



## **COMPARING THE LEADING SOLVENTS**

Not all premium-grade solvents are equal in optimizing test results

# Abstract

Laboratories performing pharmaceutical or food safety/ authenticity analyses must have high confidence in the purity and identity of the product under test. Scientists working in these facilities require high-purity solvents for chromatography, a technique used to separate and analyze complex mixtures.

Honeywell Research Chemicals and third-party labs have performed comprehensive studies of the performance and quality characteristics of the leading solvent brands. Testing revealed that the Honeywell line of solvents has a better impurity profile than products from other major suppliers – driving better outcomes for analytical chemists.

Chromatograms from internal and external tests show significant false peaks associated with some solvent products. Honeywell solvents, on the other hand, help chromatographers optimize their testing results, while reducing the amount of waste by minimizing the need to repeat experiments.

This whitepaper is intended for Quality Control (QC)/Quality Assurance (QA) personnel in the pharmaceutical, biotechnology, chemical, food and beverage, and industrial sectors who are concerned about the efficacy of the solvents used in their mission-critical analytical procedures.

Different industries require different grades of solvents for their analytical procedures. For example, food and beverage manufacturers are primarily interested in Gas Chromatography (GC) and Mass Spectrometry (MS) solvents. Pharmaceutical companies are mainly concerned with Liquid Chromatography-Mass Spectrometry (LC-MS) and GC-Headspace products.

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*A growing number of laboratories in pharmaceuticals, biotechnology and other industries are willing to invest in premium-grade solvent products to ensure accurate results from their analytical procedures.*

## Introduction

In analytical applications, chromatographers must verify the purity and identity of a given substance. If they use a solvent containing unacceptable levels of impurities, it can result in false-positive readings or errors requiring repeat experiments to be performed.

A growing number of testing laboratories in pharmaceuticals, biotechnology and other industries are willing to invest in premium-grade solvent products to ensure they receive accurate results from critical analytical procedures.

### Need for High-Quality Solvents

Today, the demand for high-quality solvents and reagents employed in mass spectrometry, gas chromatography and other analytical applications has never been greater.

The need to eliminate potential contaminants, compromised results and false readings in analytical laboratories is crucial, so only the highest quality solvent products should be used.

### Key Analytical Requirements

There are many diverse requirements for high-purity solvents in a laboratory environment. Chemists and researchers frequently employ two key types of analysis:

#### LC-MS Analysis

The combined technique of Mass Spectrometry (MS) and High Performance Liquid Chromatography (HPLC) is commonly known as Liquid Chromatography-Mass Spectrometry (LC-MS). Pairing these two analytical methods reduces experimental error and improves accuracy. The LC-MS technique

is very useful in applications involving a large number of compounds, such as environmental effluents.

Analytical laboratories have some very specific requirements for solvents used in LC-MS. In order to be suitable for this application, they will generally have been through an additional purification step as well as rigorous testing. Different manufacturers use different techniques to achieve high purity, and while all might claim to be the same standard, very often they are not. Poor quality solvents can contain particulate matter that blocks inlet and inline filters and columns, and contaminates detector cells, but, most importantly, they can make low-level detection difficult.

#### Residual Solvent Analysis

The determination of residual solvents is one of the most important Gas Chromatography (GC) applications for Quality Assurance/Quality Control (QA/QC) in the pharmaceutical industry. Residual solvents are organic volatile or semi-volatile impurities left over from the synthesis of Active Pharmaceutical Ingredients (APIs) from the manufacturing process of the final pharmaceutical products, or from packaging and storage.

Depending on the toxicity, residual solvents in pharmaceuticals pose a severe risk for the patient. They also have a potential impact on the crystalline form, possibly affecting solubility, stability, and bioavailability.

GC Headspace is ideally suited for residual solvent analysis because of its ability to quantify individual solvents. Moreover, headspace sampling is significantly more robust than direct liquid injections of API solutions.

*Research chemists can realize gains in accuracy, efficiency and productivity by selecting a manufacturer who offers multiple grades of solvent to meet their specific application requirements.*

## Choosing the Right Solution

In every organic chemistry lab, there is a range of solvents to choose from for specific applications. So where do users begin in selecting the right product?

Numerous benefits can be derived from selecting the most appropriate solvent grade. These include minimal rework, greater reproducibility of results, less challenging methods transfer, improved instrument sensitivity, and greater accuracy (i.e., fewer erroneous peaks). Such benefits can offset any additional cost for a higher-purity product, making the selection of a better grade a worthwhile investment.

## Not All Suppliers are Alike

When sourcing solvents, it's important to know the product that is being purchased. Sometimes it can be hard to tell the difference between leading brands; often the packaging is very similar, and they may have similar or the same product numbers.

In addition, the selection of an appropriate solvent supplier is an important consideration. Laboratories can realize gains in accuracy, efficiency and productivity by selecting a manufacturer who offers multiple grades to suit multiple applications, and whose manufacturing processes are focused on controlling potential variables to ensure that users get reliable results.

## Evaluating the Leading Products

Throughout the field of analytical chemistry, a number of studies have been conducted to compare the quality and performance of the leading high-purity solvent brands. The findings of these tests have significant implications for research chemists working in public and private laboratories around the world.

## How the Tests Were Conducted

### *Internal Study No. 1*

Recently, Honeywell Research Chemicals' Quality Assurance Department performed an in-depth examination of the leading analytical solvents in the chromatography marketplace. The quality and purity of Honeywell Chromasolv™ products were evaluated against solvent brands from three leading global laboratory chemical suppliers.

Honeywell Chromasolv LC-MS Acetonitrile (ACN) and Methanol (MeOH) – products #34967 and #34966 – were tested against LC-MS-grade solvents from leading competitors using the following procedure:

- MS System: Shimadzu MS-8030
- Ionization: ESI+
- Mass Range: 100-2,000 m/z
- Sample: Direct injection after 1:40 concentration with five ppb Reserpine as a standard based on the sample

To check the lot-to-lot consistency of Honeywell Chromasolv LC-MS #34967, a comparison was made between this product and a Honeywell standard HPLC grade at an absorption rate of 200 nm.

Figures 1 and 2 clearly show that Honeywell Chromasolv LC-MS solvents have a much better impurity profile than competitive products. This is valid for both Acetonitrile and Methanol. For Acetonitrile, Honeywell Chromasolv only has two impurity signals whereas competitors range from two up to 23 impurity signals. The same outcome is true for Methanol, where Honeywell Chromasolv only shows one impurity signal compared with 3 to 12 for competitors.

*Honeywell Chromasolv solvents have been custom-designed to meet the requirements of specific analytical methods, and are suitable for use in a wide range of industries.*

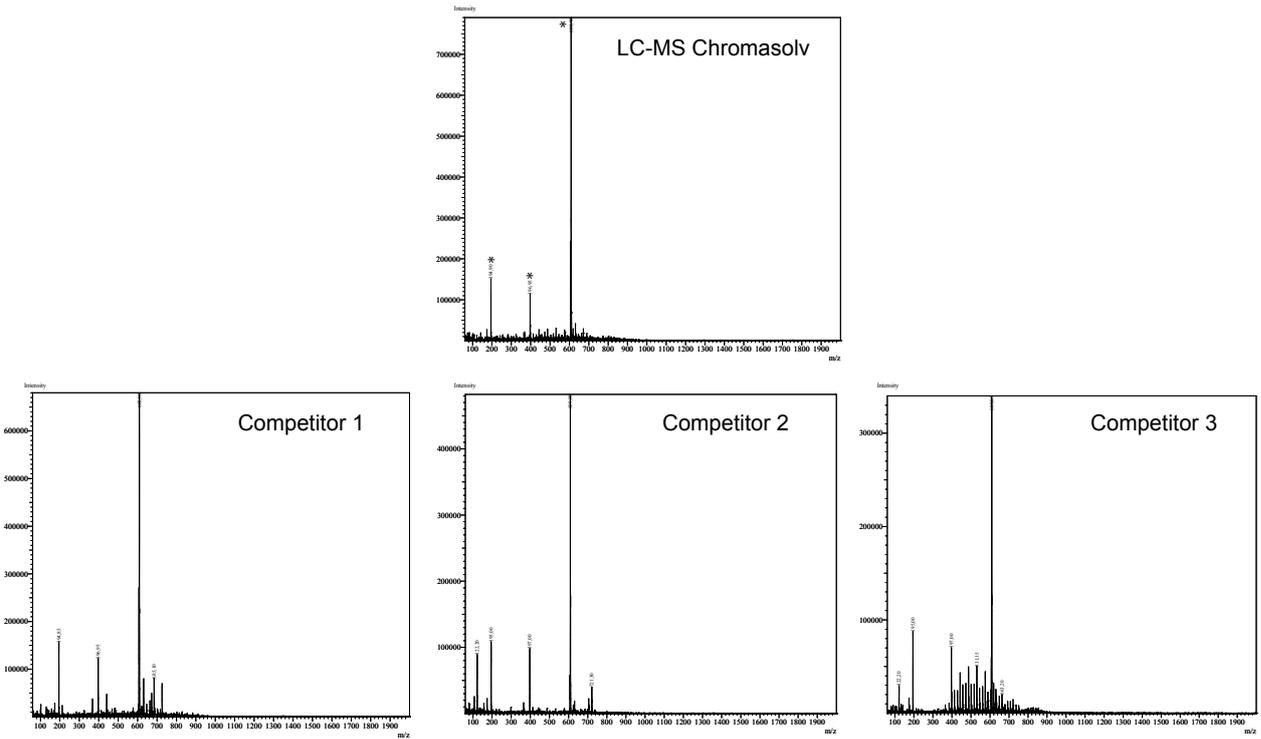


Fig. 1:  
ESI+-mass spectra of Acetonitrile LC-MS Chromasolv versus competitors 1-3, spiked with reserpine 5ppb (\* fragment ions of reserpine)

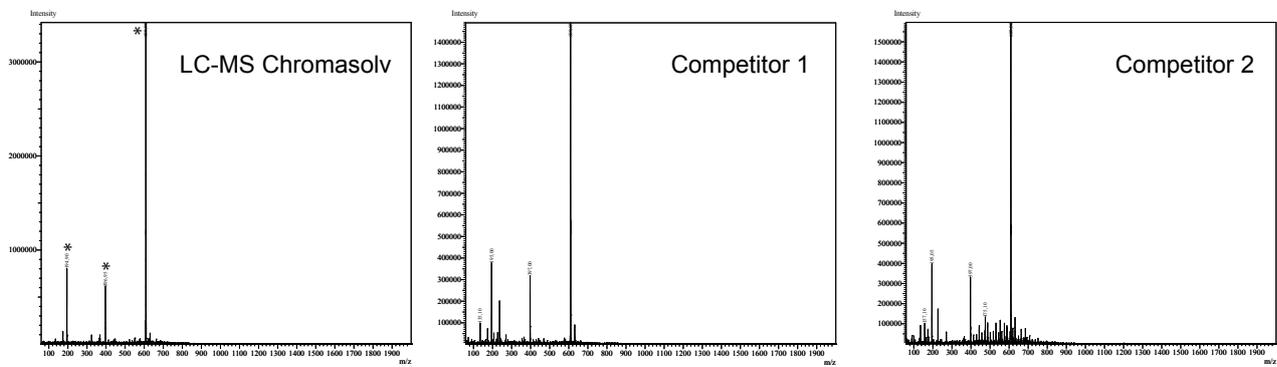


Fig. 2:  
ESI+-mass spectra of Methanol LC-MS Chromasolv versus competitors 1-2, spiked with reserpine 5ppb (\* fragment ions of reserpine)

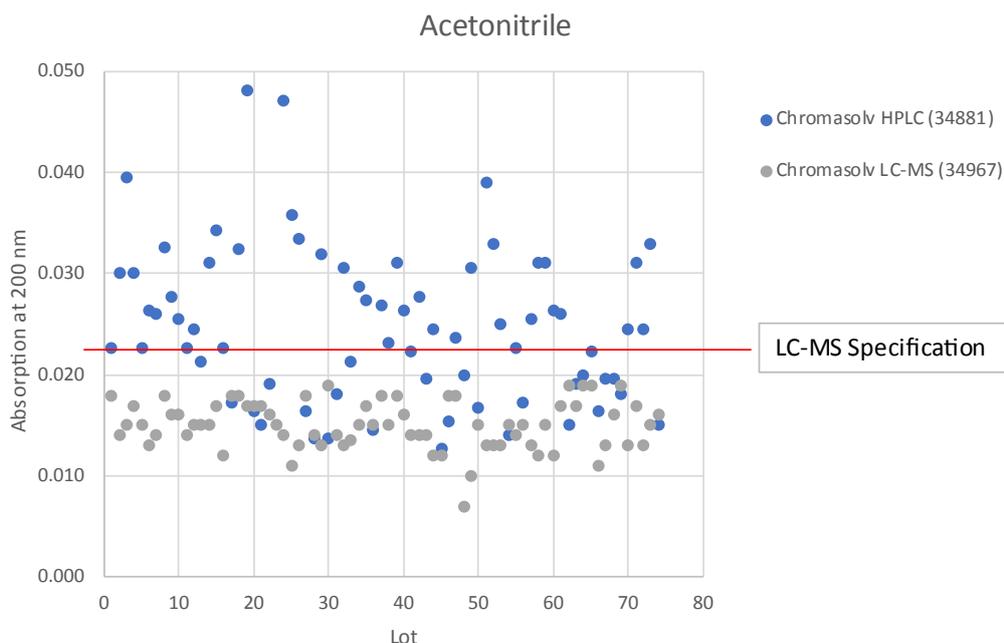


Fig. 3: Lot-to-lot UV absorption (200 nm) variations for Acetonitrile LC-MS Chromasolv (grey) vs HPLC Chromasolv (blue).

### Lot-to-lot Variation

Testing as illustrated in Figure 3 clearly indicates that Honeywell Chromasolv LC-MS ensures a very high consistency from lot-to-lot.

These results underscore the importance of choosing the right solvent quality to support the analytical task at hand. High purity and sensitive ultraviolet (UV) gradient methods can give only a rough picture of a solvent and its suitability for MS detection. Relying on sub-par solvents, especially during method development, may lower the

apparent cost per sample, but has a serious negative impact on Limit of Quantification (LOQ) while also negatively affecting the lifetime of the instrument. Honeywell Chromasolv LC-MS solvents are application tested, offer low impurities, and provide high reliability to help scientists avoid the hidden costs resulting from signal suppression.

Static Headspace GC (GC-HS) is a commonly used technique in the analysis of Organic Volatile Impurities (OVIs). This technique concentrates volatile analytes and allows their analysis free from the sample matrix.

The purity of dissolution solvents used in the headspace analysis is essential for avoiding extraneous peaks in the subsequent chromatographic analysis, and preventing interference with the analytes of interest. Many protocols followed by laboratories doing OVI analysis call for the analysis of an acceptable blank, and some published methodologies require the analysis of a blank to verify the absence of interfering peaks.

Honeywell Chromasolv GC-Headspace Solvent *N,N*-Dimethylformamide (DMF) #51781 was tested against competitive products (see Fig. 4), and Honeywell

Chromasolv GC-Headspace Solvent Dimethyl sulfoxid (DMSO) #51779 was tested against a lower grade DMSO (see Fig. 5).

The testing procedure involved:

- GC System: Shimadzu GC 2010 plus with FID and HS-20 Headspace Sampler
- Column: Agilent VF-624ms 30m x 0,32 mm, 1,8  $\mu$ m
- Oven Temp: 40 °C to 240 °C
- Sample: 1 mL solvent pro 20 mL vial
- Equilibrating: 80 °C for 60 minutes

Figure 4 shows that Honeywell Chromasolv GC-Headspace DMF has a much better impurity profile than competitive products, and Figure 5 illustrates why it is important to use an application-tested solvent for OVI.

The data presented in the following charts clearly demonstrate the superior performance of the high-purity Honeywell Chromasolv GCHeadspace grade solvent.

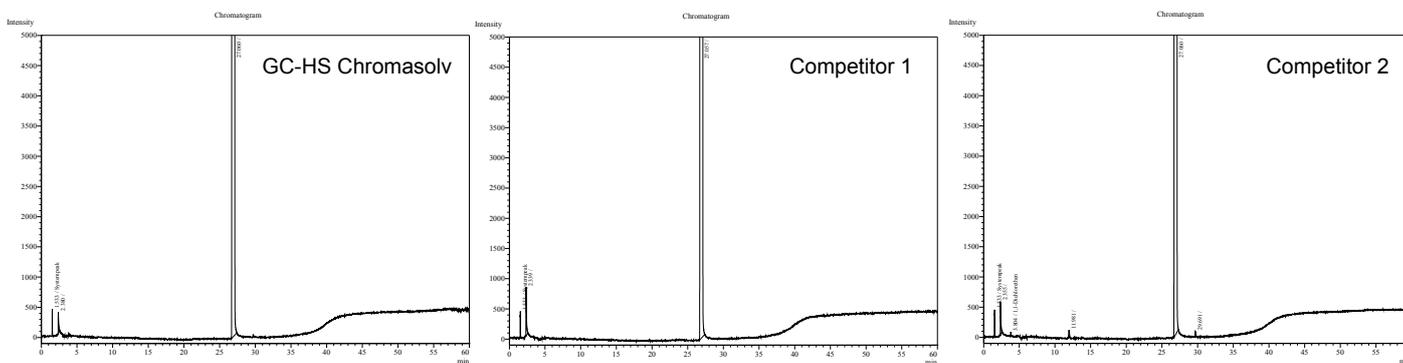


Fig. 4: Comparison GC-HS Chromatograms for DMF versus competitors 1-2

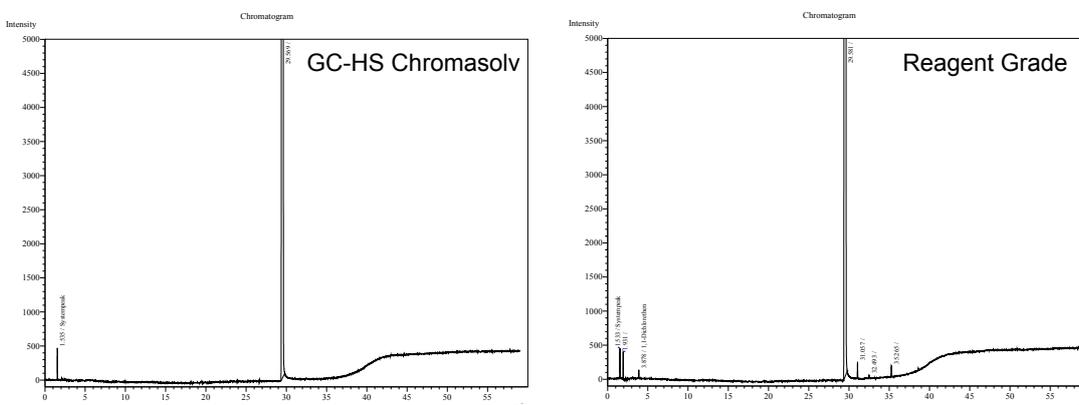


Fig. 5: DMSO GC-HS Chromasolv versus DMSO Reagent grade

### ***Third-party Study No. 1***

Honeywell identified an external lab with broad experience in LC-MS analysis and a variety of instruments to compare the quality of Honeywell Chromasolv LC-MS solvents to products from several major suppliers. The experimental setup was intended to evaluate

- 1) total ion count (TIC) trace while pumping 100% solvent into an MS system, and
- 2) pesticide analysis in water via LC-MS. The focus of the second test was on quenching effects by using different solvents.

The competitor samples were purchased via normal distribution channels, and represented typical average quality. The Honeywell samples were chosen at random from ongoing production. One batch was tested for each solvent (Methanol and Acetonitrile) from each supplier. The instrument used was an Agilent 6400 Triple Quad combined with 1200 HPLC system.

The comparison of the different suppliers showed that Chromasolv LC-MS solvents can be considered as a premium brand. In general, the quality variation of LC-MS products seemed to be higher for MeOH and ACN.

Just by changing the solvent, there can be significant changes in the signal-to-noise ratio, which determines the lowest limit of detection. Additionally, the individual impurity profile of the solvent has a strong impact on the potential quenching effects.

### ***Third-party Study No. 2***

As a part of a formal bid process a customer in Norway conducted a thirdparty study of high-purity LC-MS solvents as part of a formal bid process.

The blind test involved an UHPLC-MS analysis of the leading solvent brands. Saveen & Werner AB, a leading supplier of reagents and test kits for life sciences, and a distributor of products for plastics, glass, instruments, chemicals and consumables for analytical laboratories participated in the formal bid with Honeywell Acetonitrile and methanol in UHPLC-MS quality.

Solvents were tested based on:

- Interfering tops
- Background noise
- Pollution of equipment

One of the key criteria for the evaluation was the signal height (i.e., sensitivity) of the solvents. Experience has shown that impurities such as surfactants can reduce sensitivity. They can result in unwanted signals and high background noise. Furthermore, particles can cause high backpressure and even block columns. The tests also looked at peak shape. Some impurities can result in a broader peak. Solvents that met the criteria for interfering tops and background noise were tested over time for contamination of equipment. Honeywell Chromasolv products proved to be superior to competitive offerings on all parameters. They had significantly lower background noise and impurity signals than six other major solvents.

Quality testing was done for MeOH and ACN in UHPLC quality, and for both products, Chromasolv received the maximum score of 10,0 versus a average score for the six competitors of 4.2 for ACN and 7.5 for MeOH.

### ***Third-party Study No. 3***

Another series of third-party studies has highlighted the value and advantages of Honeywell Burdick & Jackson LC-MS solvents compared with other available products.

During the most recent study, a standard HPLC-MS methodology was used for one test, including direct MS injection with 100% mobile phase, and an HPLC-tandem with trip-quad MS (TQMS) detection was employed for another test. The study involved four Nitrofuran chemicals and one Ketoconazole drug as signal mark compounds for setting up the LC-MS database.

The MeOH test procedure involved:

- SHIMADZU LCMS-8040
- LC20 Series HPLC and Triple Quad MS 8040
- Compare Honeywell Burdick & Jackson LC-MS Methanol #LC230 versus equivalent competitor product

Test Method:

- LC Condition: (without column)
  - Flow Rate: 0.4 mL/min
  - B Conc.: 100%
- MS Condition:
  - Nebulizing Gas Flow: 3 L/min
  - Heating Gas Flow: 15 L/min
  - Interface Temperature: 350 °C
  - DL Temperature: 250 °C
  - Heat Block Temperature: 400 °C
  - Drying Gas Flow: 5 L/min
  - Mode: Q3 Scan, m/z 50-1000, Scan Speed: 5000 u/s

Test Results:

Comparison of Honeywell B&J MeOH, LC230 shown as black line versus competitor shown as pink line.

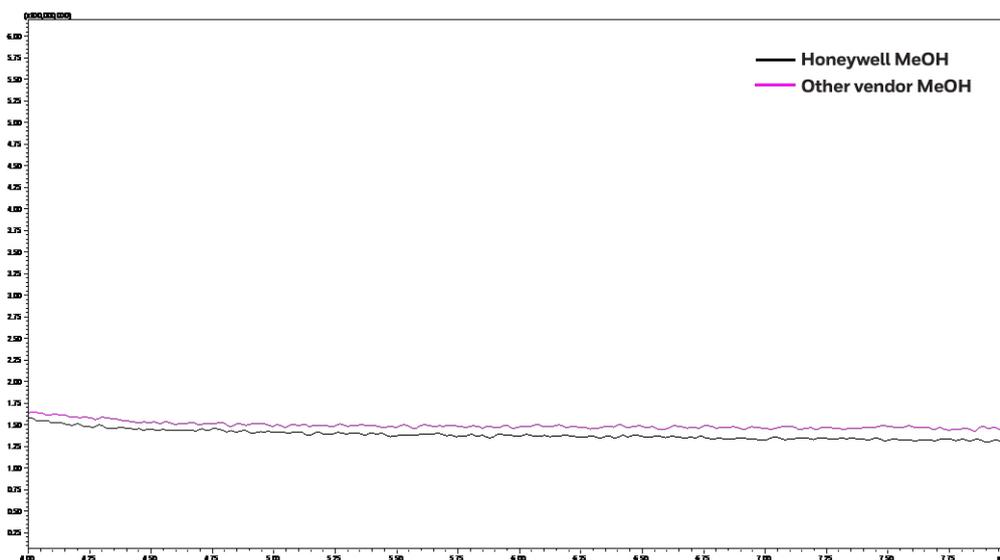


Fig. 6:  
(ESI+) TIC-MS for Q3 Scan baseline comparison.

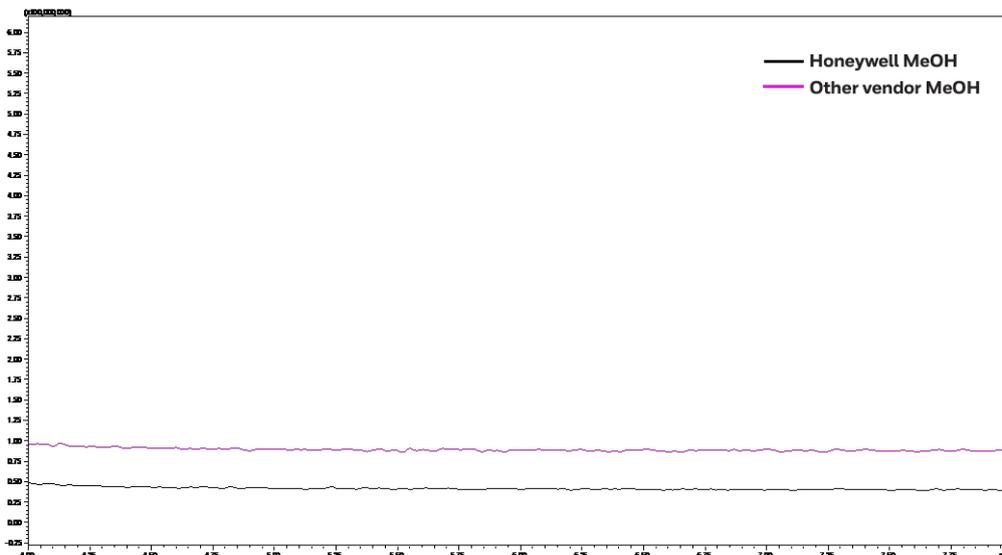


Fig. 7:  
ESI(-) TIC-MS for Q3 Scan baseline.

Response analysis of Nitrofurans

- LC Condition: (without column)
  - Flow Rate: 0.4 mL/min
  - B Conc.: 100%

- MS Condition:
  - Nebulizing Gas Flow: 3 L/min
  - Heating Gas Flow: 15 L/min
  - Interface Temperature: 350 °C
  - DL Temperature: 250 °C
  - Heat Block Temperature: 400 °C
  - Drying Gas Flow: 5 L/min
  - Scan Mode: Multiple reaction monitoring (MRM) mode
  - Injection: 1ppb- 4 chemicals mixture (injection: 1 µL)

Major nitrofurantoin antibiotic metabolites in food:

Compound	Parent ion	Daughter ion	Detective mode
SEM	209	165.9	positive
AHD	249	104	positive
AOZ	236.1	103.8	positive
AMOZ	335.1	261.9	positive

Abbreviations:  
 SEM = semicarbazide  
 AHD = 1-aminohydantoin  
 AOZ = 3-amino-2-oxazolidinone  
 AMOZ = 5-morpholine-methyl-3-amino-2-oxazolidinone

*Honeywell solvents can help chromatographers optimize their testing procedures, while reducing the amount of waste by minimizing the need to repeat experiments.*

### Comparisons signal-to-noise ratios (S/N) in Methanol

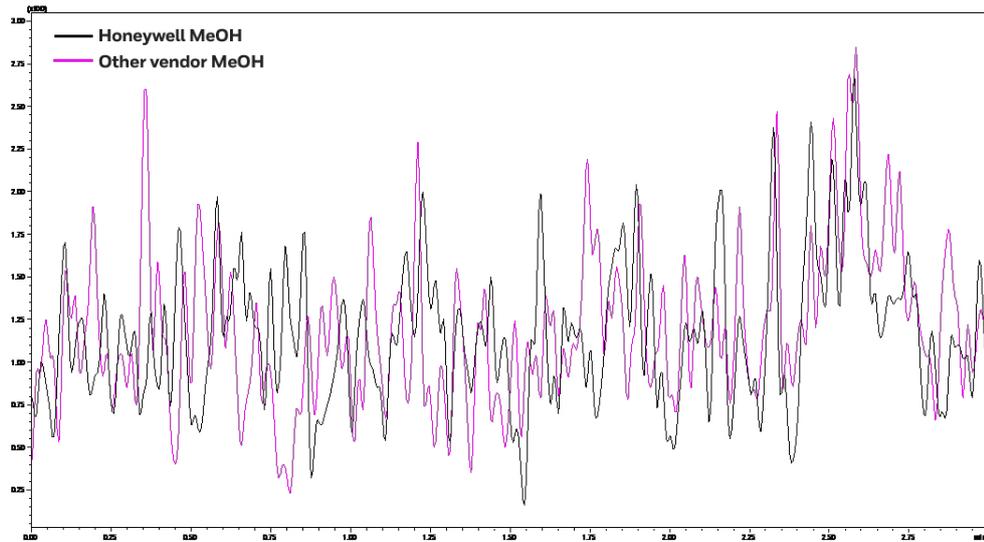


Fig. 8:  
SEM (MRM: 209>165.9 ion pair channel)

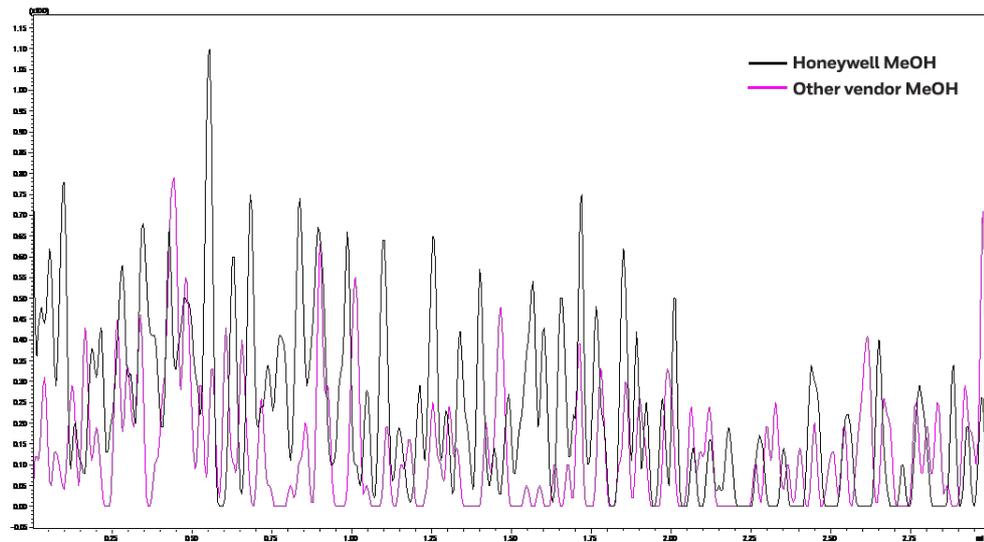


Fig. 9:  
AHD (MRM: 249>104 ion pair channel)

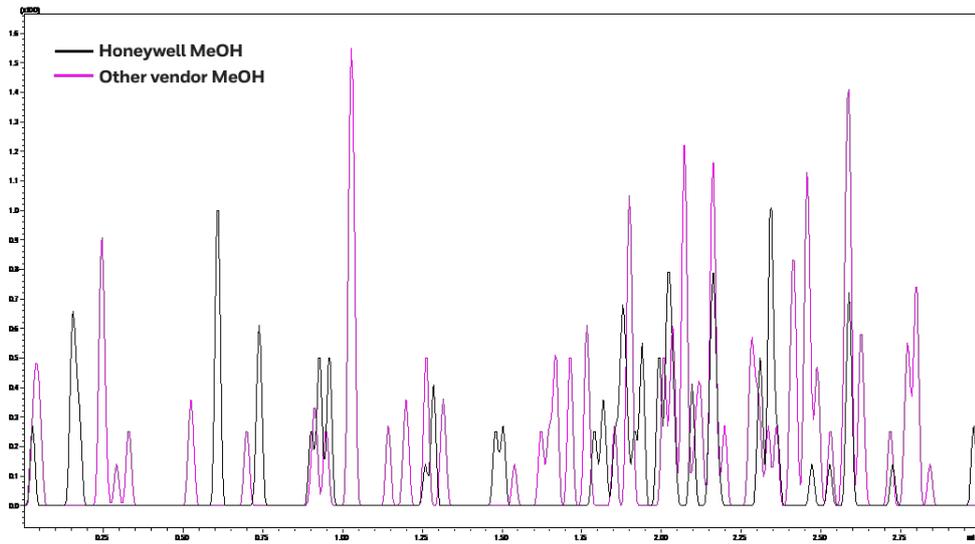


Fig. 10:  
AOZ (MRM: 236.1>103.8 ion pair channel)

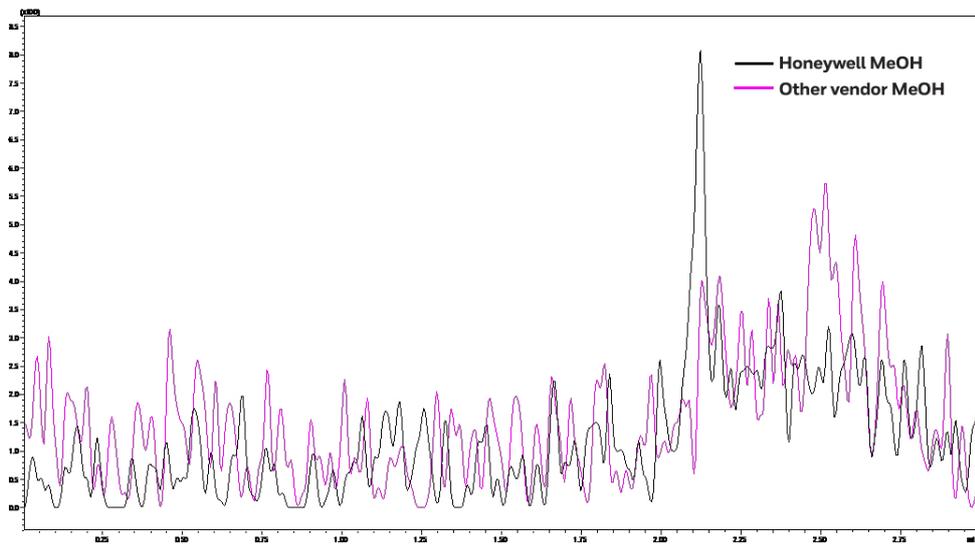


Fig. 11:  
AMOZ (MRM: 335.1>261.9 ion pair channel)

*Honeywell solvents have a superior impurity profile compared with leading competitors. They dramatically improve customers' analytical performance – assuring accurate and valid test results.*

### Comparisons MS spectra of nitrofurans in B&J versus competitor LC-MS Methanol

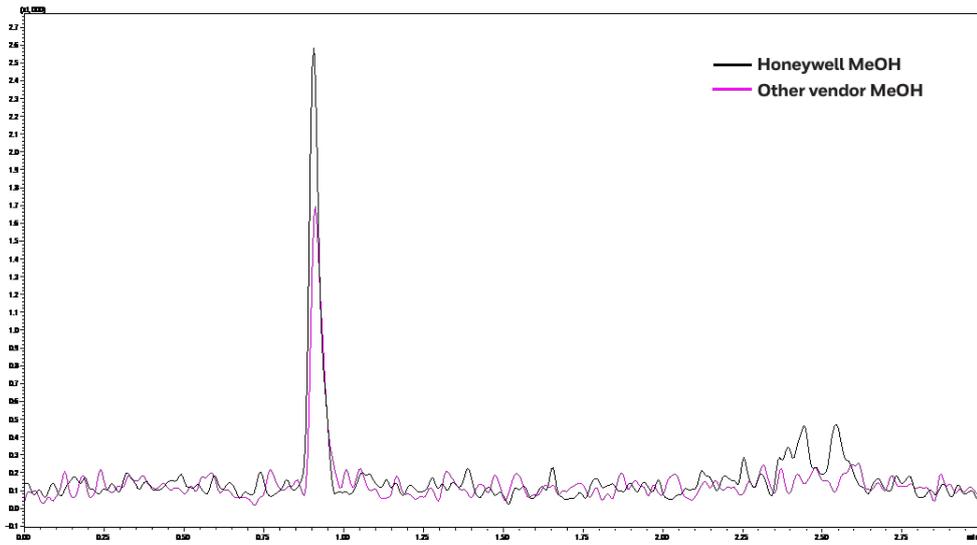


Fig. 12:  
SEM (MRM: 209>165.9 ion pair channel)

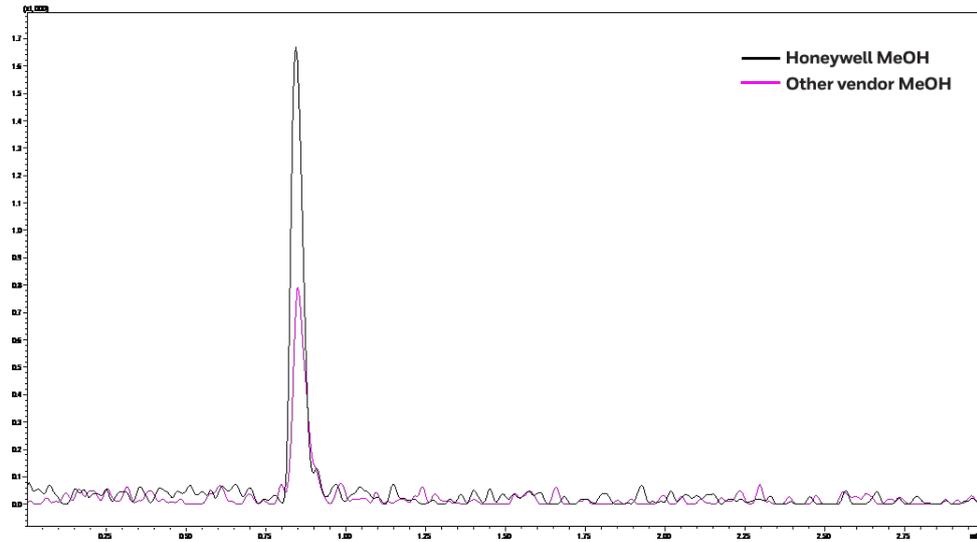


Fig. 13:  
AHD (MRM: 249>104 ion pair channel)

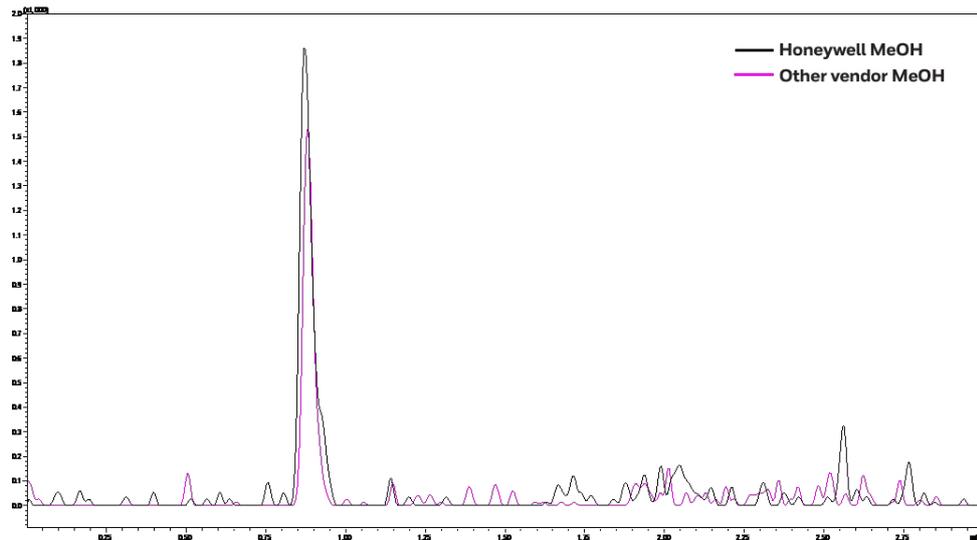


Fig. 14:  
AOZ (MRM: 236.1>103.8 ion pair channel)

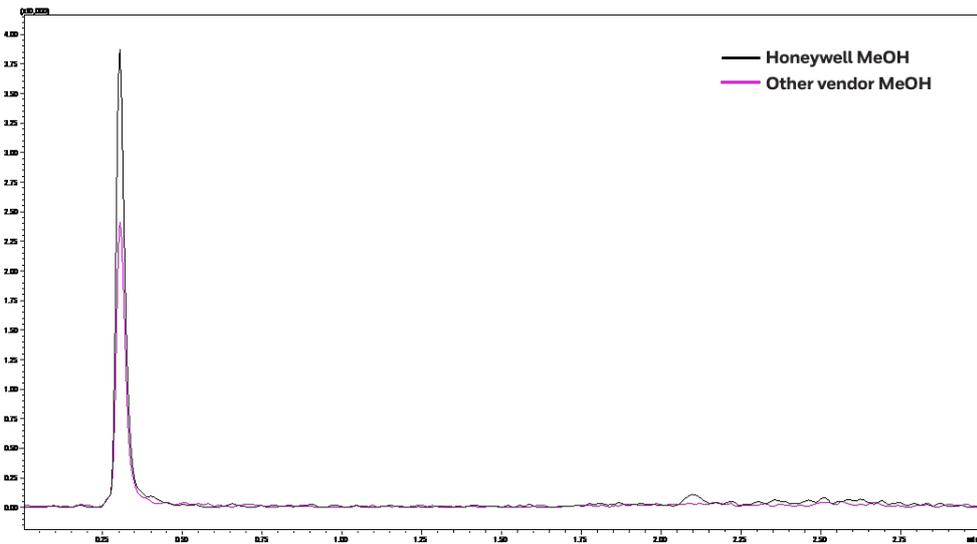


Fig. 15:  
AMOZ (MRM: 335.1>261.9 ion pair channel)

**Results:**

Background noise of the LC-MS Methanol (LC230-2.5) sample is slightly lower than that of the competitor's LC-MS methanol sample.

Honeywell's LC-MS Methanol also performed better in the Nitrofurans, including AHD and AMOZ. A higher S/N was observed in the very high sensitivity test.

For LC-MS-grade Acetonitrile, the Burdick & Jackson solvent demonstrated similar performance to the MS baseline and LC-MS ion pair signal/noise response. With LC-MS-grade Methanol, however, it provided better MS baseline performance, and for certain chemicals, it showed higher response when a very low detection limit was specified.

For example, on the Nitrofuran chemical AMOZ, the Honeywell product had 20% higher signal to noise (S/N) response when using LC230 MeOH than the leading competitor. Using AHD, there was >50% higher response. This is an important advantage for end-users with critical trace-detect requirements, as a better S/N ratio enables significantly lower detection limits. It is also a key factor for laboratories testing bio-samples.

In summary, third-party testing has demonstrated the consistency of the Honeywell product line, as well as its high quality over time.

**Conclusions**

**Higher Purity:** Honeywell solvents have a superior impurity profile compared with leading competitors in the marketplace. Through rigorous evaluations, these solvents have been shown to dramatically improve customers' analytical performance – assuring accurate and valid test results.

**Better Consistency:** Honeywell has confirmed that its solvents offer a unique level of purity for demanding LC-MS procedures. They have extremely low lot-to-lot variation as measured against other HPLC-grade products and demonstrate excellent overall consistency.

For instance, Chromasolv LC-MS has fewer peaks than competitive products, both on ACN and MeOH running solvents with Reserpin. The Chromasolv solution peaks at 609 Reserpin, with peaks at 195 and 397 fragments with Reserpin as a standard. All competitive products have an impurity profile for ACN and MeOH that can result in incorrect results from analysis.

Evaluation of DMSO Chromasolv GC-Headspace versus DMSO reagent-grade quality found a significant difference in the impurity profile – with the potential to affect lab results. Honeywell has verified that Chromasolv GC-Headspace has a much better impurity profile than the leading competitors, and as such, is the most suitable product for headspace analysis.

**Reduced Time and Cost:** Experience in labs worldwide has shown that Honeywell solvents can reduce the time and costs involved with having a chemist repeat testing to obtain the correct results. If the wrong solvent is used for analytical purposes, and renders erroneous results, it is impossible to prove the provenance of a manufacturer's product.

**Lower Risk:** An effective solvent solution can lessen the risk of a pharmaceutical or biotechnology company releasing a product to the marketplace that doesn't have the proper purity and identity.

*Chromasolv solvents are tested for LC-MS applications using the reserpine procedure to ensure very low levels of impurities for high-sensitivity spectra, and to maintain utmost system integrity.*

## About Honeywell Solvents

### Chromasolv™ Solvents

Honeywell Chromasolv LC-MS Acetonitrile and Methanol, and Chromasolv GC-Headspace solvents are part of the industry-leading Chromasolv™ brand. These solvents are produced and supplied by the original product innovator, Honeywell Research Chemicals.

The Chromasolv product family includes a line of high-purity, chromatography-grade solvents. There are four varieties of solvent in this series: HPLC and Ultra-High-Performance Liquid Chromatography (UHPLC) reagents for top-tier HPLC applications, HPLC Gradient for general-purpose clean up, GC-Headspace for gas chromatography procedures, and LC-MS solvents for liquid chromatography purposes. The purity profile of each of these products is tailored to its specific applications.

Honeywell Chromasolv™ solvents are used in a variety of analytical applications such as preparative separations utilizing LC-MS, HPLC, API purity quantitation, and pesticide analysis at trace levels. They have been custom-designed to meet the requirements of key analytical methods, and are suitable for use in a wide range of industries.



Honeywell Chromasolv LC-MS solvents were designed with low content of alkaline impurities, such as calcium, magnesium, potassium and sodium, which can interfere with analysis by forming artifacts with the analyte. The solvents ensure that specification requirements are met regardless of differences in the nature of the chemicals and their behavior. They can also be adapted to special chromatographic needs with high-purity additives.

Honeywell Chromasolv GC-Headspace solvents were developed specifically for the identification and quantification of residual solvents in pharmaceuticals using GC Headspace methods described in monographs from the United States Pharmacopeia (USP) and the European Pharmacopoeia (Ph. Eur.) and following the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines.

### Burdick & Jackson™ Solvents

Honeywell Burdick & Jackson solvents are intended for a wide range of high-purity applications, including liquid and gas chromatography, spectrophotometry, pesticide residue analysis, organic synthesis and combinatorial chemistry.

The solvents' exceptional lot-to-lot consistency means that standardized HPLC and GC-Headspace methods do not have to be continually recalibrated or adjusted when solvent lots are changed. Low trace impurities, low water content and low particulate levels also

*Burdick & Jackson GC-Headspace solvents have been designed to analyze low-volatile substances, especially with environmental relevance such as pesticides, preservatives or metabolites.*

help protect expensive columns and system components. This industry-leading consistency results in lower operating costs.

The Burdick & Jackson LC-MS product line is known for its premium quality. The solvents have been developed for extremely low impurity applications. LC-MS has become an important tool in biopharmaceutical applications as well as environmental analysis.

The production of Burdick & Jackson GCHeadspace solvents in large, homogenous batches utilizing state-of-the-art multi-step purification ensures high lot-to-lot consistency.

### **Advantages in Chromatography**

Honeywell solvents for LC-MS and HPLC-MS offer highly purified solutions for the most demanding applications. They undergo several distinct and relevant tests to ensure highest quality for reliable analysis.

For example, Chromasolv solvents are tested for LC-MS applications using the reserpine procedure to ensure very low levels of impurities (e.g., alkaline and metal ions, particles, non-volatile compounds) for high-sensitivity spectra, and to maintain utmost system integrity.

Burdick & Jackson LC-MS solvents meet the requirements of the latest generation of instrumentation regarding impurities (e.g., trace metals and other contaminants). Through the low content of particles and fluorescent impurities as well as the high UV transmittance of these solvents, exact and reproducible results in LC-MS applications are guaranteed.

Accurate and reliable GC-Headspace analysis requires the use of very pure solvents with extremely low concentrations of the defined residual solvents. Honeywell Chromasolv GC-Headspace solvents ensure this level of purity through special, state-of-the-art production and application tests, thus they can consistently deliver the reliability, accuracy and analytical safety users need.

Burdick & Jackson GC-Headspace solvents have been designed to analyze low-volatile substances, especially with environmental relevance such as pesticides, preservatives or metabolites. Each lot is characterized via high resolution capillary GC with Electron Capture Detection (ECD), Phosphorous and Nitrogen Selective Detector (PND) or GC-ECD/PND mode.





# Honeywell

**In the United States:**

For customer service, call 1-800-766-7000

To fax an order, use 1-800-926-1166

To order online: [fishersci.com](http://fishersci.com)

**In Canada:**

For customer service, call 1-800-234-7437

To fax an order, use 1-800-463-2996

To order online: [fishersci.ca](http://fishersci.ca)

