BIOSPECTRA

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SODIUM HYDROXIDE 1N TESTING METHODS

TABLE OF CONTENTS

1. PURPOSE:

1.1. To provide Laboratory personnel with a procedure for analyzing Sodium Hydroxide 1N In-Process, Finished Goods, and Stability.

2. SCOPE:

2.1. Applies to the analysis of Sodium Hydroxide 1N In-Process, Stability, and Finished Goods in the Laboratory. Methods include testing for Sodium Hydroxide 1N sold by BioSpectra.

3. RESPONSIBILITIES:

3.1. The Laboratory Manager 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 the 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. REFERENCES:

5.1. BSI-ATM-0074, Analytical Method of Analysis: Sodium Hydroxide via ICP-MS
5.2. BSI-SOP-0019, Result Reporting
5.3. BSI-SOP-0098, Balance SOP
5.4. BSI-SOP-0126, Laboratory Notebooks
5.5. BSI-SOP-0135, Laboratory Chemicals
5.6. BSI-SOP-0140, Standardization of Titrants
5.7. BSI-SOP-0242, Bangor Portable Turbidimeter and Calibration SOP
5.8. BSI-SOP-0303, NexION 350X ICP-MS SOP
5.9. BSI-SOP-0345, Nexgen-PTS Endotoxin Reader SOP
5.10. BSI-SOP-0350, Anton Paar DMA 35 Portable Density Meter Operation and Calibration
5.11. *ACS Reagent Chemicals*, current edition
5.12. USP-NF current edition

6. EQUIPMENT:

6.1. Analytical Balance
6.2. Hach Portable Turbidimeter Model 2100 Q, or equivalent
6.3. Endosafe PTS Endotoxin Reader, or equivalent
6.4. NexION 350X ICP-MS
6.5. Anton Paar DMA 35 Portable Density Meter

7. REAGENTS:

7.1. **1N Acetic Acid:** Dilute 57 mL of glacial acetic acid to 1 L with purified water.
7.2. **10% Ammonium Hydroxide:** Dilute 35 mL of 29% ammonium hydroxide to 100 mL with purified water.
7.3. **29% Ammonium Hydroxide:** Purchased commercially
7.4. **Ammonium Peroxydisulfate Crystals:** Purchased commercially
7.5. **Ammonium Thiocyanate:** Purchased commercially
7.6. **30% Ammonium Thiocyanate:** Dissolve 30 g of ammonium thiocyanate in water, and dilute with water to 100 mL.
7.7. **Buffer (pH ~9-10):** Purchased commercially
7.8. **Ferrous Ammonium Sulfate Hexahydrate:** Purchased commercially

7.9. **Glacial Acetic Acid, concentrated:** Purchased commercially
7.10. **Glycerin:** Purchased commercially
7.11. **Glycerin Base:** To 200 g of glycerin add water to total weight of 235 g. Add 140 mL of 1N NaOH, 50 mL of purified water and mix.
7.12. **Hydrochloric Acid (HCl), concentrated:** Purchased commercially
7.13. **Hydrochloric Acid (HCl, 0.02N):** Slowly add 20 mL of 0.1N Hydrochloric acid to 80 mL of purified water to make a total volume of 100 mL.
7.14. **Iron Standard (0.01 mg of Fe in 1 mL):** Dissolve 0.702 g of ferrous ammonium sulfate hexahydrate in 10 mL of 10% Sulfuric Acid Reagent Solution, and dilute with water to 100 mL. To 10 mL of this solution, add 10 mL of 10% sulfuric Acid Reagent solution, and dilute with water to 1 L.
7.15. **LAL Reagent Water:** Generated in-house or purchased commercially
7.16. **Lead Nitrate:** Purchased commercially
7.17. **Lead Stock Solution (0.1 mg of Pb in 1 mL):** Dissolve 0.160 g of lead nitrate in 100 mL of dilute nitric acid (1:99), and dilute with purified water to 1 L. The solution should be prepared and stored in containers free from lead.
7.18. **Litmus:** Purchased commercially
7.19. **Methyl Orange:** Purchased commercially
7.20. **Nitric Acid (HNO3), concentrated:** Purchased commercially
7.21. **Dilute nitric acid (1:99):** Dilute 1 mL of 69% nitric acid in 99 mL of purified water.
7.22. **pH paper:** Purchased commercially
7.23. **Phenolphthalein:** Purchased commercially
7.24. **Potassium Carbonate:** Purchased commercially.
7.25. **15% Potassium Carbonate:** weigh 15.000 g of Potassium carbonate and transfer to a 100-mL volumetric flask. Dilute to volume with purified water.
7.26. **Potassium Hydrogen Phthalate (KHP):** Purchased commercially
7.27. **Potassium Hydrogen Phthalate (KHP) Preparation:** Crush and dry a suitable amount of KHP at 120°C for 2 hours. Allow to cool to ambient temperature in a desiccator.
7.28. **Potassium Pyroantimonate TS:** Purchased commercially
7.29. **Purified Water:** Generated in-house or purchased commercially
7.30. 0.**1N Silver Nitrate TS:** Purchased commercially
7.31. **Sodium Hydroxide (NaOH, 1N):** Purchased commercially
7.32. **Sulfuric Acid (H2SO4), concentrated:** Purchased commercially
7.33. 10**% Sulfuric Acid Reagent Solution:** In a well-ventilated fume hood, slowly add 30 mL of 96% sulfuric acid to 375 mL of purified water, cool and dilute with water to 500mL.
7.34. **1N Sulfuric Acid (H2SO4):** Purchased commercially
7.35. **Thioacetamide:** Purchased commercially
7.36. **Thioacetamide TS:** Dissolve 4 g of thioacetamide in purified water to make 100 mL.

8. ANALYTICAL PROCEDURES:

NOTE: USP general chapters are used for Assay %, Chloride, Endotoxins, and Identification testing. Normality is adapted from a customer supplied method. The primary method for Heavy Metals (as Pb)and Iron (Fe) is an in-house validated method. Alternate method for Heavy Metals (as Pb) utilizes USPand ACS general chapters and for Iron (Fe) the ACS general chapter is utilized.

IN-PROCESS TESTING

8.1. **DENSITY @ 20° ± 1°C** **REPORT:**

8.1.1. The Laboratory or Manufacturing to perform a density check of the material.
8.1.2. Laboratory Procedure: Perform a water check on the DMA 35 Density Meter before the sample analysis. Refer to BSI-SOP-0350 for instrument operation and water check analysis.
8.1.3. Record the Density of the sample from the DMA 35 Density Meter. Refer to BSI-SOP-0350 for instrument operation and sample analysis.
8.1.4. Ensure that the sample is at 20° ± 1°C for analysis.
8.1.5. Refer to the current batch record for density specification.
8.1.6. Clean the Density Meter immediately after use following BSI-SOP-0350, DMA 35 Density Meter SOP.

8.2. **NORMALITY** **REPORT:**

8.2.1. Refer to Section 8.9. for sample preparation and testing.
8.2.2. **If an adjustment is required, determine assay % of the sample utilizing the following procedure:**
8.2.2.1. Accurately weigh 30-40 g of sample and add 40 mL of purified water in a clean flask. Stopper the flask and cool to room temperature. Add 150 µL phenolphthalein as the indicator. Titrate using previously standardized 1N sulfuric acid to a colorless endpoint (V_1). Add 150 µL Methyl Orange as the indicator. Titrate using previously standardized 1N sulfuric acid to a pink endpoint (V_2).

$$\% NaOH = \frac{V_2 \times N\ H_2SO_4 \times 4.00}{Sample\ Weight\ (g)}$$

FINISHED GOOD TESTING

8.3. **APPEARANCE AND COLOR** **REFER TO SUMMARY SHEET:**

8.3.1. Transfer 50 mL of sample into a Nessler tube.
8.3.2. In order to pass, test solution is complete, clear, and colorless. Verify the solution appearance against a clear and colorless reference solution, such as purified water, and view against a color comparison plate with suitable lighting.

8.4. **CHLORIDE** **REFER TO SUMMARY SHEET:**

8.4.1. Thoroughly rinse Nessler tubes using purified water prior to use.
8.4.2. Sample Preparation:
8.4.2.1. Weigh 2.0 g of sample and quantitatively transfer to a 50-mL Nessler Color Comparison Tube using purified water.
8.4.2.2. Dilute to ~20 mL with purified water.
8.4.2.3. Slowly, using extreme caution, acidify the sample with nitric acid tolitmus.
8.4.2.4. Dilute to ~40 mL with purified water.

8.4.3. 5 ppm Standard Preparation:
8.4.3.1. Dilute 14.1 µL of 0.02N HCl to ~40 mL with purified water.
8.4.4. Analysis:
8.4.4.1. To both the sample and standard solutions, add 1 mL of concentrated nitric acid and 1 mL of 0.1N Silver Nitrate TS.
8.4.4.1.1. Dilute both the sample and standard solutions to 50mL with purified water.
8.4.4.1.2. Mix and allow solutions to sit for 5 minutes using a calibrated timer.
8.4.4.1.3. 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.

8.5. **ENDOTOXINS** **REFER TO SUMMARY SHEET:**

8.5.1. Pipet 0.200 mL of sample into a sterile vial and add 1.600 mL of LAL reagent water.
8.5.2. Add ~0.01 mL of concentrated HCl to acidify.
8.5.3. Check the pH of the solution with pH paper: solution must be acidic.
8.5.3.1. If basic add HCl in increments of 0.001 mL until acidic.
8.5.4. Once acidic add sufficient buffer of a pH range ~9-10 until the solution is between pH 6-8.
8.5.5. Add approximately 0.025 mL of buffer.
8.5.6. Dilute with LAL reagent water to a final volume of 10 mL.
8.5.7. Follow the Endosafe Nexgen PTS Endotoxin Reader SOP for sample analysis.
8.5.7.1. The dilution factor is 50.

8.6. **HEAVY METALS (Pb)** **REFER TO SUMMARY SHEET:**

8.6.1. Refer to BSI-ATM-0074 for primary method of analysis.
8.6.2. Alternate Method:
8.6.2.1. Standard and Solution Prep:
8.6.2.1.1. Lead Standard Solution (0.01 mg of Pb in 1 mL): Dilute 10 mL of lead stock solution to 100 mL with purified water. This must be prepared at time of use.
8.6.2.1.2. Thioacetamide-Glycerin Base: Thoroughly mix 1 mL of thioacetamide with 5 mL of glycerin base. Heat in a boiling bath of 20 seconds. Prepare immediately before use.
8.6.2.2. Procedure:
8.6.2.2.1. **Note:** Prepare in a hood and use caution for standard and sample prep to avoidspattering of sample.
8.6.2.2.2. Sample Preparation: Weigh 30 g of sample into a suitable beaker and carefully neutralize with 1 mL of nitric acid.
8.6.2.2.3. Standard Preparation: Weigh 10 g of sample into a suitable beaker and add 0.3 mL of concentrated nitric acid. Add 2 mL of 0.01 mg of Lead Standard Solution.
8.6.2.2.4. 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.
8.6.2.2.5. Transfer the solutions to separate Nessler Color Comparison tubes. Add 1.2 mL of freshly prepared thioacetamide-glycerin base to each of the solutions and mix. QS each tube to 50 mL and mix.

8.6.2.3. Any brown color produced in the sample solution must not exceed that in the standard solution to be reported as ≤ 1 ppm.

8.7. **IDENTIFICATION (SODIUM)** **REFER TO SUMMARY SHEET:**

8.7.1. Pipette 1 mL of sample into a test tube containing 25 mL of purified water.
8.7.2. Add 2 mL of 15% potassium carbonate and heat to boiling
8.7.3. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation
8.7.4. No precipitate should be formed at this stage of analysis.
8.7.5. Add 4 mL Potassium Pyroantimonate TS and heat to boiling.
8.7.6. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.
8.7.7. A dense precipitate must form in order to pass test.

8.8. **IRON** **REFER TO SUMMARY SHEET:**

8.8.1. Refer to BSI-ATM-0074 for primary method of analysis.
8.8.2. Alternate Method:
8.8.2.1. Procedure:
8.8.2.1.1. Sample Preparation: To 20 g of sample, add 0.1 mL of phenolphthalein indicator solution, neutralize with hydrochloric acid and dilute with water to 40 mL.
8.8.2.1.2. 0.01 mg Iron Standard Preparation: Pipette 1 mL of Iron Standard (0.01 mg of Fe in 1 mL) and dilute each with water to 40 mL.
8.8.2.1.3. To the sample and standard solutions add 30-50 mg of ammonium peroxydisulfate crystals, 2 mL of hydrochloric acid, and 3 mL of Ammonium Thiocyanate Reagent Solution and mix.
8.8.2.2. Any red color in the sample must not exceed the 0.01 mg standard Solution to report as < 0.5 ppm.

8.9. **NORMALITY** **REFER TO SUMMARY SHEET:**

8.9.1. Burette Preparation:
8.9.1.1. Allow the NaOH 1N sample to come to 25° ± 2°C.
8.9.1.2. Prime the 50 mL burette by filling it with the NaOH 1N sample solution. Empty the burette and repeat.
8.9.1.3. Fill the burette to the required volume with the NaOH 1N sample solution.
8.9.2. Sample Preparation:
8.9.2.1. Weigh ~6.1 g of the previously dried KHP into a beaker.
8.9.2.2. Add 100 mL of purified water down the sides of the beaker to avoid the loss of KHP.
8.9.3. Analysis Procedure:
8.9.3.1. To the KHP solution, add 150 µL phenolphthalein indicator.
8.9.3.2. Titrate the KHP using the sample solution in the burette, to a pink endpoint.
8.9.3.3. Calculate the normality using the following equation:

$$N = \frac{(KHP\ weight\ g)}{(0.20423)(mL\ of\ NaOH\ sample\ solution)}$$