

Application News

Gas Chromatograph HS-20 NX / Nexis™ GC-2060

Residual Solvent Analysis in Pharmaceuticals with N₂ Carrier Gas Using Nexis GC-2060 and HS-20 NX

— JP 18 and USP <467> / Water-Insoluble Samples —

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User Benefits

- ◆ The newly designed FID delivers outstanding sensitivity, ensuring highly accurate and reliable analysis.
- ◆ Achieve full compliance with JP and USP guidelines using N₂ carrier gas, which is highly affordable and readily available.
- ◆ Easily analyzes *tert*-butyl alcohol and Cyclopentyl methyl ether, the Class 2 solvents added in the ICH Q3C (R8) guideline.

■ Introduction

For the analysis of residual solvents in pharmaceuticals, headspace gas chromatography (HS-GC) is widely used to target Class 1 and Class 2 solvents, in accordance with USP General Chapter <467> and JP18 (Japanese Pharmacopoeia, 18th Edition). These regulatory tests demand high sensitivity and reproducibility. The newly developed FID for the Nexis GC-2060 offers superior detection sensitivity compared to conventional models, enabling highly sensitive analysis. Additionally, due to recent helium supply shortages and rising costs, there is a growing demand for alternative analysis using nitrogen (N₂) as a carrier gas.

This application note presents the analysis of Class 1 and Class 2 water-insoluble samples using the Nexis GC-2060 with N₂ carrier gas, compliant with Supplement II to the Japanese Pharmacopoeia. DMSO was used as the sample solvent.

* Some modifications were made to the USP and JP sample preparation protocols.

■ Analytical Conditions

The instrument configuration and analytical conditions for water-insoluble samples are summarized in Table 1. To comply with USP and JP18 guidelines, Class 1 and Class 2 solvents were tested under two different methods (Procedure A and Procedure B) each utilizing distinct column types, column temperatures, and split ratios.

Table 1 Analytical Conditions for Water-insoluble samples

GC Conditions (Procedure A / Procedure B)	
Model	: Nexis GC-2060
Detector	: FID (Flame Ionization Detector)
Column	: A) SH-I-624Sil MS (P/N 227-36066-02) (0.53 mm I.D. × 30 m, d.f.= 3.0 μm) B) SH-PolarWax (P/N 221-75972-30) (0.32 mm I.D. × 30 m, d.f.= 0.25 μm)
Column Temperature	: A) 40°C (20 min) – 10°C/min – 240°C (20 min) Total 60 min B) 50°C (20 min) – 6°C/min – 165°C (20 min) Total 59.17 min
Injection Mode	: A) Split 1:5 B) Split 1:10
Carrier Gas Controller	: Linear velocity (N ₂)
Linear Velocity	: 35 cm/sec
Detector Temperature	: 250°C
FID H ₂ Flow Rate	: 40 mL/min
FID Make up Flow Rate	: 30 mL/min (N ₂)
FID Air Flow Rate	: 170 mL/min

HS Conditions (Common to Procedure A and Procedure B)	
Model	: HS-20 NX
Oven Temperature	: 80°C
Sample Line Temperature	: 90°C
Transfer Line Temperature	: 105°C
Vial Shaking Level	: Off
Vial Volume	: 20 mL
Vial Equilibrating Time	: 45 min
Vial Pressurizing Time	: 1 min
Vial Pressure	: 68.9 kPa
Loading Time	: 0.5 min
Load Equilib. time	: 0 min
Needle Flush Time	: 5 min
Injection Volume	: 1 mL

■ Analysis of Class 1 standard Solution

Chromatograms obtained for the Class 1 standard solution using Procedure A and Procedure B are shown in Fig. 1 and 2, respectively. In addition, the signal-to-noise (S/N) ratio for each peak and the repeatability over six consecutive injections are summarized in Table 2 (for Procedure A) and Table 3 (for Procedure B).

In Procedure A, carbon tetrachloride showed an excellent S/N ratio of 15, with a relative standard deviation (%RSD) of 2% or less for individual peak areas. In Procedure B, 1,2-dichloroethane achieved an outstanding S/N ratio of 99, with a %RSD of 3% or less for individual peak areas, demonstrating highly favorable results.

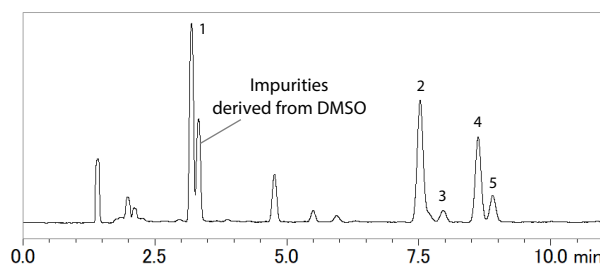


Fig. 1 Chromatogram of Class 1 Standard Solution (Procedure A)

Table 2 S/N Ratio and Repeatability of Class 1 Standard Solution (Procedure A)

Peak No.	Compounds	S/N ratio ave. ^{*1} (n = 6)	%RSD ^{*1} (n = 6)
1	1,1-Dichloroethane	256	2.23
2	1,1,1-Trichloroethane	145	1.48
3	Carbon tetrachloride	15	2.62
4	Benzene	140	1.44
5	1,2-Dichloroethane	38	1.21

*1 S/N ratios and %RSD are reference values and are not guaranteed.

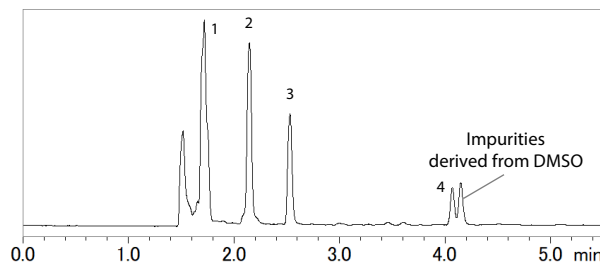


Fig. 2 Chromatogram of Class 1 Standard Solution (Procedure B)

Table 3 S/N Ratio and Repeatability of Class 1 Standard Solution (Procedure B)

Peak No.	Compounds	S/N ratio ave. ^{*2} (n = 6)	%RSD ^{*2} (n = 6)
1	1,1-Dichloroethane	379	2.09
2	1,1,1-Trichloroethane + Carbon tetrachloride	351	1.83
3	Benzene	227	1.43
4	1,2-Dichloroethane	99	1.25

*2 S/N ratios and %RSD are reference values and are not guaranteed.

■ Analysis of Class 2 standard Solution

Chromatograms obtained using Procedure A and Procedure B are presented in Figure 3 and Figure 4, respectively (Class 2A: black, Class 2B: pink, TBA/CPME/MiBK: blue). Regarding system suitability, both methods yielded excellent results: Procedure A achieved a resolution of 1.0 or greater between the acetonitrile and dichloromethane peaks (Figure 3), while Procedure B achieved a resolution of 1.0 or greater between the acetonitrile and *cis*-1,2-dichloroethene peaks.

Note that the mixed standard sample containing *tert*-butyl alcohol (TBA), Cyclopentyl methyl ether (CPME), and Methyl isobutyl ketone (MiBK) was prepared separately to meet the specified concentrations.

■ Conclusion

Using the Nexis GC-2060 with nitrogen (N₂) carrier gas, we successfully achieved the analytical precision required by the Japanese Pharmacopoeia (JP18) and USP General Chapter <467>. The HS-GC method delivered excellent S/N ratios and high repeatability for the analysis of residual solvents in water-insoluble pharmaceutical samples.

Related Applications

1. Residual Solvent Analysis in Pharmaceuticals with N₂ Carrier Gas Using Nexis GC-2060 and HS-20 NX — JP 18 and USP <467> / Water-soluble Samples — [Application News No. 01-01173-EN](#)

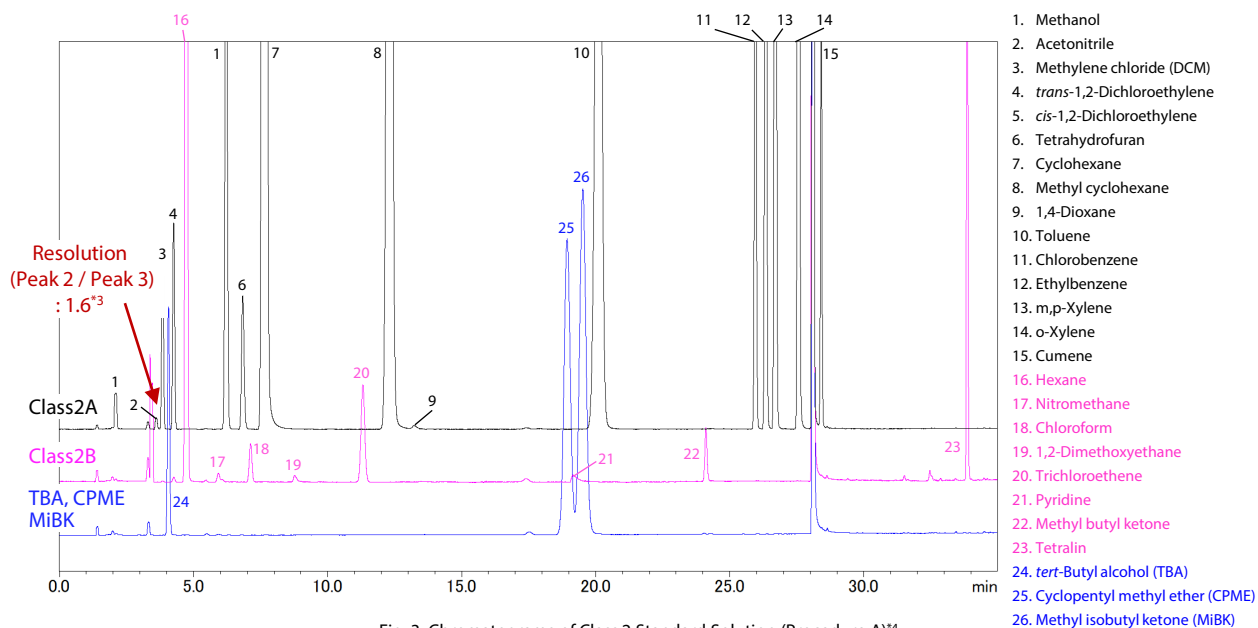


Fig. 3 Chromatograms of Class 2 Standard Solution (Procedure A)*4

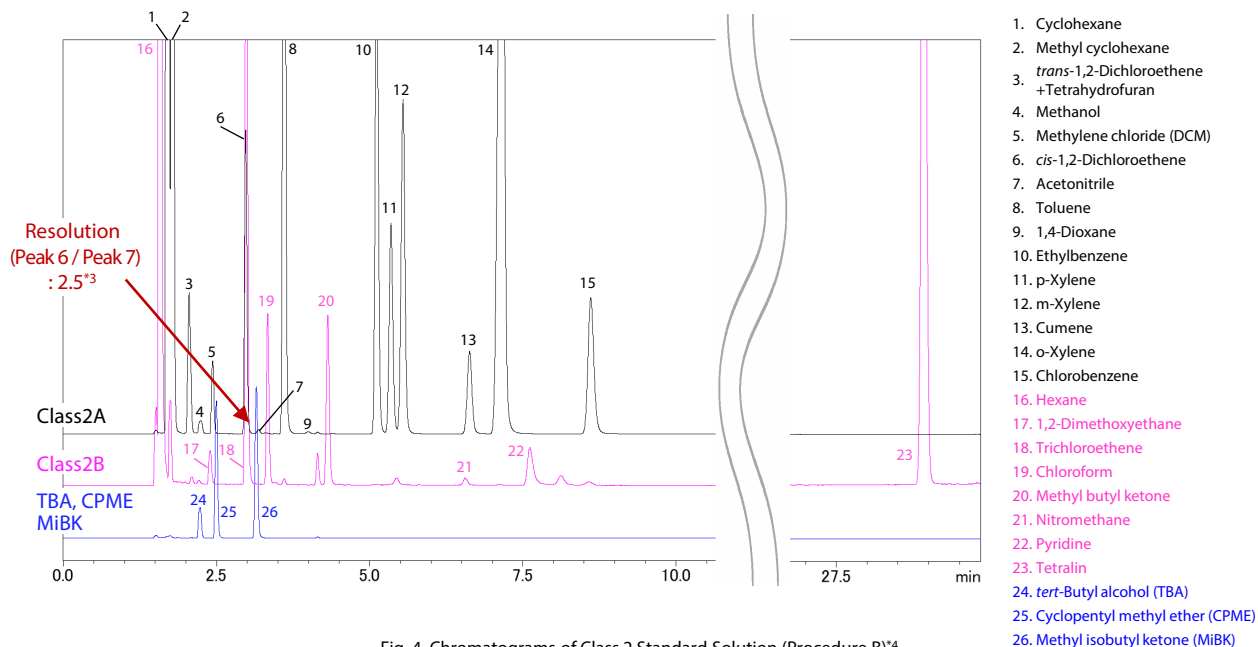


Fig. 4 Chromatograms of Class 2 Standard Solution (Procedure B)*4

*3 The resolution values are reference values and are not guaranteed.

*4 The chromatograms in Figures 3 and 4 are displayed with different magnification scales.

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Related Products

Some products may be updated to newer models.



➤ Nexis GC-2060
Gas Chromatograph



➤ HS-20 NX series
Headspace Sampler

Related Solutions

➤ Pharmaceutical and
Biopharmaceutical

➤ Small Molecule
Pharmaceutical

➤ Life Science

➤ Price Inquiry

➤ Product Inquiry

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➤ Other Inquiry