Accelerating GC/MS E&L Analysis with Advanced Software Analysis Tools

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About NSF International

NSF's mission is to improve human and planet health. Businesses, regulators and consumers look to us to facilitate the development of public health standards and to provide services that help protect food, water, consumer products and the environment.

What we do:

- Certification
- Standards Development
- Consulting
- Training and Education

Testing Drinking Water Equipment

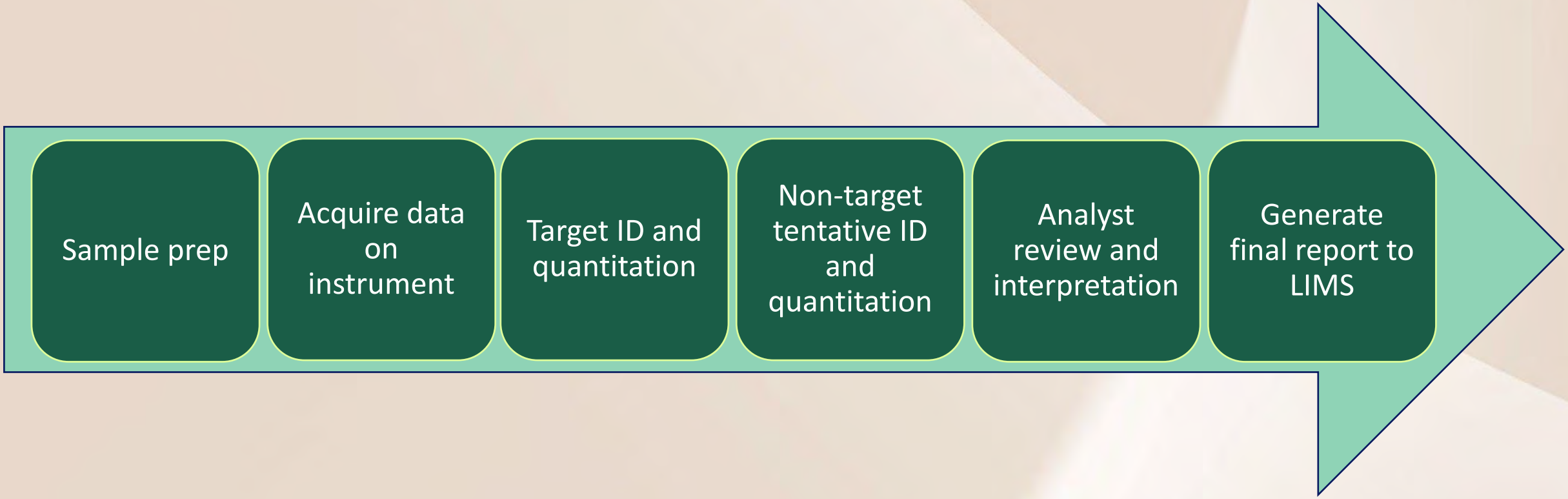
Drinking Water Chemicals(NSF/ANSI 60): Chemicals that may be added to potable water for the purposes of coagulation and flocculation, softening, precipitation, sequestering, pH adjustment, corrosion/scale, and disinfection and oxidation chemicals, as well as miscellaneous treatment and water supply chemicals.

Drinking Water Equipment (NSF/ANSI 61): Anything that delivers a drinking water supply, products such as faucets, pipes, and pumps filtration media. Including water filtration systems to reduce contaminants such as PFOA and PFOS.

Target compounds in Samples are analyzed by GC/MS for identification and quantitation by a modified version EPA 625.

Non-target compounds are tentatively identified (**Tentatively Identified Compounds (TICs)**) and quantitated using a single-point calibration against internal standards.

Overall Workflow



Overall Goals

- The software solution must be vendor independent as global sites use different brands of instruments
- Analysis tools should be easy-to-learn and automate as much of the process as possible to reduce training costs and minimize user error
- The expertise required for review and interpretation must be simplified and automated to reduce the dependence on scarce, expensive, highly experienced Analysts
- LIMS interfacing must be flexible, easy to implement, and robust

Target Analysis Requirements

- Capable of building multi-level quantitative calibrations
- Easily and seamlessly import GC/MS data from vendor neutral formats such as ANDI-MS NetCDF
- Familiar user interface to simplify operation and reduce training
- Easy but flexible report generation for LIMS integration

Target Analysis Software Solution

Thermo Scientific Chromeleon CDS 7.3[1]

- Sold and licensed independently of instrument hardware
- Familiar “Excel”-like user interface
- Accepts Data from a number of industry standard data formats and easily imports them including ANDI-MS netCDF
- Powerful, customizable reports for LIMS integration without coding

[1]Thermo Scientific
Waltham, MA

But! Exporting data from vendor software to ANDI-MS netCDF was a tedious manual process and not universally supported

Solution:

CANDI[1]: a powerful universal data format conversion tool

- Converts data from all major vendor GC/MS formats to ANDI-MS netCDF
- Runs in manual mode, batch mode or can be called programmatically
- Converts profile mode data (required for accurate mass) to centroid mode data (used by Chromeleon) automatically as needed

[1]Cerno Bioscience
Las Vegas, NV

Non-Target Analysis Challenges

- 7,000-8,000 samples evaluated annually by a team of 3-4 scientists
- The established work-flow was tedious, with analysts manually combing through spectra and chromatograms, evaluating every chromatographic peak individually. One by one
- “Dirty” samples could sometimes take hours or even days to process with hundreds of unknown peaks
- Reviewing complex matrices for co-elutions or other chromatographic interferences required intensively trained analysts and lengthy data review
- Once reduced, quantitation was also tedious and manual
- Report generation and LIMS integration was done with a complex excel macro that was difficult to maintain
- The sample backlog could get up to 6 months at times

Non-Target Analysis Requirements

- Shorten analysis time
- Fully automate the peak mixture deconvolution and quantitation
- Provide a vendor-neutral platform
- Standardize analysis across different labs and instrumentation
- Reduce the expertise required for analysis
- Improve the confidence in compound identification
- Automate reporting and LIMS system integration

Non-Target Analysis Solution

GC/ID Version 5.0[1]

- Is vendor neutral, works with all commercial GC/MS systems and directly reads all major vendor data file formats
- Fully automates peak deconvolution and quantitation
- Provides superior identification confidence by combining library search, retention index (RI), and accurate mass validation in an automated full run analysis (composite scoring)
- Modern Python scripting allowed for fast and easy NSF specified customizations to be delivered ahead of schedule

[1]Cerno Bioscience
Las Vegas, NV

Non-Target Analysis Solution Python Customizations

- Identify internal standards, surrogates and target compounds so the analyst doesn't have to spend time evaluating them
- Quantitate unknown compounds based on their response factor relative to the nearest internal standard
- Annotate Targets, IStd's, Surrogates to simplify review
- Filter out compounds below an established reporting limit so they are not shown to user, simplifying the review process
- Allow reviewer to easily choose compound "class" for uncertain absolute ID's

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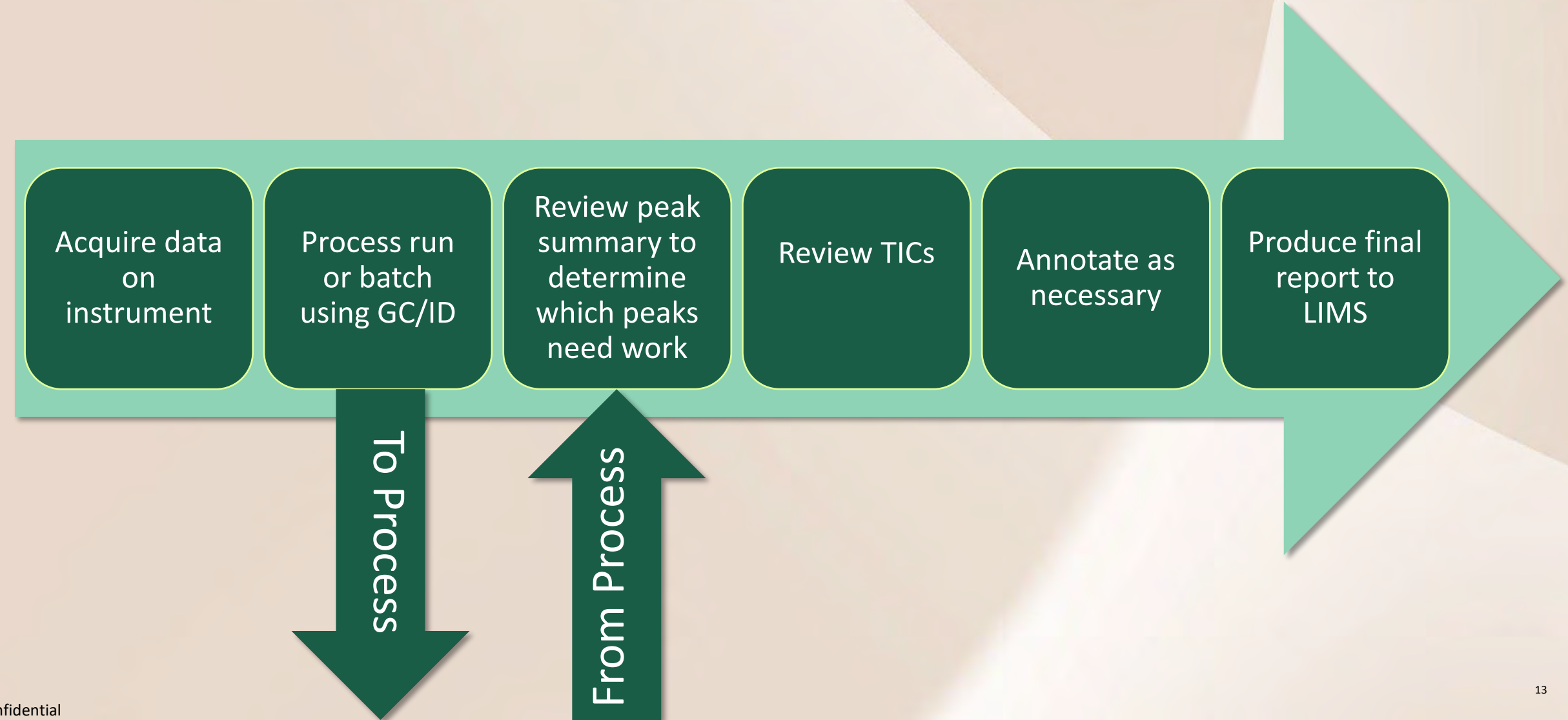
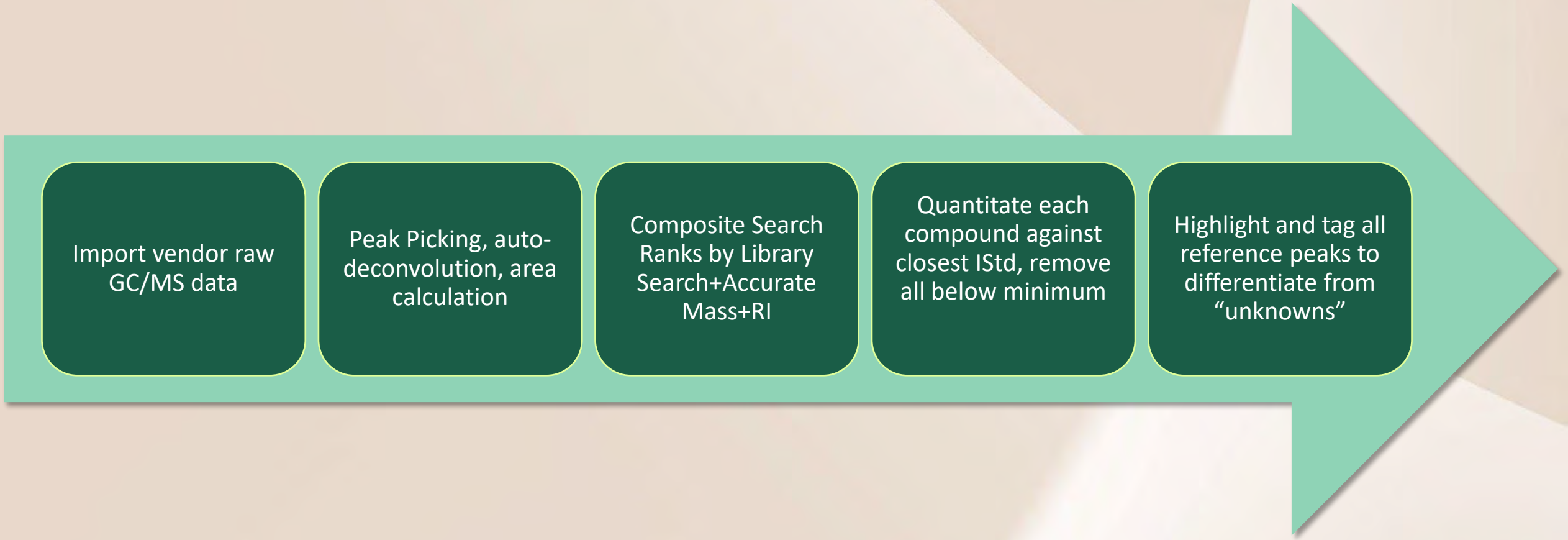
Las Vegas, NV

Workflow | Interpretation of the Data



Workflow | Processing of Data



“Composite” Scoring Reduces Ambiguity, Speeds Review

How do we Know?

Because it weighs *MW, Reverse Library Search, Forward Library Search, Retention Index*

Conventional Library results are not definitive!

Composite Scoring

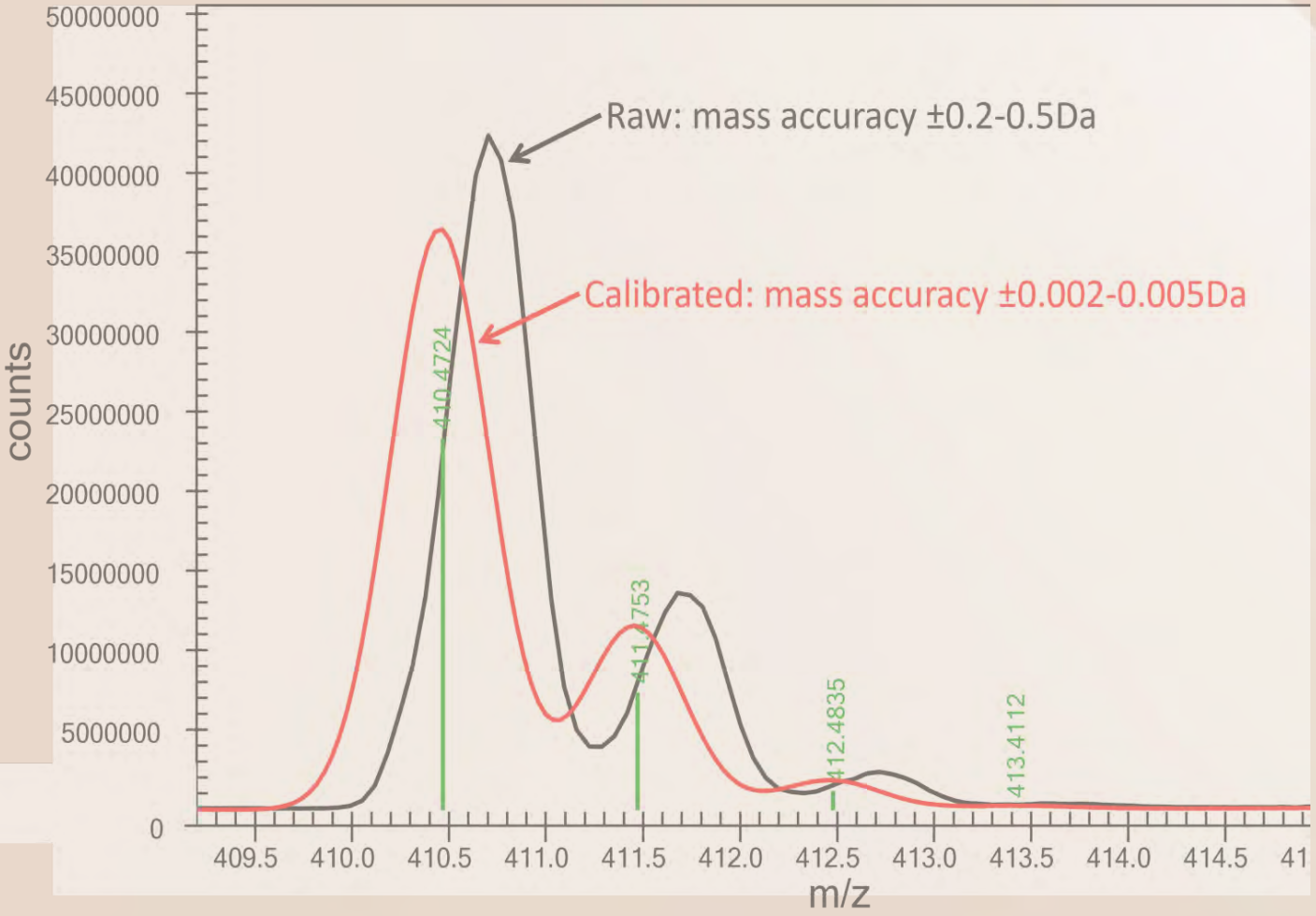
Hit	Match	NIST	RevS	SA-M	SA-F	RIFit	MW	Formula	Name
1	96.96	932	932	99.28	99.18	94.62	95.953	C2H2Cl2	Ethene, 1,2-dichloro-, (E)-
2	92.88	932	932	99.28	99.18	69.38	95.953	C2H2Cl2	1,2-Dichloroethylene
3	88.36	968	968	99.28	99.18	54.38	95.953	C2H2Cl2	Ethene, 1,2-dichloro-, (Z)-
4	86.96	867	876	99.28	99.18	57.62	95.953	C2H2Cl2	Ethene, 1,1-dichloro-
5	76.6	422	423	98.45	99.18	94.62	97.969	C2H4Cl2	Ethane, 1,1-dichloro-
6	64.5	642	644	97.24	99.18	0	95.98	C2H5ClS	Chloromethylmethyl sulfide
7	50.68	787	806	26.28	99.18	0	153.959	C4H4Cl2O2	Dihydro-4,5-dichloro-2(3H)-fur
8	41.97	479	512	14.48	85.65	82.38	93.938	C2Cl2	Ethyne, dichloro-
9	37.42	661	662	-29.09	99.18	0	233.885	C4H5BrCl2O2	Methyl 3-bromo-2,2-dichloro
10	37.09	487	777	-25.77	99.18	0	123.985	C4H6Cl2	Cyclobutane, 1,1-dichloro-
11	34.67	599	600	-26.37	99.18	0	189.936	C4H5Cl3O2	Methyl 2,3,3-trichloropropan

What’s the right answer?

Wrong! It’s this one

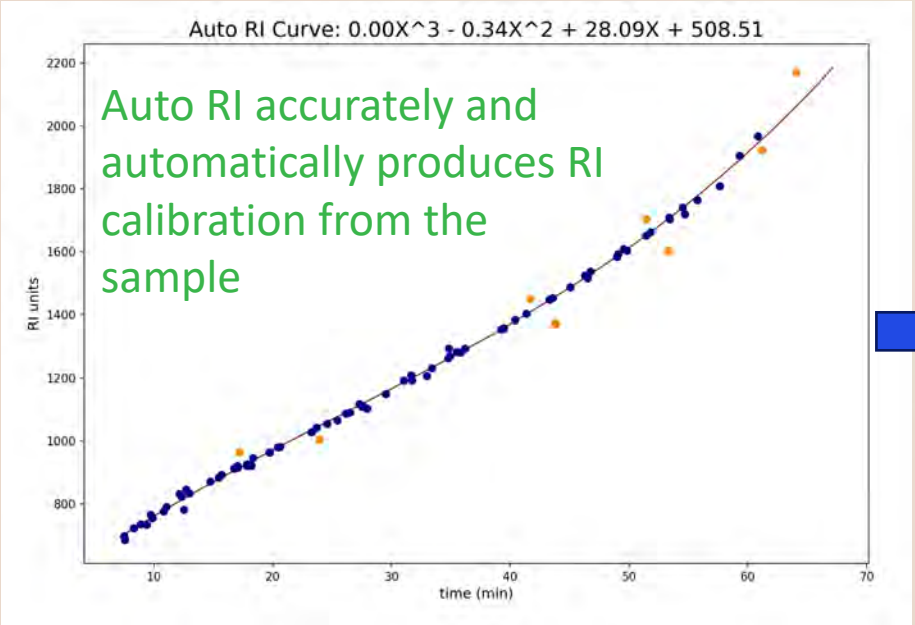
Are you sure?

Accurate Mass on SQ GC/MS



- Obtains the formula for molecular and fragment ions in the sample using profile data.
- Calibrate full spectrum data with built in PFTBA gas using Cerno's patented calibration
- Apply calibration to sample data
- Confirm accurate mass molecular ion formula and fragments against Hit list to validate search match

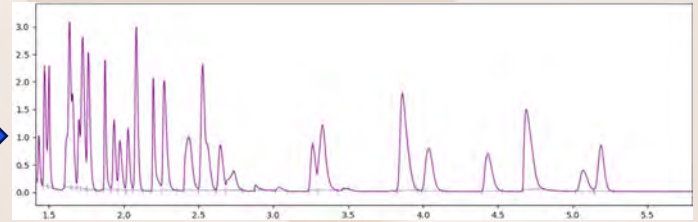
GC Retention Index Calibration with GC/ID

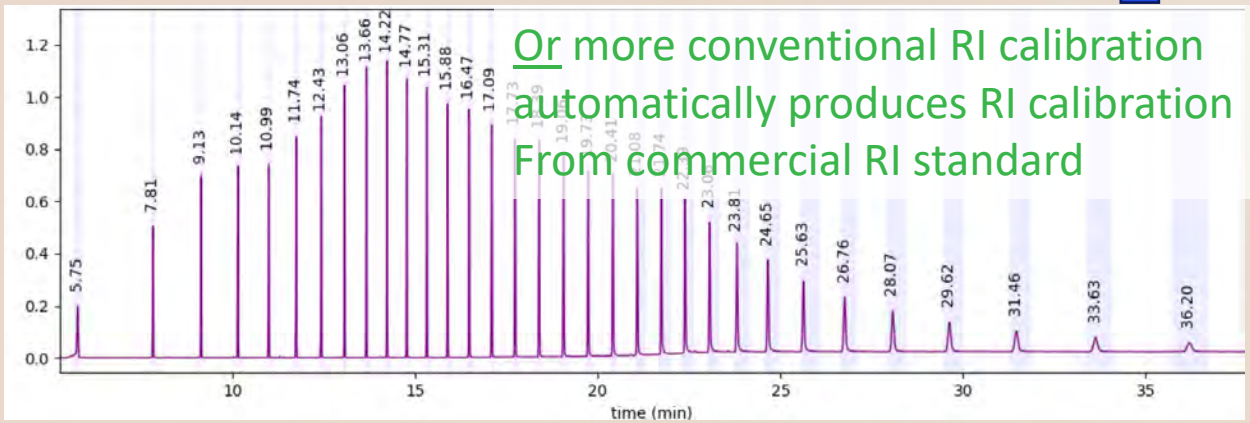


Auto RI accurately and automatically produces RI calibration from the sample

Calibrated GC

Fully RI calibrated chromatogram





Or more conventional RI calibration automatically produces RI calibration From commercial RI standard

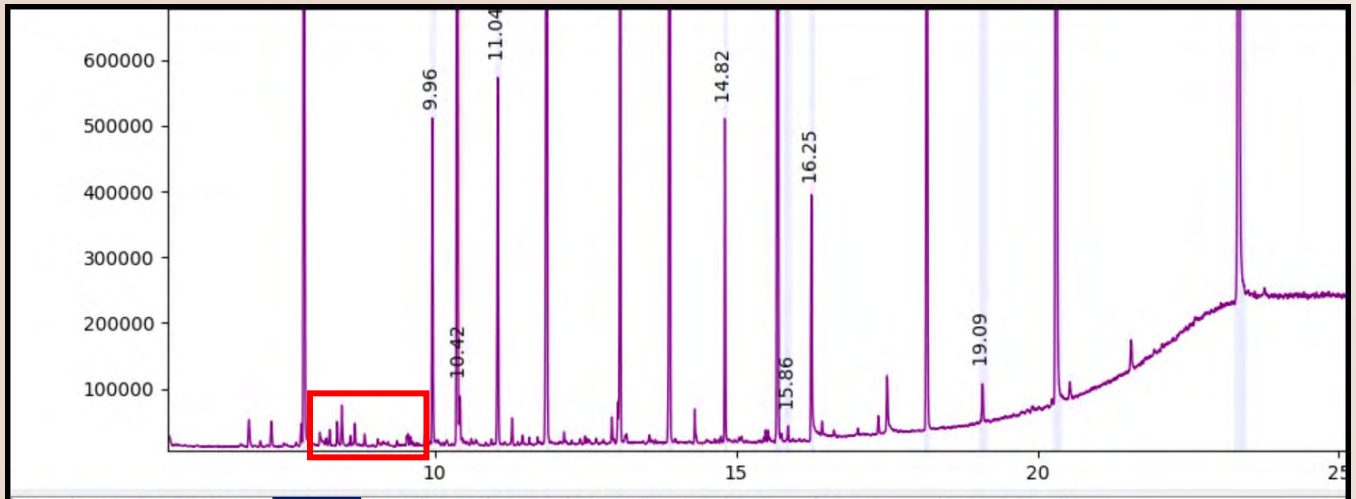
New NIST database with “full” RI coverage

RI match for every compound for superior identification

Hit	Match	NIST	RIFit	Name
1	96.96	932	94.62	Ethylene, 1,2-dichloro-, (E)-
2	92.88	932	69.38	1,2-Dichloroethylene
3	88.36	968	54.38	Ethylene, 1,2-dichloro-, (Z)-
4	86.96	867	57.62	Ethene, 1,1-dichloro-

Typical “Clean” Run

Python scripting enabled custom, optimized workflow



Peak	Time	Quant	Mix	Match	NIST	RevS	SA-M	SA-F	RI-Fit	MW	CAS	Formula	Name	
1	7.83	28.54	1/1	99.16	833	834	97.28	99.16	81.1	100.089	62238-37-3	C6H12O	3-Penten-1-ol, 2-methyl-	←Unk
2	9.96	7.90	1/1	67.55	876	882	60.36	0.00	98.9	100.080	13127-88-3	C6D6O	S:Phenol-d6-	
3	10.37	40.61	1/1	98.73	961	962	98.73	0.00	82.8	149.994	3855-82-1	C6D4Cl2	I:1,4-Dichlorobenzene-D4	
4	10.42	0.63	2/2	98.60	919	929	-25.65	98.60	97.5	130.136	104-76-7	C8H18O	T:1-Hexanol, 2-ethyl-	
5	11.04	9.72	1/1	98.36	896	901	98.36	0.00	97.5	128.063	4165-60-0	C6D5NO2	S:Nitrobenzene-D5	
6	11.86	40.00	1/1	96.93	921	922	96.93	0.00	72.8	136.113	1146-65-2	C10D8	I:Naphthalene-D8	
7	13.08	14.09	1/1	99.40	960	960	99.40	98.49	98.0	172.069	321-60-8	C12H9F	S:1,1'-Biphenyl, 2-fluoro-	
8	13.89	40.00	1/1	95.73	909	909	88.20	0.00	96.4	164.141	15067-26-2	C12D10	I:Acenaphthene-d10	
9	14.82	4.44	1/1	98.14	955	955	98.14	97.42	96.0	327.773	118-79-6	C6H3Br3O	S:Phenol, 2,4,6-tribromo-	
10	15.69	40.00	1/1+1	92.98	890	890	92.98	0.00	94.6	188.141	1517-22-2	C14D10	I:Phenanthrene-D10	
11	15.86	0.21	1/1+1	99.09	875	897	-8.29	99.09	73.4	278.152	84-69-5	C16H22O4	T:1,2-Benzenedicarboxylic	
12	16.25	3.92	1/1	98.73	927	927	98.23	98.73	94.0	256.240	57-10-3	C16H32O2	n-Hexadecanoic acid	←Unk
13	18.16	19.53	1/1	97.70	913	913	92.65	0.00	94.9	244.197	1718-51-0	C18D14	S:p-Terphenyl-d14	
14	19.09	0.79	1/1+1	99.04	890	890	-78.89	99.04	94.6	312.136	85-68-7	C19H20O4	T:Butyl benzyl phthalate	
15	20.31	40.00	1/1+2	94.03	895	898	91.50	0.00	91.6	240.169	1719-03-5	C18D12	I:Chrysene-D12	
16	23.34	40.00	1/1+1	91.63	873	882	91.63	0.00	90.2	264.169	1520-96-3	C20D12	I:Perylene-D12	

Review time for “unknowns” from hours to minutes for “clean” runs and days to hours for “dirty” runs!

- Batch processes at <4sec/run (avg, multi-threaded)
- Confidently identifies all peaks (composite “Match” score)
- Accurately quantitates all peaks in run against closest IStd even with co-elution
- Filters out all peaks below quant minimum threshold
- Highlights and visually tags Targets, IStd, Surrogates to simplify user review
- Clearly indicates “Unknowns” that need attention
- Creates custom report for LIMS system (both parsable text and hyperlinked PDF)

Summary

Best of breed software solutions unchained from vendor specific solutions ready for global roll out

- Simplify user interface and LIMS report generation
- Fully automated tedious manual processing methods
- Eliminated 6 month sample backlog, samples analyzed as the are run
- Reduced review time for “clean” samples from hours to minutes
- Reduced review time for “dirty” samples from days to hours
- Produces comprehensive custom report for LIMS integration and customer reports


Thank You!
Questions?