System Parameter and Performance Comparison Between Agilent 7697A and Agilent G1888A Headspace Samplers for USP <467>

Technical Overview

Introduction

The Agilent 7697A Headspace Sampler introduced onboard electronic pneumatics control and several instrument control enhancements to improve performance over earlier models of headspace units sold by Agilent, such as the Agilent G1888A Headspace Sampler. With this introduction came the addition of several method parameters that were not in earlier models. This technical overview will explain those differences and show that, with these new parameters, the 7697A Headspace Sampler gives similar or better resolution, precision, and accuracy as the G1888A Headspace Sampler. It will also provide data on comparative studies between the two instruments that show the 7697A Headspace Sampler meets the System Suitability requirements for USP Method <467>.

This detailed comparison of the 7697A Headspace Sampler and the G1888A Headspace Sampler provides a resource for method transfer and S.O.P. documentation to laboratories replacing a G1888A Headspace Sampler with a 7697A Headspace Sampler. This document can be referenced in preparing USP Method <467> method transfer documentation.

No comparative testing was done with the Agilent 7694 Headspace Sampler. However, because the pneumatics of the 7694 Headspace Sampler are similar to the pneumatics of the G1888A Headspace Sampler, similar results are expected. Therefore, if migrating from the 7694 Headspace Sampler to the 7697A Headspace Sampler, this technical overview can also be used for reference.

Agilent Technologies

Analysis of Residual Solvents by USP Method <467>

Analysis of residual solvents in pharmaceuticals is extremely important to protect patient safety. Quality assurance (QA) labs routinely use Unites States Pharmacopeia (USP) Method <467> for this purpose [1]. The basic method is used worldwide for quality control, and closely follows ICH Q3C guidelines [2].

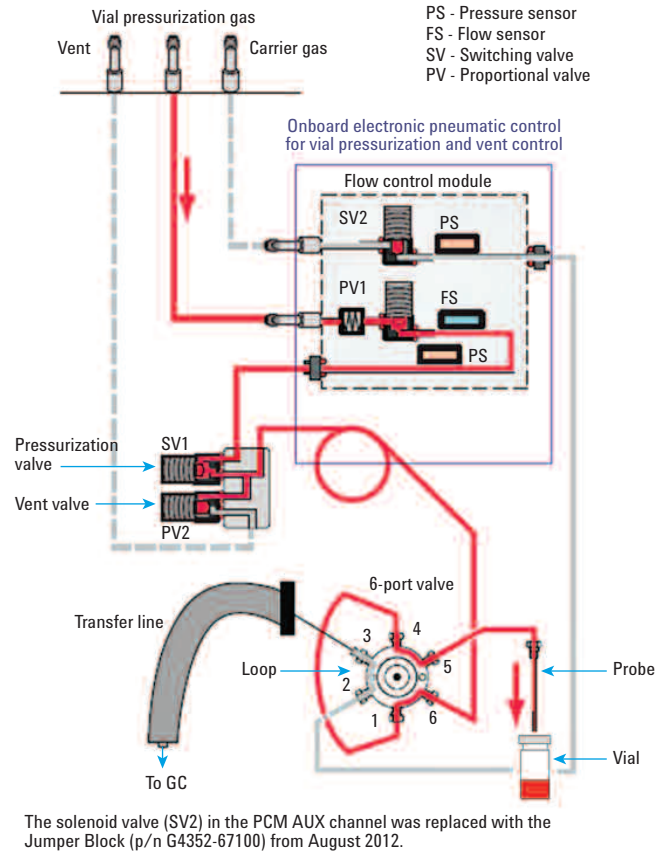
Residual solvents in pharmaceuticals may remain from the manufacturing process of the active pharmaceutical ingredients (APIs) or final product. The levels of residual solvents must be monitored and controlled for a number of reasons including safety, effect on crystalline form, solubility, bioavailability, and stability. All drug substances, excipients, and products must be monitored.

Changes and Improvements in the Agilent 7697A Headspace Sampler

Use of advanced pneumatics, excellent thermal zone control, and precise timing yielded improved repeatability and precision for residual solvent analysis with the Agilent 7697A Headspace Sampler compared to previous generation samplers [3]. Previous generation headspace samplers, such as the Agilent G1888A Headspace Sampler, were designed to vent the pressurized vial to ambient pressure while filling the sample loop. The 7697A Headspace Sampler introduced the use of onboard electronic pneumatics control to allow the headspace to control the final vial pressure seen in the sample loop during the sample loop filling process. Controlling this pressure removes any effects from ambient atmospheric pressure fluctuations in the laboratory, which can provide more repeatable results. It can also allow for better sensitivity from the instrument.

With these improvements, several significant differences can be noted between the G1888A Headspace Sampler and the 7697A Headspace Sampler. One advantage of incorporating the onboard pneumatics control is that a GC AUX module no longer has to be purchased for vial pressurization. Unlike the G1888A Headspace Sampler, in which the vial pressurization plumbing went from the gas supply to the GC AUX module, to the headspace, now only a supply of gas is required to be plumbed into the vial pressurization bulkhead on the back of the 7697A Headspace Sampler. Figure 1 shows the flow path of the 7697A Headspace Sampler, and Figure 2 shows the flow path of the G1888A Headspace Sampler [4].

Despite the differences in pneumatic control, the 7697A Headspace Sampler uses the same sampling technology as the G1888A Headspace Sampler. They both use the same core methodology of valve and loop headspace sampling. Because of this equivalence, there should be no need to do a complete method revalidation when making the transition from the G1888A to the 7697A Headspace Sampler. A method transfer might be needed, and many people follow USP <1224> to transfer methods. It is up to each laboratory to document the changes after system migration.



The solenoid valve (SV2) in the PCM AUX channel was replaced with the Jumper Block (p/n G4352-67100) from August 2012.

Figure 1. Agilent 7697A Headspace Sampler flow path in standby mode (standard installation, without the optional carrier PCM).

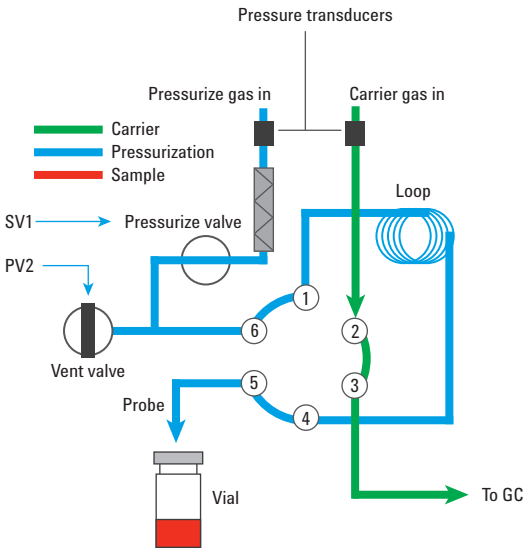


Figure 2. Agilent G1888A Headspace Sampler flow path in standby mode.

Explanation of Method Parameters

Loop fill behavior

Agilent G1888A Settings	Agilent 7697A Settings
Passive Backpressure Control (Vent to ambient pressure)	Active Backpressure Control (Decrease final loop pressure to a setpoint)

The onboard electronic pneumatics control allows the Agilent 7697A Headspace Sampler to achieve active or passive backpressure control of the sample loop filling. The Agilent G1888A Headspace Sampler uses only passive backpressure control to vent the vial contents through the sample loop down to ambient pressure. The default loop fill mode on the 7697A Headspace Sampler uses active pressure control. In this control mode, the final loop pressure is dropped to draw sample from the headspace vial through the sample loop and out the vent before injection. The **Final Loop Pressure** setpoint of the 7697A Headspace Sampler is dependent on the initial vial fill pressure if the **Loop Fill Mode** is set to *Default*. The 7697A Headspace Sampler can run in passive backpressure control by setting the Final Loop Pressure to 0 psig, but it is not recommended. The instrument would no longer be able to provide atmospheric pressure compensation for the final loop pressure, and this could lead to run-to-run fluctuations in chromatography if changes in atmospheric pressure occur during the course of an analytical sequence.

Vial and loop settings

Agilent G1888A Settings	Agilent 7697A Settings
Vial Pressurization Time	Vial Fill Mode (“Flow to Pressure”) or (“To Pressure”)
Vial Pressure	Fill Pressure
Loop Fill Time	Loop Fill Mode (Default or Custom)

Adding the capacity of backpressure control to the 7697A Headspace Sampler means there are a few different method parameters between the two headspace units. In the G1888A Headspace Sampler, the vial pressurization parameters were set by **Vial Pressurization Time** and **Vial Pressure**. The sample loop was filled by the **Loop Fill Time** and **Loop Equilibration Time** method parameters.

The 7697A Headspace Sampler requires specific vial and loop settings such as **Vial Fill Mode**, **Fill Pressure**, and **Loop Fill Mode**. These parameters are used to achieve the active backpressure control discussed earlier.

The default Vial Fill Mode is *Flow to Pressure*. The headspace uses a calculated flow rate to pressurize the vial to the pressure specified by the Fill Pressure parameter. The headspace will dynamically reduce the flow rate as the vial pressure setpoint is approached to prevent overshooting the setpoint. This Fill Pressure parameter is similar to the Vial Pressure parameter in the Agilent G1888A Headspace Sampler. The two modes of vial pressurization on the Agilent 7697A Headspace Sampler, *Flow to Pressure* and *To Pressure*, when compared using Class 2A solvents, are nearly equivalent in repeatability on most solvents, as seen in Table 1. Using the *To Pressure* mode can pressurize the vial in half the time compared to *Flow to Pressure* because in the former the maximum available flow rate is used until the setpoint is reached rather than dynamically reducing the flow rate as the setpoint is approached. Using *To Pressure* improves the repeatability for cyclohexane and methylcyclohexane, which have very low partition coefficients in water [5]. For more details on the study comparing *Flow to Pressure* and *To Pressure*, refer to application note 5990-9106EN [5].

Table 1. Residual Solvent RSDs for Two Modes of Vial Pressurization on an Agilent 7697A Headspace Sampler (n = 10 Injections)

Class 2A compound	Flow to pressure	To pressure
Methanol	1.92	2.27
Acetonitrile	2.09	2.37
Dichloromethane	0.81	1.44
trans-1,2-Dichloroethene	1.54	1.84
cis-1,2-Dichloroethene	1.00	1.7
THF	1.06	1.47
Cyclohexane	4.88	1.52
Methylcyclohexane	5.01	1.43
1,4-Dioxane	2.36	2.36
Toluene	1.56	1.81
Chlorobenzene	1.14	1.5
Ethylbenzene	1.99	1.85
m,p-Xylene	1.92	1.89
o-Xylene	1.56	1.93

In the default Loop Fill Mode, the headspace uses the initial vial pressure, which is known from the Fill Pressure, to calculate an optimum flow rate and final loop pressure for filling the sample loop. These values are calculated by the instrument and not set by the user. If you would like to set these parameters, choose the Custom Loop Fill Mode. Then you can specify the **Loop Ramp Rate**, **Final Loop Pressure**, and **Loop Equilibration Time**. The Final Loop Pressure directly affects the sensitivity of the system. For more information on choosing these values, refer to the Agilent 7697A Headspace Sampler Advanced Operation guide.

Operating the Agilent 7697A Headspace Sampler in active backpressure control allows the system to retain more sample on the column during injection. This can overload the column and lead to poor peak shape. If this happens, one simple method adjustment is to reduce the Final Loop Pressure to a lower value by changing the Loop Fill Mode from *Default* to *Custom*. As discussed earlier, entering 0 psig leaves the final loop pressure subject to fluctuations in ambient pressure. Entering a low pressure, for example, 2 or 4 psig, could be used where a lower response is expected than under Default conditions, but the atmospheric pressure compensation of the 7697A Headspace Sampler would still be active.

Vial shaking settings

Agilent G1888A Settings	Agilent 7697A Settings (1–9)
High	7
Low	5

The shaking speed on the 7697A Headspace Sampler takes into account both acceleration and frequency, and has nine different levels of shaking (1–9) as opposed to just High or Low available with the Agilent G1888A Headspace Sampler. Both also have the option of turning off shaking. In terms of acceleration, the 7697A Headspace Sampler shaking level 4 is equivalent to the G1888A Headspace Sampler *High*. The 7697A Headspace Sampler shaking level 3 is equivalent to the G1888A Headspace Sampler *Low*. In terms of frequency, the 7697A Headspace Sampler shaking level 6 is either High or Low on the G1888A Headspace Sampler (100 shakes per minute). For method development starting conditions, if the G1888A Headspace Sampler shaking level was High, a recommended starting level on the 7697A Headspace Sampler is 7. If the G1888A Headspace Sampler shaking level was Low, a recommended starting level on the 7697A Headspace Sampler is 5.

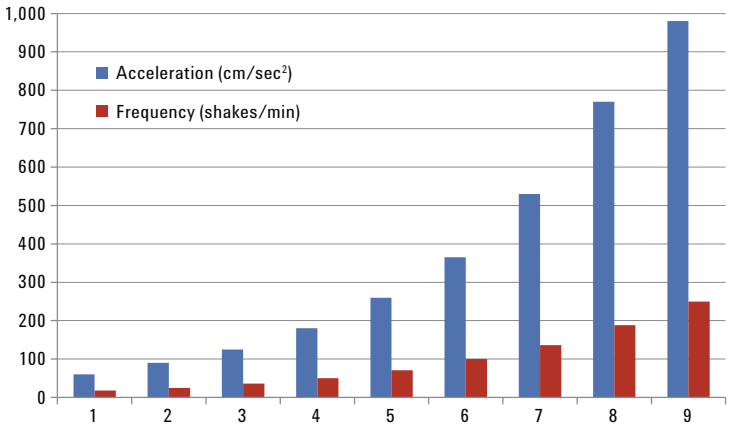


Figure 3. Graph of acceleration and frequency for the nine levels of shaking available on the Agilent 7697A Headspace Sampler.

Temperature settings

Both systems require acceptable oven, loop, and transfer line temperatures. These settings do not need to change when converting from an Agilent G1888A Headspace Sampler to an Agilent 7697A Headspace Sampler. If the user would like to change these parameters to take advantage of the advanced thermal control, they should take into consideration the recommendations in the white paper, *Thermal Zone Considerations for the Agilent 7697A Headspace Sampler*, when determining the appropriate temperature zone setpoints [6]. The white paper discusses how there no longer needs to be a temperature difference between the oven and loop zones, and recommends running these two zones at the same temperature for best peak area precision.

Timing settings

When converting from a G1888A Headspace Sampler to a 7697A Headspace Sampler, timing settings such as **Vial Equilibration**, **Injection Duration**, and **GC Cycle Time** should not be affected. On the 7697A Headspace Sampler, there is an additional parameter on the headspace front panel, **Pressure Equilibration**. Pressure Equilibration is the time allotted for the vial to equilibrate at pressure during vial pressurization. The default value is 0.10 minutes. The equivalent parameter can be set in the software as **Pressure Equilibration Time**. The user will notice that there are no longer timing settings for vial pressurization or loop fill. They are now replaced as part of the Vial Fill Mode and Loop Fill Mode.

Carrier settings

Agilent G1888A Settings	Agilent 7697A Settings
GC Control	GC Control
–	HS Control (with optional PCM module)
GC + HS Control (Manual pressure control of HS)	GC + HS Control (With optional carrier PCM module)

Having the GC control the carrier gas into the 7697A Headspace Sampler is the default and recommended installation setup. This is unchanged from the standard mode for the G1888A Headspace Sampler. For users with the optional carrier PCM Module on the 7697A Headspace Sampler, HS or GC + HS Control of the carrier gas is available as well. If using HS control, the headspace provides and controls the carrier gas to the GC. This mode is usually used if the 7697A Headspace Sampler is connected to a non-Agilent GC. When in this mode, the GC column dimensions must be correctly entered into the 7697A Headspace Sampler front panel so that the headspace can have accurate control of the carrier gas through the GC. If using GC + HS Control, the GC maintains and uses its own carrier gas supply, and the headspace uses its own carrier gas supply. The headspace provides an additional flow into the GC inlet. This setup is similar to running the G1888A Headspace Sampler in manual pressure control mode. Although the recommendation is to have the GC control the carrier gas, the 7697A Headspace Sampler can be run in this mode if a similar setup to an existing G1888A Headspace Sampler is needed.

Sequence actions settings

Agilent G1888A Settings	Agilent 7697A Settings
Continue	Continue
Abort	Abort
Wait	Skip or Pause

Sequence actions allow the user control over certain types of headspace or GC errors (for example, Vial Missing, Wrong Vial Size, Leak Detected, or System Not Ready) that can occur when handling sample vials for a run or a sequence of runs. If one of these errors is detected, the user can control what the Agilent 7697A Headspace Sampler does in response by setting the following actions: **Continue**, **Skip**, **Pause**, or **Abort**.

For example, System Not Ready: when the headspace becomes Ready, it checks if the GC is Ready. If the GC is not ready for a new injection, the headspace follows the specified action. The default setting is Abort.

For the Agilent G1888A Headspace Sampler, the options are **Continue**, **Wait**, or **Abort**. You will notice that Wait, which waited until the GC was ready to inject the sample, is no longer an option on the 7697A Headspace Sampler but is now replaced by Skip or Pause. Skip will skip the current sample vial, then continue processing with the next sample vial in the sequence. Pause will pause the sequence, but any vials in the oven will continue to be processed, including the current vial, if applicable. For headspace models with a 111-vial tray, no other vials will be moved into the vial oven. For the 12-vial model, the headspace processes the current vial and then stops. The advantages of Skip or Pause are they do not ignore the Vial Equilibration Time, as Wait did. This means the user will have more consistent processing of the vials for more consistent chromatography.

Transfer line diameter

The G1888A Headspace Sampler only had one option for the transfer line, the deactivated 0.8 mm id Siltek transfer line. The 7697A Headspace Sampler now has several options for transfer line diameter (0.25 mm, 0.32 mm, 0.45 mm, or 0.53 mm id), since it uses replaceable deactivated fused silica or ProSteel deactivated stainless steel. This gives more options for method development and optimization. The standard transfer line used on the 7697A Headspace sampler is one with a 0.53 mm id, and is the recommended starting id for method development.

Peak resolution can be impacted by the choice of sample loop volume and headspace transfer line diameter. As the headspace sample loop volume decreases, it is a good idea to reduce the transfer line inner diameter.

Summary of Method Parameters

Below are recommended method settings for the Agilent 7697A Headspace Sampler when migrating from the Agilent G1888A Headspace Sampler. Other method parameters should stay the same when migrating from the G1888A Headspace Sampler to the 7697A Headspace Sampler. This is not a guarantee of performance but a good starting point of method development. The method can be optimized by adjusting the Final Loop Pressure, Shaking, and Vial Fill Mode. Increasing GC split flow or septum purge flow can improve resolution as well.

		Agilent 7697A Headspace Sampler	
Function	**Agilent G1888A Headspace Sampler**	**Higher sensitivity**	**More similar resolution**
Vial	Vial pressurization time = XX	Vial fill mode = Default	Vial fill mode = Default
	Vial pressure = XX	Fill pressure = 15 psi	Fill pressure = 15 psi
Loop	Loop fill time = XX	Loop fill mode = Default	Loop fill mode = Custom
			Loop fill ramp rate = 20 mL/min
			Final loop pressure = 4 psi
Shaking	Low	5	5
	High	7	7

Note: XX is the current G1888A method setting.
Method settings based on using a 20-mL headspace vial.

Comparative Studies

System suitability for USP <467>

USP <467> has the following requirements for system suitability that must be met:

Procedure A (Identification) – A means of determining if any residual solvents are present in the sample at a detectable level.

- Signal-to-Noise (S/N) of 1,1,1-trichloroethane > 5
- S/N of all Class 1 solvents > 3
- Resolution of acetonitrile and methylene chloride > 1

Procedure B (Confirmation) – Once a residual solvent is identified to be above the acceptable limit, Procedure B is performed to confirm analyte identity.

- S/N of benzene > 5
- S/N of all Class 1 solvents > 3
- Resolution of acetonitrile and *cis*-dichloroethene > 1

The 7697A Headspace Sampler not only meets these requirements, but it also gives similar or better results than the G1888A Headspace Sampler. The following comparative studies were performed to demonstrate that the system suitability requirements are met and to demonstrate the accuracy and precision performance of the instruments.

Signal-to-noise

A comparative study of the Agilent 7697A Headspace Sampler and Agilent G1888A Headspace Sampler showed that both systems deliver similar S/N results, which exceed the specifications set by USP <467> (Figure 4, Table 2).

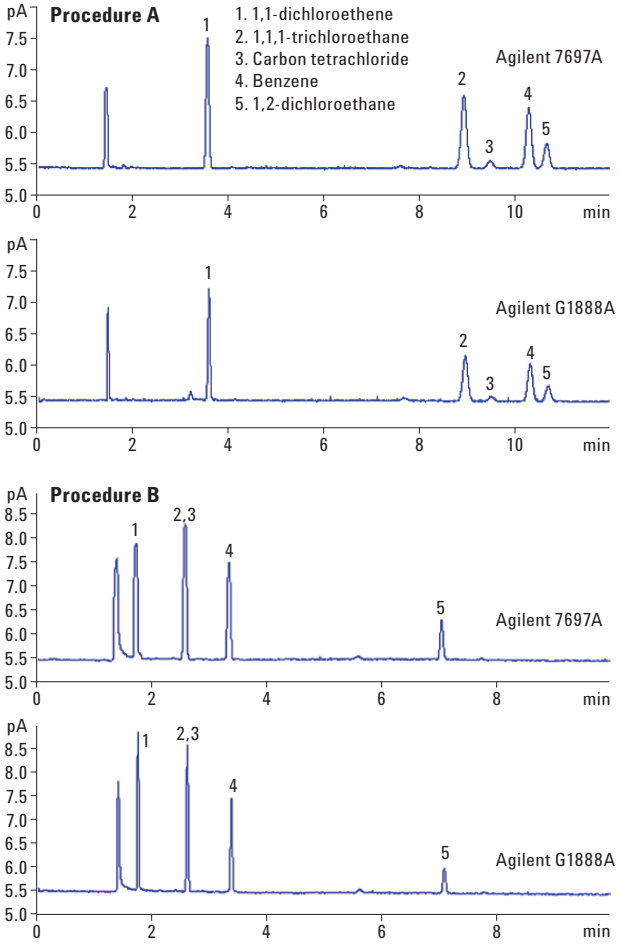


Figure 4. Comparative chromatograms of Procedure A and Procedure B for the Agilent 7697A and Agilent G1888A Headspace Samplers, at USP limit concentrations.

Table 2. S/N for 1,1,1-Trichloroethane and Benzene for Procedure A and Procedure B for the Agilent 7697A and Agilent G1888A Headspace Samplers

	S/N Procedure A		S/N Procedure B	
Compound	**Agilent 7697A**	**Agilent G1888A**	**Agilent 7697A**	**Agilent G1888A**
1,1,1-Trichloroethane	35.7	26.2	87.6	101.9
Benzene	29.8	21.3	63.1	64.7

The Agilent 7697A Headspace Sampler met the required S/N and gave similar results to the Agilent G1888A Headspace Sampler. All Class 1 solvents gave a S/N above 3 for both Procedure A and Procedure B. For Procedure A, both instruments had a S/N for 1,1,1-trichlorethane more than five times greater than the requirement. The 7697A Headspace Sampler gave a slightly better S/N than the G1888A Headspace Sampler for these solvents. For Procedure B, both instruments had a S/N for benzene more than 12 times above the requirement, with the 7697A Headspace Sampler giving similar results to the G1888A Headspace Sampler.

Resolution

Figure 5 shows that both instruments met the resolution requirements set by USP <467>, Figure 5A is for Procedure A and Figure 5B is for Procedure B.

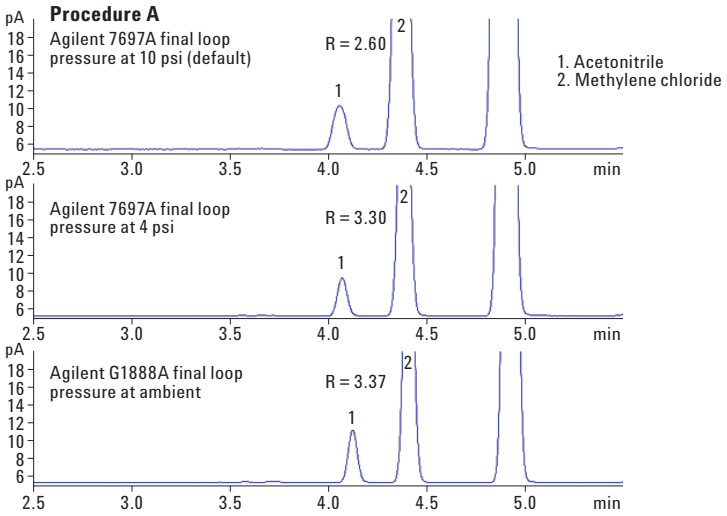


Figure 5A. Acetonitrile (1) and methylene chloride (2) resolution comparison between Agilent 7697A and Agilent G1888A Headspace Samplers on an Agilent J&W DB-624UI column (p/n 123-0334UI) with a 20-mL vial. The top chromatogram shows the 7697A in Default Loop Fill Mode. The middle chromatogram shows the 7697A with similar resolution to the G1888A, which is shown in the bottom chromatogram.

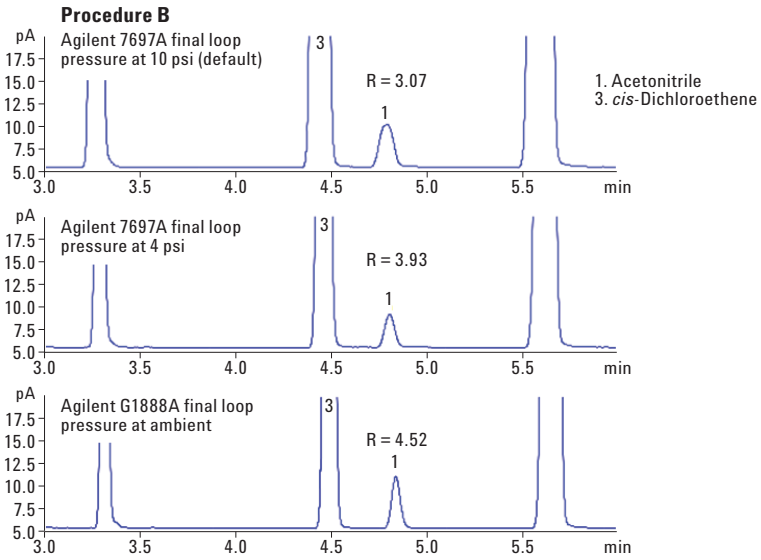


Figure 5B. Acetonitrile (1) and cis-dichloroethene (3) resolution comparison between the Agilent 7697A and Agilent G1888A Headspace Samplers on an Agilent J&W HP-INNOWax column (p/n 19091N-113) with a 20-mL vial. The top chromatogram shows the 7697A in Default Loop Fill Mode. The middle chromatogram shows the 7697A with similar resolution to the G1888A, which is shown in the bottom chromatogram.

As discussed earlier in the section on Vial and Loop Settings, using the active back-pressure control allows the Agilent 7697A Headspace Sampler to retain more sample on the column. You can adjust the amount of sample that makes it to the column by adjusting the Final Loop Pressure in the Loop Fill Mode. If you want higher sensitivity out of the instrument, using the Default parameters set by the Loop Fill Mode will usually achieve this. If you choose to run the 7697A Headspace Sampler with higher sensitivity you will notice the peaks are wider as a result of the increased area counts. This may affect your resolution but allows you to run the system at its optimum performance. Reducing the Final Loop Pressure on the 7697A Headspace Sampler can improve your resolution, but may result in a change in sensitivity. Regardless of the Loop Fill Mode selected, the 7697A headspace sampler clearly exceeds the resolution requirements set in USP <467>.

Precision

Application notes have previously been published showing the area count precision results of both the Agilent G1888A Headspace Sampler and the 7697A Headspace Sampler. When coupled to an Agilent 7890A GC, the G1888A Headspace Sampler repeatability was mostly below 5 % RSD. For complete details, refer to application note 5989-9726EN [7]. Performance on an Agilent 7890B GC would be comparable to the 7890A GC.

The 7697A Headspace Sampler offers an improvement on area count precision. When connected to a 7890A GC, the repeatability was generally better than 2.5 % RSD for Class 1, Class 2A, and Class 2B solvents. The results were regardless of vial size (10 mL or 20 mL) or inlet type (S/SL inlet or VI inlet). For complete details see application note 5990-7625EN [3]. This level of performance can be attributed to precise EPC controlled vial sampling, complete inert sample path, and stable thermal zones. The use of controlled venting (Custom Loop Fill Mode) in the 7697A Headspace Sampler allows the user flexibility over the final pressure when

filling the sample loop, as discussed earlier. As a general rule for method development, the final vial pressure should be set between 2.0 psi (Normal Temperature and Pressure-NTP) and 10.0 psi (NTP) in order to achieve the best repeatability. The optimal pressure used is dependent on vial size. This control leads to better results and depending on the analyte partition coefficient (k), it can also enhance sensitivity [3].

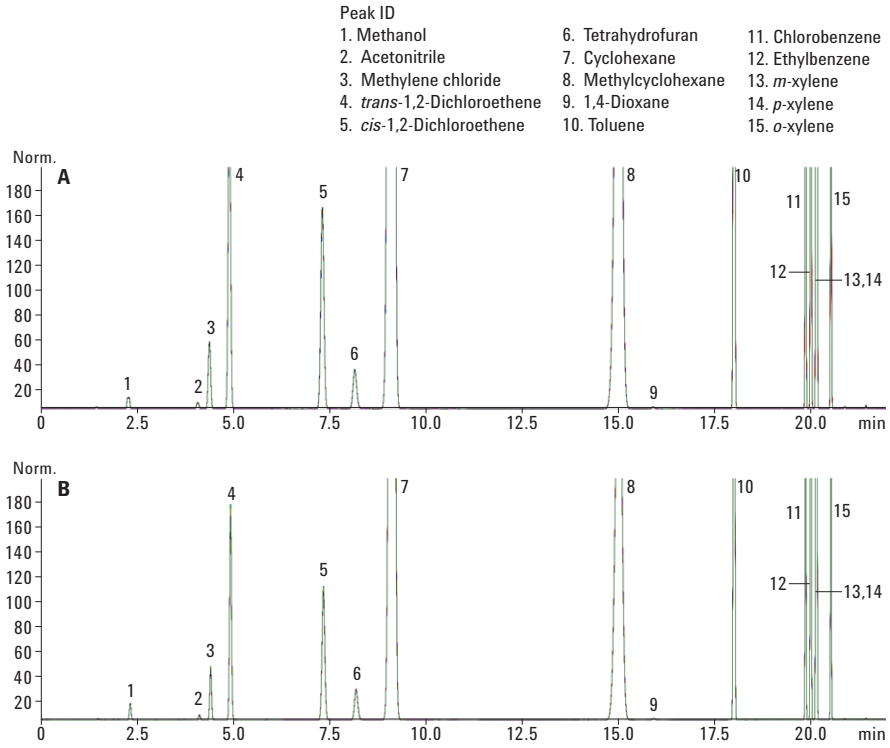


Figure 6. Overlay of chromatograms for Class 2A compounds for A) Agilent 7697A and B) Agilent G1888A Headspace Samplers.

Table 3. % RSD Comparison of Agilent 7697A and Agilent G1888A Headspace Samplers. RSD is for Seven Injections

Peak no.	1	2	3	4	5	6	7	8	9	10	11	12	13,14	15
Agilent 7697A	1.54	0.48	1.65	1.86	1.71	0.79	1.63	1.29	1.64	1.66	1.44	1.39	1.33	1.27
Agilent G1888A	1.33	6.72	1.90	2.00	2.00	1.21	1.94	1.84	1.48	2.01	2.02	1.97	1.99	2.02

Accuracy

By performing a comparative study of the Agilent 7697A Headspace Sampler and Agilent G1888A Headspace Sampler, the accuracy of the two instruments was compared. Figure 7 shows the linearity curves for both instruments. Headspace samples were prepared for Class 2A solvents at concentrations ranging from about five times below USP limits to six times above to demonstrate accuracy. For example, according to USP <467> Procedure A, the limit concentration in prepared headspace vials for methanol is 30.0 ng/µL. The concentrations used for linearity were 2.52, 12.58, 25.17, and 151.00 ng/µL in water.

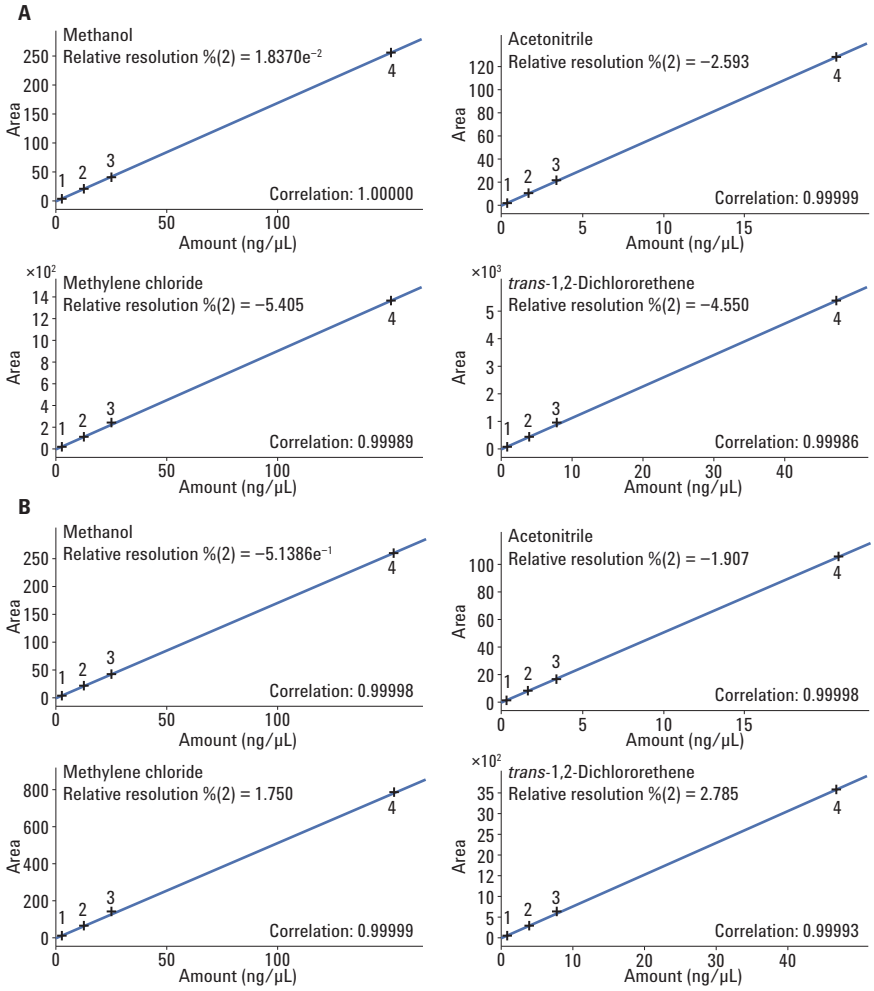
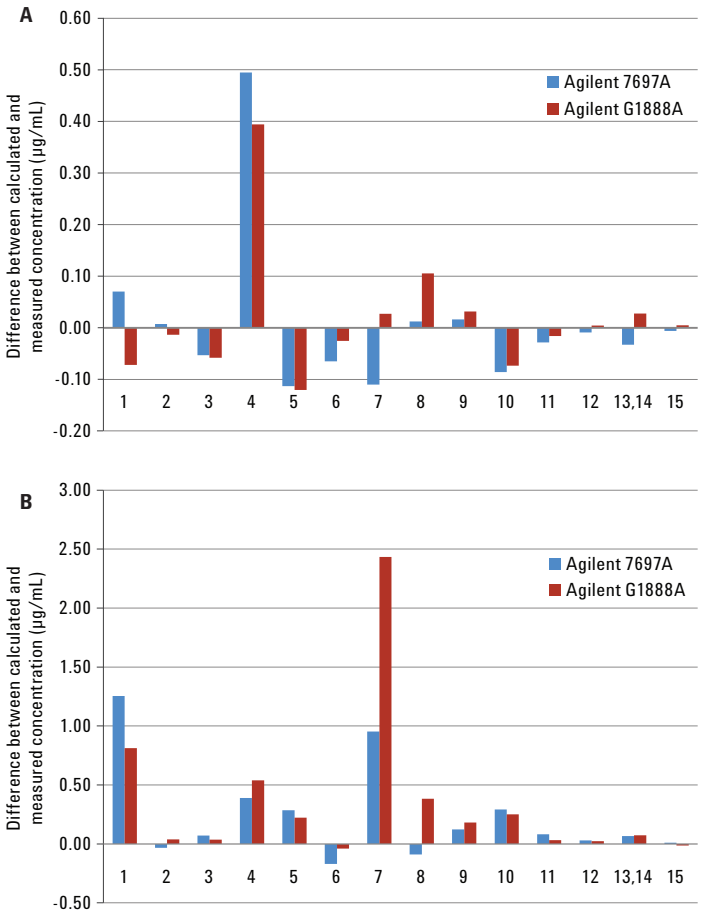


Figure 7. A few comparative calibration curves for both A) Agilent 7697A and B) Agilent G1888A Headspace Samplers for Class 2A solvents from about five times below to six times above limit values.

Two different concentration samples (low and high) were then run against the calibration tables to test the difference between the measured and calculated concentrations. Figure 8 shows the results of these tests.



A		Calculated concentration (µg/mL)
1.	Methanol	5.03
2.	Acetonitrile	0.69
3.	Methylene chloride	1.00
4.	*trans*-1,2-Dichloroethene	1.57
5.	*cis*-1,2-Dichloroethene	1.57
6.	Tetrahydrofuran	1.21
7.	Cyclohexane	6.50
8.	Methylcyclohexane	1.98
9.	1,4-Dioxane	0.63
10.	Toluene	1.49
11.	Chlorobenzene	0.60
12.	Ethylbenzene	0.62
13.	*m*-xylene, 14. *p*-xylene	2.69
15.	*o*-xylene	0.33

B		Calculated concentration (µg/mL)
1.	Methanol	50.33
2.	Acetonitrile	6.87
3.	Methylene chloride	10.03
4.	*trans*-1,2-Dichloroethene	15.73
5.	*cis*-1,2-Dichloroethene	15.73
6.	Tetrahydrofuran	12.07
7.	Cyclohexane	65.00
8.	Methylcyclohexane	19.77
9.	1,4-Dioxane	6.33
10.	Toluene	14.90
11.	Chlorobenzene	6.00
12.	Ethylbenzene	6.17
13.	*m*-xylene, 14. *p*-xylene	26.87
15.	*o*-xylene	3.28

Figure 8. Difference between calculated and measured concentrations for both A) low and B) high concentration samples. The calculated concentration for a given peak number is shown in the corresponding tables. The figure shows the measured concentration from the instrument minus the calculated concentration from the table for both the Agilent 7697A, in blue, and the Agilent G1888A, in red. See the text for additional explanation.

Both the Agilent 7697A Headspace Sampler and Agilent G1888A Headspace Sampler gave similar average results for the accuracy, with the highest deviation overall from cyclohexane, due to its low K in water. For the low concentration sample, both instruments gave an average measured concentration within 10 % of the calculated concentration. For the high concentration sample, both instruments gave an average measured concentration within 6 % of the calculated concentration.

Discussion

The 7697A Headspace Sampler is able to provide similar or better results than the G1888A Headspace Sampler in regards to S/N, resolution, precision, and accuracy. Due to the onboard electronic pneumatics control used on the 7697A Headspace Sampler, there are a few new method parameters that the G1888A Headspace Sampler did not have. This also allows the 7697A Headspace Sampler to be more sensitive than the G1888A Headspace Sampler. If needed, you can change the sensitivity of the headspace by adjusting method or instrument parameters such as the final loop pressure, sample loop volume, or injection port split ratio.

Since the 7697A Headspace Sampler is not using a new technology, the user should not have to do a complete method revalidation of their methods based on the G1888A Headspace Sampler. Many people follow USP <1224> to transfer methods, but use your professional judgment to determine what is most appropriate for your laboratory.

Appendix

Sample preparation and method parameters used for this technical overview are listed below:

Sample preparation procedure

Two Stock solutions of residual solvents in DMSO were used:

5190-0490 Residual Solvent Revised Method 467 Class 1

5190-0492 Residual Solvent Revised Method 467 Class 2A 1 ampule of 1 mL

Class 1 residual solvent preparation

Step 1.	Add 1 mL of stock solution to 9 mL of DMSO and dilute to 100 mL with water.
Step 2.	Dilute 1 mL from step 1 to 100 mL with water.
Step 3.	Dilute 10 mL from step 2 to 100 mL with water.
Sample	Add 5 mL of water to 1 mL from step 3 in a 20-mL HS vial.

Compound	Concentration	Unit
1,1-Dichloroethene	66.7	ng/mL
1,1,1-Tricloroethane	83.3	ng/mL
Carbon tetrachloride	33.3	ng/mL
Benzene	16.7	ng/mL
1,2-Dichloroethane	41.7	ng/mL

Class 2A residual solvent preparation

Step 1. Dilute 1 mL of stock solution to 100 mL with water.

Sample Add 5 mL of water to 1 mL from step 1 in a 20-mL HS vial.

Compound	Concentration	Unit
Methanol	25.2	µg/mL
Acetonitrile	3.4	µg/mL
Methylene chloride	5.0	µg/mL
trans-1,2-Dichloroethene	7.9	µg/mL
cis-1,2-Dichloroethene	7.9	µg/mL
Tetrahydrofuran	6.0	µg/mL
Cyclohexane	32.5	µg/mL
Methylcyclohexane	9.9	µg/mL
1,4-Dioxane	3.2	µg/mL
Toluene	7.5	µg/mL
Chlorobenzene	3.0	µg/mL
Ethylbenzene	3.1	µg/mL
m-xylene	10.9	µg/mL
p-xylene	2.6	µg/mL
o-xylene	1.6	µg/mL

GC parameters

Instrument	Agilent 7890B GC
Oven temperature (initial)	40 °C
Hold time	15 minutes
Post run	50 °C
Program	
#1 Rate	20 °C/min
#1 Value	240 °C
#1 Hold time	3 min
Equilibration time	1 min
Front SS inlet He	
Mode	Split
Heater	On 140 °C
Pressure	On 11.264 psi
Total flow	On 18 mL/min
Septum purge flow	On 3 mL/min
Gas saver	Off
Split ratio	5 :1
Split flow	12.5 mL/min
Liner	Agilent 5181-8818: 250 µL (Splitless, straight liner, deactivated)
Procedure A	Agilent 123-0334UI DB SELECT 624UI, 30 m × 320 µm, 1.8 µm
Procedure B	Agilent 19091N-113 HP-INNOWax, 30 m × 320 µm, 1.8 µm
In	Front SS Inlet He
Out	Back detector FID
(Initial)	40 °C
Pressure	11.264 psi
Flow	2.5 mL/min
Average velocity	39.235 cm/sec
Holdup time	1.2744 minutes
Back detector FID	
Heater	On 250 °C
H_2 Flow	On 40 mL/min
Air Flow	On 400 mL/min
Makeup flow (combined)	On 30 mL/min
Carrier gas flow correction	Included in makeup flow
Flame	On
Electrometer	On

HS parameters

	Agilent 7697A Headspace Sampler	Agilent G1888A Headspace Sampler
Temperature settings	Oven temperature 80 °C Loop temperature 90 °C Transfer line temperature 100 °C	Same
Transfer line	Transfer line type DB-ProSteel Transfer line diameter 0.53 mm	Transfer line type Deactivated 0.8 mm id Siltek
Timing settings	Vial equilibration 30.00 minutes Injection duration 0.50 minutes GC cycle time 35.00 minutes	Same Oven stabilization time 1.00 minute
Vial and loop settings	Vial size 20 mL Loop size 1 mL Fill mode *Default* (fill flow 50 mL/min, fill pressure 15 psi, hold time 0.1 minutes) Fill pressure 5 psi Loop fill mode Custom Loop ramp rate 20 psi/min Loop final pressure 10 psi Loop equilibration time 0.1 Vial shaking OFF Vial pressurization gas nitrogen	Vial size 20 mL Loop size 1 mL Vial pressurization time 0.20 minutes Vial pressure 15.00 psi Loop equilibration time 0.05 minutes Loop fill time 0.20 minutes Vial shaking OFF Vial pressurization gas nitrogen

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