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RESIDUAL SOLVENTS BY HEADSPACE GC-FID: GLYCERIN

TABLE OF CONTENTS

1. PURPOSE:

1.1. To provide Laboratory Analysts and/or qualified designees with a procedure for analyzing Residual Solvents by Headspace GC-FID in Glycerin.

2. SCOPE:

2.1. This Analytical Method applies to the analysis of Residual Solvents by Headspace GC-FID in Glycerin.
2.2. Residual Solvents in Glycerin specifications:

Table 1: Residual Solvents in Glycerin Specifications

Analyte	Specification
Methanol	≤ 3000ppm

3. RESPONSIBILITIES:

3.1. The Laboratory Technology Manager is responsible for the control, implementation, training, and maintenance of this procedure
3.2. The Laboratory Analysts, and/or qualified designees, are responsible for performing the testing stated in this procedure.
3.3. Safety: Standard laboratory safety regulations apply. Before working with any chemical, read and understand the Safety Data Sheet (SDS).

4. REFERENCES:

4.1. BSI-PRL-0348, Analytical Method Validation Protocol: Residual Solvents by Headspace GC-FID
4.2. BSI-RPT-2196, Analytical Method Validation Report: Residual Solvents by Headspace GC-FID – Glycerin
4.3. BSI-SOP-0098, Balance SOP
4.4. BSI-SOP-0126, Laboratory Notebooks
4.5. BSI-SOP-0134, Pipette SOP
4.6. BSI-SOP-0161, Waste Handling SOP
4.7. BSI-SOP-0316, Shimadzu QP2010S GC/MS SOP
4.8. ICH Q3A
4.9. USP NF <467> Residual Solvents
4.10. USP NF <621> Chromatography

5. MATERIALS AND EQUIPMENT:

5.1. All materials and equipment utilized in this analysis are outlined in this section.
5.2. Equipment and Instrumentation:
  5.2.1. Analytical Balance
  5.2.2. Micropipettes
  5.2.3. GC-FID
    5.2.3.1. Make: Shimadzu
    5.2.3.2. Model: GC-2010 with Head-Space Autosampler
  5.2.4. GC Column:
    5.2.4.1. Make: Phenomenex
    5.2.4.2. Model: Zebron ZB-624, 30m x 0.25mm x 1.40µm
    5.2.4.3. Part Number:7HG-G005-27
5.3. Reagents and Reference Standards:
  5.3.1. **Glycerin:** In-House or Purchased Commercially.
  5.3.2. **Methanol Certified Reference Standard:** Purchased Commercially.
  5.3.3. **Purified Water:** In-House or Purchased Commercially.
5.4. Supplies:
  5.4.1. 20mL Headspace Vials and Caps
  5.4.2. Beakers
  5.4.3. Class A Volumetric Flasks
  5.4.4. Crimper
  5.4.5. Micropipette Tips
  5.4.6. Transfer Pipettes
  5.4.7. Vespel Graphite Ferrule

6. METHOD PARAMETERS:

6.1. **HS-20**
  6.1.1. Oven Temp: 80.0°C
  6.1.2. Sample Line Temp.: 150.0°C
  6.1.3. Transfer Line Temp: 155.0°C
  6.1.4. Shaking Level: 1
  6.1.5. Injection Count: 1
  6.1.6. Pressurizing Gas: 176.2 kPa
  6.1.7. Equilibrating Time: 15.00 minutes
  6.1.8. Pressurization Time: 0.50 minutes
  6.1.9. Pressure Equilibration Time: 0.50 minutes
  6.1.10. Load Time: 1.00 minute
  6.1.11. Load Equilibration Time: 0.50 minutes
  6.1.12. Injection Time: 1.00 minute
  6.1.13. Needle Flush Time: 1.00 minute
  6.1.14. GC Cycle Time: 7.00 minutes
  6.1.15. Check System Ready: Off
  6.1.16. Extended System Ready Check: Off
  6.1.17. Check GC Ready: Off
  6.1.18. Extended GC Ready Check: Off
  6.1.19. Needle Check: Yes
  6.1.20. Action on Leak Check Error: Stop
  6.1.21. Action with No Vial in Tray: Stop

6.2. **GC-2010**

6.2.1. Column Oven Temperature: 80.0°C
6.2.2. Injection Mode : Split
6.2.3. Flow Control Mode: Linear Velocity
6.2.4. Pressure: 175.2 kPa
6.2.5. Total Flow: 50.7 mL/minute
6.2.6. Column Flow: 2.32 mL/minute
6.2.7. Linear Velocity: 47.6 cm/second
6.2.8. Purge Flow: 2.0 mL/minute
6.2.9. Split Ratio: 20
6.2.10. High Pressure Injection: OFF
6.2.11. Carrier Gas Saver: OFF
6.2.12. Splitter Hold: OFF
6.2.13. Oven Temp Program:

Table 2: Oven Temperature Program

Rate (°C/minute)	Temperature (°C)	Hold Time (minutes)
--	80.0	6.00

6.3. **Ready Checks**

6.3.1. Column Oven: YES
6.3.2. HS: NO
6.3.3. FID: YES
6.3.4. HS Carrier: YES
6.3.5. HS Purge: YES
6.3.6. APC1: YES
6.3.7. FID Makeup: YES
6.3.8. FID1 H2: YES
6.3.9. FID1 Air: YES
6.3.10. External Wait: NO
6.3.11. Auto Flame On: Yes
6.3.12. Auto flame Off: Yes
6.3.13. Reignite: Yes
6.3.14. Auto Zero After Ready: Yes
6.3.15. Equilibrium Time: 3.0 minutes
6.3.16. CRG(INJ): OFF
6.3.17. APC1: 75.0kPa

7. SAMPLE PREPARATION:

7.1. **Pre-Requisite Solutions:**

7.1.1. <u>10000ppm Methanol Stock Solution:</u>

7.1.1.1. Prepare a 10000 mg/L (ppm) solution of Methanol in Purified Water by weighing 0.50g of Methanol Certified Reference Standard directly into a 50mL volumetric flask, dissolving in Purified Water, filling to volume with Purified Water, and mixing thoroughly.

7.1.1.2. Calculate the actual methanol concentration using the Certificate of Analysis (CoA) purity.

$$Methanol\ Stock\ Concentration\ (ppm) = \frac{Methanol\ Weight\ (mg)}{Stock\ Solution\ Volume\ (L)} \times CoA\ Purity$$

7.2. **Calibration Standards:**

7.2.1. Blank (0% Level):

7.2.1.1. Purified water or equivalent.

7.2.2. Calibration Level 1 (50% Level):

7.2.2.1. In a 100mL volumetric flask, add 1.50mL of *10000ppm Methanol Stock Solution*, dissolve in Purified Water, fill to volume with Purified Water, and mix well.

7.2.2.2. Pipette 10mL of standard into a 20mL headspace vial, crimp to seal, and mix thoroughly.

7.2.3. Calibration Level 2 (80% Level):

7.2.3.1. In a 100.mL volumetric flask, add 2.40mL of *10000ppm Methanol Stock Solution*, dissolve in Purified Water, fill to volume with Purified Water, and mix well.

7.2.3.2. Pipette 10mL of standard into a 20mL headspace vial, crimp to seal, and mix thoroughly.

7.2.4. Calibration Level 3 (100% Level):

7.2.4.1. In a 100mL volumetric flask, add 3.00mL of *10000ppm Methanol Stock Solution*, dissolve in Purified Water, fill to volume with Purified Water, and mix well.

7.2.4.2. Pipette 10mL of standard into a 20mL headspace vial, crimp to seal, and mix thoroughly.

7.2.5. Calibration Level 4 (120% Level):

7.2.5.1. In a 100mL volumetric flask, add 3.60mL of *10000ppm Methanol Stock Solution*, dissolve in Purified Water, fill to volume with Purified Water, and mix well.

7.2.5.2. Pipette 10mL of standard into a 20mL headspace vial, crimp to seal, and mix thoroughly.

7.2.6. Calibration Level 5 (150% Level):

7.2.6.1. In a 100mL volumetric flask, add 4.50mL of *10000ppm Methanol Stock Solution*, dissolve in Purified Water, fill to volume with Purified Water, and mix well.

7.2.6.2. Pipette 10mL of standard into a 20mL headspace vial, crimp to seal, and mix thoroughly.

7.3. **Sample Solutions:**

7.3.1. Glycerin Sample Solution:

7.3.1.1. Weigh 1.0g of sample into a 20mL headspace vial, add 10mL of Purified Water, dissolve, crimp to seal, and mix thoroughly.

7.3.1.2. **NOTE:** Enter the dilution factor of 10 into the software.

8. CALCULATIONS:

8.1. Calibration Standard Concentration (ppm)

$$Standard\ Concentration\ (ppm) = \frac{Stock\ Solution\ Concentration\ \left(\frac{mg}{L}\right) \times Volume\ of\ Stock\ Solution\ (mL)}{Final\ Volume\ of\ Calibration\ Standard\ (mL)}$$

9. PERFORMANCE PARAMETERS:

9.1. **System Suitability / Calibration:**

9.1.1. Calibrate the GC-FID using the *Blank (0% Level)* and Calibration Level 1 through 5 and determine the Calibration Coefficient (r^2).

9.1.2. Acceptance Criteria:

9.1.2.1. A Calibration Coefficient (r^2) of NLT 0.95.

9.2. **Sample Analysis:**

9.2.1. Analyze Sample Solutions using the appropriate method parameters and a suitable Calibration Curve

9.3. **Result Reporting:**

9.3.1. The Limit of Quantitation (LOQ) for this method is the 50% calibration level after applying the dilution factor.

9.3.2. Sample Solution Results:

9.3.2.1. Report any value below the Limit of Quantitation (LoQ) as less than the 50% calibration standard concentration multiplied by the dilution factor of the sample.

9.3.2.2. For values greater than the 50% calibration standard concentration multiplied by the dilution factor of the sample, report the result to the nearest whole number.

10. DOCUMENTATION PROCEDURES:

10.1. Sample Preparation:

10.1.1. Record all related raw data including balance printouts if applicable in associated laboratory notebook.

10.1.2. Record lots numbers, associated calculations, and any variance to solution preparations described in the preceding protocol with justification.

10.1.3. Initial and date all applicable printouts and attachments as per laboratory notebooks SOP.

10.2. Instrument Run:

10.2.1. Print and initial and date sequence/batch file.

10.2.2. Data processing is automated and performed within the method during data acquisition, any changes to the integration parameters should be justified with supporting evidence for the change, and saved to the associated method file.