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SODIUM HYDROXIDE 5N TESTING METHODS

TABLE OF CONTENTS

1.	PURPOSE:.....	3
2.	SCOPE:.....	3
3.	RESPONSIBILITIES:	3
4.	SAFETY:	3
5.	EQUIPMENT:	3
6.	REAGENTS:	3
7.	REFERENCES:	4
8.	ANALYTICAL PROCEDURES:	5

1. PURPOSE:

- 1.1. To provide Laboratory personnel with a procedure for analyzing Sodium Hydroxide 5 N In-Process, Stability, and Finished Good samples.

2. SCOPE:

- 2.1. Applies to the analysis of Sodium Hydroxide 5N In-Process, Stability, and Finished Goods in the Laboratory. Methods include testing for all grades of Sodium Hydroxide 5N sold by BioSpectra; only the specific tests required for the requested grade must be tested.

3. RESPONSIBILITIES:

- 3.1. The Laboratory Manager, or qualified designee is responsible for training, maintenance, and implementation of this procedure.
- 3.2. Laboratory personnel are responsible for compliance with the terms of this procedure. This includes notifying Laboratory Management if any analyses fail to meet their respective specifications.

4. SAFETY:

- 4.1. Causes SEVERE skin burns and eye damage. Standard laboratory safety regulations apply. Before working with any chemical, read and understand the Safety Data Sheet (SDS).

5. EQUIPMENT:

- 5.1. Analytical Balance
- 5.2. Burette
- 5.3. Calibrated Oven
- 5.4. Calibrated Pipette
- 5.5. Calibrated Thermometer
- 5.6. Calibrated Timer
- 5.7. Hach Portable Turbidimeter Model 2100 Q, or equivalent
- 5.8. Anton Paar DMA 35 Portable Density Meter
- 5.9. Endosafe PTS Endotoxin Reader, or equivalent
- 5.10. NexION 350X ICP-MS

6. REAGENTS:

- 6.1. **0.02N Hydrochloric Acid (HCl):** Slowly add 20 mL of 0.1N Hydrochloric Acid to 80 mL of purified water to make a total volume of 100 mL.
- 6.2. **0.1N Hydrochloric Acid (HCl):** Purchased Commercially.
- 6.3. **1N Acetic Acid:** Dilute 57mL of glacial acetic acid to 1L with purified water.
- 6.4. **1N Sodium Hydroxide (NaOH):** Purchased Commercially.
- 6.5. **10% Ammonium Hydroxide:** Dilute 35mL of 29% ammonium hydroxide to 100mL with purified water.
- 6.6. **10% Sulfuric Acid:** Slowly add 30mL of 96% Sulfuric Acid to 375 mL of purified water. Cool and dilute with water to 500mL.
- 6.7. **29% Ammonium Hydroxide:** Purchased Commercially.
- 6.8. **30% Ammonium Thiocyanate:** Dissolve 30g of ammonium thiocyanate in water and dilute with water to 100mL.

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- 6.9. **Ammonium Peroxydisulfate Crystals:** Purchased Commercially.
- 6.10. **Ammonium Thiocyanate:** Purchased Commercially.
- 6.11. **Endosafe PTS Cartridge 1-0.01 EU/mL:** Purchased Commercially.
- 6.12. **Ferrous Ammonium Sulfate Hexahydrate:** Purchased Commercially.
- 6.13. **Glacial Acetic Acid, concentrated:** Purchased Commercially.
- 6.14. **Glycerin:** Purchased Commercially.
- 6.15. **Glycerin Base:** To 200g of glycerin, add water to a total weight of 235g. Add 140mL of 1N NaOH, 50mL of purified water and mix.
- 6.16. **Hydrochloric Acid, concentrated:** Purchased Commercially.
- 6.17. **Iron Standard (0.01mg of Fe in 1mL):** Dissolve 0.702g of ferrous ammonium sulfate hexahydrate in 10mL of 10% sulfuric acid and dilute with water to 100mL. To 10mL of this solution, add 10mL of 10% sulfuric acid and dilute with water to 1L.
- 6.18. **LAL Reagent Water:** Purchased Commercially.
- 6.19. **Lead Nitrate:** Purchased Commercially.
- 6.20. **Lead Stock Solution (0.1mg of Pb in 1mL):** Dissolve 0.160g of lead nitrate in 100mL of dilute nitric acid (1:99) and dilute with purified water to 1L. The solution should be prepared and stored in containers free from lead.
- 6.21. **Litmus Paper:** Purchased Commercially
- 6.22. **Nitric Acid (HNO₃):** Purchased Commercially
- 6.23. **Nitric Acid, dilute (1:99):** Dilute 1mL of 69% nitric acid in 99mL of purified water.
- 6.24. **Phenolphthalein:** Purchased Commercially.
- 6.25. **Phenolphthalein Indicator:** Dissolve 1.0 g of phenolphthalein in 100 mL of reagent grade alcohol.
- 6.26. **pH 9-10 Buffer (0.25M Tris Base):** Purchased Commercially.
- 6.27. **Potassium Carbonate:** Purchased Commercially.
- 6.28. **Potassium Carbonate (15%):** Weigh 15.000g of Potassium Carbonate and transfer to a 100mL volumetric flask. Dissolve and dilute to volume with purified water.
- 6.29. **Potassium Hydrogen Phthalate (KHP):** Crush and dry a suitable amount of KHP at 120°C for 2 hours. Allow to cool to ambient temperature in a desiccator.
- 6.30. **Potassium Pyroantimonate TS:** Purchased Commercially.
- 6.31. **Purified Water:** In-house or Purchased Commercially.
- 6.32. **Reagent Alcohol:** Purchased Commercially.
- 6.33. **Sulfuric Acid, Concentrated:** Purchased Commercially.
- 6.34. **0.1N Silver Nitrate (AgNO₃) TS:** Purchased Commercially
- 6.35. **Thioacetamide:** Purchased Commercially.
- 6.36. **Thioacetamide TS:** Dissolve 4g of thioacetamide in purified water to make 100mL.

7. REFERENCES:

- 7.1. BSI-MEM-0130, Endosafe NexGen PTS Endotoxin Reader: Qualified Products
- 7.2. BSI-SOP-0019, Result Reporting
- 7.3. BSI-SOP-0098, Balance SOP
- 7.4. BSI-SOP-0126, Laboratory Notebooks
- 7.5. BSI-SOP-0135, Laboratory Chemicals
- 7.6. BSI-SOP-0140, Standardization of Titrants

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- 7.7. BSI-SOP-0242, Bangor Portable Turbidimeter and Calibration SOP
- 7.8. BSI-SOP-0244, VWR Gravity Convection Oven Operation and Calibration (Model Number 414005-106)
- 7.9. BSI-SOP-0303, NexION 350X ICP-MS SOP
- 7.10. BSI-SOP-0345, Endosafe nexgen-PTS Endotoxin Reader SOP
- 7.11. BSI-SOP-0350, Anton Paar DMA 35 Portable Density Meter Operation and Calibration
- 7.12. *ACS Reagent Chemicals*, current edition
- 7.13. *USP-NF* current edition

8. ANALYTICAL PROCEDURES:

8.1. IN-PROCESS TESTING:

8.1.1. NORMALITY (CONFIRMATION 1 AND 2) REFER TO BATCH RECORD:

8.1.2. **KHP (Potassium Hydrogen Phthalate) Preparation:**

- 8.1.2.1. Crush and dry a suitable amount of KHP at 120°C for 2 hours. Allow to cool to ambient temperature in a desiccator.

8.1.3. **Burette Preparation:**

- 8.1.3.1. Fill a 25-mL volumetric flask with sample. Quantitatively transfer the aliquot to a 250-mL volumetric flask with purified water. Rinse the 25-mL flask by filling the flask halfway with purified water, shaking it, then transferring the rinse to the 250-mL volumetric flask. Perform the rinse procedure in duplicate. Fill the 250-mL volumetric flask to volume with purified water. Mix well and cool to 25° ± 2°C. QS the sample solution to 250 mL after cooling is complete.
- 8.1.3.2. Prime the 50-mL burette by filling it with the diluted sample solution. Empty the burette and repeat.
- 8.1.3.3. Fill the burette to the required volume with the prepared sample solution.

8.1.4. **Sample Preparation:**

- 8.1.4.1. Weigh 4.0 – 4.2 g of the previously dried KHP into a 250-mL beaker.
- 8.1.4.2. Add 100 mL of purified water down the sides of the beaker to avoid the loss of KHP.

8.1.5. **Analysis Procedure:**

- 8.1.5.1. To the KHP solution, add 150 µL phenolphthalein indicator.
- 8.1.5.2. Titrate the KHP using the sample solution in the burette, to a pink endpoint.
- 8.1.5.3. Calculate the normality using the following equation:

$$N = \frac{KHP\ Weight\ (g) \times KHP\ Purity \times 10}{0.20423 \times mL\ of\ NaOH\ Sample\ Solution}$$

Where:

$$KHP\ Purity = \frac{Assay\ percent\ of\ KHP}{100} \quad (from\ manufacturer's\ CoA)$$

$$0.20423 = \frac{Formula\ weight\ of\ KHP}{1000} 10 = Dilution\ Factor$$

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FINISHED GOOD TESTING:

- 8.1.6. **APPEARANCE AND COLOR** :
- 8.1.6.1. Transfer 2 mL of sample into a 4 mL (10-mm) glass comparison tube.
 - 8.1.6.2. Transfer 2 mL of purified water into a separate 4 mL (10-mm) glass comparison tube.
 - 8.1.6.3. View the tubes vertically against a color comparison plate with suitable lighting. In order to pass, the test solution is complete, clear, and colorless when compared to purified water.
 - 8.1.6.4. For Stability Testing: If the sample does not pass specification when compared to purified water, it can be compared to another sample determined to be passing (such as the Finished Goods lot retain) as a direct comparison to make the qualitative determination for Appearance and Color.
- 8.1.7. **CHLORIDE** :
- 8.1.7.1. Thoroughly rinse Nessler tubes using purified water prior to use.
 - 8.1.7.2. **Sample Preparation:**
 - 8.1.7.2.1. Weigh 2.0 g of sample and quantitatively transfer to a 50-mL Nessler Color Comparison Tube using purified water.
 - 8.1.7.2.2. Dilute to ~20 mL with purified water.
 - 8.1.7.2.3. Slowly, using extreme caution, acidify the sample with nitric acid to litmus.
 - 8.1.7.2.4. Dilute to 40 mL with purified water.
 - 8.1.7.3. **5 ppm Standard Preparation:**
 - 8.1.7.3.1. Dilute 14.1 µL of 0.02N HCl to ~40 mL with purified water.
 - 8.1.7.4. **Analysis:**
 - 8.1.7.4.1. To both the sample and standard solutions, add 1 mL of concentrated nitric acid and 1 mL of 0.1N Silver Nitrate TS. Dilute the sample and standard to 50 mL with purified water.
 - 8.1.7.4.2. Mix and allow solutions to sit for 5 minutes using a calibrated timer.
 - 8.1.7.4.3. After 5 minutes, the turbidity in the sample solution does not exceed the turbidity produced by the standard when viewed against a dark background. Analyze turbidity utilizing the turbidity meter and record the sample NTU results.
- 8.1.8. **ENDOTOXIN** :
- 8.1.8.1. Pipette 0.200 mL of sample into a sterile vial and add 1.600 mL of LAL reagent water.
 - 8.1.8.2. Check the pH of the solution with pH paper.
 - 8.1.8.2.1. If the solution is basic, add HCl in small increments until the solution is acidic.
 - 8.1.8.3. Once acidic, add sufficient pH 9-10 buffer solution until the pH is between 6-8.
 - 8.1.8.4. Dilute to 10 mL with LAL reagent water.
 - 8.1.8.5. Follow the Endosafe Nexgen PTS Endotoxin Reader SOP for sample analysis.
 - 8.1.8.5.1. The dilution factor is 50.

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8.1.9. **HEAVY METALS (Pb)** :

Primary Method

8.1.9.1. Standard and Solution Preparation:

- 8.1.9.1.1. Lead Standard Solution (0.01mg of Pb in 1mL): Dilute 10mL of lead stock solution to 100mL with purified water. This must be prepared at the time of use.
- 8.1.9.1.2. Thioacetamide-glycerin base: Thoroughly mix 1mL of thioacetamide with 5mL of Glycerin base. Heat in a boiling bath for 20 seconds. Prepare immediately before use.

8.1.9.2. Procedure:

- 8.1.9.2.1. Note: Prepare in hood, and use caution for standard and sample preparation to avoid spattering of sample.
- 8.1.9.2.2. Sample Preparation: Weigh 30g of sample into a suitable beaker and carefully add 9mL of concentrated nitric acid.
- 8.1.9.2.3. Standard Preparation: Weigh 10g of sample and add 3mL of concentrated nitric acid. Add 2mL of 0.01mg Lead Standard Solution (0.01mg/mL Pb).
- 8.1.9.2.4. Place both the standard and sample on a hot plate and evaporate to dryness. Cool and dissolve each residue with 20 mL of purified water. Adjust the pH to between 3 and 4 utilizing a pH meter, with 1N acetic acid or 10% ammonium hydroxide.
- 8.1.9.2.5. Transfer the solutions to separate Nessler Color Comparison tubes. Add 1.2mL of freshly prepared thioacetamide-glycerin base to each of the solutions and mix. QA each tube to 50mL and mix.
- 8.1.9.2.6. Any brown color produced in the sample solution must not exceed that in the standard solution to be reported as ≤ 1 ppm.

Alternate Method

8.1.9.3. Refer to NexION 350X ICP-MS SOP.

8.1.10. **IDENTIFICATION (SODIUM)** :

- 8.1.10.1. Pipette 1 mL of sample into a test tube containing 25 mL of purified water.
- 8.1.10.2. Add 2 mL of 15% Potassium Carbonate and heat to boiling.
- 8.1.10.3. Allow to cool in an ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.
- 8.1.10.4. Add 4 mL of Potassium Pyroantimonate TS and heat to boiling.
- 8.1.10.5. Allow to cool in an ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.
- 8.1.10.6. A dense precipitate must form in order to pass test.

8.1.11. **IRON (Fe)** :

Primary Method

8.1.11.1. Procedure:

- 8.1.11.1.1. Sample Preparation: To 20g of sample, add 0.1mL of phenolphthalein indicator solution, neutralize with hydrochloride acid and dilute with water to 40mL.

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- 8.1.11.1.2. 0.01mg Iron Standard Preparation: Pipette 1mL of Iron Standard (0.01mg of Fe in 1mL) and dilute with water to 40mL.
- 8.1.11.1.3. To the sample and standard solutions, add 2mL of hydrochloric acid and dilute to 50mL with purified water. Add 30-50mg of ammonium peroxydisulfate crystals and 3mL of 30% Ammonium Thiocyanate and mix.
- 8.1.11.1.4. Any red color in the sample must not exceed the 0.01mg standard solution to report as <0.5ppm.

Alternate Method

8.1.11.2. Refer to NexION 350X ICP-MS SOP.

8.1.12. **NORMALITY** :

8.1.12.1. **KHP (Potassium Hydrogen Phthalate) Preparation:**

- 8.1.12.1.1. Crush and dry a suitable amount of KHP at 120°C for 2 hours. Allow to cool to ambient temperature in a desiccator.

8.1.12.2. **Burette Preparation:**

- 8.1.12.2.1. Fill a 25-mL volumetric flask with sample. Quantitatively transfer the aliquot to a 250-mL volumetric flask with purified water. Rinse the 25-mL flask by filling the flask halfway with purified water, shaking it, then transferring the rinse to the 250-mL volumetric flask. Perform the rinse procedure in duplicate. Fill the 250-mL volumetric flask to volume with purified water. Mix well and cool to 25° ± 2°C. QS the sample solution to 250 mL after cooling is complete.
- 8.1.12.2.2. Prime the 50-mL burette by filling it with the diluted sample solution. Empty the burette and repeat.
- 8.1.12.2.3. Fill the burette to the required volume with the prepared sample solution.

8.1.12.3. **Sample Preparation:**

- 8.1.12.3.1. Weigh 4.0 – 4.2 g of the previously dried KHP into a 250-mL beaker.
- 8.1.12.3.2. Add 100 mL of purified water down the sides of the beaker to avoid the loss of KHP.

8.1.12.4. **Analysis Procedure:**

- 8.1.12.4.1. To the KHP solution, add 150 µL phenolphthalein indicator.
- 8.1.12.4.2. Titrate the KHP using the sample solution in the burette, to a pink endpoint.
- 8.1.12.4.3. Calculate the normality using the following equation:

$$N = \frac{KHP\ Weight\ (g) \times KHP\ Purity \times 10}{0.20423 \times mL\ of\ NaOH\ Sample\ Solution}$$

Where:

$$KHP\ Purity = \frac{Assay\ percent\ of\ KHP}{100} \quad (from\ manufacturer's\ CoA)$$

$$0.20423 = \frac{Formula\ weight\ of\ KHP}{1000} \quad 10 = Dilution\ Factor$$

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