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Application News

No. G290

Gas Chromatograph

Analysis of Residual Solvents in drug products using Nexis GC-2030 combined with HS-20 head space sampler - USP <467> Residual Solvents Procedure A -

Residual solvents in pharmaceuticals are defined as volatile organic compounds used in or generated from the manufacture of drug substances, pharmaceutical additives, or drug products. They are strictly controlled according to risk classifications from Class 1 to Class 3, which are based on the risk to human health.

Headspace GC methods specified in the USP (U.S. Pharmacopeia), General Chapters <467> Residual Solvents, are commonly used for analysis of residual solvents. This Application News presents data obtained using the Shimadzu HS-20 Headspace Sampler and Nexis GC-2030 Gas Chromatograph, from Class 1 and Class 2 standard solutions, in accordance with Water-Soluble Articles, Procedure A, in USP <467> Residual Solvents.

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Fig. 1 Nexis GC-2030 + HS-20

Class1

Fig.2 shows the Class 1 standard solution chromatogram. Procedure A requires that the S/N ratio obtained for 1,1,1-Trichloroethane in this chromatogram be 5 or higher. As shown, the S/N ratio was 220. Even for carbon tetrachloride, which had the lowest sensitivity level, the S/N was 20.

Table 3 indicates the S/N ratio of each peaks and the repeatability of the peak area (n=6).

Table 3 S/N ratio and Repeatability of Class1

No.	Compounds	S/N ratio	%RSD (n=6)
1	1,1-Dichloroethane	320	2.8
2	1,1,1-Trichloroethane	220	2.3
3	Carbon tetrachloride	20	2.9
4	Benzene	170	2.5
5	1,2-Dichloroethane	60	3.4

Instruments and Analytical Conditions

Table 1 GC Method for USP 467 Procedure A

Model	: Nexis GC-2030
Detector	: FID-2030
Headspace Sampler	: HS-20
Column	: SH-Rxi-624 Sil MS (0.32 mm I.D. × 30 m, d.f. = 1.8 µm)
Column Temperature	: 40 °C (20 min) - 10 °C /min - 240 °C (20 min) Total 60 min
Injection Mode	: Split 1 : 5
Carrier Gas Controller	: Constant Linear Velocity (He)
Linear Velocity	: 35 cm/sec
Detector Temperature	: 250 °C
FID H2 Flow Rate	: 40 mL/min
FID Make up Flow Rate	: 30 mL/min (He)
FID Air Flow Rate	: 400 mL/min
Injection Volume	: 1 mL

Table 2 HS-20 Method for USP 467 Procedure A

Oven Temperature	: 80 °C
Sample Line Temperature	: 110 °C
Transfer Line Temperature	: 120 °C
Vial Stirring	: Off
Vial Volume	: 20 mL
Vial Heat-retention Time	: 60 min
Vial Pressurization Time	: 1 min
Vial Pressure	: 75 kPa
Loading Time	: 1 min
Needle Flush Time	: 5 min

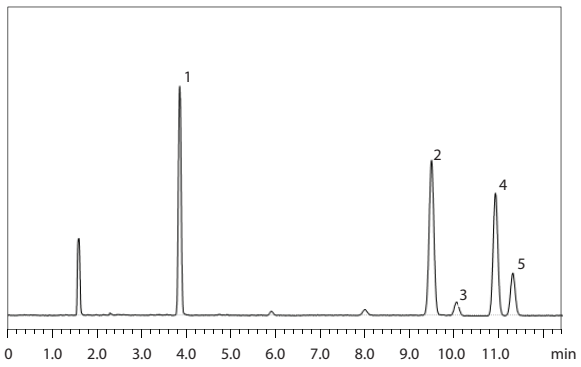
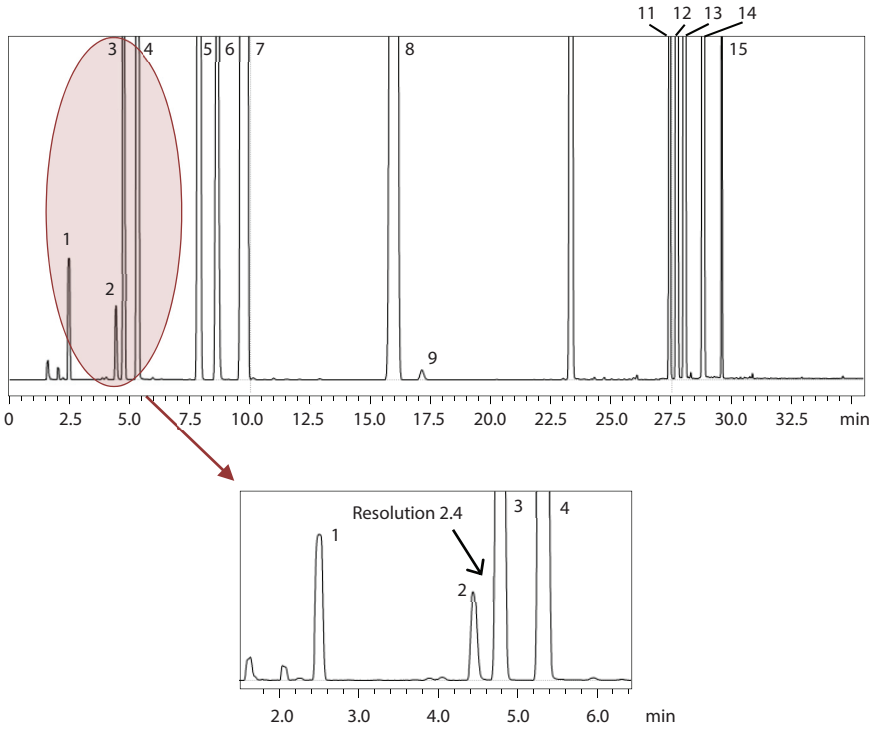


Fig. 2 Chromatogram of WATER-SOLUBLE ARTICLES Class1 Standard Solution by Procedure A

Class2

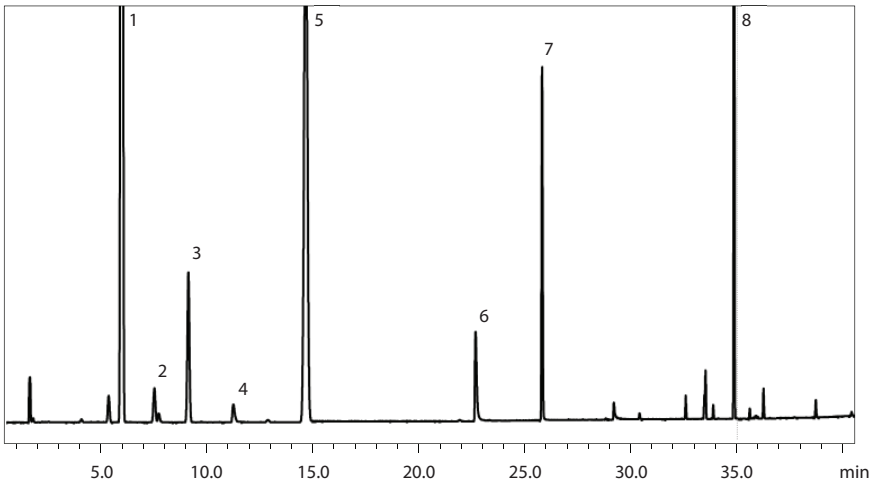
Due to the large number of components in the Class 2 standard solution, it was separated into two mixtures: A and B. Respective measurement results are shown in Fig.3 and Fig.4. Procedure A requires that the resolution for acetonitrile and methylene chloride in the Class 2 standard solution Mixture A chromatogram be 1.0 or greater.

Fig.3 shows that, using the Restek SH-Rxi-624SilMS low-bleed column, the specified peaks are completely separated, with a resolution of 2.4.



1: Methanol
2: Acetonitrile
3: Methylene chloride (DCM)
4: trans-1,2-Dichloroethylene
5: cis-1,2- Dichloroethylene
6: Tetrahydrofuran
7: Cyclohexane
8: Methylcyclohexane
9: 1,4-Dioxane
10: Toluene
11: Chlorobenzene
12: Ethylbenzene
13: m,p-Xylene
14: o-Xylene
15: Cumene

Fig. 3 Chromatogram of WATER-SOLUBLE ARTICLES Class 2A Standard Solution by Procedure A



1: Hexane
2: Nitromethane
3: Chloroform
4: 1,2-Dimethoxyethane
5: Trichloroethene
6: Pyridine
7: Methylbutylketone
8: Tetraline

Fig. 4 Chromatogram of WATER-SOLUBLE ARTICLES Class 2B Standard Solution by Procedure A

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