SHIMADZU
Excellence in Science

Application News

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

Residual Solvent Analysis in Pharmaceuticals with N_2 Carrier Gas Using Nexis GC-2060 and HS-20 NX

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

Shota Hayakawa, Toyohito Wada

User Benefits

- The newly designed FID delivers outstanding sensitivity, ensuring highly accurate and reliable analysis.
- Achieve full compliance with JP and USP guidelines using N_2 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 (N_2) as a carrier gas.

This application note presents the analysis of Class 1 and Class 2 water-soluble samples using the Nexis GC-2060 with N_2 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-soluble 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-soluble 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 H2Flow 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	: 110°C
Transfer Line Temperature	: 120°C
Vial Shaking Level	: Off
Vial Volume	: 20 mL
Vial Equilibrating Time	: 60 min
Vial Pressurizing Time	: 1 min
Vial Pressure	: 75 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 23, 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 198, with a %RSD of 3% or less for individual peak areas, demonstrating highly favorable results.

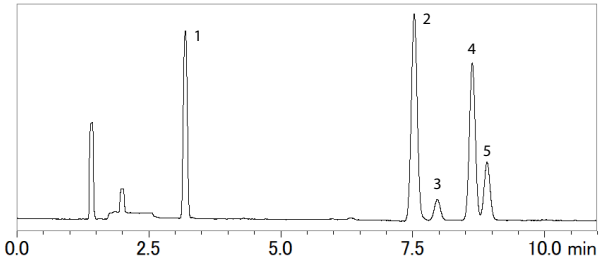


Fig. 1 Chromatogram of Class 1 Standard Solution (Procedure A)

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	331	1.23
2	1,1,1-Trichloroethane	339	1.26
3	Carbon tetrachloride	23	1.60
4	Benzene	195	1.94
5	1,2-Dichloroethane	67	0.91

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

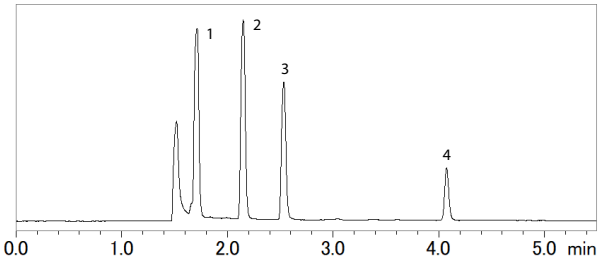


Fig. 2 Chromatogram of Class 1 Standard Solution (Procedure B)

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	157	1.73
2	1,1,1-Trichloroethane +Carbon tetrachloride	362	2.03
3	Benzene	389	1.87
4	1,2-Dichloroethane	198	1.15

*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.

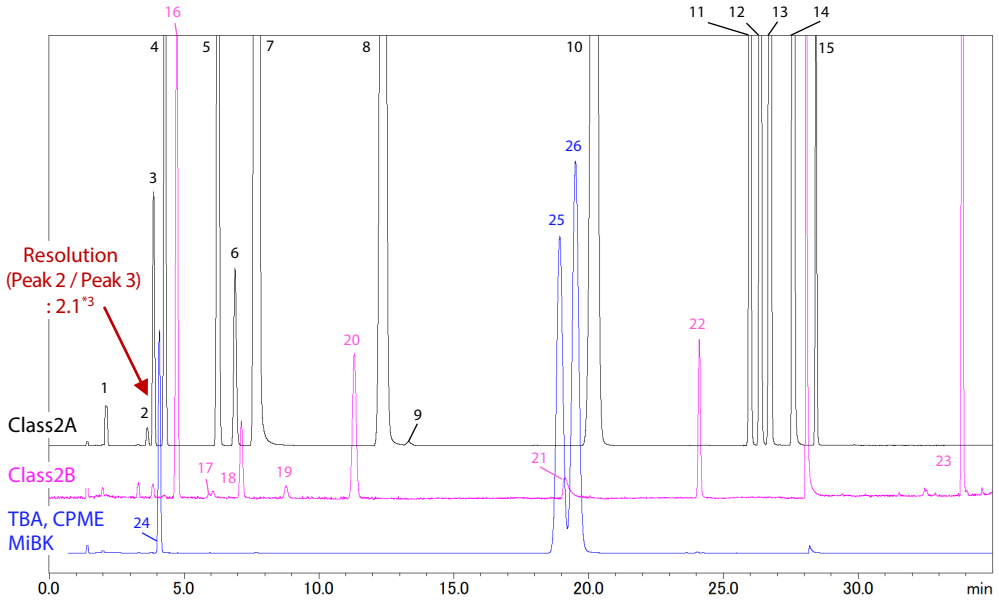
Note that the mixed standard sample containing *tert*-butyl alcohol (TBA), Cyclopentyl methyl ether (CPME), and Methyl isobutyl ketone (MiBK) was prepared separately to meet the specified concentrations.

■ Conclusion

Using the Nexis GC-2060 with nitrogen (N_2) 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-soluble pharmaceutical samples.

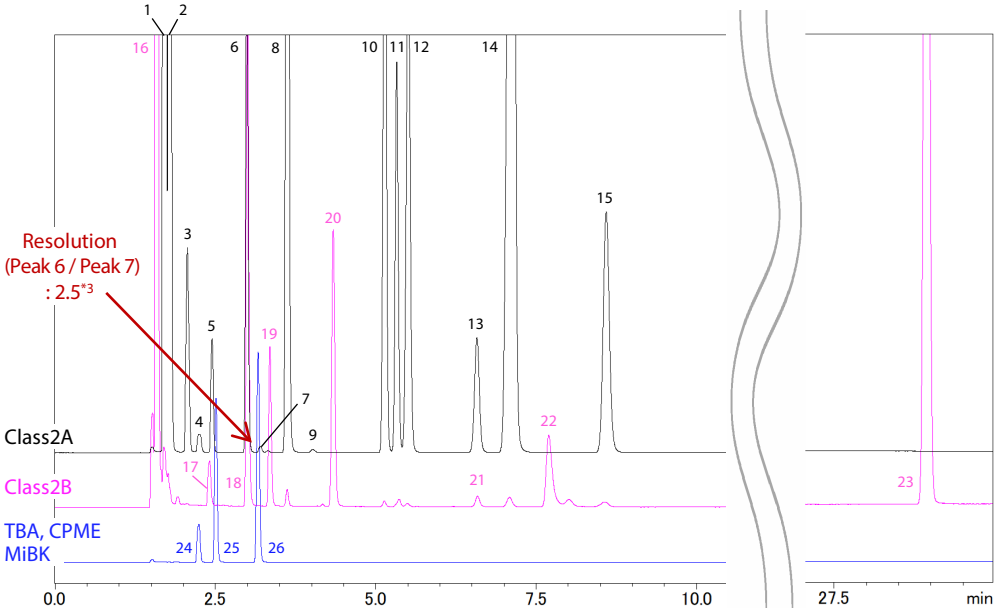
Related Applications

1. Residual Solvent Analysis in Pharmaceuticals with N2 Carrier Gas Using Nexis GC-2060 and HS-20 NX — JP 18 and USP <467> / Water-Insoluble Samples — Application News No. 01-01172-EN



1. Methanol
2. Acetonitrile
3. Methylene chloride (DCM)
4. *trans*-1,2-Dichloroethylene
5. *cis*-1,2-Dichloroethylene
6. Tetrahydrofuran
7. Cyclohexane
8. Methyl cyclohexane
9. 1,4-Dioxane
10. Toluene
11. Chlorobenzene
12. Ethylbenzene
13. m,p-Xylene
14. o-Xylene
15. Cumene
16. Hexane
17. Nitromethane
18. Chloroform
19. 1,2-Dimethoxyethane
20. Trichloroethene
21. Pyridine
22. Methyl butyl ketone
23. Tetralin
24. *tert*-Butyl alcohol (TBA)
25. Cyclopentyl methyl ether (CPME)
26. Methyl isobutyl ketone (MiBK)

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



1. Cyclohexane
2. Methyl cyclohexane
3. *trans*-1,2-Dichloroethene +Tetrahydrofuran
4. Methanol
5. Methylene chloride (DCM)
6. *cis*-1,2-Dichloroethene
7. Acetonitrile
8. Toluene
9. 1,4-Dioxane
10. Ethylbenzene
11. p-Xylene
12. m-Xylene
13. Cumene
14. o-Xylene
15. Chlorobenzene
16. Hexane
17. 1,2-Dimethoxyethane
18. Trichloroethene
19. Chloroform
20. Methyl butyl ketone
21. Nitromethane
22. Pyridine
23. Tetralin
24. *tert*-Butyl alcohol (TBA)
25. Cyclopentyl methyl ether (CPME)
26. Methyl isobutyl ketone (MiBK)

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.

01-01173-EN First Edition: Aug. 2026

SHIMADZU
Shimadzu Corporation
www.shimadzu.com/an/

› Please fill out the survey

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

› Technical Service / Support Inquiry

› Other Inquiry