direct Measurement

Measured in pH 7 buffer

Thermo Scientific Orion meters electrodes are constructed to provide a cell zero (pH_0) of pH 7. The offset potential is the potential measured at the indicated cell zero; therefore, the offset potential is the mV reading measured in pH 7 buffer.

- To determine the offset, the analyst can measure pH 7 and document the mV reading. This may be achieved by including pH 7 buffer in the calibration or by using pH 7 as the verification buffer. Compare the mV reading to the +/- 59 mV per Thermo Scientific Orion specifications.³

Method 3 – Analyst calculation

Calculated from calibration data

Another method is to calculate the offset from a calibration buffer data point. This can be done by the analyst. To calculate offset, use the following equation:

$$E_0 = E_s - \frac{(-59.16 * (T+273.15) * (\% \text{ slope}) * (\text{pHs} - 7))}{298.15 * 100}$$

Where:

- Es = mV of a pH buffer used during calibration (e.g. mV for the pH 4.01 buffer)
- T = temperature of the buffer tested (°C)
- % slope = percent slope determined during the calibration
- pHs = the true pH of the pH buffer at the temperature during testing

Example of Method 3 Equation

A pH 4.01 buffer at 35°C is used during calibration and reads a mV value of 157.4.
The displayed slope of the calibration is 95.3%. The true value of pH 4.01 buffer at 35°C is 4.02.

$$E_0 = 157.4 - \frac{(-59.16 * ((35+273.15)/298.15) * (95.3\%/100) * (4.02-7))}{100}$$

$$E_0 = -16.2 \text{ mV offset}$$

Verification

To verify the calibration, test a pH buffer that was not used during the calibration and has a value between the calibration buffers.

- Consider pH 6.86 or pH 7.00 buffer (whichever is not used during the calibration) for the purpose of verification. If desired, an alternate buffer may be chosen.

The pH reading for the buffer should agree within ± 0.05 pH units of the buffer value expected at that temperature.

- Compare the pH reading obtained to known expected values for the buffer at that temperature.
- See table at the right for expected values of pH 6.86 and pH 7.00 buffers at temperatures ranging from 0 to 100°C.

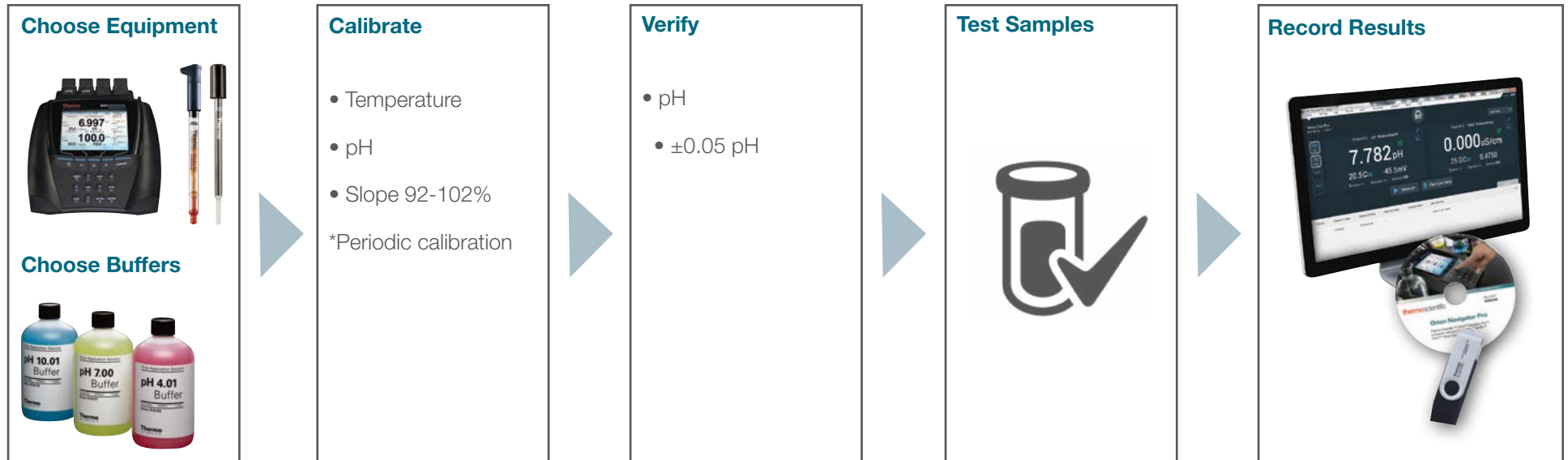
pH Buffer Values for Calibration Verification

T (°C)	pH 6.86	pH 7.00	T (°C)	pH 6.86	pH 7.00	T (°C)	pH 6.86	pH 7.00	T (°C)	pH 6.86	pH 7.00
0	6.98	7.11	25	6.86	7.00	50	6.83	6.96	75	6.85	7.01
1	6.98	7.11	26	6.86	6.99	51	6.83	6.96	76	6.85	7.01
2	6.97	7.10	27	6.86	6.99	52	6.83	6.96	77	6.86	7.02
3	6.96	7.09	28	6.86	6.99	53	6.83	6.96	78	6.86	7.02
4	6.96	7.09	29	6.85	6.99	54	6.83	6.97	79	6.86	7.03
5	6.95	7.08	30	6.85	6.98	55	6.83	6.97	80	6.86	7.03
6	6.95	7.08	31	6.85	6.98	56	6.83	6.97	81	6.86	7.03
7	6.94	7.07	32	6.85	6.98	57	6.84	6.97	82	6.86	7.04
8	6.93	7.07	33	6.85	6.98	58	6.84	6.97	83	6.87	7.04
9	6.93	7.06	34	6.85	6.98	59	6.84	6.97	84	6.87	7.05
10	6.92	7.06	35	6.84	6.97	60	6.84	6.97	85	6.87	7.05
11	6.92	7.05	36	6.84	6.97	61	6.84	6.97	86	6.87	7.06
12	6.91	7.05	37	6.84	6.97	62	6.84	6.98	87	6.87	7.06
13	6.91	7.04	38	6.84	6.97	63	6.84	6.98	88	6.87	7.07
14	6.9	7.04	39	6.84	6.97	64	6.84	6.98	89	6.87	7.07
15	6.9	7.03	40	6.84	6.97	65	6.84	6.98	90	6.88	7.08
16	6.9	7.03	41	6.84	6.97	66	6.84	6.98	91	6.88	7.08
17	6.89	7.02	42	6.84	6.97	67	6.84	6.99	92	6.88	7.09
18	6.89	7.02	43	6.84	6.96	68	6.84	6.99	93	6.88	7.10
19	6.88	7.02	44	6.83	6.96	69	6.85	6.99	94	6.88	7.10
20	6.88	7.01	45	6.83	6.96	70	6.85	6.99	95	6.88	7.11
21	6.88	7.01	46	6.83	6.96	71	6.85	7.00	96	6.89	7.11
22	6.87	7.01	47	6.83	6.96	72	6.85	7.00	97	6.89	7.12
23	6.87	7.00	48	6.83	6.96	73	6.85	7.00	98	6.89	7.13
24	6.87	7.00	49	6.83	6.96	74	6.85	7.01	99	6.89	7.13
									100	6.89	7.14

Thermo Scientific Orion pH Values for 6.86 and 7.00 Buffers at temperatures from 0 to 100 °C



Preparing to Measure pH in a Highly-Regulated Lab



Footnotes:





¹ For details and exact language, see: USP <791> pH General Chapter, The United States Pharmacopeial Convention, www.usp.org.

² Per written communication with Mr. Antonio Hernandez-Cardoso, Senior Scientific Liaison, United States Pharmacopeia, November 7, 2014. AHC@usp.org.

³ Per written communication with Mr. Antonio Hernandez-Cardoso, Senior Scientific Liaison, United States Pharmacopeia, April 29, 2019. AHC@usp.org.

Next steps

Conduct your pH testing with confidence. Thermo Scientific Orion pH meters, electrodes, and solutions are part of a high-quality pH test method designed to assist with USP <791> pH requirements. To purchase a pH meter, electrode and calibration solutions, please contact your local Thermo Scientific Orion sales representative and reference the part numbers listed below.

Product	Description	Part Number
Meters 	Thermo Scientific™ Orion™ Versa Star Pro™ pH benchtop meter kit, includes electrode stand, 8302BNUMD ROSS Ultra™ Triode™ glass-body pH/ATC electrode, 096019 stirrer probe and 810199 ROSS pH buffer & solution kit	VSTAR12
Electrodes 	Orion ROSS Ultra Triode glass-body pH/ATC electrode	8302BNUMD
	Orion ROSS Ultra Triode epoxy-body pH/ATC electrode	8157BNUMD
	Orion ROSS Sure-Flow glass-body pH electrode	8172BNWP
	Orion ROSS Sure-Flow epoxy-body pH electrode	8165BNWP
	Orion ATC temperature probe with stainless steel body	927007MD
Solutions 	Orion pH 1.68 buffer, 475 mL	910168
	Orion pH 4.01 buffer, 475 mL	910104
	Orion pH 6.86 buffer, 475 mL	910686
	Orion pH 7.00 buffer, 475 mL	910107
	Orion pH 10.01 buffer, 475 mL	910110
	Orion pH 12.46 buffer, 475 mL	910112
Software 	Orion™ Navigator Pro™ Computer Software for Orion Versa Star Pro meters, includes one software license on CD and user manual	VSTAR-NPCD
	Orion Navigator Pro Computer Software for Orion Versa Star Pro meters, includes one software license on USB flash drive and user manual	VSTAR-NPUSB

For more information on the Orion Navigator Pro computer software, visit thermofisher.com/orionsoftware



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