Agilent's GC Analyzer Solutions: Introduction to the Controlled Substances Analyzer

Get your laboratory on the Analytical ***"FAST TRACK"***

December 2013

Today's Challenges
Expecting More from Less

Business Challenges

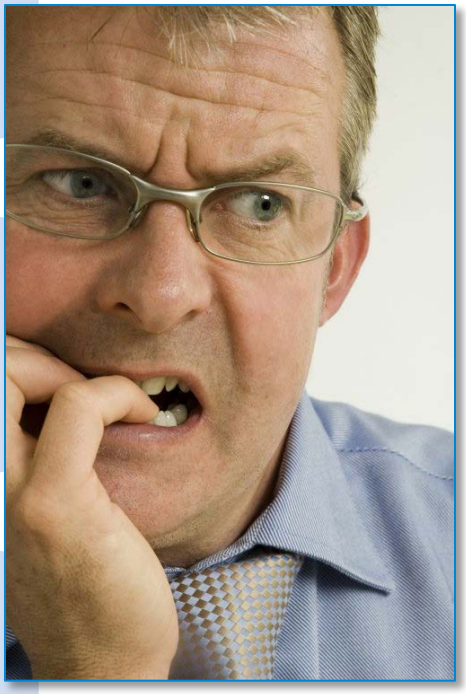
- Increasing cost of ownership
- Trace analysis in complex matrices

Resource Allocation

- Less time for method development
- Limited technical experience

Optimizing Efficiency

- Demands for higher throughput
- Quicker return on capital investment

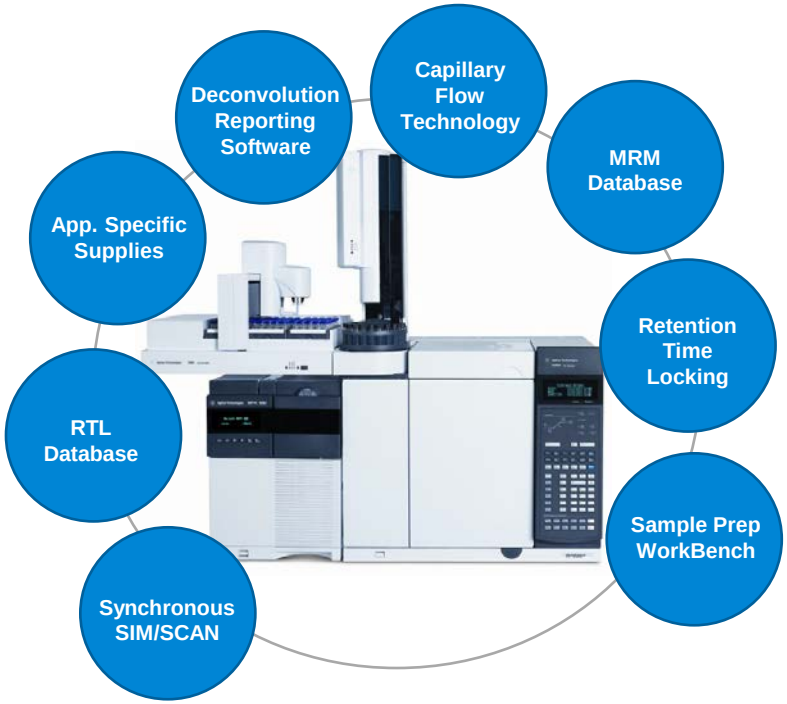


Analyzer Portfolio

Resolving the Your Search for Value

What is an “Analyzer”?

An Analyzer is a factory-configured GC or GC/MSD system constructed, tuned and tested for the application prior to delivery to the customer’s laboratory.



Pre-Configured Analyzers

Increasing the Value Proposition

Common Components

Std. HW, SW

w/o Analyzer

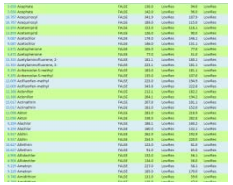
App. optimized consumables

Customer Configured

Factory Configured with Chemical Testing Field Verification

System with application setup

Familiarization



Application report

Analyzer Solution

Focus your team on analyses; not method development!

Analytical Requirements

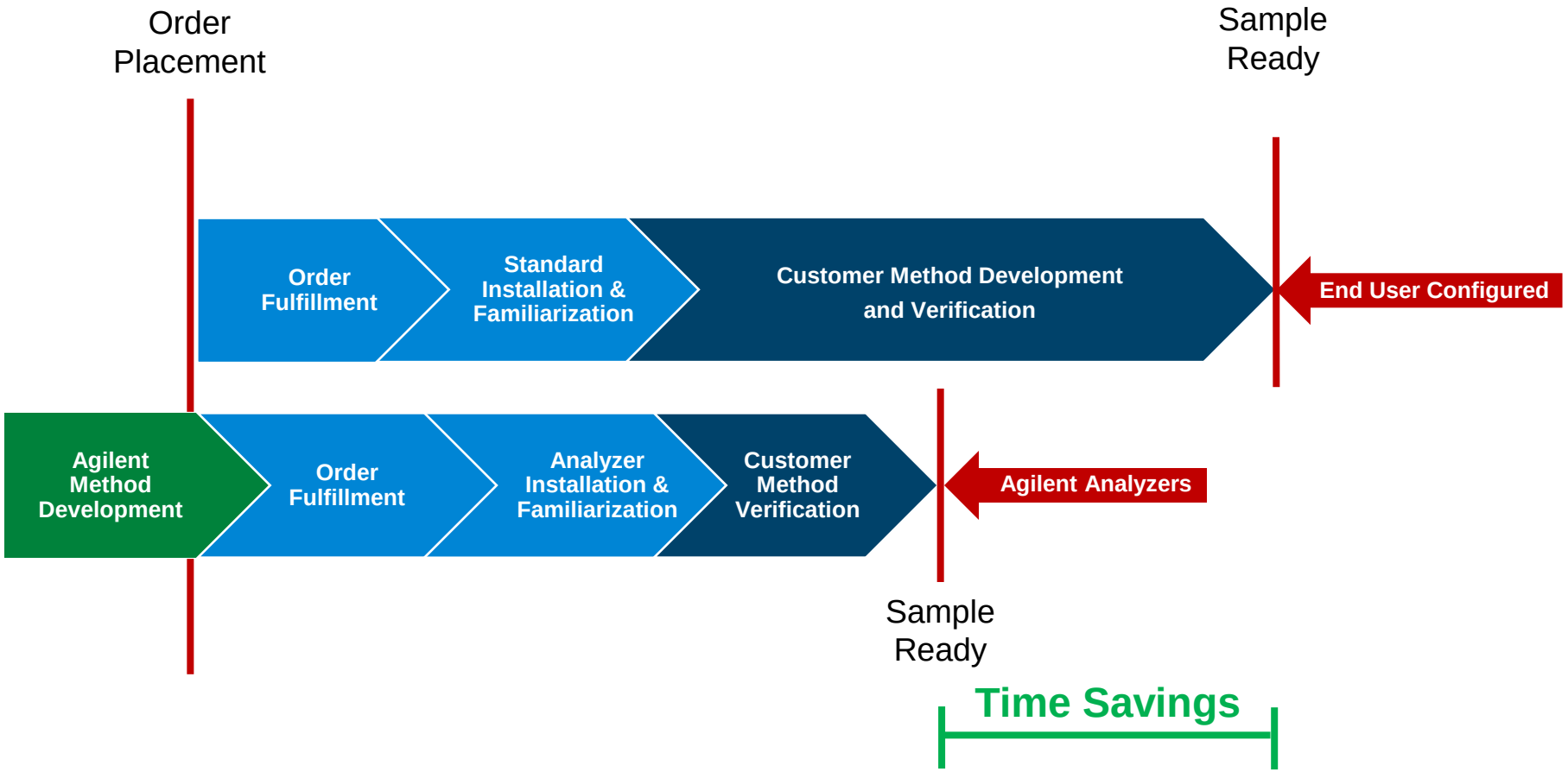
Customer's Responsibility

Agilent Provides

Customer's Responsibility

Intrinsic Value of Analyzers and Application Kits

Reduce the time required for system deployment



…Faster Application Startup with a Guaranteed Method

Controlled Substances Analyzer

… IDENTIFY Drugs of Abuse Targets with Confidence!

Developed in Collaboration with:

Sarah Keeling and Fran Diamond
NMS Labs, Willow Grove, PA

Analysis of Controlled Substances: Challenges

Routine Seized Drug Analysis

Multiple sample types:

- Pharmaceuticals. examples: oxycodone, hydrocodone
- Illicit drugs. examples: heroin, cocaine
- Botanical materials. examples: marijuana, synthetic marijuana (Spice)
- Syringe residues. examples: heroin, methamphetamine
- Charred pipe residues. examples: crack cocaine, hashish

Analyte list constantly growing

- Synthetic cannabinoids. examples: JWH-018, PB-22
- Designer stimulants. examples: MDPV, BZP
- Novel psychoactive substances

Analysis of Controlled Substances: Challenges

Routine Seized Drug Analysis

Laboratory Needs:

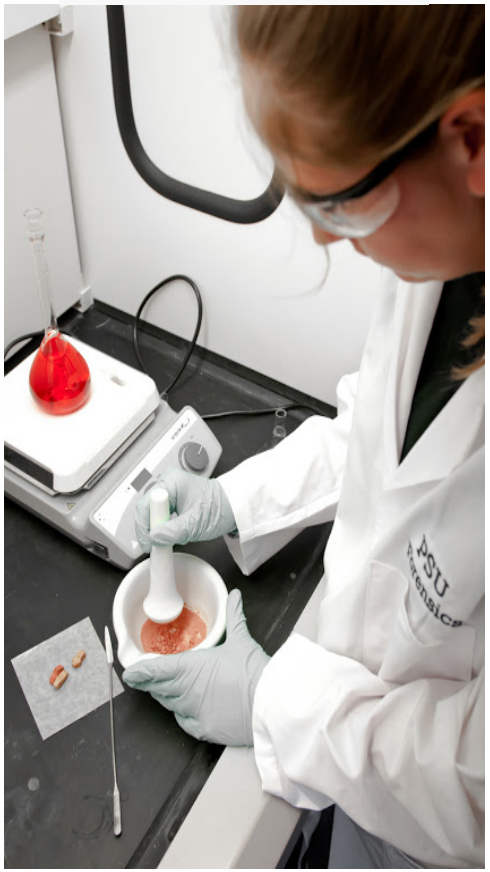
- Analyze complex mixtures by GC/MS
- Efficiency of testing
- Speed of analysis
- High quality results
- Time efficient data processing
- Simple sample prep

Analytical Challenges

- Samples of varying nature
- Identify closely related analytes: isomers, analogs, etc.
- Variable concentrations: column overload to trace concentrations
- Complex matrix: cutting agents, adulterants, non-volatile compounds

Current Situation

Routine Seized Drug Analysis



Expanding list of new drug targets

Long Cycle Times (23.0 Min)

Carry-over interferences between samples

PBM Based Searching

Manual Data Review

- Manual Spectrum subtraction
- Manual Baseline Review

Methods vary from lab-to-lab

- In place validation per lab SOP
- Limited standardization of method

Inconsistent spectral libraries and retention times

Cost of Analysis with Helium Carrier

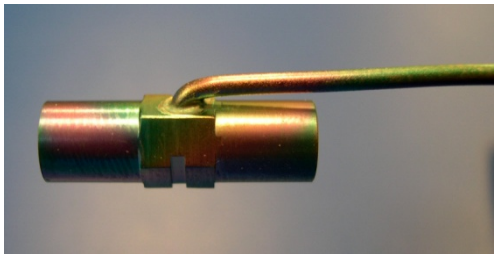
Wanted to Create a New Configuration

Rapid Identification of Seized Drug Samples

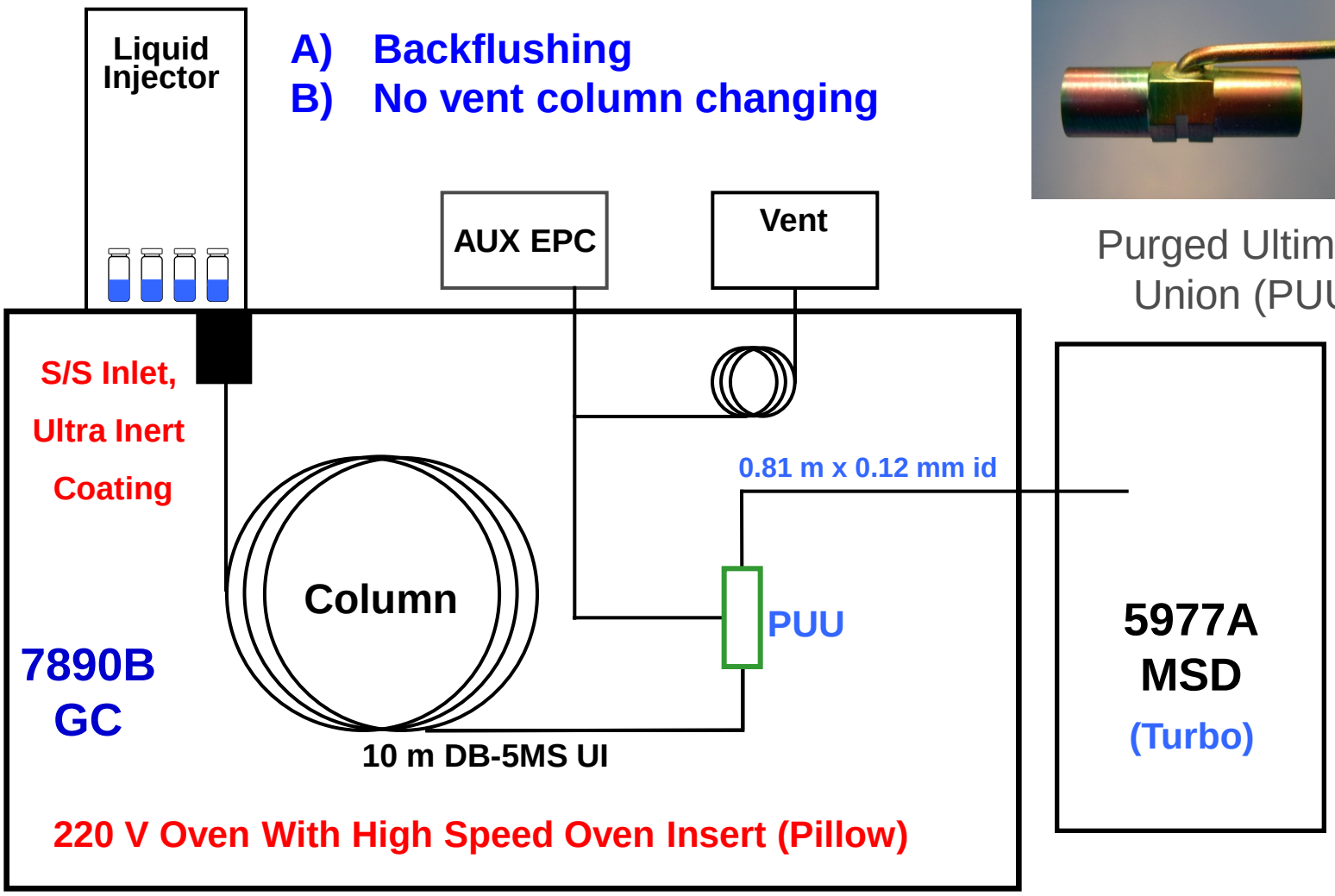
- **Reduce operating expense:** Use hydrogen carrier gas
- **High speed analysis:** from 23.0 to 13.5 min run-to-run for analysis to Vardenafil
- **Backflushing:** Minimize column trimming and eliminate sample carry-over
- **Retention Time Locking (RTL):** Precise RT matching column-to-column, instrument-to-instrument, and lab-to-lab
- **Deconvolution Reporting Software:** Rapid reliable compound identification
- **New 460 compound database:** Comprehensive list of controlled substances including new psycho active substances (synthetic cannabinoid, and “Bath Salt” compounds)
- **Ultra Inert Flow Path:** **Inlet to Detector** Minimizes sample decomposition

Configuration of Controlled Substance Analyzer

Post column Capillary Flow Technology (PUU) device provides:



Purged Ultimate Union (PUU)



Method Parameters for Hydrogen Carrier

Controlled Substance Analyzer

Ramp	'C/min	'C	Hold min
Initial		50	1
Ramp 1	60	325	4
Runtime	9.58 min		
Backflush	325 'C/min for 1.0 min		

Inlet	Split/Splitless
Temp	265 'C
Mode	Pulsed Splitless, Constant Flow
Flow	1.4 (adj to lock)
Pulse Press	11 psi
Pulse time	0.3 min
Purge time	1 min
Purge Flow	50 mL/min

Column	DB-5MSUI part # (100-2000)
	10m x 0.25 mm id x 0.25 um film
Outlet Pressure	Programmed for constant MSD restrictor flow (2.81 psig initial)

Injection volume 1 uL
RT locked to Proadifen at 5.039 min

MSD	Agilent 5977
Solvent Delay	2.3 min
Acquisition Mode	Scan
Scan Range	40 to 570
Threshold	0
Sampling	2
TID	ON
Quad Temp	200 'C
Source Temp	300 'C
Transfer Line	300 'C
Tune	Atune, Gain Normalized 1X

Backflush Device	Purged Ultimate Union with overpressure vent
MSD Restictor	0.81 m x 0.12 mm id Inert fused silica tubing
Restrictor Flow	2.0 mL/min Constant Flow
Backflush Time	1.0 min
Backflush Temp	325
Backflush Press	40

Controlled Substances Analyzer

… Development Challenges using
Hydrogen Carrier Gas

Incompatibility of O-Rings with H2 Carrier

Restek Publication

SeparationScience
PREMIER LEARNING FOR ANALYTICAL CHEMISTS

North America
Volume 5, Issue 5
2013

Identification of Allergens in Common Snack foods using Transportable Single-quadrupole GC–MS

Ghost Peaks in Gas Chromatography Part 2: The Injection Port
Jaap de Zeeuw

Identification of Flavour and Fragrance Allergens in Common Snack foods using Transportable Single-quadrupole GC–MS
Suli Zhao

Comparison of Regulated Methods Using Ion Chromatography for Bromate Analysis in Drinking Water
Richard F. Jack

Selective Therapeutic Monitoring of Drugs and Their Pharmacologically Active Metabolites by Liquid Chromatography
Gellért Karvaly, Judit Szaniszló and József Fürész

Analysis of Beer by Comprehensive 2D-LC

Transition metals in feedwater using post-column reaction and subsequent UV/VIS detection

High-performance screening of pollutants in water usingGC×GC/TOF MS

Automated Extraction and GC/MS Determination of Phthalates in Consumer Products

Quantitation and Identification of Pharmaceuticals and Personal Care Products (PPCP) in Environmental Samples using Advanced TripleTOF® MS/MS Technology
Click here to view more>>

Incompatibility of O-Rings with H2 Carrier

Restek Publication

Figure 7

Figure 7: Deformation of "O"-ring when used with hydrogen as the carrier gas. Helium did not show this effect.

"O" – Ring Contamination

Using an Agilent gas chromatograph, the injection port also contains a "O"-ring. This ring prevents the sample from re-entering the liner after injection. The 'O' ring is a challenge as it is continuously at high temperature and it is a polymeric material that has to make a good seal. We received customer input that shared issues with deformed rings in split/splitless injection systems (see Figure 7) which caused injection issues. In this case the "O"-ring deformed and hardened using hydrogen as the carrier gas. It did not happen when helium was used.

http://www.sepscience.com/docs/Bespoke/Editions/SepSci/Sepsci0513na.pdf?utm_source=iContact&utm_medium=email&utm_campaign=eLearning%20Newsletter%20-%20North%20America&utm_content=

Incompatibility of O-Rings with H2 Carrier

Restek Publication

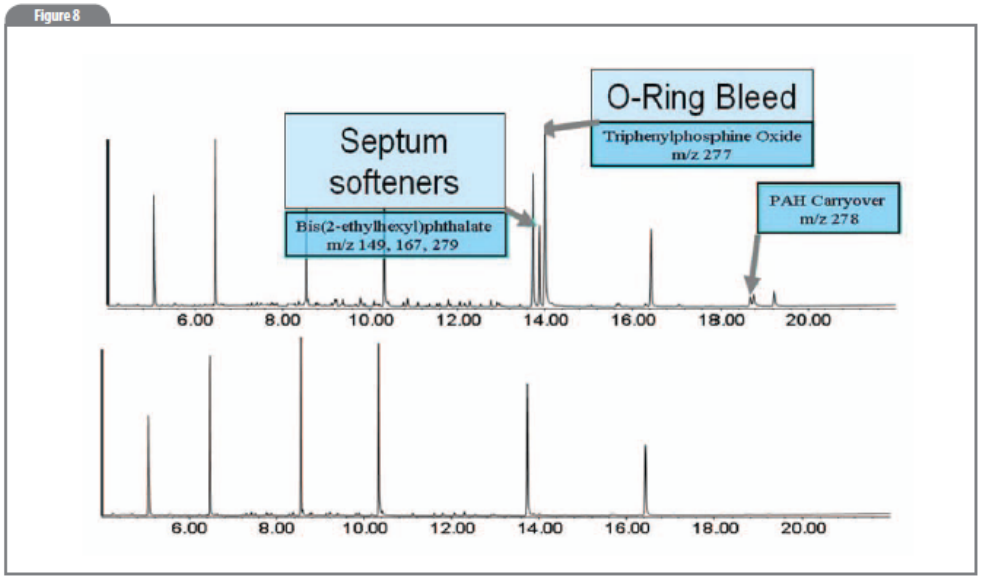


Figure 8: Ghost peaks produced by a dirty injection port. Showing peaks for triphenyl phosphine oxide(*m/z* 279) , phthalates (*m/z* 149, 167 and 277) and PAH (*m/z* 278). Full story, see ref. [4].

The "O"-ring itself can also produce ghost peaks. Figure 8 shows a peak that typically shows up as a "ghost-peak" generated by the "O"-ring. The component, triphenyl phosphine oxide, will accumulate on the column when it's set at low temperature. It has a *m/z* of 266. The same chromatogram also shows phthalate peaks that are used as septum-softeners.

It is important to make sure that "O"-rings are used with sufficient thermal stability. There are many brands of "O"-rings and problems can result — not only from the formation of ghost peaks but also from the challenge sometimes of getting liners out of injection systems, when maintenance is due.

http://www.sepscience.com/docs/Bespoke/Editions/SepSci/Sepsci0513na.pdf?utm_source=iContact&utm_medium=email&utm_campaign=eLearning%20Newsletter%20-%20North%20America&utm_content=

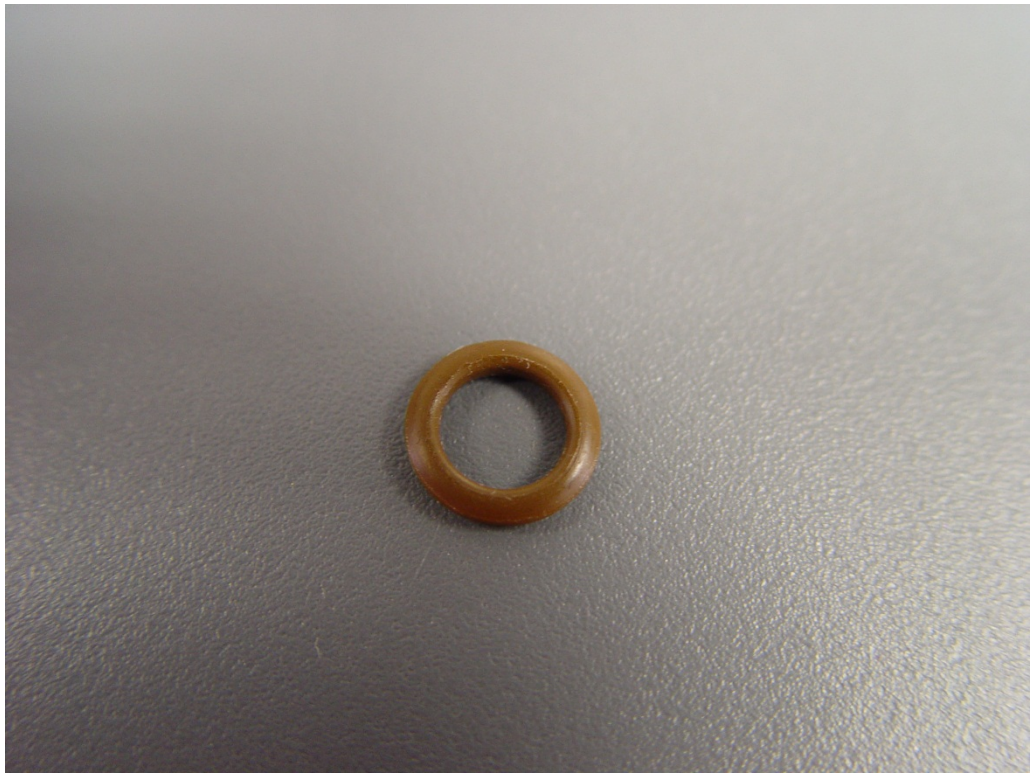
System Development: O-Ring Issues

H_2 Carrier for Controlled Substances

- Cotton swabs used to clean injection port metal.
- Swabs with dirt used to clean top of the weldment assembly.

System Development: O-Ring Issues

H_2 Carrier for Controlled Substances

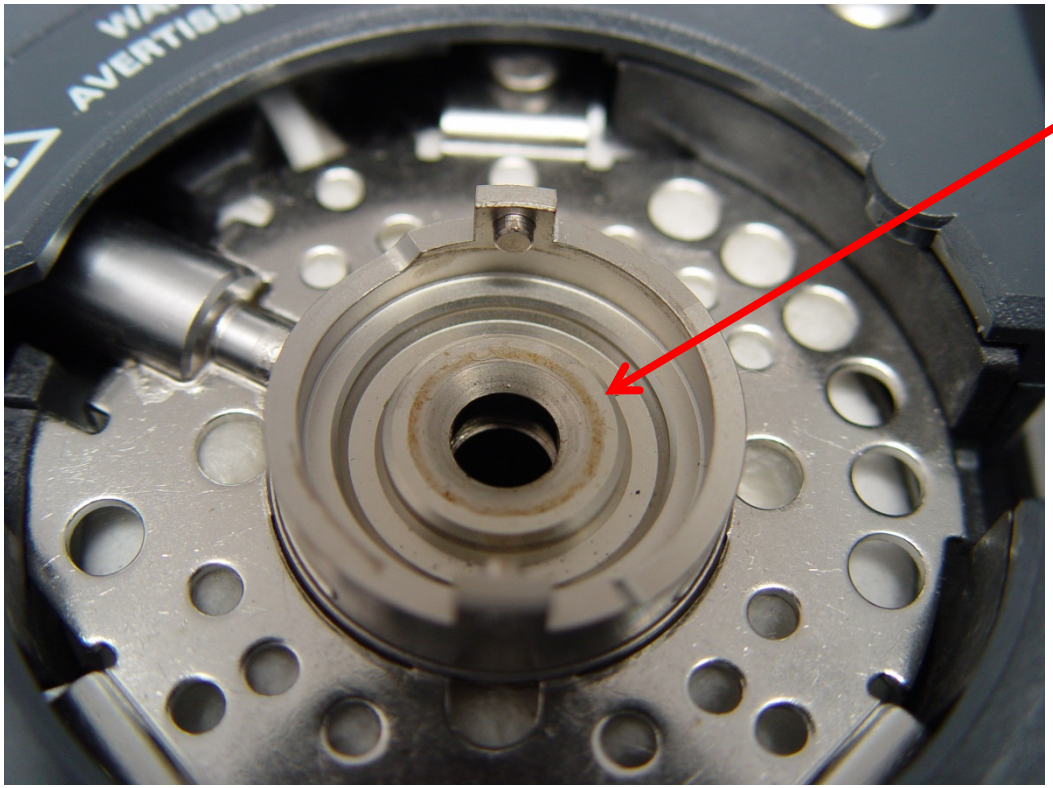


O-ring suspected of leaving a deposit (breakdown product) around the top of the weldment

Figure 7: Deformation of "O"-ring when used with hydrogen as the carrier gas. Helium did not show this effect.

System Development: O-Ring Issues

H_2 Carrier for Controlled Substances



Residue on top of inlet weldment

Problem Resolution:

- Convert to 5190-2293 Liner, UI, splitless, single taper, glasswool with o-ring
- 5188-5365 Liner O-Ring, Non-Stick 10PK
- 5190-6145 Gold Seal, Ultra Inert, w/Washer, 10/PK
- Provided UI Inlet Weldment

New Inert Flow Path for the 7890B GC / 5977A MSD

Reliability, Durability, Speed and Ease of Use

From inlet-to-detector … **COMPLETE DEACTIVATION** of sample path!

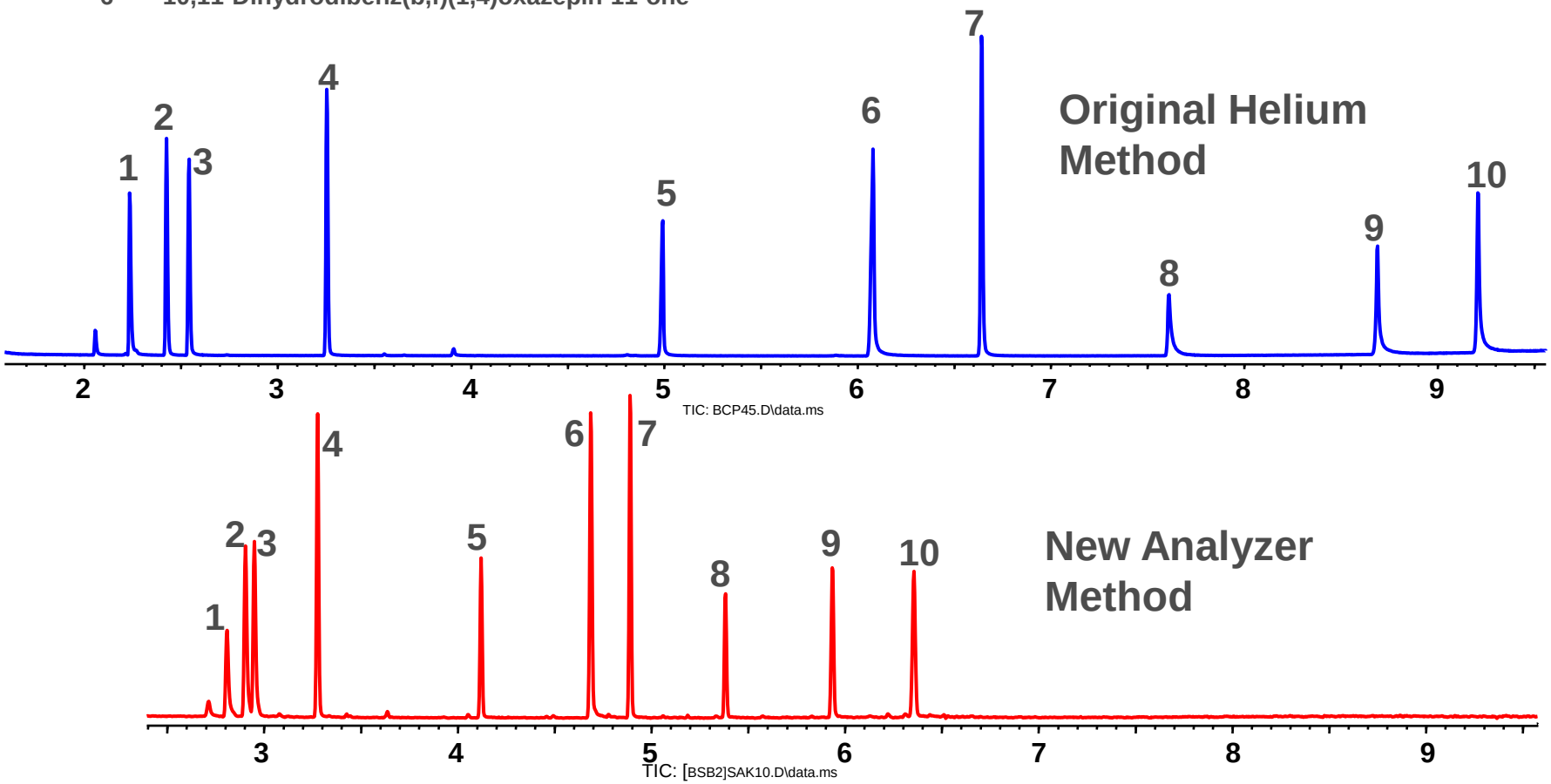
Controlled Substances Analyzer

Analytical Performance

Test Mix Chromatography

Original Helium Method and New Analyzer Method

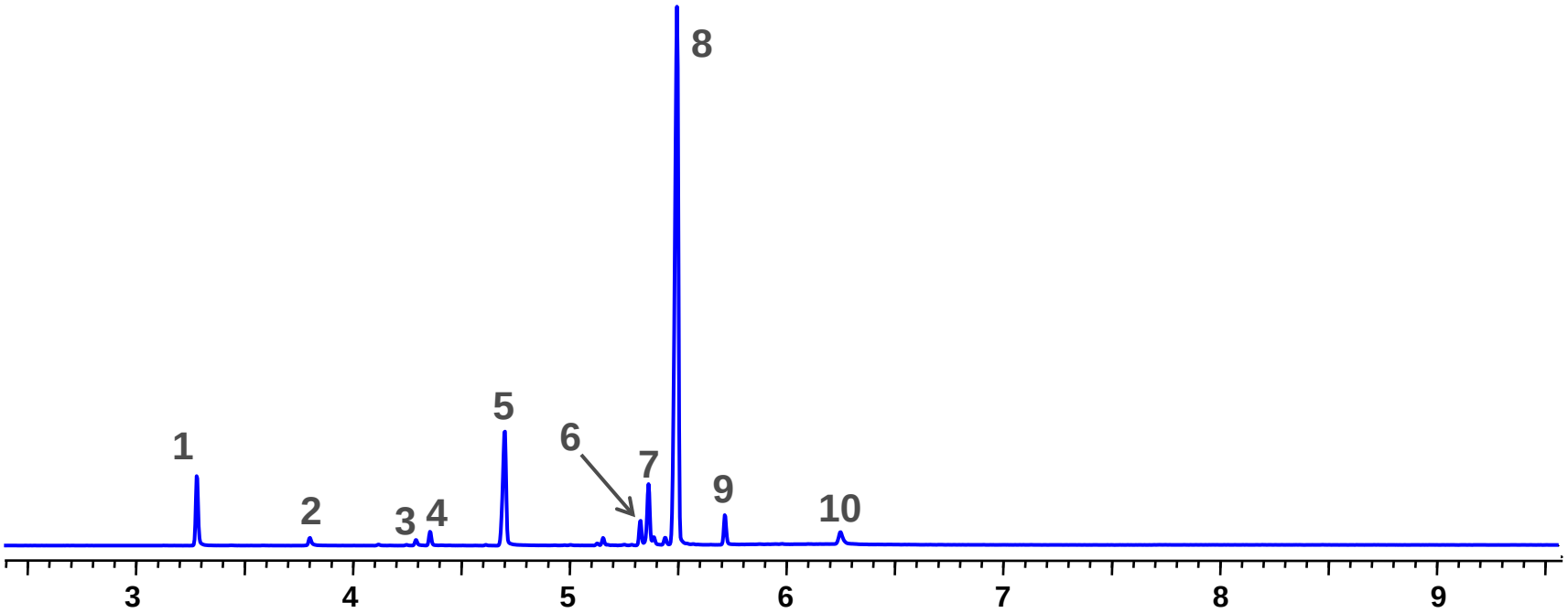
1	Amphetamine
2	Phentermine
3	Methamphetamine
4	N-Propylamphetamine
5	Pentobarbital
6	10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one
7	Cocaine
8	Oxycodone
9	Alprazolam
10	Strychnine



Example: Street Heroin

Controlled Substances Analyzer

1 N-Propylamphetamine (ISTD)
2 Benzocaine
3 Caffeine
4 Lidocaine
5 10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one (ISTD)
6 Acetylcodeine
7 6-Monoacetylmorphine
8 Heroin
9 Papaverine
10 Noscapine



DRS Report for Heroin Sample

Controlled Substances Analyzer

MSD Deconvolution Report
Sample Name: ALA33
Data File: D:\MassHunter\GCMS\1\data\Heroin_Sample.D
Date/Time: 15:14 Wednesday, Oct 2 2013

Adjacent Peak Subtraction = 1
Resolution = High
Sensitivity = Medium
Shape Requirements = Medium

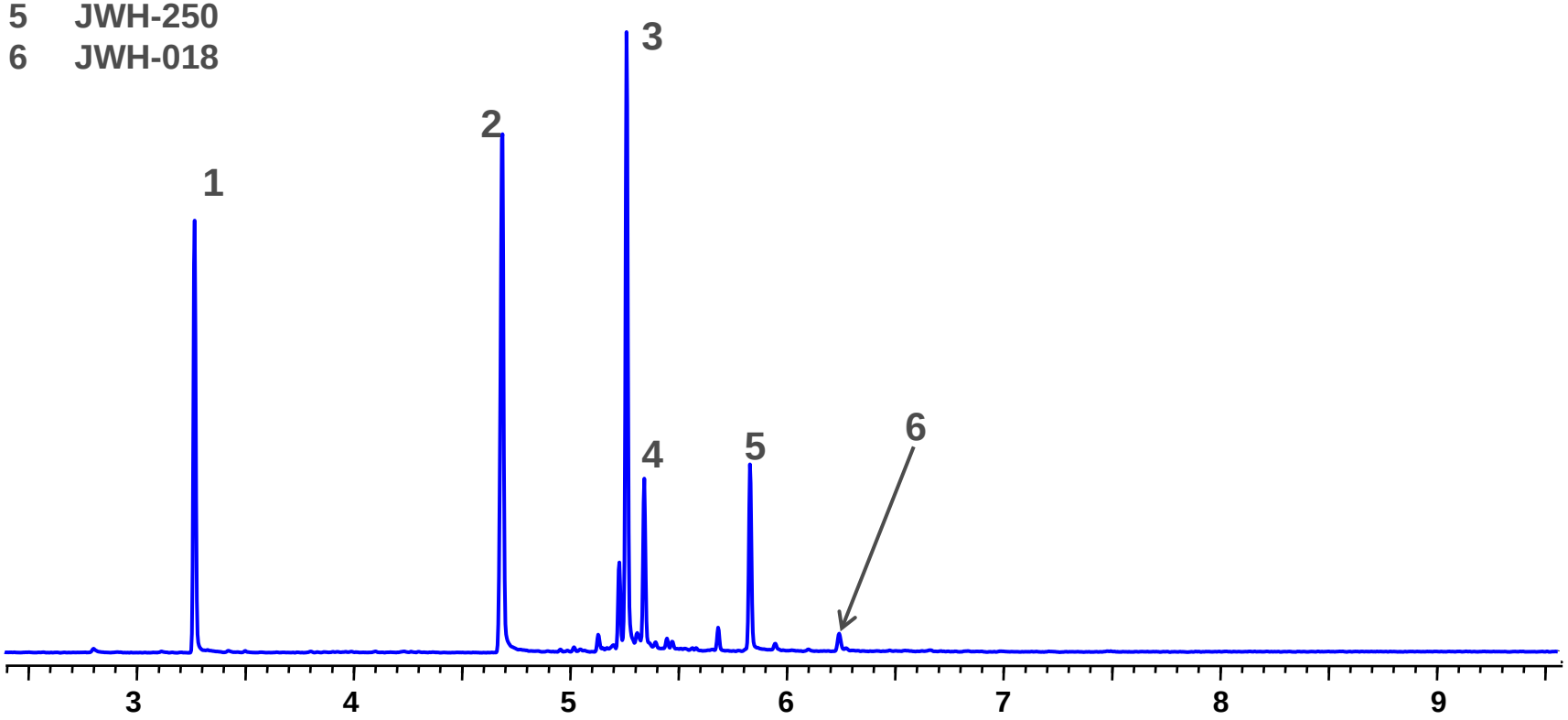
The NIST library was searched for the components that were found in the AMDIS target library.

			Amount (ng)		AMDIS		NIST	
Retention Time (R.T.)	Cas #	Compound Name	Chemstation	AMDIS	Match	R.T. Diff	Reverse Match	Hit Number
3.285	51799327	N-Propylamphetamine			99	-0.4	90	1
3.8059	94097	Benzocaine			100	-0.5	95	2
4.2958	58082	Caffeine			100	-0.4	91	1
4.3613	137586	Lidocaine			99	-0.4	92	1
4.7037	3158858	10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one			97	0.2	93	1
5.3308	6703271	Acetylcodeine			100	-0.2	95	1
5.3687	2784738	6-Monoacetylmorphine			100	0.2	95	1
5.4999	561273	Heroin			100	0.9	97	1
5.7215	58742	Papaverine			98	-0.2	94	1
6.2532	128621	Noscapine			92	-0.5	90	1

Example: Marijuana Sample

Controlled Substances Analyzer

1 N-Propylamphetamine (ISTD)
2 10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one (ISTD)
3 Delta-9-tetrahydrocannabinol (THC)
4 Cannabinol
5 JWH-250
6 JWH-018



DRS Report for Marijuana Sample

Controlled Substances Analyzer

MSD Deconvolution Report
Sample Name: KCJ06k
Data File: D:\MassHunter\GCMS\1\data\Agilent helium to hydrogen\Case 07.D
Date/Time: 15:17 Friday, Nov 1 2013

Adjacent Peak Subtraction = 1
Resolution = High
Sensitivity = Medium
Shape Requirements = Medium

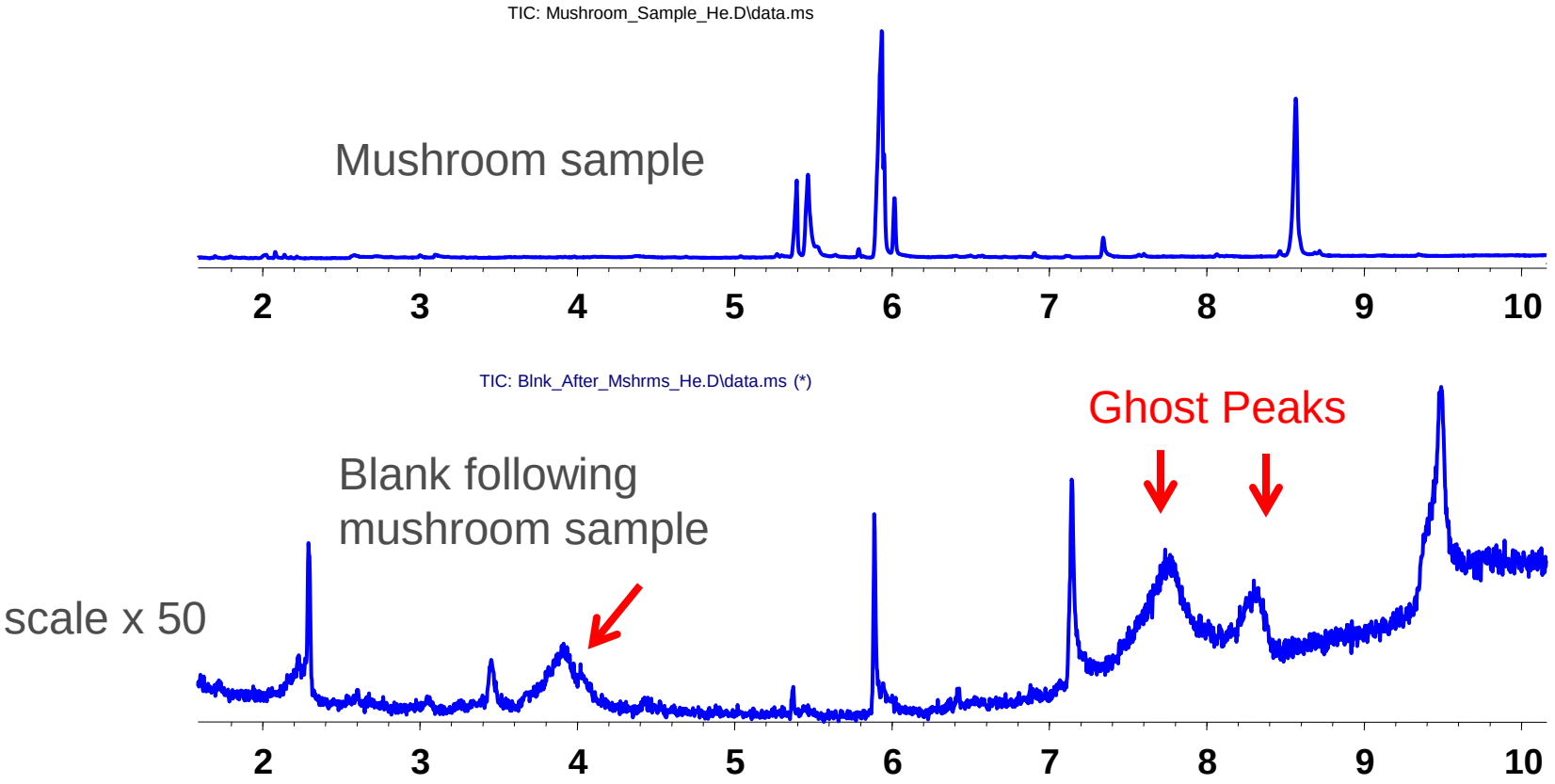
The NIST library was searched for the components that were found in the AMDIS target library.

			Amount (ng)		AMDIS		NIST	
Retention Time (R.T.)	Cas #	Compound Name	Chemstation	AMDIS	Match	R.T. Diff (sec)	Reverse Match	Hit Num.
3.2713	51799327	N-Propylamphetamine			100	-1.2	89	1
4.6926	3158858	10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one			98	-0.4	93	1
5.2699	1972083	Delta-9-tetrahydrocannabinol (THC)			100	-0.1	95	1
5.3508	521357	Cannabinol			100	0	93	1
5.8397	864445432	JWH-250			99	-0.8	89	1
6.2516	209414073	JWH-018			96	-1	89	1

Synthetic Cannabinoids

Analysis of Mushroom Drug Sample

Original Helium Method



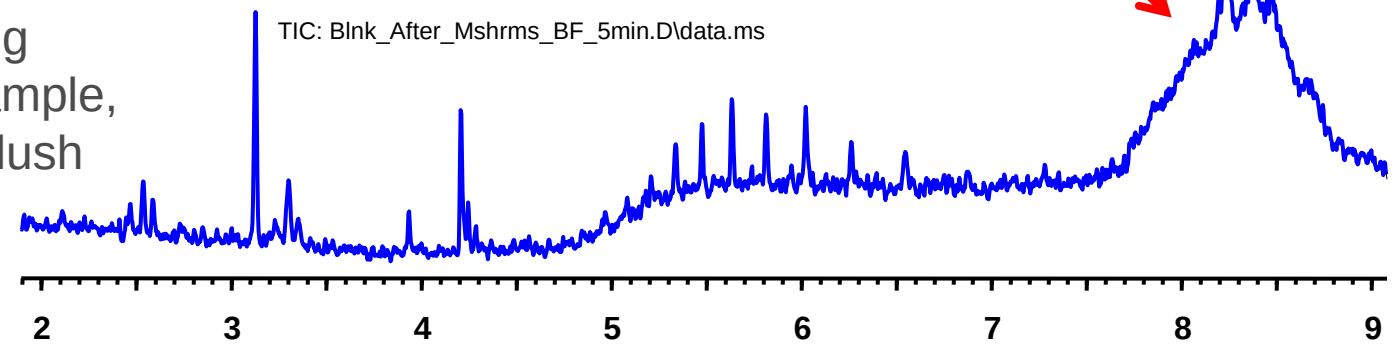
Heavy matrix compounds can carry over to following analysis, necessitating very long post run bake out

Analysis of Blank Following Mushroom Sample

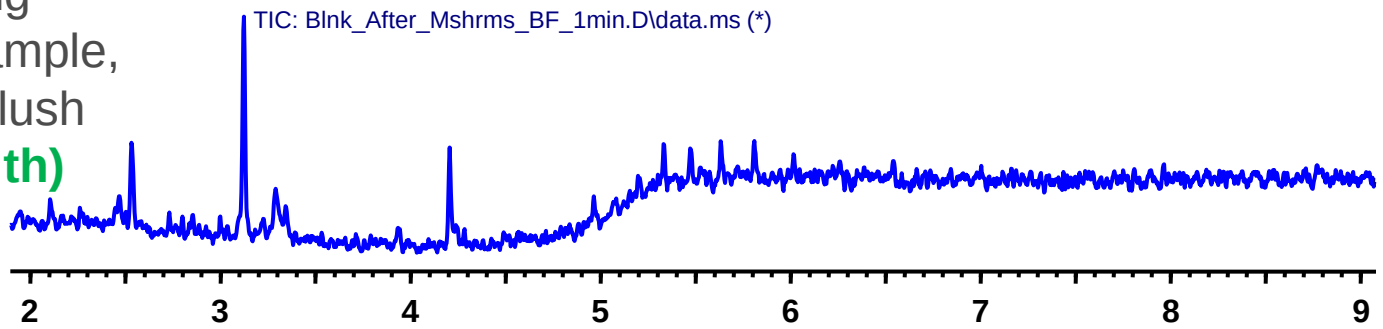
H_2 Carrier Instrument

Ghost Peaks

Blank following mushroom sample, 0.5 min backflush **(too short)**



Blank following mushroom sample, 1.0 min backflush **(correct length)**

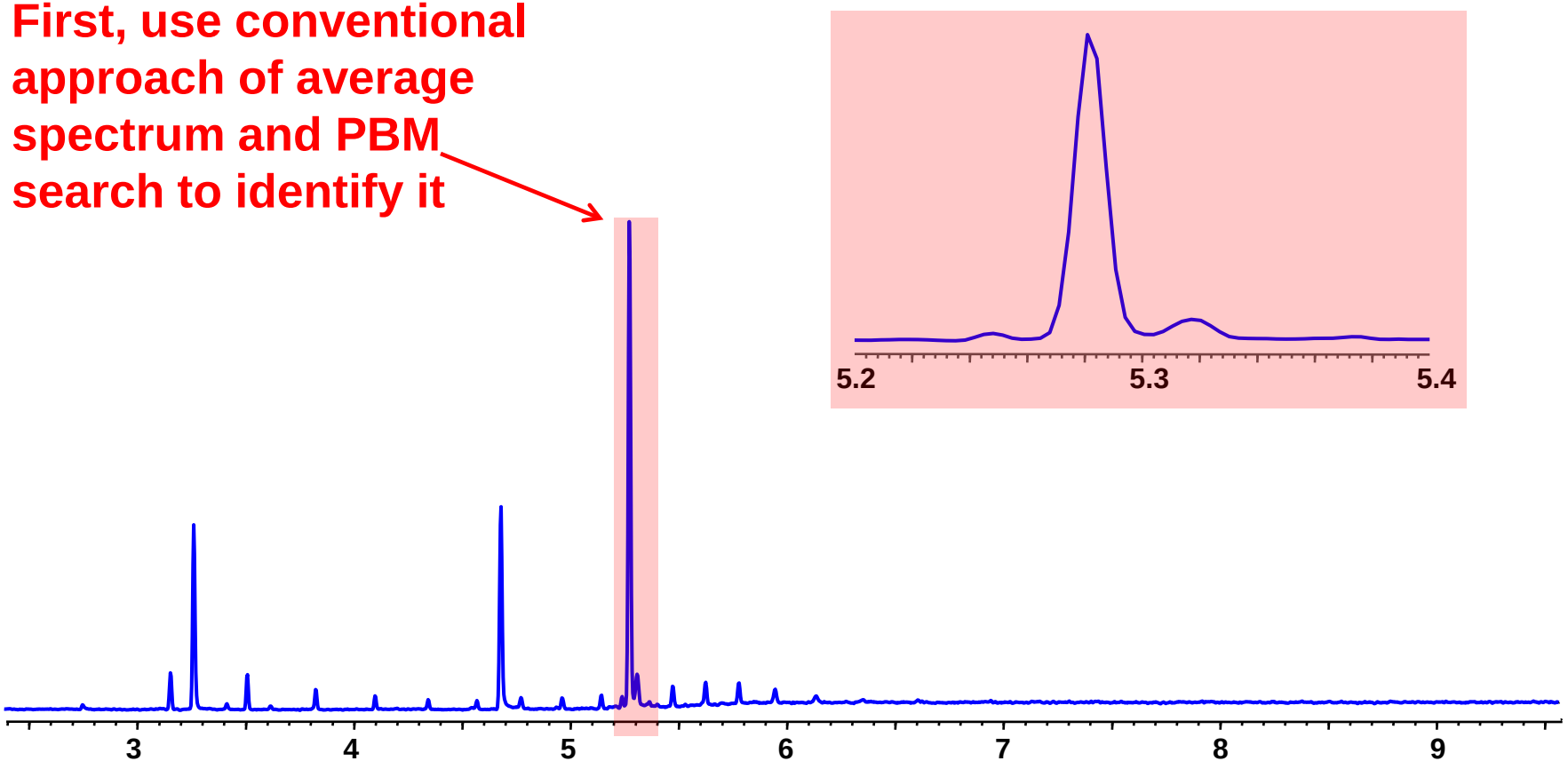


Using a 1.0 minute backflush prevents heavy matrix compounds from carrying over to next run

Deconvolution Training Standard

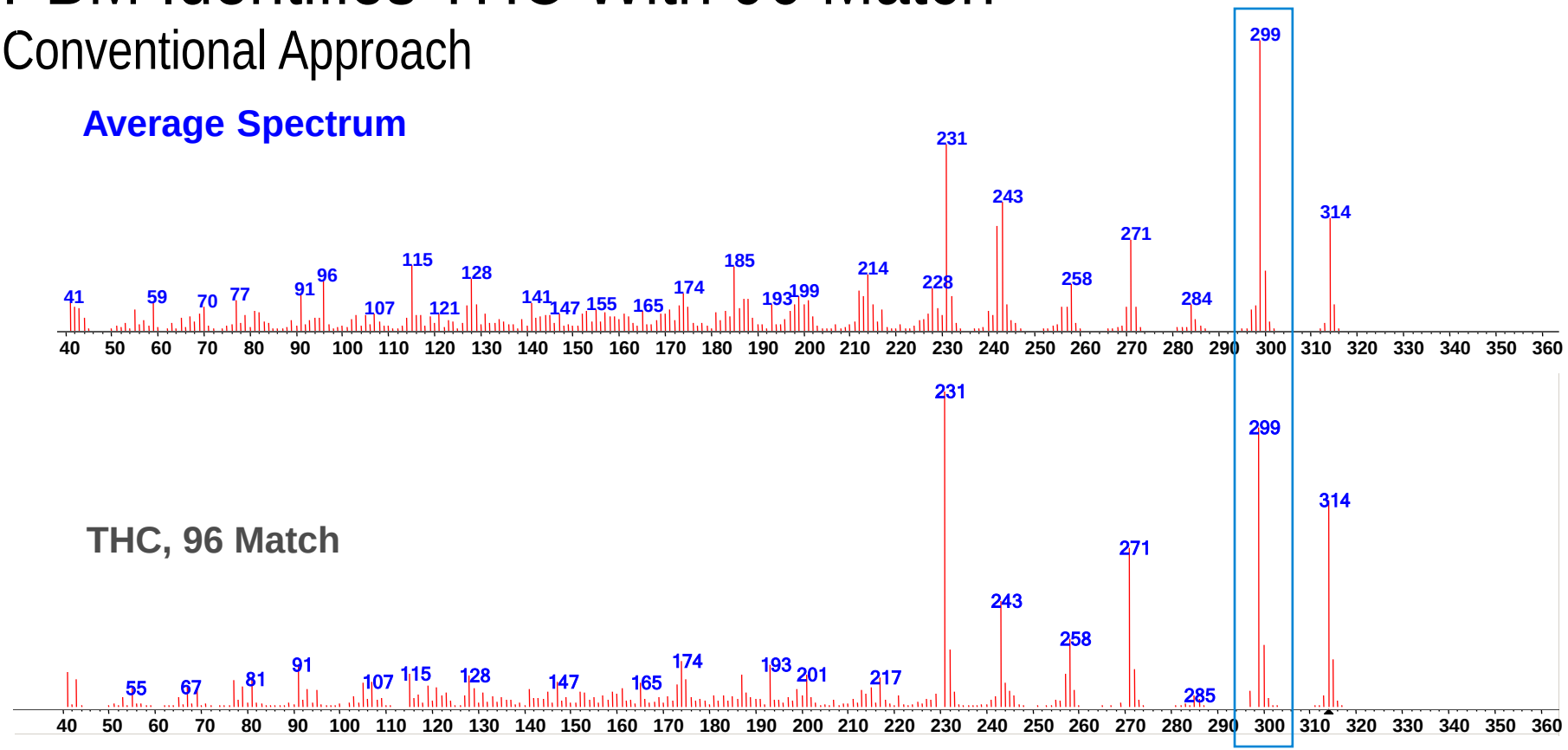
Deconvolution Reporting Software (DRS) Familiarization

What is this peak?
First, use conventional approach of average spectrum and PBM search to identify it

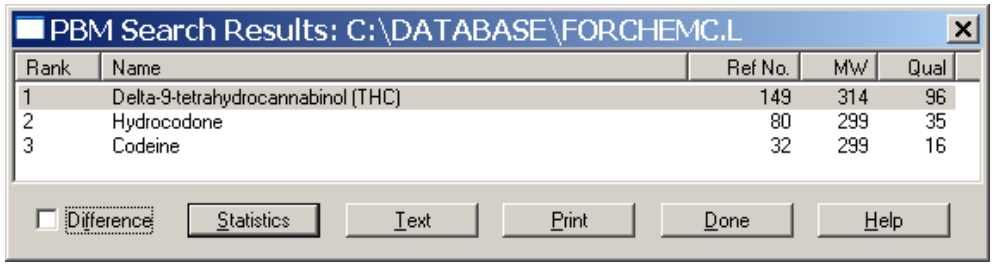


PBM Identifies THC With 96 Match

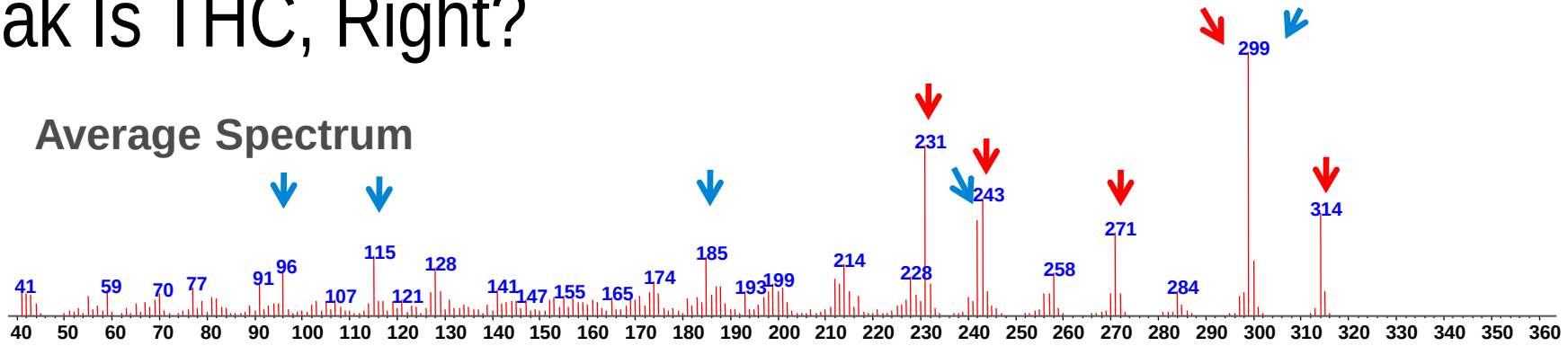
Conventional Approach

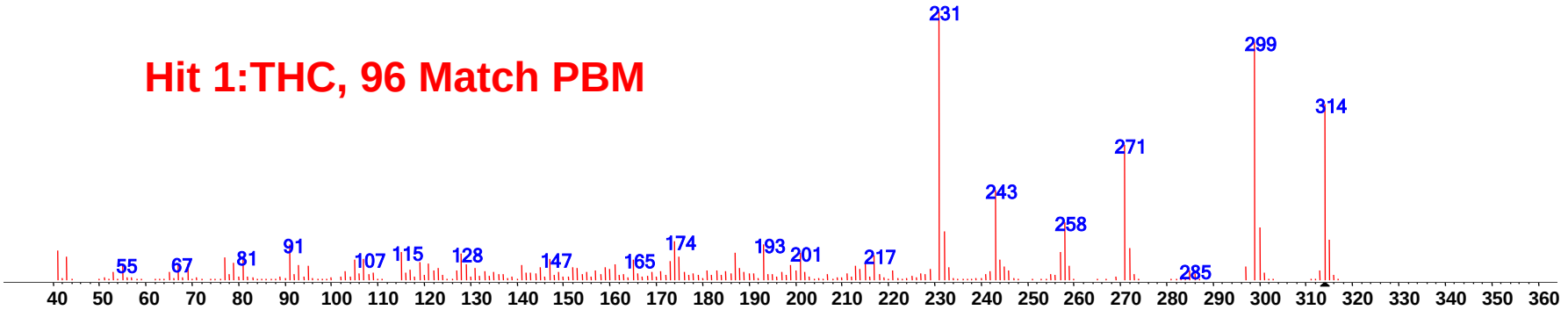


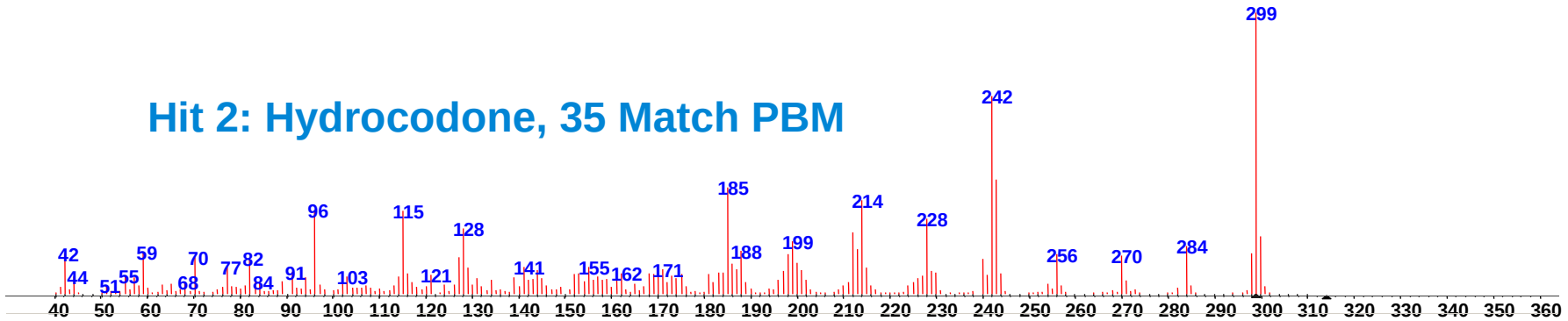
- First hit is THC with 96 PBM match.
- Second hit is hydrocodone with only 35 match



Peak Is THC, Right?

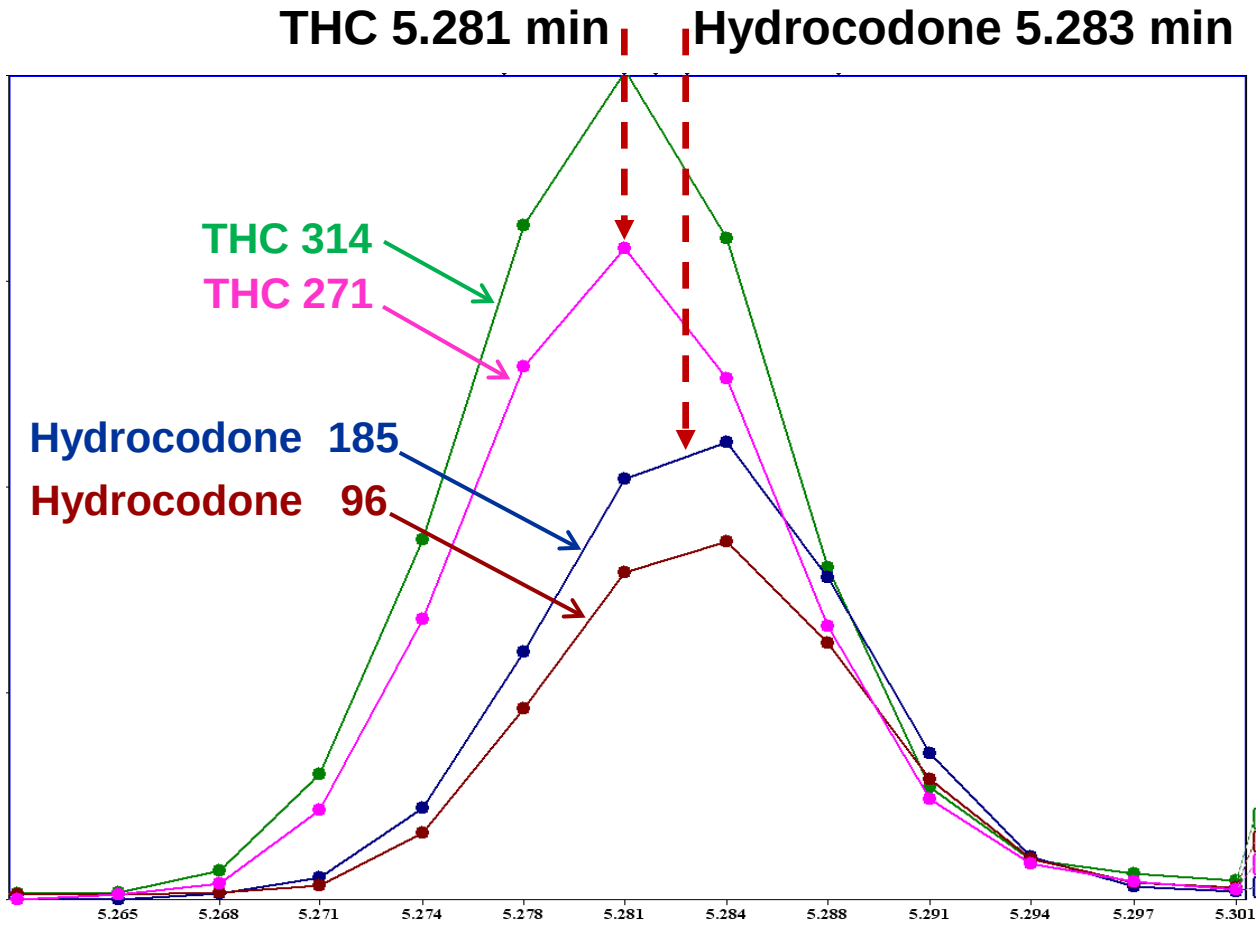






Overlap of THC and Hydrocodone

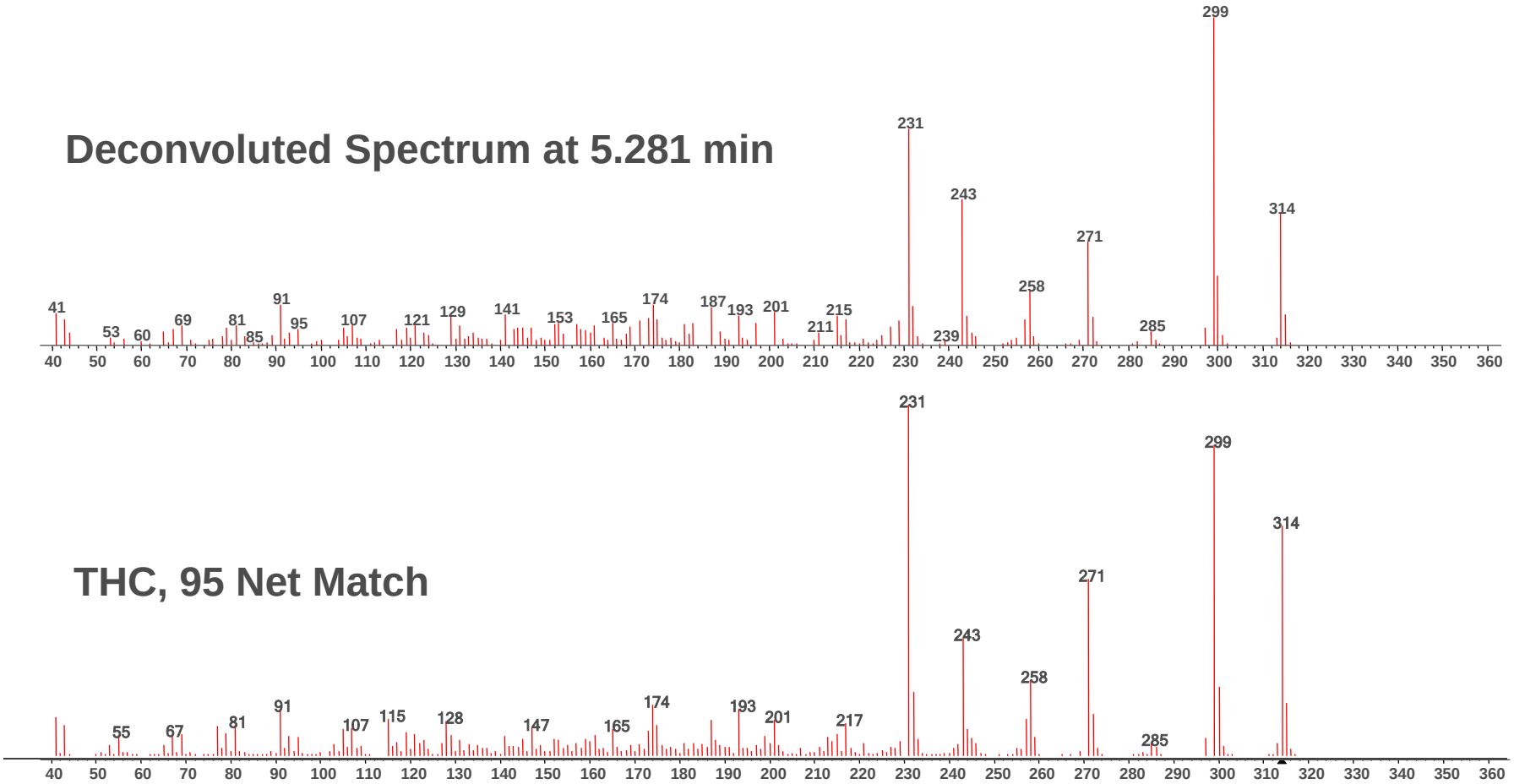
As viewed in AMDIS



- **Deconvolution finds 2 compounds closely merged together.**
- **Peaks are separated by only 0.002 min. (Less than 1 scan)**

First Peak Found By AMDIS

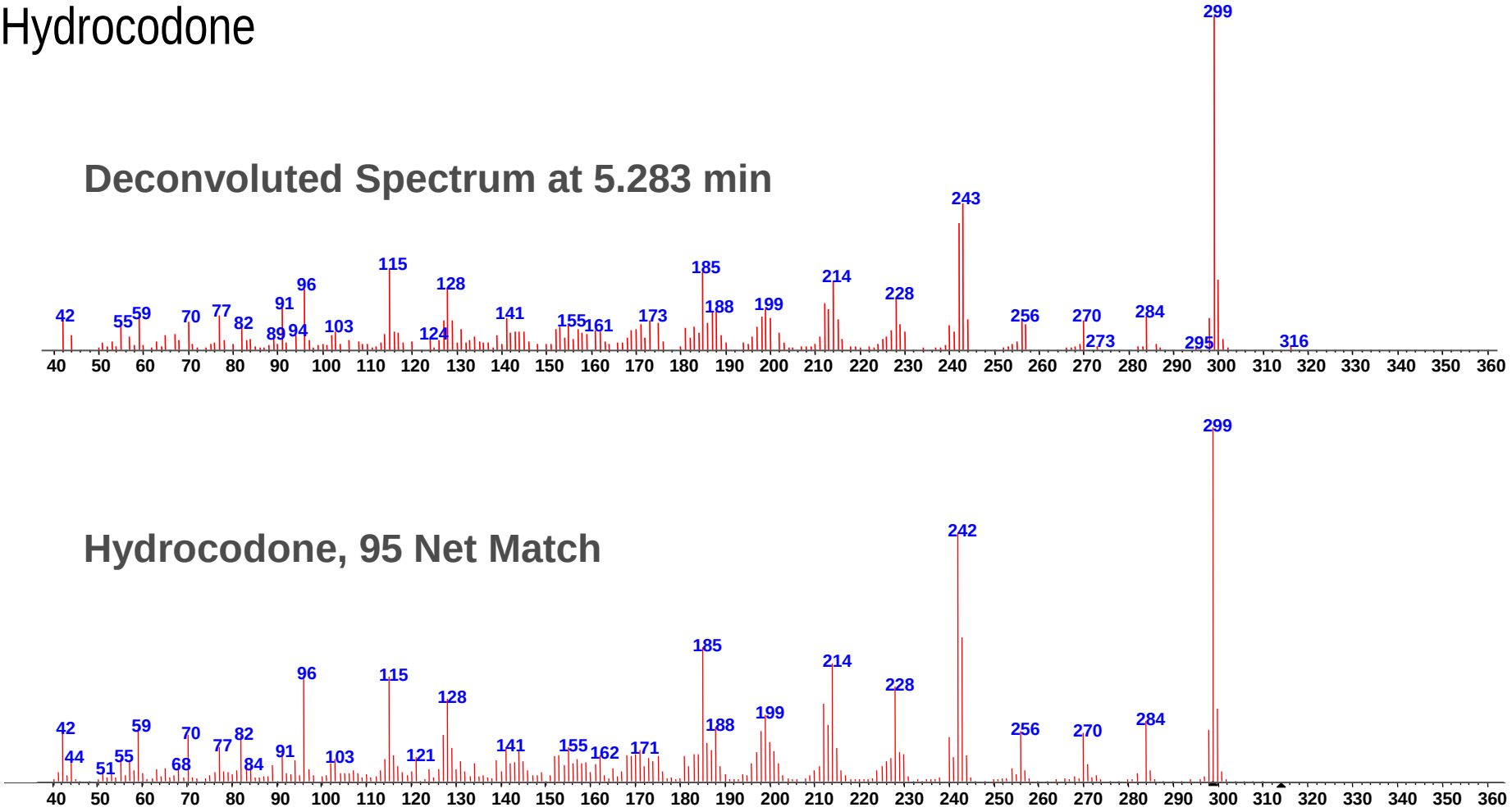
THC



AMDIS deconvolution confirms that the first peak is THC

Second Peak Found By AMDIS

Hydrocodone



This peak would probably have been missed without AMDIS deconvolution

DRS Report For Training Sample

Automated Deconvolution and Reporting

MSD Deconvolution Report
Sample Name: THC/HC
Data File: D:\MassHunter\GCMS\1\data\HCOD_THC.D
Date/Time: 17:18 Wednesday, Oct 2 2013

Adjacent Peak Subtraction = 1
Resolution = High
Sensitivity = Medium
Shape Requirements = Medium

The NIST library was searched for the components that were found in the AMDIS target library.

			Amount (ng)		AMDIS		NIST	
Retention Time (R.T.)	Cas #	Compound Name	Chemstation	AMDIS	Match	R.T. Diff	Reverse Match	Hit Number
3.2702	51799327	N-Propylamphetamine			99	-1.3	91	1
4.6881	3158858	10,11-Dihydrodibenz(b,f)(1,4)oxazepin-11-one			97	-0.7	90	1
5.2479	521379	Cannabidiol			68	5.6	64	3
5.281	1972083	Delta-9-tetrahydrocannabinol (THC)			95	0.5	85	1
5.283	125291	Hydrocodone			95	0.2	88	1
5.3145	466999	Hydromorphone			78	-0.1	67	2
5.3637	521357	Cannabinol			67	0.8	55	4

Automated report generation takes about ~ 60 sec!

New Controlled Substances Analyzer

Rapid Identifying Seized Drug Samples

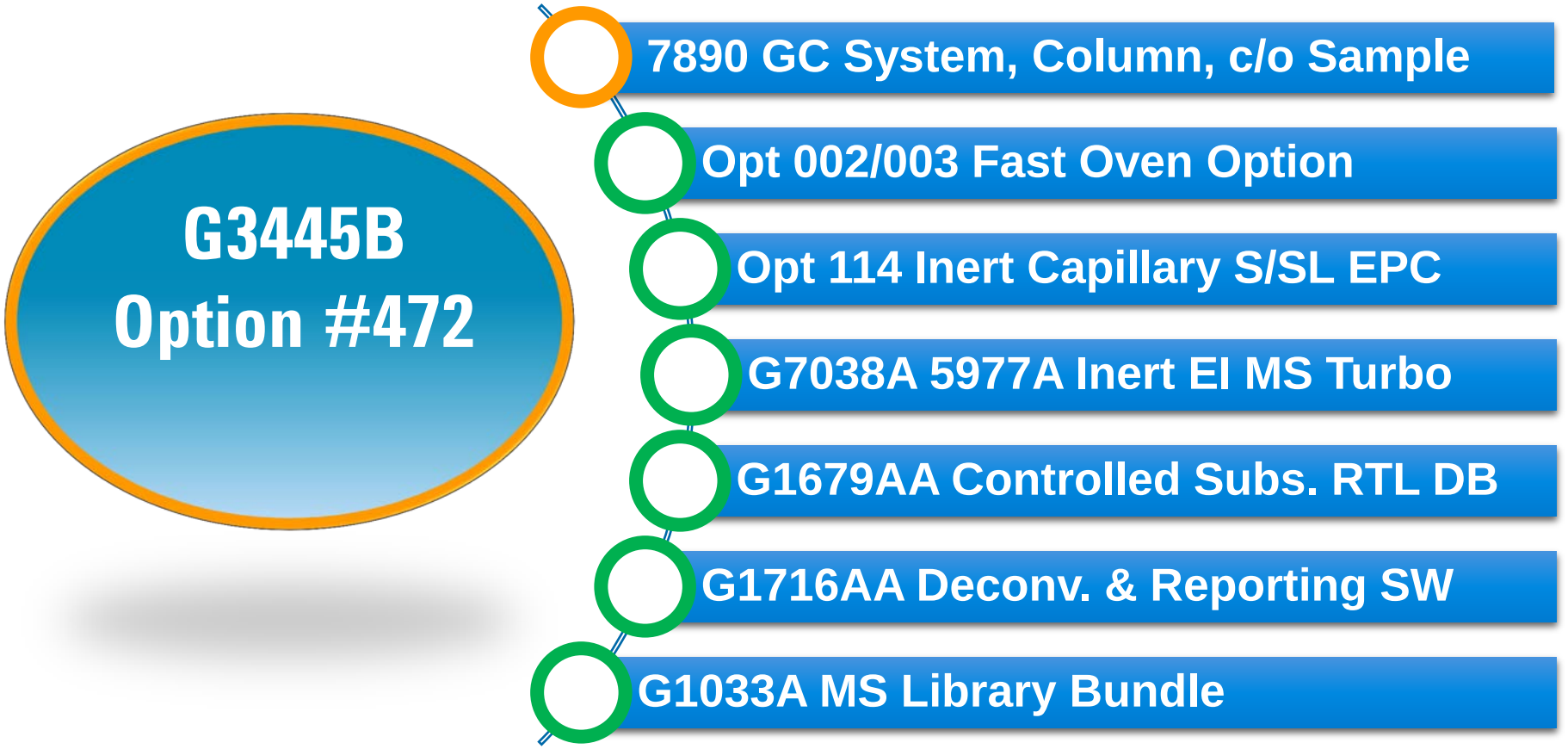
- **Reduce operating expense:** Use hydrogen carrier gas
- **High speed analysis:** from 23.0 to 13.5 min run-to-run
- **Backflushing:** Minimize column trimming and eliminate sample carry-over
- **Retention Time Locking (RTL):** Precise RT matching column-to-column, instrument-to-instrument, and lab-to-lab
- **Deconvolution Reporting Software:** Automated ,rapid and reliable compound identification
- **New 460 compound database:** Comprehensive list of controlled substances including new psycho active substances (synthetic cannabinoid, and “Bath Salt” compounds)
- **Ultra Inert Flow Path:** “Designed-in” from **Inlet-to-Detector** to minimize sample decomposition

Controlled Substances Analyzer

How do I buy it?

Controlled Substances Analyzer

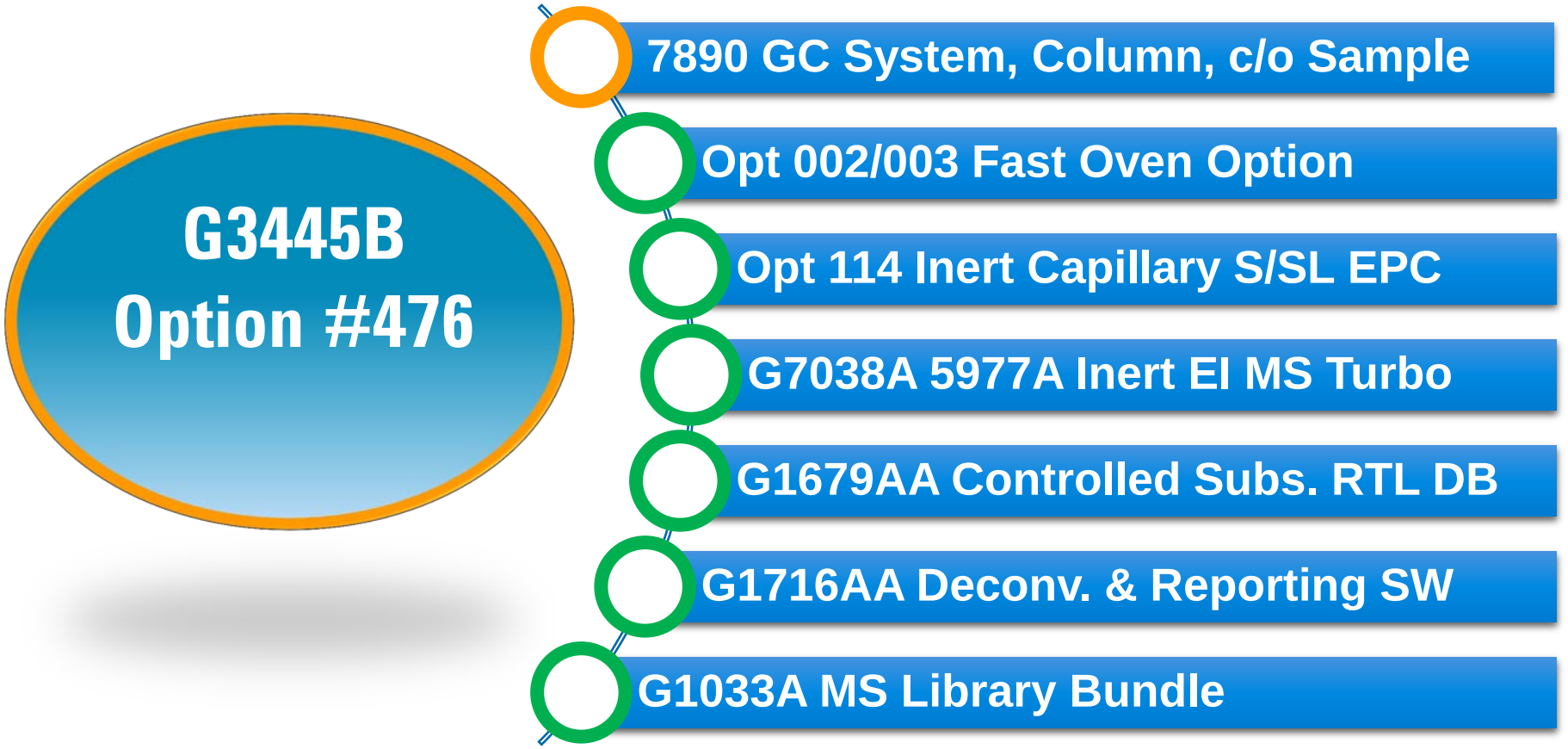
Helium Carrier Gas



Contact your Agilent Account Manager for full ordering details

Controlled Substances Analyzer

Hydrogen Carrier Gas



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Analyzer Value to Customers

Helping your customer enhance their competitive advantage

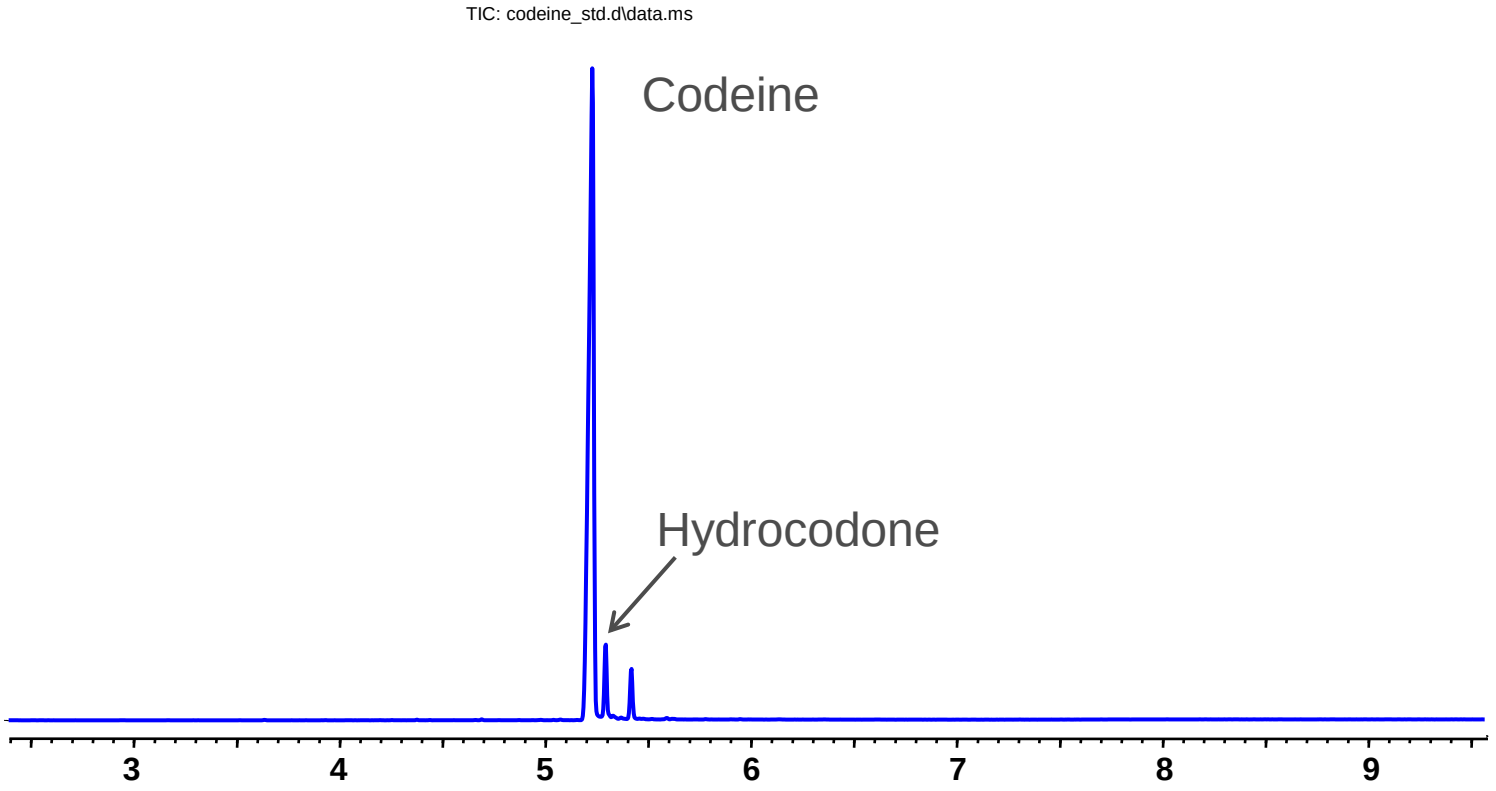
- Alleviate Resource Pressure
- Guaranteed Method
- Optimized Performance
- Advanced Technologies
- Quicker Deployment and Return

Questions or Comments

APPENDIX

Codeine, H_2 Instrument

Some hydrocodone is formed when codeine is injected. About 6% is converted.



Caffeine, H_2 Instrument

Severely overloaded caffeine peak has RT shifted outside recognition window. Use alternate window setting in AMDIS when these are encountered.