In the cannabis space, residual solvents are volatile compounds that may have been used to extract, process, or refine cannabis materials. Traces of these solvents remain present after post-extraction methods such as winterization, vacuum, and heat. Since these substances can present varied human health risk levels in consumption, testing is crucial to ensure consumers' safety.

Due to the complexity of the matrices, the analysis of residual solvents in cannabis products presents several significant challenges, such as the differences in boiling points between analytes, differences in polarity, or the need to bake out compounds before analysis.

In this article, Phenomenex analytical experts answer questions and share analytical best practices that help mitigate these challenges.

What are your suggestions for resolving critical pairs, like ethylene oxide/methanol and propane/butane?

First, you need to choose a column that has a very thick stationary phase, such as a 0.25 mm ID Zebron™ ZB-624PLUS™ column with a 1.4 micron film thickness. Then you need to increase your split ratio, so you don't send too much analyte onto the column. Also, start the run at a lower temperature, like 30 or 35°C, to provide enough focusing time for on-column separation. Finally, for the low boiling analytes, you should back off a bit on the flow rate.

Can I run residual solvents and terpenes on the same column?

Most 624-type GC columns have sufficient column selectivity to separate both residual solvents and terpenes. Therefore, you can run both methods on the same column on the same instrument (in two separate injections, of course). However, it is important to thoroughly bake out the column at the end of each run and here the high temperature stability of the Zebron™ ZB-624PLUS™ column (-20 to 300/320 °C) is an essential characteristic. Finally, while it is possible to analyze both residual solvents and terpenes on the same instrument and column, high-volume laboratories find it more productive and economical to dedicate separate instruments to the two analytical methods.

Why do I have to run the residual solvent method up to 240°C when all the analytes elute at a much lower temperature?

The residual solvent analytes will indeed all elute within the 180 to 200°C window. However, the higher temperature runup is needed because the matrix is “sticky” with terpenes and other semi-volatile and non-volatile compounds. These can cause contaminant carryover effects in subsequent analyses, especially with MS detectors. To eliminate the carryover problem, we recommend taking the final temperature of the column and transfer line to 300°C, rather than 240°C. The high temperature stability of ZB-624PLUS™ allows this more aggressive instrument “bake out”.

How do you prevent saturation of the detector for samples that have very high residual solvent content?

Since you may not know beforehand which samples have high solvent levels, we recommend having a second GC instrument with an FID detector to screen incoming samples prior to

GC-MS analysis to identify “hot” samples. This allows you to adjust the split ratio for the quantitative analysis and avoid detector saturation. This is particularly important when dealing with samples of unfamiliar origin.

How do I prevent analyte carryover in residual solvent methods?

There are several potential causes. Low-level carryover contamination can arise from either (or both) the headspace transfer lines or the mass spec transfer line. Therefore, maintaining these lines at high temperature is important. Also, what appears to be carryover may be laboratory background contamination from other operations. As will be discussed in a later question, the solution is to isolate the GC-MS as much as possible from all background sources.

What are some common headspace transfer temperatures that you recommend for different diluents?

Different diluents require different equilibrium temperatures and equilibrium times, but the transfer line temperature will be the same. If you are using water, you should limit the equilibrium temperature to 80°C and allow 45-60 minutes for complete equilibration of high boiling analytes, but keep the transfer line at 175°C to ensure complete transfer. For higher boiling diluents like DMAC or DMSO you can use a higher equilibrium temperature but shorter time. For all three diluents, however, a transfer line temperature of 175°C works well.

How can you prevent the acetonitrile used in potency analysis from contaminating

laboratory air and interfering with residual solvent analysis?

There are many potential sources and solutions: Put caps with filters or sorbent traps on your HPLC mobile phase bottles and solvent waste receptacles; don't leave residual acetonitrile in pipette barrels; do all your potency extractions and standard preparations in a fume hood; and if you are using a triple quad MS for pesticide analysis, don't discharge the vacuum exhaust from the ionization source into the lab.

Which system should you use for residual solvent analysis: GC-FID or GC-MS?

For residual solvents you definitely need to use GC-MS for accurate analysis. And, if you have the budget, you should go with GC-Triple Quad MS. In residual solvent analysis you have a lot of analytes with similar structures and the potential for a lot of matric interference, so MS is crucial for identifying the right compound. With GC-FID you only

have your reference standard, and you can't authenticate or confirm a sample result. Even with MS, residual solvent analysis in cannabis at low levels of detection is very challenging and you need all the instrumentation power you can get.

For residual solvent analysis is it best to use a liner with wool or without wool?
For residual solvent analysis you don't need a liner with glass wool because with headspace sample introduction, any material that reaches the injection port has already been vaporized (unlike in pesticide analysis). However, with residual solvent headspace analysis the liner geometry is very important. You need to use a small internal diameter liner (1-2 mm) to focus the analytes and introduce a sharp, narrow band onto the column.

Explore the Following Cannabis Testing Resources:

- *Application Note – Determination of Residual Solvents and Terpenes in Cannabis by GC-FID using Zebron™ ZB-624PLUS™ GC Column*
- *Technical Note – Expanded Mycotoxins Analysis in Cannabis Matrices by LC-MS/MS*
- *Webinar – Testing Insights and Analytical Challenges: Pesticides Methods*

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