



## BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

**SOP Title:** Measurement of pH According to the USP Using a pH Meter  
**SOP Number:** 22124  
**Revision:** 10

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#### 1. PURPOSE

This procedure describes the United States Pharmacopeia (USP) based protocol used to measure the pH of a sample solution independent of pH meter.

#### 2. SCOPE

This will apply to measurements of pH by Technical Operations in Good Manufacturing Practices/Good Laboratory Practices (GMP/GLP) applications in the Biopharmaceutical Development Program (BDP).

#### 3. RESPONSIBILITIES

3.1 The Process Analytics/Quality Control (PA/QC) Technical Operations Lead

- Defines the Procedure.

3.2 PA/QC or Technical Operations personnel

- Performs the procedure.
- Reviews data.
- Documents results of the procedure.

3.3 Biopharmaceutical Quality Assurance (BQA).

- Provides quality oversight.

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### 4. MATERIALS AND REAGENTS

Part Number	Description	BDP Approved Substitution Permitted?
21596/21597	Ross electrode	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30235	pH 1.0 Buffer	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30107	pH 4.0 Buffer	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30108	pH 7.0 Buffer	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30109	pH 10.0 Buffer	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30234	pH 12.0 Buffer	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
20140	Centrifuge tubes	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
20091	Kimwipes	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
21596	Electrode storage solution	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
30575	3M Potassium Chloride (KCl)	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
N/A	Squirt bottle or beaker containing water for rinsing electrode. The water must be deionized, distilled, Type 1, or Reverse Osmosis (RO) water quality or better.	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

### 5. EQUIPMENT

- Automated temperature compensation (ATC) probe for temperature measurement.
- Beckman 660 pH meter and printer.
- Thermo Orion A211 Benchtop pH meter and printer.

### 6. PROCEDURE

6.1 Beckman 660 pH Meter Three-Point Standardization Procedure

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**NOTE:** The standardization procedure must be done after changing electrodes. Standardization must be performed daily prior to running any samples. The pH difference of two sequential standards must not exceed four units and the expected pH of the material should fall between the standards. When the pH of a sample falls outside the expected range, the instrument should be re-standardized using the appropriate buffers which again are within four units. Standardization buffers must be aliquotted fresh daily. The fill hole must be open when the electrode is in use to permit free flow of filling solutions through the reference junction.

- 6.1.1 The electrode is rinsed with water and the excess blotted. See 4.8 for acceptable types of water.
- 6.1.2 The electrode is immersed in standard one and the solution stirred briefly. The STD arrow (second from left) is pressed to begin measuring the highlighted expected standard.
- 6.1.3 The pH meter is standardized such that the display value should match the actual pH of standard one buffer indicated by the manufacturer's label.
- 6.1.4 The electrode is rinsed with water and the excess blotted. See Materials section for acceptable types of water.
- 6.1.5 Using the tab arrow on the pH meter (third from left), the highlighted cursor is moved over to the next expected standard value (i.e., 7.00, or 10.0). The electrode is immersed in standard two and the solution stirred briefly.
- 6.1.6 The pH meter value is standardized such that the display value should match the actual pH of standard two buffer indicated by the manufacturer's label.
- 6.1.7 Repeat steps 6.1.5 to 6.1.6 for the third and final standard buffer.

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- 6.1.8 To recall the calibration data, push the Menu button (5th arrow from left) and scroll to Recall Cal Data. Press Enter. Then press More to display the buffer standard slopes. Press the Print icon (4th arrow from the left) to send the data to the printer.

The slopes must be within the values supplied in the probe documentation, which is located in each pH logbook, 92.0% - 102.0%. If the slope is not within the specified range, discard the buffers and repeat 6.1.1 – 6.1.6 using buffers from new unopened bottles. If the slopes are still out of range, the probe may be at fault. Change the electrode and repeat standardization as in 6.1.1 - 6.1.6. Inform the Area Supervisor. Record the slopes on Form 22124-01

### 6.2 pH Measurement Procedure using the Beckman 660 pH Meter.

**NOTE:** When measuring the pH of potable water, purified water, Reverse Osmosis, or WFI, add 3M KCl to each sample (approximately 30  $\mu$ L to 70  $\mu$ L of 3M KCL per 100mL of water sample). 1 drop is ~ 10  $\mu$ L. Addition of ions is necessary to obtain an accurate measurement of pH.

- 6.2.1 Rinse the electrode with Type 1 or higher quality, purified water. Blot excess water.
- 6.2.2 Immerse the electrode in the sample solution. Stir briefly. Before analyzing, be sure that the sample is  $25.0 \pm 1\pm C$  with the ATC probe.
- 6.2.3 When the reading has stabilized read the sample pH from the display. Repeat steps 6.2.1 and 6.2.2 until two successive readings result in the same value when rounded to one decimal place and record the value on the appropriate forms and logbook. Select the Print icon (last arrow from the left) to send data to the Beckman printer.
- 6.2.4 Repeat steps 6.2.1 to 6.2.3 for subsequent samples.

**NOTE:** For samples with a pH value lower than the lowest NIST-traceable standard (1.0) or higher than the highest NIST traceable standard (12.0), results will be reported as less than or greater than, respectively, the value of the standard. The actual value may be presented in parenthesis.

### 6.3 Thermo Orion Star A211 pH Meter Three-Point Standardization Procedure

- 6.3.1 Power the unit on by pushing the Power button. Power on the corresponding printer unit attached to the Thermo Orion Star benchtop pH meter.

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6.3.2 If using the 8103BNUWP (BDP PN 21597) ROSS or equivalent pH probe, ensure that the probe is filled with pH electrode solution before using.

6.3.3 User will be presented with the main screen. From here, the calibration procedure may be started. Calibration must be performed once per day and before any samples are processed.

6.3.4 The Orion Star pH Unit has the capability to auto detect the pH buffer calibration values. The table below shows the acceptable mV ranges. If the auto detected value is outside of these ranges, the user will have to input the actual buffer value from the standard bottle.

pH Buffer	mV Range
4.01	+117 mV to +236 mV
7.00	-59 mV to +59 mV
10.00	-237 mV to -264 mV

6.3.5 Press the button under the Cal. menu. Rinse the pH probe and ATC probe with Type 1 or better purified water, place into pH 4 buffer.

6.3.6 Press the Start button. The unit will try to auto assign the calibration buffer value from the measured mV. If the mV value is outside the range for the pH buffer, the user will have to enter in the correct pH value.

6.3.6.1 If the pH value needs to be corrected due to the measured mV value falling outside the appropriate range, press the Edit button.

6.3.6.2 A keypad is displayed. The user can then navigate the keypad using the arrow buttons on the unit.

6.3.6.3 Enter the actual pH buffer value. Press the Done button.

6.3.7 After entering the corrected pH buffer value or if accepting the auto detected value, press the Accept button. Press the Next button to proceed to the next calibration point.

6.3.8 Rinse the pH probe and ATC probe with Type 1 or better purified water. Place in pH 7 buffer. Repeat steps 6.3.6.1 through 6.3.6.3 and 6.3.7.

6.3.9 Rinse the pH and ATC probes with Type 1 or better purified water. Place them in pH 10 buffer. Repeat steps 6.3.6.1 through 6.3.6.3 and 6.3.7.

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6.3.10 Upon completing the calibration point for pH 10, press the Done button. The unit will return to the Main screen and will automatically print. Record the slope percentages on Form 22124-01.

6.3.11 If the slope percentages are outside the given ranges listed on Form 22124-01, re- calibrate the unit with new, un-opened buffers. If this does not correct the calibration issue, contact the area supervisor.

6.4 pH Measurement Procedure using the Thermo Orion Star A211 pH Meter.

**NOTE:** When measuring the pH of potable water, purified water, Reverse Osmosis, or WFI, add 3M KCl to each sample (approximately 30  $\mu$ L to 70  $\mu$ L of 3M KCL per 100mL of water sample). 1 drop is ~ 10  $\mu$ L. Addition of ions is necessary to obtain an accurate measurement of pH.

6.4.1 To test a sample using the Thermo Orion Star benchtop pH meter, rinse the pH and ATC probes with Type 1 or better purified water. Blot excess water from the probes.

6.4.2 Place both the pH and ATC probes in the sample solution. Stir briefly. Press the Measure button. Gently move the pH probe in and out of the sample solution three times.

6.4.3 The unit will display the current sample temperature( $^{\circ}$ C) and the pH value. It may take up to a minute for the unit to stabilize on the sample pH. Ensure that the measured temperature is  $25.0\pm 1^{\circ}$ C.

6.4.4 After the unit has locked in on a stable pH value, the data will automatically be sent to the attached printer. If the printer does not print, check the communication cable, ink cartridge, and power cable.

6.4.5 Record the sample temperature and pH values from the printout on Form 22124-01

## 7. MAINTENANCE

7.1 Good electrode care is an important requirement for accurate pH measurement and long life of the electrode. While complete instructions for specific electrode care are included with each electrode, certain important points are noted here.

7.2 The glass bulb at the end of the electrode is fragile – be careful when handling electrodes. Electrodes generally come with a vial containing storage solution protecting this glass bulb. For long-term storage, return the electrode to the storage solution in the protective vial.



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- 7.3 There may be a fill hole near the top of the electrode. Remove the tape, plug or sleeve from the fill hole. It is sealed to prevent loss of filling solution during shipment or during periods of non-use.
- 7.4 Be sure that the correct filling solution for the specific electrode is used; some require saturated AgCl and some do not.
- 7.5 When the electrode is not in use, store with the bulb and reference junction immersed in the filling/storage solution, or as recommended by the manufacturer for the specific electrode being used. Do not store the electrode with the tip immersed in tap water or deionized water.
- 7.6 Procedures described in the electrode instructions can be used to rejuvenate an electrode, but if the electrode continues to have slow response, poor span or is cracked/broken, replace it.
- 7.7 If the attached ATC probe is damaged or changed during the life of the unit(s), the unit will need to undergo calibration for the newly added probe.

### 8. DOCUMENTATION AND RECORDS

- 8.1 Each pH meter must have a BDP Equipment ID Number.
- 8.2 Each pH meter must have a logbook. Use, replacement of electrode, and maintenance are recorded when they occur. Results of standardization and sample results are recorded on Form 22124-01 each time the instrument is used. Each day's entry is initialed and dated.
- 8.3 Additionally, record pH measurements on the appropriate sample submission form (Form 22002-01) or other laboratory form accompanying the sample submission form. Printed data may be taped and then signed and dated on a separate blank sheet of paper.

### 9. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
22124-01	pH Results Data Sheet
22124-02	Equipment Log
22002-01	QC Test Request002-01