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### **1.0 Purpose**

This procedure describes the general protocol used to measure pH using various pH meters.

### **2.0 Scope**

This procedure applies to manufacturing personnel who use pH meters.

### **3.0 Authority and Responsibility**

3.1 The Director, Technical Operations, Biopharmaceutical Development Program has the authority to define this procedure.

3.2 Manufacturing is responsible for training personnel and documenting this training to Biopharmaceutical Quality Assurance (BQA), and performing this procedure.

3.3 BQA is responsible for quality oversight of this procedure.

### **4.0 Equipment and Supplies**

4.1 pH electrode.

4.2 pH standard buffers, pH 4 (BDP PN 30107), pH 7 (BDP PN 30108), pH 10 (BDP PN 30109) or BDP approved equivalent.

4.3 Beakers, centrifuge tubes, or equivalent clean containers to hold buffers.

4.4 Squir bottle or beaker with Reverse Osmosis (or higher) grade water.

4.5 Storage Buffer, BDP PN 20632 or BDP approved equivalent.

- 4.6 Automated temperature compensation (ATC) probe if the operator wants temperature compensation and/or temperature measurement.
- 4.7 Operating Manuals for various models.

## 5.0 Procedure

**NOTE:** See Attachments 1, 2, 3 and 4 for specific instruments.

- 5.1 Two-point or Three-Point pH Standardization Procedure
  - 5.1.1 Standardization must be performed at least once per day when the instrument is in use or when electrodes are changed.
  - 5.1.2 Aliquot standardization buffers from fresh stock each day.
  - 5.1.3 Standardize per meter instructions (Attachment 1, 2,3 or 4).
  - 5.1.4 Verify the standardization is acceptable.
  - 5.1.5 Repeat standardization once if the result is not acceptable. Rejuvenate or replace the probe if this is unsuccessful and repeat standardization.
- 5.2 pH Measurement Procedure
  - 5.2.1 Rinse the electrode with water.
  - 5.2.2 Immerse the electrode in the sample solution.
  - 5.2.3 Read the sample pH from the display once reading has stabilized.
  - 5.2.4 Repeat steps 5.2.1 to 5.2.3 for subsequent samples.

## 6.0 Maintenance

- 6.1 When the electrode is not in use, place in a container of storage solution, (BDP PN 20632) or as recommended by the manufacturer. Container is to be labeled with description and expiration date of storage solution.
- 6.2 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, then replace it and document the replacement in the equipment log.
- 6.3 If the electrode is to be used directly in product (intermediate or final) for non-terminal samples, it must be visibly identified with the project number and dedicated to that project.

## 7.0 Documentation

- 7.1 For Jenco Models 6009, 6071, and 6171 pH meters record the pH meter standardization and usage on Form 12181-01 (bound in logbook.)
- 7.2 The buffer preparation group will use Form 12181-02 to record pH meter standardization including product lot number in the pH Meter Logbook each time that it is used.
- 7.3 For Thermo Orion 2-Star or STARA pH meters not in buffer preparation group's lab space, record the pH meter standardization and usage on Form 12181-03 (bound in equipment log.)



- 7.4 Record pH measurements on the appropriate Batch Production Record (BPR), form, or lab book.
- 7.5 Record maintenance and cleaning per **SOP 21531, *Equipment Logs***.

## 8.0 References and Related Documents

<b>SOP 21531</b>	<i>Equipment Logs</i>
<b>Form 12181-01</b>	<i>Jenco pH Meter Standardization/Operation Log</i>
<b>Form 12181-02</b>	<i>pH Meter Logsheet</i>
<b>Form 12181-03</b>	<i>Thermo Orion 2-Star/STARA Standardization/Operation Log</i>
<b>Attachment 1</b>	<i>Operation of the Beckman Model Phi 72 pH Meter in Manual Mode</i>
<b>Attachment 2</b>	<i>Operation of the Jenco Models 6009, 6071, and 6171 pH Meters</i>
<b>Attachment 3</b>	<i>Operation of the Thermo Orion 2-Star/STARA Benchtop pH Meter</i>
<b>Attachment 4</b>	<i>Operation of the Thermo Scientific Orion Versa Star Pro Benchtop Meter</i>

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## Attachment 1

### Operation of the Beckman Model Phi 72 pH Meter in Manual Mode

**NOTE:** If the STD key shows STD 1 or STD 2, the instrument is in manual mode and the standardization procedure is described below. Use an ATC probe for this procedure.

1. Choose two standard buffers that bracket the expected pH of the sample. Generally, the pH 4 and 10 standards are used; however, other values can be entered – consult manual to change standard settings.
2. Rinse electrode with water and blot excess with towels.
3. Immerse the electrode in first STD buffer. Stir briefly.
4. Press the C (clear) key.
5. Press the pH key. The screen will show a pH reading near the value of the buffer.
6. Press STD 1 key. In manual standardization mode the standardization key is identified as either “STD 1” or “STD 2” and can be toggled to switch from one to the other.
7. The “STD 1:” indicator will flash until the instrument recognizes a stable signal. After the “STD 1:” indicator stops flashing, the value of the pH standard used will read out on the display and will appear with the “STD1:” indicator at the upper left-hand corner of the display.
8. Rinse the electrode and blot excess.
9. Immerse the electrode in STD buffer 2. Stir briefly.
10. Press the STD 2 key. The “STD2:” indicator will flash until a stable signal is recognized by the instrument. After the “STD 2:” indicator stops flashing, the value of the pH standard used will read out on the display and will appear with the “STD2:” indicator at the upper left-hand corner of the display.
11. The pH meter will automatically indicate if the slope is unacceptable. Reconditioning or replacement of the probe is described in the user manual.
12. Rinse the electrode and blot excess.
13. Immerse the electrode in sample stabilized at  $25 \pm 1^\circ\text{C}$ . Stir briefly.
14. For continuous measurement and display of pH, turn off the auto-read function by pressing AUTO. For individual reading, press the pH key. When the auto read stops flashing, the pH is displayed. To repeat the reading, press pH again.

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## Attachment 2

### Operation of the Jenco Models 6009, 6071, and 6171 pH Meters

1. Press the MODE key until the pH AUTOLOCK mode is displayed.
2. Rinse the electrode with water.
3. Immerse the electrode in pH 7 buffer and press STAND key. Wait until the WAIT indicator disappears and the SLOPE indicator begins flashing.
4. Rinse the electrode with water.
5. Immerse the electrode in either pH 4 or pH 10 buffer to bracket the expected pH of sample being measured. Press the SLOPE key. Wait until the WAIT indicator disappears.
6. The meter reading for the second buffer (pH 4 or pH 10) must be within an **allowable difference of 0.1** from the standard value.
7. Rinse the electrode with water.
8. Record the appropriate information on the Instrument Standardization/Operation Form (12181-01).
9. Immerse the electrode in the sample and press the MEASURE key. Wait until a stable reading is obtained.

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### Attachment 3

#### Operation of the Thermo Orion 2-Star/STARA Benchtop pH Meter

1. Choose two standard buffers that bracket the expected pH of the sample. Generally, pH 4, pH 7, and pH 10 standards are used. However, other values can be entered – consult manual to change standard settings.
2. Press the **Calibrate** key.
3. Rinse the electrode with WFI and blot excess with a lint-free tissue.
4. Insert the electrode into the first buffer. Stir briefly.
5. Wait for the **pH** icon to stop flashing and the ► icon to start flashing.
6. Press the **calibrate** key.
7. Rinse the electrode with WFI and blot excess with a lint-free tissue.
8. Insert the electrode into the second buffer. Stir briefly.
9. Wait for the **pH** icon to stop flashing and the ► icon to start flashing.
10. Press the **calibrate** key and then press the **measure** key to save and end calibration. The unit will display an error message if calibration fails. See the owner's manual for corrective action.
11. Rinse the electrode with WFI and blot excess with a lint-free tissue.
12. Insert the electrode into the sample. Stir briefly.
13. Press the **measure** key to take a measurement. Once the reading stabilizes the **AR** icon will stop flashing, the display will freeze, and the meter will print the data on the display (the printout will include the pH value along with the date and time. Repeat steps 11 through 13 to take a new measurement

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## Attachment 4

### Operation of the Thermo Scientific Orion Versa Star Pro

1. Choose two standard buffers that bracket the expected pH of the sample. Generally, pH 4, pH 7, and pH 10 standards are used. However, other values can be entered – consult manual to change standard settings.
2. Turn the meter on and press the Cal button and choose channel 1 (pH).
3. Message will say rinse probe and place in first standard.
4. Insert the electrode into the sample. Stir briefly.
5. Press Start (F3). Once stable, ready will display and message will state F2 accept or F3 edit.
6. If standard value is displayed correctly press F2 accept. If not press F3 and repeat.
7. Rinse probe and place in the second standard and repeat steps above.
8. For a 3 point calibration press Next and repeat steps above or for a 2 point calibration press Cal Done button and next the measure button to exit Cal mode.
9. For measurement of a sample, the meter will recognize when the probe is placed in a sample. It will continue to read at all times and once stable “Ready” will appear above the sample value. Then press Print to obtain a printout that states the final pH of the sample.