# Gas Chromatography Problem Solving and Troubleshooting

***Question:***

I am experiencing peak size irreproducibility for my headspace analysis of solvents in water. I am using a sample temperature of 45°C, an equilibration time of 10 min, and an injection time of 6 s. How do I improve the reproducibility of my analysis?

***Answer:***

There are a number of factors that impact the accuracy and precision of headspace analyses. In most cases, problems are related to the sampling conditions or the suitability of the sample. Headspace sampling is based on a fairly simple principle. If a sample (liquid or solid) is placed in a tightly sealed vial, the concentrations of the volatile compounds in the gas phase and sample phase (the open space above the sample and the liquid or solid sample, respectively) reach equilibrium after a sufficient period of time. The sample is usually heated to increase the compound concentration in the gas phase. For a constant set of conditions, the concentration of the compounds in the gas phase is directly proportional to their concentration in the sample phase. If a portion of the gas phase is properly collected and analyzed, the resulting compound concentrations reflect their amounts in the original sample.

The temperature of the sample, the time elapsed before sampling, compound affinity for the sample, and the size of the vial and sample can be critical sample variables. Organic compounds exhibit higher gas phase concentrations at higher temperatures. Sensitivity is often increased by using a higher sample temperature. The upper temperature limit is usually determined by the pressure limit of the vial sample (usually 75–100 psig) and thermal stability of the sample. Headspace samplers usually have difficulties in maintaining sample temperatures lower than 40–45°C. Even if a higher sample temperature is not needed to improve sensitivity, it may be advantageous to increase the temperature to improve the stability and reproducibility of the analysis. In general, a sample temperature that is about 20°C below the sample solvent boiling point is a good starting point. Sample temperatures above 80°C are generally not necessary or better. If a loss of response occurs at a higher sample temperature, sample degradation might be occurring. Also, a larger amount of the sample solvent is introduced into the column at a higher sample temperature. The larger solvent peak may interfere with other closely eluting peaks or adversely affect the detector's response and behavior. The best sample temperature achieves a good balance of sensitivity, sample degradation, and solvent peak size.

At a given temperature, the sample compound concentrations in the gas and sample phases do not immediately reach equilibrium. A sufficient amount of time is required before equilibrium is reached. A suitable equilibration time depends on the sample, the sample temperature, and the size of the sample and vial. Sampling before the sample is fully equilibrated results in erratic peak sizes. In general, a 10–15-min equilibration time is a good starting point. Increase the equilibration time by 10 min at a time until the analyte peaks no longer increase in size. Longer equilibration times are usually harmless but unnecessary. However, excessively long equilibration times, especially at higher sample temperatures, may increase or induce sample degradation.

Compounds with a high affinity for the sample solvent do not partition into the headspace as well as compounds with a lower affinity. This results in a lower concentration of the higher-affinity compounds in the gas phase. For example, methanol or ethanol in a water sample does not partition into the gas phase as well as hexane or benzene. Solid particulates, miscible liquids, and dissolved solids can significantly alter the distribution of compounds between the gas and sample phases. For the same concentration of a compound in a real sample (e.g., ground or drinking water) and clean solvent (e.g., deionized and organic free water), a noticeable difference in peak size between the two samples is often obtained. This is caused by sample matrix compounds altering the distribution of the compound between the two phases. Because there are no matrix compounds in the clean solvent, it is not affected, and a different concentration of the compound is measured, even though the same amount is present in the original sample. Sometimes, adding clean solvent to the sample dilutes the interferences and minimizes any associated problems; however, sensitivity is compromised due to the dilution of the sample. To improve sensitivity and reproducibility, an ionic modifier such as sulfate, phosphate or acetate buffer, or sodium chloride is added to the solvent to drive more of the compounds into the gas phase and to minimize the effect of the matrix compounds. Erratic peak sizes may be caused by changes or differences in the sample. This can be difficult to control due to the unpredictable and unknown effect and concentration of sample matrix compounds.

There are several other factors that require attention to ensure good headspace results. Any change in the size of the sample or vial results in a different concentration of the compounds in the gas phase. If the same volume of the headspace is taken for analysis, the corresponding peak sizes change. If the sample and vial sizes are changed by the same relative amount (e.g., both are increased by two times), peaks of approximately the same size are obtained. Another variable is the injection time (sampling time or loop fill time). It determines the amount or volume of gas that is used to transfer the gaseous headspace sample out of the vial and into the gas chromatograph (GC). For more concentrated samples, 5–10 s is sufficient; 10–15 s is typically used for less concentrated samples. Peak broadening usually begins to occur for times

above 15 s. Longer injection times also introduce a large amount of the sample solvent into the GC. The high amount of the solvent may alter the detector's response, thus changing the size of some of the analyte peaks. This is fairly common with water as the sample solvent. Finally, if there is a cool zone in the headspace sampler or GC, some of the sample compounds may condense in this area. Later-eluting or less volatile compounds suffer a greater loss of peak size. Problems with carryover or ghost peaks are often evident if a condensation problem exists.

For headspace analyses, changes in response or method sensitivity are usually due to a change in the sample or its environment. Care is needed to ensure consistent and sufficient sample temperature, sufficient equilibration time, and sample size and treatment. Inconsistent peak size can also be caused by problems or errors in the GC. Detectors (gas flows and purity, temperature, cleanliness, and operation), columns (activity or contamination), and injectors (cleanliness, leaks, flow rates, and operation) are some of the more common sources of peak size problems. These areas should be investigated if there are no apparent problems with the headspace sampler, conditions, or samples.

The purpose of *Chromatography Problem Solving and Troubleshooting* is to have selected experts answer chromatographic questions in any of the various separation fields (GC, GC–MS, HPLC, TLC, SFC, HPTLC, open column, etc.). If you have questions or problems that you would like answered, please forward these to the *Journal* editorial office with all pertinent details: instrument operating conditions, temperatures, pressures, columns, support materials, liquid phases, carrier gas, mobile phases, detectors, example chromatograms, etc. In addition, if you would like to share your expertise or experience in the form of a particular question accompanied by the answer, please forward to JCS Associate Editor, *Chromatography Problem Solving and Troubleshooting*, P.O. Box 48312, Niles, IL 60714. All questions/answers are reviewed to ensure completeness. The *Journal* reserves the right not to publish submitted questions/answers.

Dean Rood
Associate Editor