GMP-Authorized Laboratory
(ANMDM Romania, Certificate No: 045/2024/RO)

Residual Solvents Analysis of Pharmaceutical API's and finished products

Introduction

One of Scient's main objectives is to help our customers in their pharmaceutical development phase as well as pharmaceutical QC testing. Different organic solvents are used for the manufacture of API's and may contribute to the residual solvents remaining in the final pharmaceutical product. Chapter 2.4.24 of European Pharmacopeia in conjunction with chapter 5.4 are used to identify, control and quantify Residual Solvents classified into 3 major classes.

- ✓ Class 1 solvents are considered hazardous, and should be avoided during manufacturing.
- ✓ Class 2 solvents are considered less severely toxic, and should be limited.
- ✓ Class 3 solvents pose less risk to human health than Class 1 or Class 2 solvents.

In **Figure 1**, the peak-to-peak signal-to-noise ratio (S/N) calculated for 1,1,1-trichloroethane in Class 1 standard solution was 416, more than 5:1 (required by Eur. Ph.) and all peaks in Class 1 system suitability showed S/N >3:1.

Table 1. HS-GC-MS analytical parameters used for residual solvents content determination

Perkin Elmer TurboMatrix S40	
Oven temperature (°C)	105
Needle temperature (°C)	110
Loop temperature (°C)	110
Incubation time (min)	45.0
Pressurization time (min)	1.0
Vial pressure (psi)	20.0
Perkin Elmer GC Clarus 680	
Column	624SilMS 30mx0.32mmx1.8µm
Injector temperature (°C)	140
Injection time (min)	0.05
Injection mode	split injection @ split ratio 20:1
Carrier gas, Mode/Flow	He, constant @ 1.50 mL/min
GC oven temperature program	
Temperature 1 (°C)	40
Hold time 1 (min)	5
Temperature 2 (°C)	240
Rate (°C/min)	30
Hold time 2 (°C)	1
Perkin Elmer MS SQ8T	
Inlet temperature (°C)	180
Source temperature (°C)	150
Acqusition mode	EI+ @ 70eV, both FullScan and SIR mode

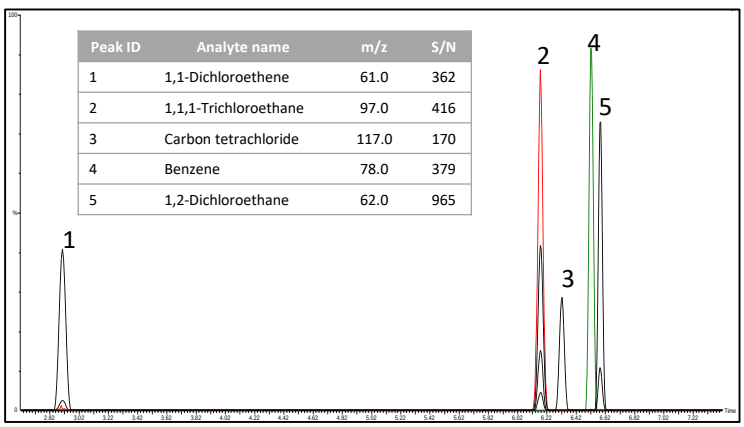

Figure 1. Peak-to-peak signal-to-noise (S/N) ratios for Class 1 residual solvents as System Suitability solution for water-insoluble products.

Using the powerful resolving power of Clarus SQ8T mass spectrometer, benzene and 1,2-dichloroethane peaks are well separated based on their specific m/z ion ratios (**Figure 2**).

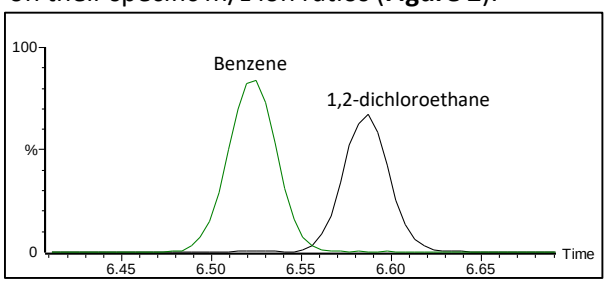

Figure 2. Chromatographic separation between Benzene and 1,2-Dichloroethane in Class 1 Residual Solvents.

In **Figure 3**, the resolution (Res) between the acetonitrile and dichloromethane peak, was automatically calculated using the Communique report software, meeting the acceptance criteria as required, both for water-soluble and water-insoluble products.

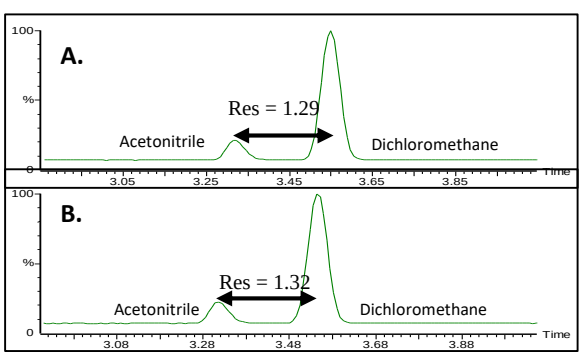

Figure 3. Chromatographic resolution (Res) between Acetonitrile and Dichloromethane for **A.** water-soluble and **B.** water-insoluble products. The acceptance criteria from Chapter 2.4.24 of Eur. Ph. is met (Res ≥1.0).