BIOSPECTRA

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SODIUM HYDROXIDE 2N TESTING METHODS

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1. PURPOSE:

1.1. To provide Laboratory personnel with a procedure for analyzing Sodium Hydroxide 2N In-Process, Stability, and Finished Good samples.

2. SCOPE:

2.1. Applies to the analysis of Sodium Hydroxide 2N In-Process, Stability, and Finished Goods in the Laboratory. Methods include testing for all grades of Sodium Hydroxide 2N sold by BioSpectra; only the specific tests required for the requested grade must be tested.

3. RESPONSIBILITIES:

3.1. The Director of Laboratory Testing is responsible for training, maintenance and implementation of this procedure.

3.2. Laboratory Analysts are responsible for compliance with the terms of this procedure. This includes notifying the Laboratory Supervisor, Laboratory Manager, and/or Director of Laboratory Testing 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-0760, Sodium Hydroxide 2N 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-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-0244, VWR Gravity Convection Over Operation and Calibration (Model Number 414005-106)
5.9. BSI-SOP-0303, NexION 350X ICP-MS SOP
5.10. BSI-SOP-0345, Endosafe nexgen-PTS Endotoxin Reader SOP
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. Calibrated Oven
6.6. Calibrated Pipettes

7. REAGENTS:

7.1. **Endosafe PTS Cartridge 1-0.01 EU/mL** - Purchased commercially.
7.2. **Hydrochloric Acid (HCl) (concentrated)** – Purchased commercially.
7.3. **Hydrochloric Acid (0.02 N HCl)** - Dilute 20 mL of HCl 0.1 N to 100 mL with purified water. Can be purchased commercially.
7.4. **LAL Reagent Water** - Purchased commercially.
7.5. **Methyl Orange** – Dissolve 0.10g of methyl orange in 100mL of purified water. Filter if necessary.
7.6. **Nitric Acid (HNO3) Concentrated (Reagent Grade)** – Purchased commercially.
7.7. **Phenolphthalein** – Dissolve 1.0g of phenolphthalein in 100mL of reagent grade alcohol.
7.8. **pH Paper / Litmus Paper** - Purchased commercially.
7.9. **Potassium Hydrogen Phthalate (KHP)** - Prepare an appropriate sample container at 120 °C for 30 minutes. Allow to cool in desiccator. Crush and dry a suitable amount of potassium hydrogen phthalate. Dry at 120 °C for 2 hours. Cool and store in desiccator in a closed container. Stable for 3 months.
7.10. **Silver Nitrate, 0.1 N TS** - Purchased commercially.
7.11. **Sulfuric Acid (1N H2SO4)** – Purchased commercially
7.12. **Tris Base Solution (0.25M)** – Purchased commercially

8. ANALYTICAL PROCEDURES:

8.1. **IN-PROCESS TESTING:**

8.1.1. **APPEARANCE** **REPORT:**

8.1.1.1. Transfer 50 mL of sample into a Nessler tube.
8.1.1.2. Inspect the sample to ensure it is particulate free.

8.1.2. **NORMALITY (CONFIRMATION 1 AND 2) REFER TO SUMMARY SHEET:**

8.1.2.1. **Burette preparation:**
8.1.2.1.1. Allow the NaOH 2N sample to come to 25°C ± 2°C.
8.1.2.1.2. Prime the 50 mL burette by filling it with the NaOH 2N sample solution. Empty the burette and repeat.
8.1.2.1.3. Fill the burette to the required volume with the NaOH 2N sample solution.

8.1.2.2. **Sample preparation:**
8.1.2.2.1. Weigh 12.0 g of the previously dried KHP into a 250 mL beaker.
8.1.2.2.2. Add 100 mL of purified water down the sides of the beaker to avoid the loss of KHP.

8.1.2.3. **Analysis Procedure:**
8.1.2.3.1. To the KHP solution, add phenolphthalein indicator.
8.1.2.3.2. Titrate the KHP using the sample solution in the burette, to a pink endpoint.
8.1.2.3.3. Calculate the normality using the following equation:

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

$$KHP\ Purity = Assay\ percent\ of\ KHP/100\ (from\ manufacturer's\ CoA)$$

$$0.20423 = Formula\ weight\ of\ KHP/1000$$

NOTE:

- **If Confirmation 1 sample is in specification, perform Normality on the Confirmation 2 sample. Both must be in specification to release for packaging.**
- **If Confirmation 1 sample is out of specification, perform Assay % (w/w) and inform appropriate Laboratory Management of both results to make adjustment to the blend.**

8.1.3. **ASSAY** **REPORT:**

8.1.3.1. NOTE: only required if Normality Confirmation sample is out of specification.
8.1.3.2. Perform a manual standardization or titrant check of 1N Sulfuric Acid per Standardization of Titrants.
8.1.3.3. Accurately weigh 10-15 g of sample and add 100 mL of purified water in a clean flask. Stopper the flask and allow to cool to room temperature.
8.1.3.4. Add phenolphthalein as the indicator and titrate using previously standardized 1N Sulfuric Acid to a colorless endpoint (V1).
8.1.3.5. Add Methyl Orange as the indicator.
8.1.3.6. Titrate using previously standardized 1N Sulfuric Acid to a pink endpoint (V2).
8.1.3.7. Calculate the percentage of Sodium Hydroxide using the following equation:

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

8.2. **FINISHED GOOD TESTING:**

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

8.2.1.1. Transfer 50 mL of sample into a Nessler tube.
8.2.1.2. In order to pass, the test solution is complete, clear and colorless, and free from particulate matter.
8.2.1.3. 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.
8.2.1.4. 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.

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

8.2.2.1. Thoroughly rinse Nessler tubes using purified water prior to use.
8.2.2.2. **Sample Preparation:**
8.2.2.2.1. Weigh 2.0 g of sample and quantitatively transfer to a 50 mL Nessler Color Comparison Tube using purified water.
8.2.2.2.2. Dilute to ~20 mL with purified water.
8.2.2.2.3. Slowly, using extreme caution, acidify the sample with Nitric Acid to litmus.
8.2.2.2.4. Dilute to 40 mL with purified water.
8.2.2.3. **5 ppm Standard Preparation:**
8.2.2.3.1. Dilute 14.1 µL of 0.02N HCl to ~40 mL with purified water.
8.2.2.4. **Analysis:**
8.2.2.4.1. To both the sample and standard solutions, add 1 mL of concentrated nitric acid and 1 mL of 0.1N Silver Nitrate TS. Dilute each tube to 50 mL with purified water.

8.2.2.4.2. Mix and allow solutions to sit for 5 minutes using a calibrated timer.
8.2.2.4.3. 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.

8.2.3. **ENDOTOXINS** **REFER TO SUMMARY SHEET:**
8.2.3.1. Pipet 0.200 mL of sample into a sterile vial and add 1.600 mL of LAL reagent water.
8.2.3.2. Add concentrated Hydrochloric acid to acidify.
8.2.3.3. Check the pH of the solution with pH paper: solution must be acidic.
8.2.3.3.1. If basic, add HCl in increments until acidic.
8.2.3.3.1.1. Add approximately 1-2 µL of HCl.
8.2.3.4. Once acidic add sufficient buffer of a pH range ~9-10 until the solution is between pH 6-8.
8.2.3.4.1. Add approximately 0.3 mL of buffer.
8.2.3.5. Dilute with LAL reagent water to a final volume of 10 mL.
8.2.3.6. Follow the Endosafe Nexgen PTS Endotoxin Reader SOP, BSI-SOP-0345, for sample analysis.
8.2.3.6.1. The dilution factor is 50.

8.2.4. **HEAVY METALS (PB)** **REFER TO SUMMARY SHEET:**
8.2.4.1. Refer to NexION 350X ICP-MS SOP, BSI-SOP-0303.

8.2.5. **IDENTIFICATION (SODIUM)** **REFER TO SUMMARY SHEET:**
8.2.5.1. Pipette 1 mL of sample into a test tube containing 25 mL of purified water.
8.2.5.2. Add 2 mL of 15% Potassium Carbonate and heat to boiling.
8.2.5.3. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.
8.2.5.4. No precipitate should be formed at this stage of analysis.
8.2.5.5. Add 4 mL Potassium Pyroantimonate TS and heat to boiling.
8.2.5.6. Allow to cool in ice bath and as necessary, rub the inside of the test tube with a glass rod to initiate precipitation.
8.2.5.7. A dense precipitate must form in order to pass test.

8.2.6. **IRON** **REFER TO SUMMARY SHEET:**
8.2.6.1. Refer to NexION 350X ICP-MS SOP, BSI-SOP-0303.

8.2.7. **NORMALITY** **REFER TO SUMMARY SHEET:**
8.2.7.1. **Burette preparation:**
8.2.7.1.1. Allow the NaOH 2N sample to come to 25°C ± 2°C.
8.2.7.1.2. Prime the 50 mL burette by filling it with the NaOH 2N sample solution. Empty the burette and repeat.
8.2.7.1.3. Fill the burette to the required volume with the NaOH 2N sample solution.
8.2.7.2. **Sample preparation:**
8.2.7.2.1. Weigh 12.0 g of the previously dried KHP into a 250 mL beaker.
8.2.7.2.2. Add 100 mL of purified water down the sides of the beaker to avoid the loss of KHP.
8.2.7.3. **Analysis Procedure:**
8.2.7.3.1. To the KHP solution, add phenolphthalein indicator.

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

8.2.7.3.3. Calculate the normality using the following equation:

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KHP Purity = Assay Percent of KHP/100 (from manufacture's CoA)

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