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SODIUM HYDROXIDE 2N TESTING METHODS

TABLE OF CONTENTS

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

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 Laboratory Manager 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 applicable 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-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 Oven 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 BATCH RECORD:**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 150 µL of 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 150 µL of phenolphthalein as the indicator and titrate using previously standardized 1N Sulfuric Acid to a colorless endpoint (V1).
- 8.1.3.5. Add 150 µL of 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 150 µL of 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:

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

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

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