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SODIUM HYDROXIDE 0.5N

TESTING METHODS

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1. PURPOSE:

1.1. To provide the Quality Control (QC) Laboratory personnel with a procedure for analyzing Sodium Hydroxide 0.5N In-Process, Stability, and Finished Good samples.

2. SCOPE:

2.1. Applies to the analysis of Sodium Hydroxide 0.5N for In-Process, Stability, and Finished Goods in the QC Laboratory. Methods include testing for Sodium Hydroxide 0.5N sold by BioSpectra.

3. RESPONSIBILITIES:

3.1. The Executive Director of Quality Control is responsible for training, maintenance and implementation of this procedure.
3.2. The QC Analysts are responsible for compliance with the terms of this procedure. This includes notifying the Executive Director of Quality Control 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. *ACS Reagent Chemicals*, current edition
5.2. *USP-NF* current edition
5.3. Anton Paar DMA 35 Portable Density Meter Operation and Calibration, DCN:19-002946
5.4. Laboratory Chemicals
5.5. Balance SOP
5.6. Blue M Convection Oven Operation and Calibration SOP
5.7. Laboratory Nexgen-PTS Endotoxin Reader SOP, DCN:18-002735
5.8. Laboratory Notebooks
5.9. Result Reporting

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

7. ANALYTICAL PROCEDURES: PRODUCT IS NON-COMPENDIAL

NOTE: USP general chapters are used for Assay %, Chloride, Endotoxins, and Identification testing. Normality is 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 USP and ACS general chapters and for Iron (Fe) the ACS general chapter is utilized.

7.1. **IN-PROCESS TESTING:**

7.1.1. **DENSITY @20°±1°C REPORT:**

7.1.1.1. QC or Manufacturing to perform a density check of the material.

7.1.1.1.1. If QC analysis: Perform a water check on the DMA 35 Density Meter before the sample analysis. Refer to DCN: 19-002946 for instrument operation and water check analysis.

7.1.1.1.2. Record the Density of the sample from the DMA 35 Density Meter. Refer to DCN: 19-002946 for instrument operation and sample analysis.

7.1.1.1.3. Ensure that the sample is at 20°±1°C for analysis.

7.1.1.1.3.1. Density ~1.02g/mL

7.1.1.1.4. Clean immediately after use following DMA 35 Density Meter SOP.

7.1.2. **NORMALITY REPORT:**

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

For an exact assay % required for adjustment:
Accurately weigh 30-40g of sample and add 40 mL of purified water in a clean flask. Stopper the flask and cool to room temperature. Add Phenolphthalein as the indicator. Titrate using previously standardized 1 N Sulfuric Acid to a colorless endpoint (V_1). Add Methyl Orange as the indicator. Titrate using previously standardized 1 N Sulfuric Acid to a pink endpoint. (V_2).

Calculate the percentage of Sodium Hydroxide using the following equations:

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

7.2. **FINISHED GOOD TESTING:**

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

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 REFER TO SUMMARY SHEET:**

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. 5ppm Standard Preparation:
7.2.2.3.1. Dilute 14.1µL 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 1mL of concentrated nitric acid and 1mL of 0.1N Silver Nitrate TS.
7.2.2.4.2. Dilute both tubes to 50 mL and mix. Allow solutions to sit for 5 minutes using a calibrated timer.
7.2.2.4.3. 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.

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

7.2.3.1. Pipet 0.200mL of sample into a sterile vial and add 1.600mL of LAL reagent water.
7.2.3.2. Add ~0.01mL of concentrated HCl 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 of ~ 0.001mL until acidic.
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 0.025mL 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 (AS PB) REFER TO SUMMARY SHEET:**
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 time of use.
7.2.4.2.3. Dilute nitric acid (1:99): Dilute 1mL of 69% nitric acid in 99mL of purified water.
7.2.4.2.4. 1N Acetic Acid: Dilute 57mL of glacial acetic acid to 1L with purified water.
7.2.4.2.5. 10% ammonium hydroxide: Dilute 35mL of 29% ammonium hydroxide to 100mL with purified water.
7.2.4.2.6. Glycerin base: To 200g of glycerin add water to total weight of 235. Add 140mL of 1N NaOH, 50mL of purified water and mix.
7.2.4.2.7. Thioacetamide: Dissolve 4g of thioacetamide in purified water to make 100mL.

7.2.4.2.8. Thioacetamide-glycerin base: Thoroughly mix 1mL of thioacetamide with 5mL of Glycerin base. Heat in a boiling bath of 20 seconds. Prepare immediately before use.

7.2.4.3. Procedure:
Note: Prepare in a hood, and use caution for standard and sample prep to avoid spattering of sample.

7.2.4.4. Sample Preparation: Weigh 30g of sample into a suitable beaker and carefully neutralize with 1mL of nitric acid.

7.2.4.5. Standard Preparation: Weigh 10g of sample and add 0.3mL of concentrated nitric acid. Add 2mL of 0.01mg of Lead Standard Solution.

7.2.4.6. Place both the standard and sample on a hot plate and evaporate to dryness. Cool and dissolve each residue with 20mL of purified water. Adjust the pH to between 3 and 4 utilizing a pH meter, with 1N acetic acid or 10% ammonium hydroxide.

7.2.4.7. 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.

7.2.4.8. 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 REFER TO SUMMARY SHEET:**

7.2.5.1. Pipette 25mL of sample into a test tube.

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 REFER TO SUMMARY SHEET:**

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

7.2.6.2. Alternate Method:

7.2.6.3. Standard and Solution Preparations:

7.2.6.3.1. 30% ammonium thiocyanate: Dissolve 150 of ammonium thiocyanate in water, and dilute with water to 500mL.

7.2.6.3.2. 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.

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

7.2.6.3.2.2. 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.

7.2.6.4. Procedure:
7.2.6.5. Sample Preparation: To 10g of sample, add 0.1mL of phenolphthalein indicator solution, neutralize with hydrochloric acid and dilute with water to 40mL.
7.2.6.6. 0.02mg Iron standard preparation: Pipette 2mL of 0.01mg of Iron standard and dilute each with water to 40mL.
7.2.6.7. 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.
7.2.6.8. Any red color in the sample must not exceed the 0.02mg Standard solution.

7.2.7. **NORMALITY REFER TO SUMMARY SHEET:**
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. Allow the 0.5 N NaOH sample to cool to 25°±2°C.
7.2.7.2.2. Prime the 50mL burette by filling it with the 0.5N NaOH sample solution. Empty the burette and repeat.
7.2.7.2.3. Fill the burette to the required volume with the 0.5N NaOH sample solution.
7.2.7.3. Sample preparation:
7.2.7.3.1. Weigh ~3.0g of the previously dried KHP into a 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 0.5N NaOH sample solution in the burette, to a pink endpoint.
7.2.7.4.3. Calculate the normality using the following equation:

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