BIOSPECTRA
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SODIUM HYDROXIDE 10N TESTING METHODS

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1. PURPOSE:

1.1. To provide the laboratory personnel with a procedure for analyzing Sodium Hydroxide 10N In-Process, Stability, and Finished Good samples.

2. SCOPE:

2.1. Applies to the analysis of Sodium Hydroxide 10 N In-Process, Stability, and Finished Goods in the Laboratory. Methods include testing for all grades of Sodium Hydroxide 10 N sold by BioSpectra; only the specific tests required for the requested grade must be tested.

3. RESPONSIBILITIES:

3.1. The laboratory manager is responsible for training, maintenance and implementation of this procedure.

3.2. The laboratory personnel are responsible for compliance with the terms of this procedure. This includes notifying the laboratory manager 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-FRM-0717, Sodium Hydroxide 10N Analytical Procedure
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-0133, Blue M Convection Oven Operation and Calibration SOP
5.6. BSI-SOP-0135, Laboratory Chemicals
5.7. BSI-SOP-0140, Standardization of Titrants
5.8. BSI-SOP-0242, Bangor Portable Turbidimeter and Calibration SOP
5.9. BSI-SOP-0255, XL200 pH mV Conductivity Meter SOP
5.10. BSI-SOP-0303, NexION 350X ICP-MS SOP
5.11. BSI-SOP-0345, Laboratory Nexgen-PTS Endotoxin Reader SOP
5.12. BSI-SOP-0350, Anton Paar DMA 35 Portable Density Meter Operation and Calibration
5.13. *ACS Reagent Chemicals*, current edition
5.14. *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. XL200 pH mV Conductivity Meter

7. ANALYTICAL PROCEDURES:

7.1. IN-PROCESS TESTING:

7.1.1. ASSAY >30.5%:

7.1.1.1. Perform a manual standardization or titrant check of 1N Sulfuric Acid per Standardization of Titrants.
7.1.1.2. Accurately weigh 3.5 – 7.5g of sample and add 40mL of purified water in a clean flask. Stopper the flask and allow to cool to room temperature.
7.1.1.3. Add Phenolphthalein as the indicator and titrate using previously standardized 1N Sulfuric Acid to a colorless endpoint (V1).
7.1.1.4. Add Methyl Orange as the indicator.
7.1.1.5. Titrate using previously standardized 1N Sulfuric Acid to a pink endpoint (V2).
7.1.1.6. Calculate the percentage of Sodium Hydroxide using the following equation:

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

7.1.2. DENSITY @20°±1°C 1.354-1.395:

7.1.2.1. QC or Manufacturing to perform a density check of the material.
7.1.2.2. 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.
7.1.2.3. Record the Density of the sample from the DMA 35 Density Meter. Refer to BSI-SOP-0350 for instrument operation and sample analysis.
7.1.2.4. Ensure that the sample is at 20°±1°C for analysis.
7.1.2.5. Clean immediately after use following DMA 35 Density Meter SOP

7.1.3. CHLORIDE < 5 PPM:

7.1.3.1. ***Note:*** *Record <5ppm or >5ppm in the batch record.*
For QC Release to Dilute to Normality, the confirmation 1 and 2 samples must be run against a freshly prepared 5ppm standard only.

7.1.3.2. **Sample preparation:**
7.1.3.2.1. Thoroughly rinse Nessler tubes using purified water prior to use.
7.1.3.2.2. Weigh 2.0g of sample and quantitatively transfer to 50mL Nessler Color Comparison Tube using purified water.
7.1.3.2.3. Dilute sample to ~20mL with purified water.
7.1.3.2.4. Slowly, using extreme caution, acidify the sample with nitric acid to litmus.
7.1.3.2.5. Dilute to 40mL with purified water.
7.1.3.3. **Standard Preparation**: Standard preparation for internal reporting only.
7.1.3.3.1. 5ppm Limit: Dilute 14.1µL of 0.02N HCl to ~40mL with purified water.
7.1.3.4. **Procedure:**
7.1.3.4.1. To the standard and sample solutions prepared above, add 1mL of concentrated nitric acid and 1mL of 0.1N Silver Nitrate TS.
7.1.3.4.2. Dilute each tube to 50mL with purified water.
7.1.3.4.3. Mix and allow to sit for 5 minutes, using a calibrated timer.

7.1.3.4.4. 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.

7.1.3.4.5. For Cold Water Regen samples, the turbidity in the sample solution can not exceed that of the standard in order to report as <5ppm. If the turbidity of the sample exceeds that of the standard, report as >5ppm and **notify QA/QC Management and Process Technology.**

7.1.3.4.6. For Assay/Chloride Confirmation samples, the sample NTU must be >2NTU from the standard NTU in order to be considered acceptable. If the sample NTU value falls within 2NTU of the standard, run the sample in triplicate. **Notify QA/QC Management prior to proceeding.**

7.1.4. **NORMALITY** **REPORT:**

7.1.3.1. Refer to Section 7.2.7 for sample preparation and testing.

7.2. FINISHED GOOD TESTING:

7.2.1. APPEARANCE AND COLOR CLEAR, COLORLESS LIQUID:

7.2.1.1. Transfer 50mL of sample into a Nessler tube.

7.2.1.2. 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.

7.2.2. CHLORIDE ≤ 5PPM:

7.2.2.1. Thoroughly rinse Nessler tubes using purified water prior to use.

7.2.2.2. **Sample Preparation:**

7.2.2.2.1. Weigh 2.0g of sample and quantitatively transfer to a 50mL Nessler Color Comparison Tube using purified water.

7.2.2.2.2. Dilute to ~20mL with purified water.

7.2.2.2.3. Slowly, using extreme caution, acidify the sample with nitric acid to litmus.

7.2.2.2.4. Dilute to ~40mL with purified water.

7.2.2.3. **5 ppm Standard Preparation:**

7.2.2.3.1. Dilute 14.1 µL of 0.02N HCl to ~40mL with purified water.

7.2.2.4. **Analysis:**

7.2.2.4.1. To both the sample and standard solutions, add 1 mL of concentrated nitric acid and 1 mL of 0.1N Silver Nitrate TS.

7.2.2.4.2. Dilute both the sample and standard solutions to 50mL with purified water.

7.2.2.4.3. Mix and allow solutions to sit for 5 minutes using a calibrated timer.

7.2.2.4.4. 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.

7.2.3. **ENDOTOXINS** **≤2.0 EU/ML:**

7.2.3.1. Pipet 0.200mL of sample into a sterile vial and add 1.600 mL of LAL reagent water.
7.2.3.2. Add 0.160mL of concentrated Hydrochloric acid to acidify.
7.2.3.3. Check the pH of the solution with pH paper: solution must be acidic.
7.2.3.3.1. If basic add HCl in increments until acidic.
7.2.3.3.1.1. Add approximately 0.2mL of HCl.
7.2.3.4. Once acidic add sufficient buffer of a pH range ~9-10 until the solution is between pH 6-8.
7.2.3.4.1. Add approximately 0.3mL of buffer.
7.2.3.5. Dilute with LAL reagent water to a final volume of 10mL.
7.2.3.6. Follow the Endosafe Nexgen PTS Endotoxin Reader SOP for sample analysis.
7.2.3.6.1. The dilution factor is 50.

7.2.4. **HEAVY METALS (PB)** **≤ 1PPM:**

7.2.4.1. Refer to NexION 350X ICP-MS SOP for primary method of analysis.

Alternate Method:
7.2.4.2. Standard and Solution Prep:
7.2.4.2.1. 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.
7.2.4.2.2. 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.
7.2.4.2.2.1. Dilute nitric acid (1:99): Dilute 1mL of 69% nitric acid in 99mL of purified water.
7.2.4.2.3. 1N Acetic Acid: Dilute 57mL of glacial acetic acid to 1L with purified water.
7.2.4.2.4. 10% Ammonium Hydroxide: Dilute 35mL of 29% ammonium hydroxide to 100mL with purified water.
7.2.4.2.5. Glycerin Base: To 200g of glycerin add water to total weight of 235. Add 140mL of 1N NaOH, 50mL of purified water and mix.
7.2.4.2.6. Thioacetamide: Dissolve 4g of thioacetamide in purified water to make 100mL.
7.2.4.2.7. 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.
7.2.4.3. Procedure:
7.2.4.3.1. Note: Prepare in hood, and use caution for standard and sample prep to avoid spattering of sample.
7.2.4.3.2. Sample Preparation: Weigh 30g of sample into a suitable beaker and carefully add 18mL of concentrated nitric acid.
7.2.4.3.3. Standard Preparation: Weigh 10g of sample and add 5mL of concentrated nitric acid. Add 2mL of 0.01mg Lead Standard Solution.

7.2.4.3.4. 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.

7.2.4.3.5. 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. QS each tube to 50mL and mix.

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

7.2.5. **IDENTIFICATION (SODIUM) PASSES TEST:**

7.2.5.1. Pipette 1mL of sample into a test tube containing 25mL of purified water.

7.2.5.2. Add 2mL of 15% Potassium Carbonate and heat to boiling

7.2.5.3. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation

7.2.5.4. No precipitate should be formed at this stage of analysis.

7.2.5.5. Add 4mL Potassium Pyroantimonate TS and heat to boiling.

7.2.5.6. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.

7.2.5.7. A dense precipitate must form in order to pass test.

7.2.6. **IRON ≤ 2PPM:**

7.2.6.1. Refer to NexION 350X ICP-MS SOP for primary method of analysis.

Alternate Method:

7.2.6.2. Standard and Solution Preparations:

7.2.6.2.1. 30% ammonium thiocyanate: Dissolve 150g of ammonium thiocyanate in water, and dilute with water to 500mL.

7.2.6.2.2. Iron Standard (0.01mg of Fe in 1mL): Dissolve 0.702g of ferrous ammonium sulfate hexahydrate in 10mL of 10% sulfuric acid reagent solution, and dilute with water to 100mL.

7.2.6.2.2.1. To 10mL of this solution, add 10mL of 10% sulfuric acid reagent solution, and dilute with water to 1L.

7.2.6.2.2.2. 10% sulfuric acid reagent solution: In a well- ventilated fume hood, slowly add 30mL of 96% sulfuric acid to 375mL of purified water, cool and dilute with water to 500mL.

7.2.6.3. Procedure:

7.2.6.3.1. Thoroughly rinse glassware with purified water prior to use.

7.2.6.3.2. Sample Preparation: To 10g of sample, add 0.1mL of phenolphthalein indicator solution, neutralize with hydrochloric acid (solution will turn from pink to clear) and dilute with water to 40mL in a graduated cylinder. Transfer to a Nessler Color Comparison Tube.

7.2.6.3.3. 0.02mg Iron Standard Preparation: Pipette 2mL of 0.01mg of Iron standard into a graduated cylinder and dilute to 40mL with purified water. Transfer to a Nessler Color Comparison Tube.

7.2.6.3.4. To the sample and standard solutions add 30-50mg of ammonium peroxydisulfate crystals, 3mL of hydrochloric acid, and 3mL of ammonium thiocyanate reagent solution, and mix.

7.2.6.3.5. Any red color in the sample must not exceed the 0.02mg Standard solution.

7.2.7. **NORMALITY** **9.9 -10.1 N:**

7.2.7.1. KHP (Potassium Hydrogen Phthalate) preparation:

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

7.2.7.2. Burette preparation:

7.2.7.2.1. Fill a 25mL volumetric flask with sample. Quantitatively transfer the aliquot to a 250mL volumetric flask with purified water. Rinse the 25mL flask by filling the flask halfway with purified water, shaking it, then transferring the rinse to the 250mL volumetric flask. Perform the rinse procedure in duplicate. Fill the 250mL volumetric flask to volume with purified water. Mix well and cool to 25°±2°C. QS the sample solution to 250mL after cooling is complete.

7.2.7.2.2. Prime the 50mL burette by filling it with the diluted sample solution. Empty the burette and repeat.

7.2.7.2.3. Fill the burette to the required volume with the prepared sample solution.

7.2.7.3. Sample preparation:

7.2.7.3.1. Weigh 8.0000 – 8.2000g of the previously dried KHP into a 250mL beaker.

7.2.7.3.2. Add 100mL of purified water down the sides of the beaker to avoid the loss of KHP.

7.2.7.4. Analysis Procedure:

7.2.7.4.1. To the KHP solution, add phenolphthalein indicator.

7.2.7.4.2. Titrate the KHP using the sample solution in the burette, to a pink endpoint.

7.2.7.4.3. Calculate the normality using the following equation:

$$N = \frac{(KHP\ weight\ g)(KHP\ Purity)(10)}{(0.20423)(mL\ of\ NaOH\ sample\ solution)}$$

7.2.8. **SODIUM CARBONATE** **≤0.6%:**

7.2.8.1. **Preparation of 6N sulfuric acid Solution:**

7.2.8.1.1. To a 1L volumetric flask containing 600ml of cooled Purified Water, add slowly (using caution) 169mL of 96% sulfuric acid in small increments allowing to cool in between each addition. Dilute to the mark, mix thoroughly. Reagent may already be prepared.

7.2.8.1.2. Following the Standardization of Titrants SOP, perform a single check of the 6N sulfuric Acid normality concentration when the reagent is first prepared:

7.2.8.2. **Sample Analysis:**

7.2.8.2.1. Accurately weigh 48g of sample in an iodine flask then add 100mLof purified water. Stopper, swirl to mix, water seal the flask, and chill to room temperature in an ice bath.

7.2.8.2.2. While in an ice bath, slowly add the calculated volume of 6N sulfuric acid reagent required from the calculation below. Wash down the flask sides with purified water, swirl to mix, water-seal the flask, and then chill to room temperature.

$$mL\ of\ 6N\ sulfuric\ acid\ to\ add = \frac{(29.9)^{1}(sample\ weight)}{(4.00)(N\ of\ 6N\ Sulfuric\ Acid)} - 5mL$$

[1] Theoretical assay value of a 9.95N Sodium Hydroxide. (Low end of target range to avoid the over addition of 6N Sulfuric Acid)

7.2.8.2.3. Titrate with a standardized 1N H_2SO_4 and phenolphthalein TS usinga 50mL buret to a precise clear endpoint (V_1); add methyl orange indicator and continue the titration to the first pink endpoint (V_2). Calculate the % Na_2CO_3 using the following equation:

$$\%\ Na_2CO_3 = \frac{(V_2 - V_1)\ x\ N\ of\ Titrant\ x\ 10.6}{sample\ weight\ (g)}$$