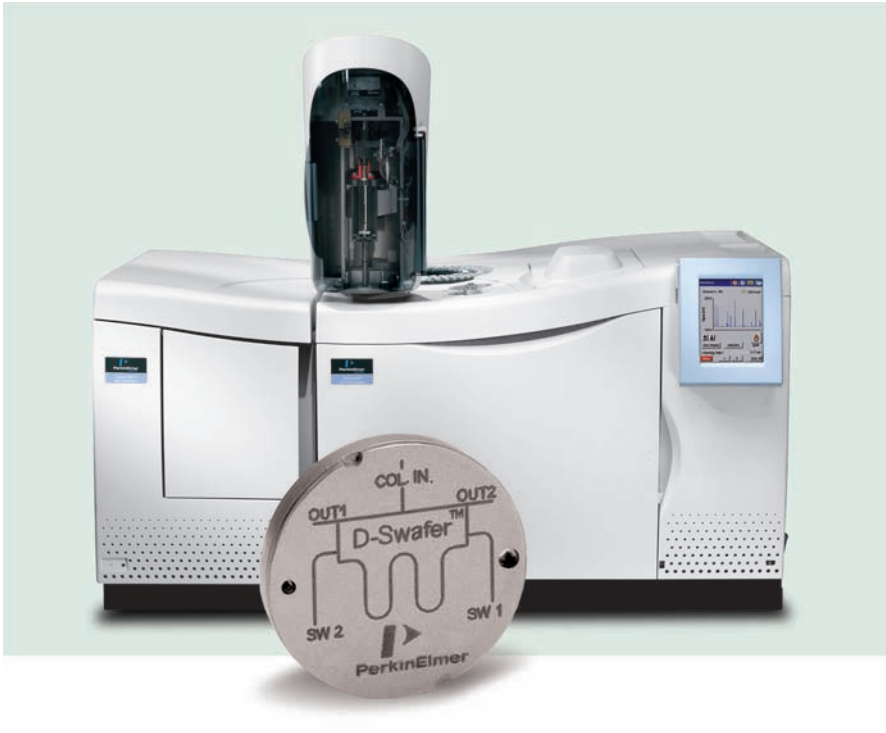


APPLICATION NOTE

Gas Chromatography/
Mass Spectrometry

**Author**

**Andrew Tipler**

**Senior Scientist**
**PerkinElmer**

# Using the D-Swafer to Investigate Solvent Impurities by Heartcutting GC/MS

## Introduction

Solvents are widely used in the pharmaceutical and food industries for a variety of purposes. It is important that such solvents are carefully quality-control (QC) tested prior to use to ensure that no unsafe levels of impurities are present.

Gas chromatography (GC) is normally the preferred technique for the determination of impurities in solvents. The inclusion of a mass spectrometric (MS) detector enables the identities of the impurities to be established.

Because many solvents are produced by fractional distillation, their impurities will have similar boiling points to that of the solvent. Thus in GC, the retention times will be similar to that of the solvent and the risk of co-elution can be high.

Furthermore, if the MS is kept active during solvent elution, contamination of the ion source or analyzer may result, and the risk of filament damage is greatly increased. This application note describes a heartcutting technique that allows the entire injected sample to reach the detector and yet resolve the issues with solvent-peak resolution and potential detector damage.

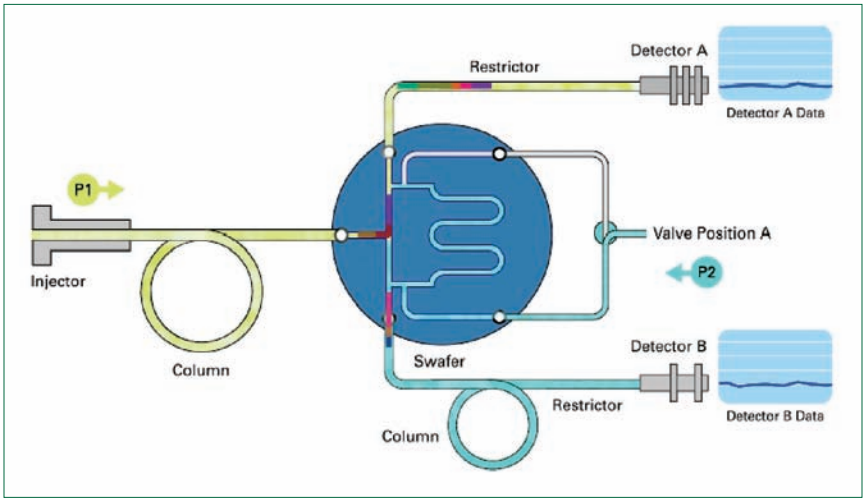


*Figure 1.* The D-Swafer in the D4 configuration for classic heartcutting.

## Method

For this work, a D-Swafer™ Dean's Switch was configured as shown in Figure 1. This is a classic Dean's switch configuration, enabling cuts to be directed from the effluent of the first column into the inlet of the second column.

Tables 1 and 2 (Page 2) give further details of the analytical system and conditions applied.

The Swafer Setup Utility software, which is included with the product, was used to determine the geometry of the restrictor tubing connected to the FID. This is necessary to balance the flow rate in the secondary column in order for the Swafer switching to function correctly.

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***Table 1.*** Gas Chromatograph Configuration.

| Component | Description |
|---|---|
| Gas Chromatograph | Clarus® 600 GC |
| Heartcutting Device | D-Swafer in D4 configuration |
| Injector | Split/splitless |
| Detector 1 | Flame ionization |
| Detector 2 | Clarus 600 T MS |
| Column 1 | 15 m x 0.25 mm x 1.0 µm Elite-1 |
| Column 2 | 30 m x 0.25 mm x 1.0 µm Elite Wax |
| Restrictor | 58 cm x 0.10 mm deactivated fused silica |

***Table 2.*** Analytical Conditions.

| | Setting | Value |
|---|---|---|
| Oven | Temperature | 60 ˚C isothermal for 8 min |
| Carrier Gas | | Helium |
| Injector | Temperature | 225 ˚C |
| | Carrier-Gas Pressure (P1) | 23 psig (159 kPa) |
| | Split Flow | 100 mL/min |
| Midpoint | Pressure (P2) | 16 psig (110 kPa) |
| Detector 1 (FID) | Temperature | 250 ˚C |
| | Air Flow Rate | 450 mL/min |
| | Hydrogen Flow Rate | 45 mL/min |
| | Range | x20 |
| | Attenuation | x64 |
| Detector 2 (MS) | Temperature | 200 ˚C |
| | Mass Range | 15 to 150 Da |
| | Scan Time | 0.2 sec |
| | Interscan Delay | 0.1 sec |
| Sample Injection | | 1 µL by Autosampler in Fast Mode |
| Swafer Switching Valve (V4) Timed Events | | See Results section |

## Samples

For this work, 5 samples of analytical-grade dichloromethane (DCM) from different suppliers and a single sample of ethyl acetate were analyzed.

## Results

The 5 DCM samples were exampled first. With the Swafer switching solenoid valve (V4) turned off, the effluent from Column 1 was directed to Detector 1 – the flame ionization detector (FID). Figure 2 shows the chromatography observed on the FID from one of the DCM samples.

With the relatively high split flow being applied, the FID will not provide very good detection limits for the impurities. Figure 2 shows a number of impurities around the main DCM peak that are only just above the background noise level. In practice, this will not be a limitation because the superior sensitivity of the MS system will allow much better detection limits to be obtained when these impurities are cut to the second column.

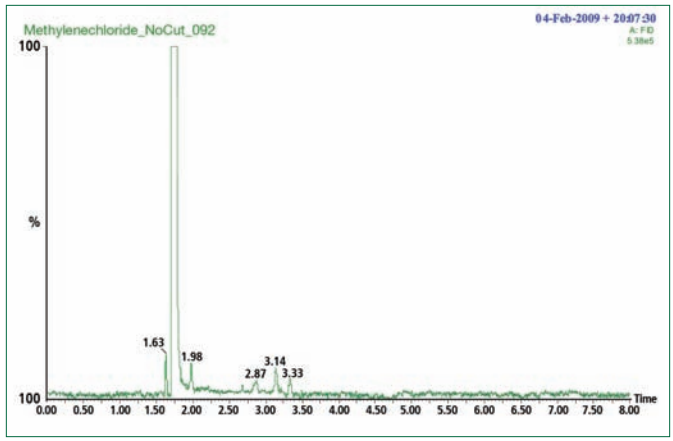


*Figure 2.* Chromatogram on Detector 1 (FID) of DCM sample 3, showing small impurity peaks.

To check that the D-Swafer was working correctly, the signal was monitored on the MS detector while the chromatography was directed to the FID. Figure 3 shows that none of the sample reached the MS detector while the D-Swafer was switched to the other channel.

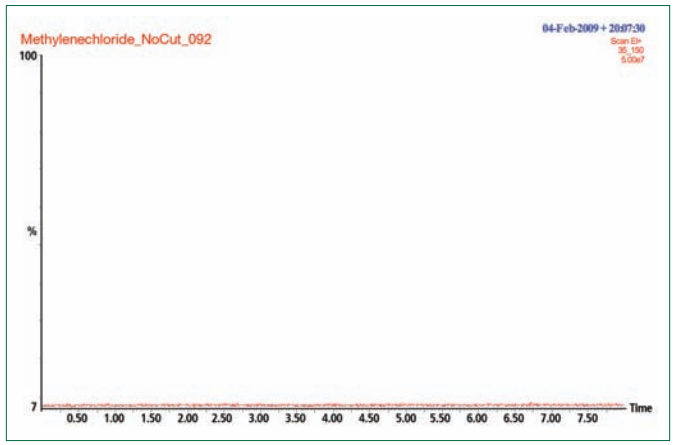


*Figure 3.* Signal seen on the MS while the D-Swafer is switched to the FID.

When V4 was switched on for the whole run, all effluent from Column 1 will be directed to the inlet of Column 2 and so the chromatography will occur in both columns and will appear at Detector 2 – the MS. Figure 3 shows the total ion chromatogram for DCM sample 3. Note the much better sensitivity to the impurity compounds than from the FID.

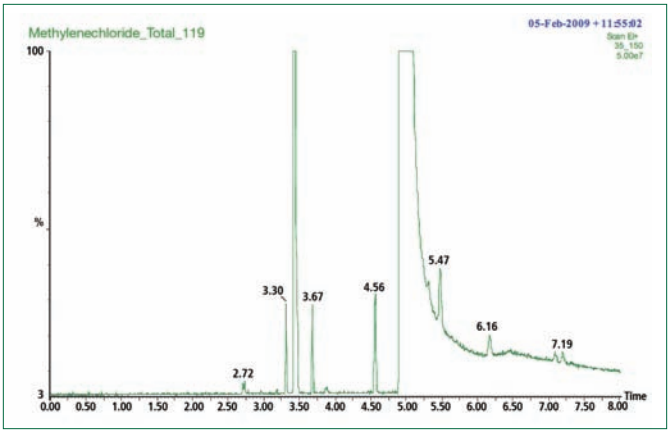


*Figure 4.* Total ion chromatogram on Detector 2 (MS) of DCM sample 3.

In Figure 4, we see the solvent peak dominates the chromatography around it and probably obscures some smaller peaks.

A run was made with V4 turned on at the start of the run and switched on during the solvent-peak elution on Column 1 and then switched off again. This sidecutting technique has the effect of removing a large fraction of the solvent, yet allowing the rest of the sample to enter Column 2. Figure 5 shows a chromatogram run this way.

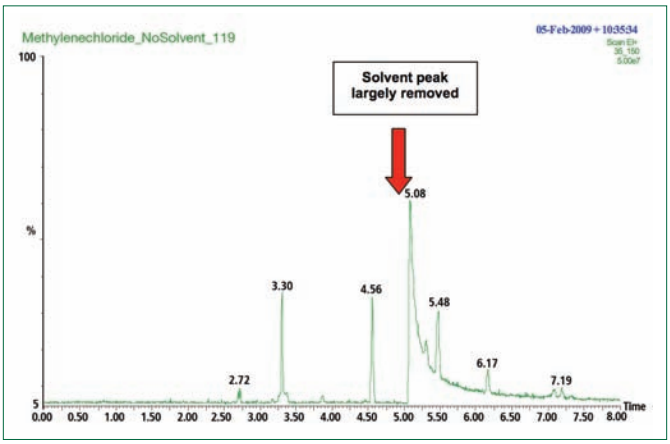


*Figure 5.* Total ion chromatogram on Detector 2 (MS), with solvent peak removed, of DCM sample 3. The switching valve was turned off between 1.68 and 1.80 minutes (refer to Figure 2 for context) but was on for the rest of the run.

Inspection of Figure 5 shows that much of the solvent has been removed by the sidecutting method. This removal is better illustrated by Figure 6, which shows the two chromatograms at a larger scale. Thus, sidecutting is a highly effective technique to keep solvent away from the MS detector.

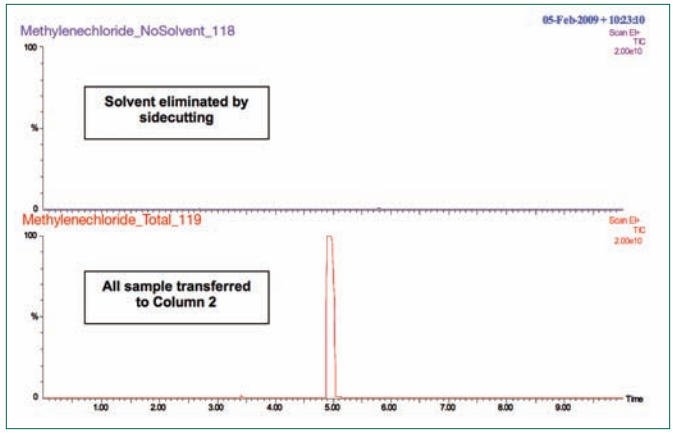


*Figure 6.* Chromatograms shown in Figures 4 and 5 plotted together at a larger scale to show the efficacy of sidecutting for solvent removal.

Although this sidecutting technique allows the sample to be processed on the MS without the potential damage and interference from the solvent peak, it does not take into account any peaks which will co-elute with the solvent on Column 1 – these peaks would not enter Column 2 or be seen by the MS.

Close examination of Figure 5 reveals that two peaks are missing from this chromatogram at approximately 3.42 and 3.67 minutes that were present in Figure 4. These clearly must co-elute on Column 1.

To enable these (and possibly other) peaks that co-elute with the solvent to be transferred to the second column for separation, a peak-sectioning technique was used to deliver time-incremented narrow heartcuts of the solvent peak from successive runs of the same DCM sample. Figure 7 shows how the solvent peak was sectioned into six 0.02-minute heartcuts. This approach allows the area under the solvent peak on Column 1 to be fully mapped by Column 2 without exposing the MS detector to large amounts of solvent.

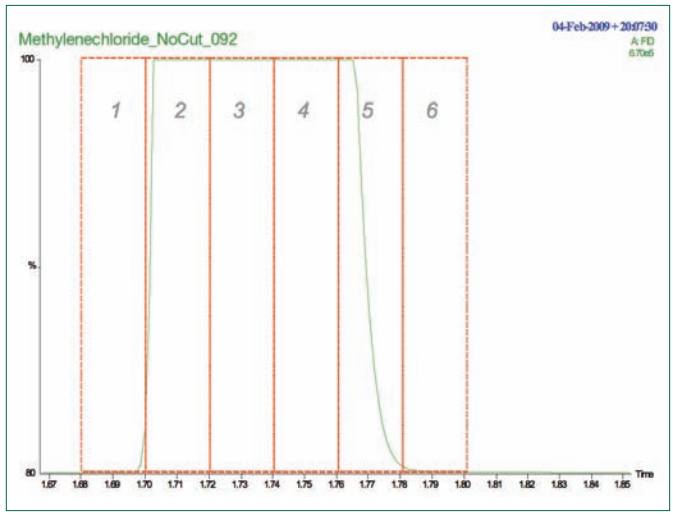


*Figure 7.* Sectioning the DCM solvent peak into six 0.02-minute heartcuts.

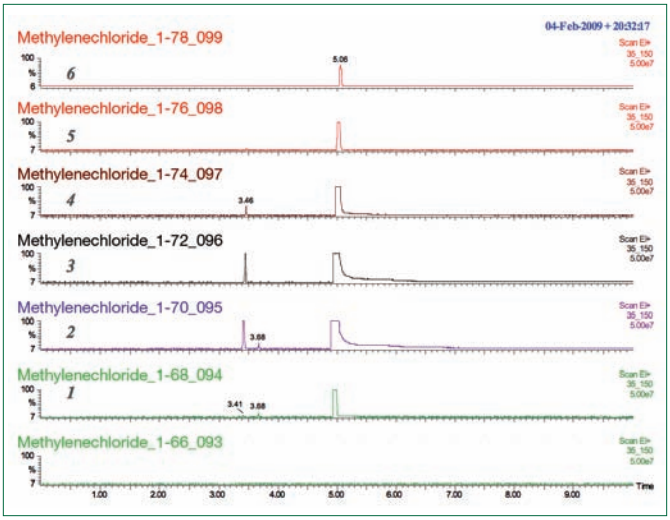


*Figure 8.* Chromatograms from successive 0.02-minute heartcuts.

***Table 3.*** Tentative MS Assignment of Compound Identities in DCM Samples Using the Solvent Sidecutting and Heartcut Sectioning Technique.

| Retention Time (min) | MS Identification | DCM Sample 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| 3.30 | 2-Methylbutane | | | √ | | |
| 3.41+ | Branched Chain Pentene* | √ | | √ | √ | √ |
| 3.68+ | Dichloroethylene* | √ | √ | √ | √ | √ |
| 3.75 | Branched Chain Hexane* | | | | √ | |
| 3.87 | Acetone | √ | | √ | | |
| 3.90 | Branched Chain Hexane* | | | | √ | |
| 4.56 | Branched Chain Hexene* | | | | √ | √ |
| 4.56 | Dichloroethylene* | √ | √ | √ | √ | |
| 4.65 | Ethanol | | | | √ | |
| 4.70 | Isopropanol | | | | √ | |
| 4.91# | Trimethyl Oxirane | | | | √ | |
| 5.31 | 1-Chlorobutane | | | √ | | |
| 5.48 | 2-Chloro-2-Methylbutane | √ | | √ | | |
| 5.79 | Cyclohexene | | √ | | √ | |
| 6.02 | Acetonitrile | | | | √ | |
| 6.17 | 2-Butanone | | | √ | | |
| 7.08 | Hexyl Alcohol* | | | √ | | √ |
| 7.19 | Chloroform | | √ | √ | √ | |

*+ Peak co-eluting with solvent in Column 1*
*# Peak co-eluting with solvent in Column 2*
** Isomer not determined*

Figure 8 shows the six chromatograms obtained from the successive solvent cuts. The 'lost' peaks at approximately 3.4 and 3.7 minutes are now apparently recovered.

In Figure 8, we have effectively delivered the whole solvent to the second column and have been able to prevent gross overloading of the column and the detector and are able to recover two components that would have been otherwise lost. By combining these data with those from Figure 5, we are able to provide a comprehensive result for the impurities in this type of sample without the associated problems of large solvent peaks. Table 3 shows the impurities identified in the five DCM samples using this technique. In all cases, the impurity peaks were well separated from the DCM peak.

The next sample examined was a batch of ethyl acetate that had significantly more impurities than the DCM samples previously examined.

Figures 9, 10, 11 and 12 show the chromatography on the FID, the total sample on the MS, the sample with the solvent removed by sidecutting, and the heartcut-sectioned solvent peak respectively. Table 4 (Page 6) lists the compounds identified in this sample.

In this analysis, there are three peaks that elute with the solvent peak on Column 1: n-hexane, 1-chloro-2-methylpropane and 2-butanol.

What is also of particular interest from these data are the three peaks that elute between 5.00 and 5.30 minutes. These would co-elute with the solvent peak on Column 2 and so they would only be seen when the solvent is eliminated by sidecutting, as shown in Figure 11 (Page 5).

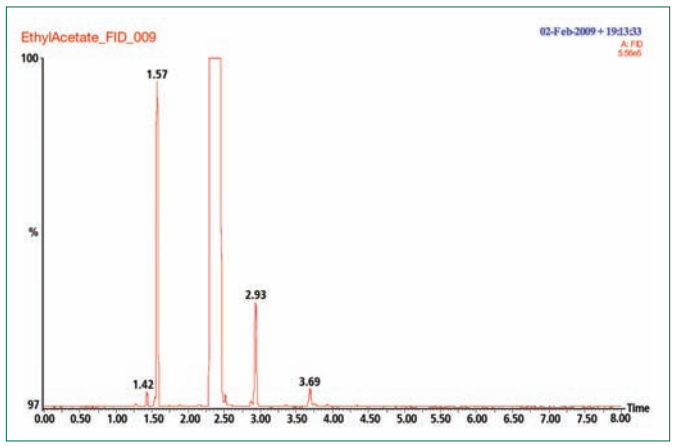


*Figure 9.* Sample of ethyl acetate on Column 1 and the FID.

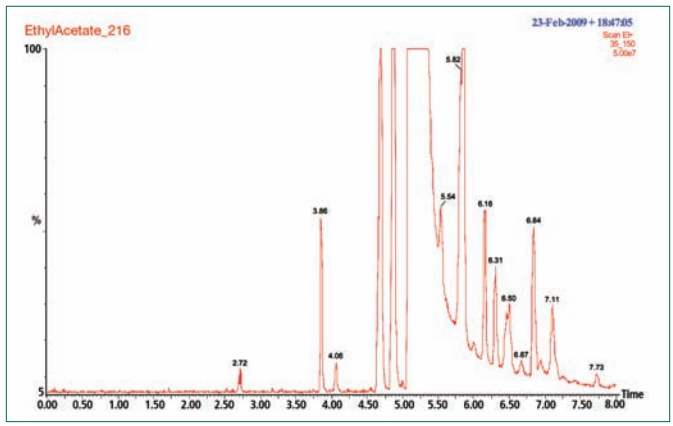


*Figure 10.* Chromatogram of total ethyl acetate sample transferred to Column 2 and the MS detector.

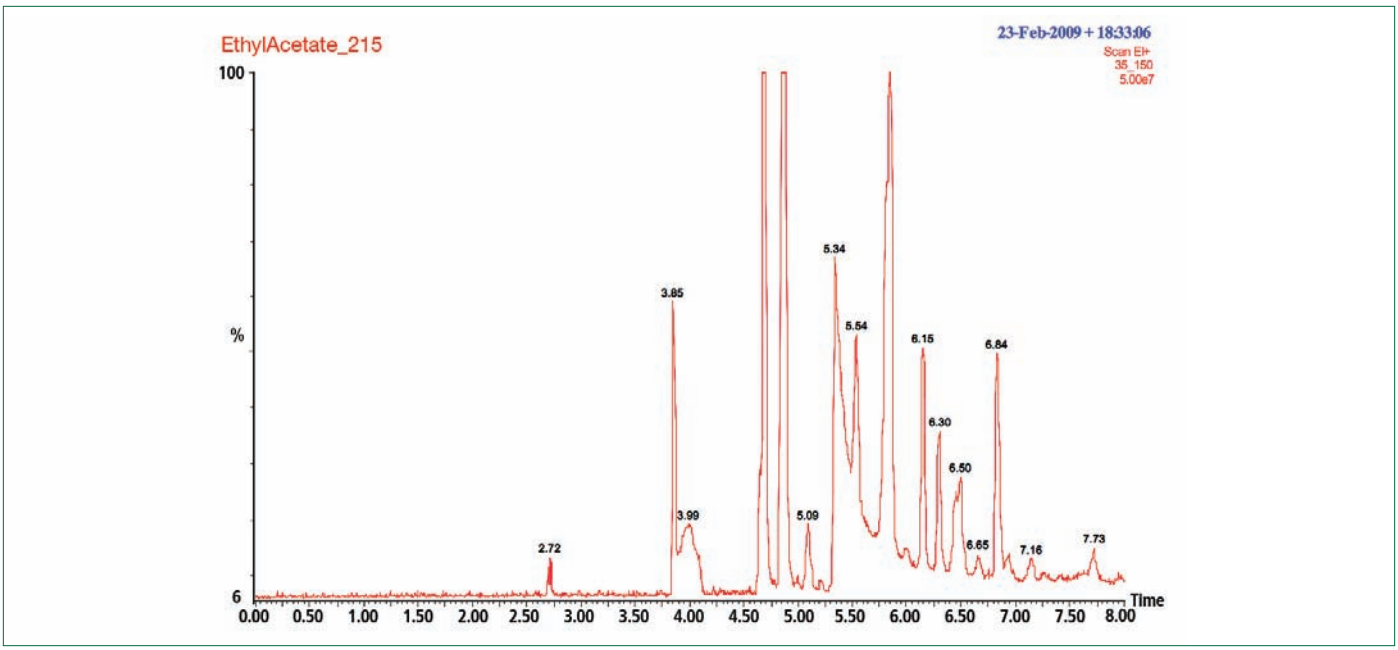


*Figure 11.* Chromatogram of ethyl acetate sample with the solvent removed by sidecutting on Column 2 and the MS detector.

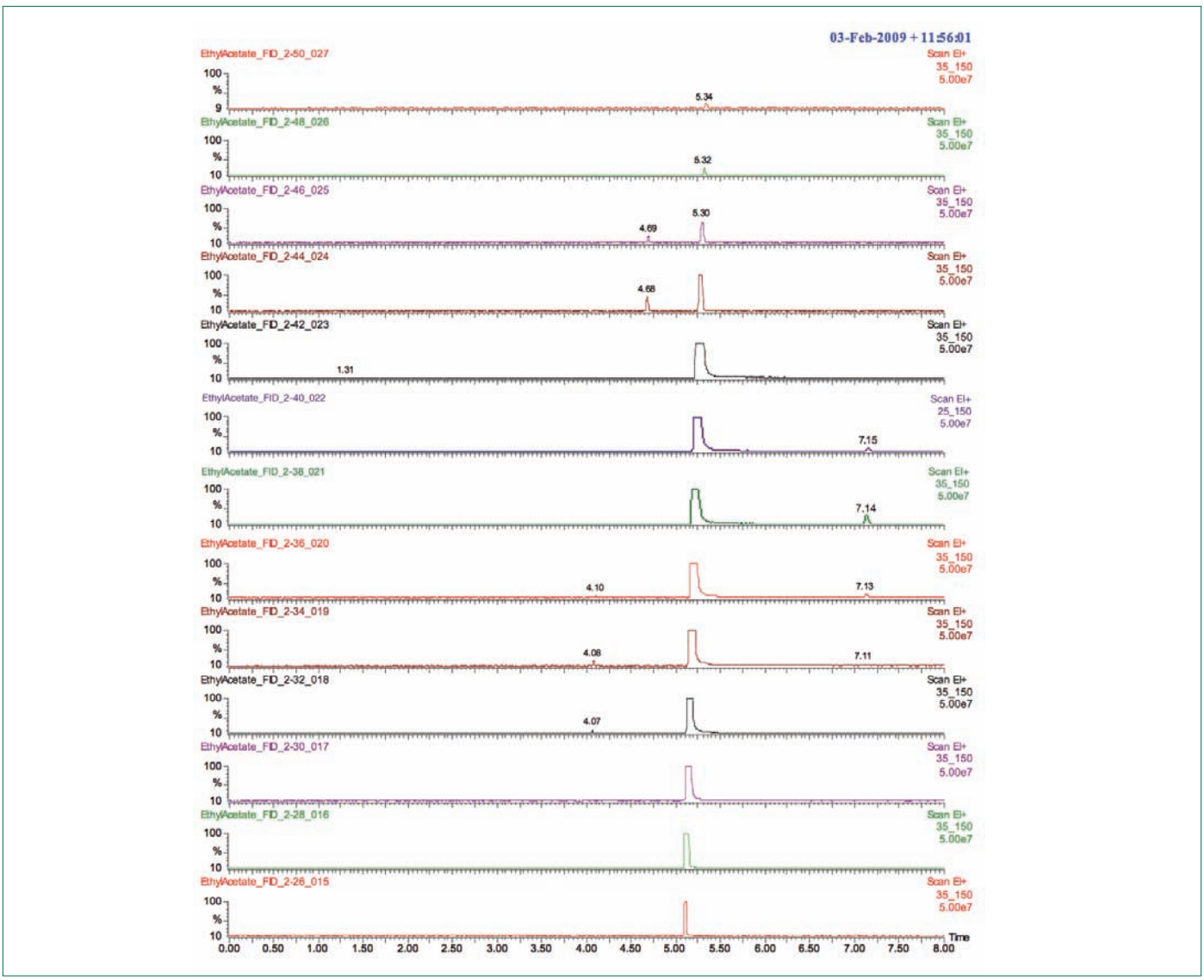


*Figure 12.* Ethyl acetate solvent peak sectioned by heartcutting into Column 2 and the MS.

***Table 4.*** Tentative MS Assignment of Compound Identities in Ethyl Acetate Sample Using the Solvent Sidecutting and Heartcut Sectioning Technique.

| Retention Time (min) | MS Identification |
|---|---|
| 3.85 | Acetone |
| 4.06+ | n-Hexane |
| 4.65 | Ethanol |
| 4.68+ | 1-Chloro-2-Methylpropane |
| 4.69 | Isopropanol |
| 4.86 | 1-Ethoxy-2-Methyl-Propane |
| 5.01# | Dichloromethane |
| 5.09# | 2-Butanone |
| 5.20# | Tetrahydrofuran |
| 5.54 | Branched Chain Octane* |
| 5.75 | n-Heptane |
| 5.81 | Isopropyl Acetate |
| 5.85 | 1-Ethoxybutane |
| 5.99 | Branched Chain Nonane* |
| 6.15 | Pentanone* |
| 6.30 | 1-Ethoxybutene |
| 6.45 | 3-Methyl-2-Butanol |
| 6.50 | Isopropyl Propionate |
| 6.65 | Branched Chain Undecane* |
| 6.84 | 1,2-Dimethoxypropane |
| 6.94 | Ethoxy Acetic Acid |
| 7.13+ | 2-Butanol |
| 7.16 | 2-Methylpropyl Formate |
| 7.73 | n-Propyl Acetate |

*+ Peak co-eluting with solvent in Column 1*
*# Peak co-eluting with solvent in Column 2*
** Isomer not determined*

## Conclusion

This sidecutting and heartcutting technique provides a comprehensive and reliable method for revealing the low-level impurities of solvents. Although the solvent-peak sectioning process entails several repeat chromatograms of the same sample, these runs are fairly short and isothermal, so the total analytical time is just 50 minutes. This time would be needed to fully map the obscured components. In the samples examined here, only two additional peaks were found in the sectioned chromatograms, so the method could be optimized just to apply heartcuts to the affected sections and so reduce the number of runs necessary.

Although we have shown the application of this technique just to samples of dichloromethane and ethyl acetate, the same approach could be extended to other solvents or any sample where there is an interest in identifying and quantifying compounds at low levels that co-elute with other relatively large peaks.

**PerkinElmer, Inc.**
940 Winter Street
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P: (800) 762-4000 or
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