



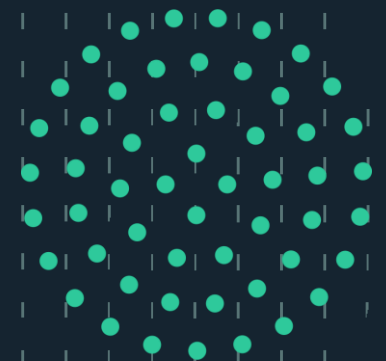
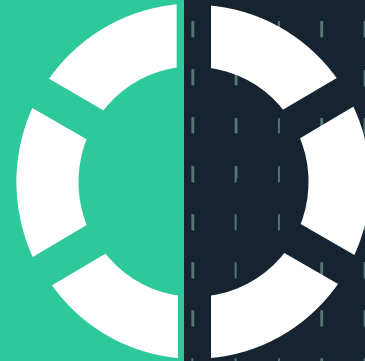
Unlocking the potential of High Throughput Purification with Advanced Automated Impurity Analysis

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Dotmatics, A Siemens Company

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About Virscidian

We are a software company that is on a mission to deliver:



Drug Discovery Software-enabled Synthesis to Registration & HTS Screening Workflows



End-to-end analytical software solutions that mimic and extend your natural laboratory workflows



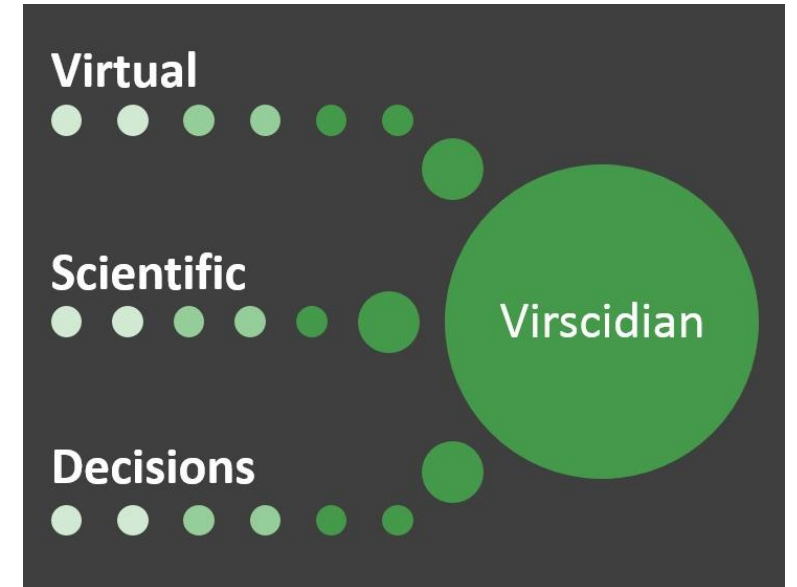
Desktop and enterprise products developed for high to low sample throughput workflows



Best in class workflow driven LC/MS Automated data processing, results creation, review-by-exception



Acquired in Aug. 2024 by **Dotmatics**, which was subsequently acquired by **Siemens** in Apr. 2025, to accelerate scientific research and improve data-driven decision-making for our customers and partners, providing them with a broader range of innovative solutions.



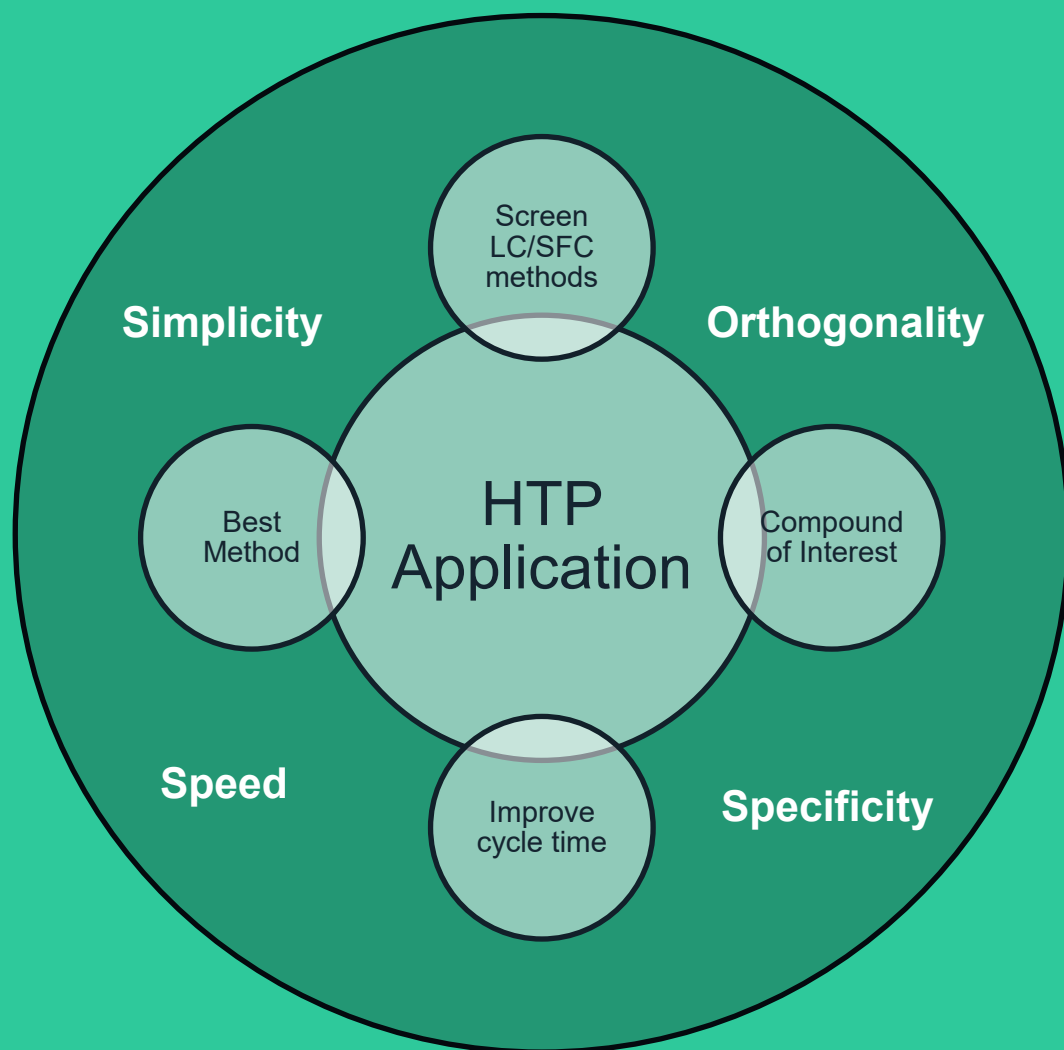
Outline

Evolution of Method Selection

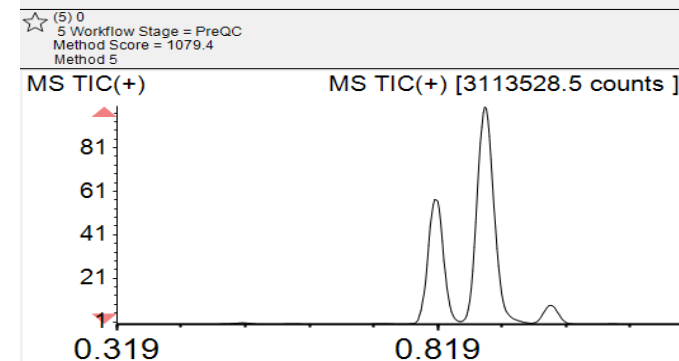
Advanced Automated
Impurity Analysis



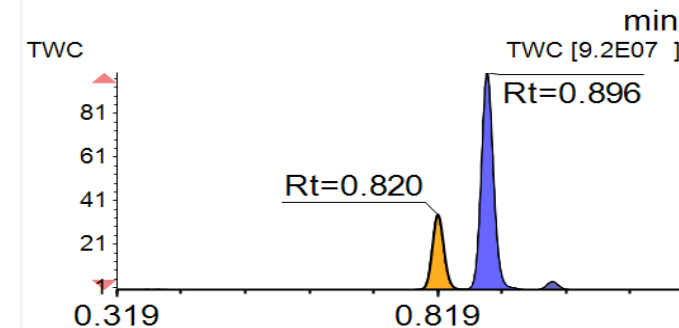
Initial Application & Approach Approach



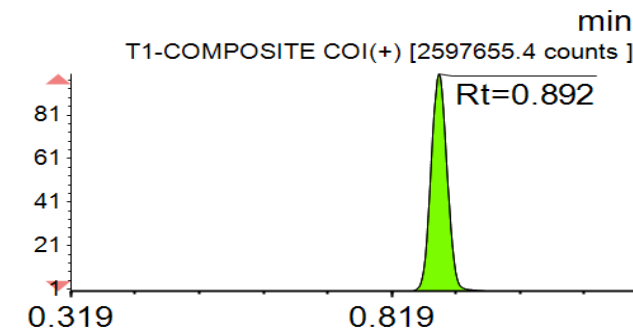
MS-TIC



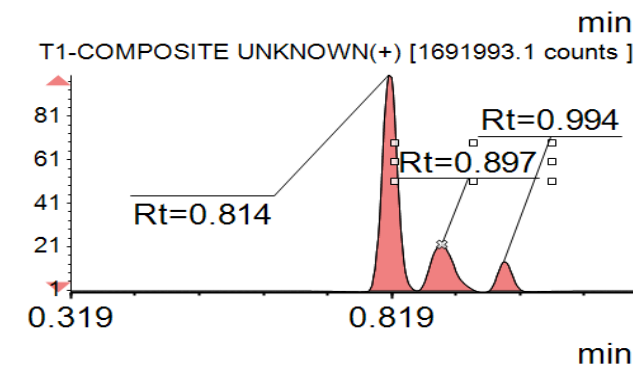
UV-TWC



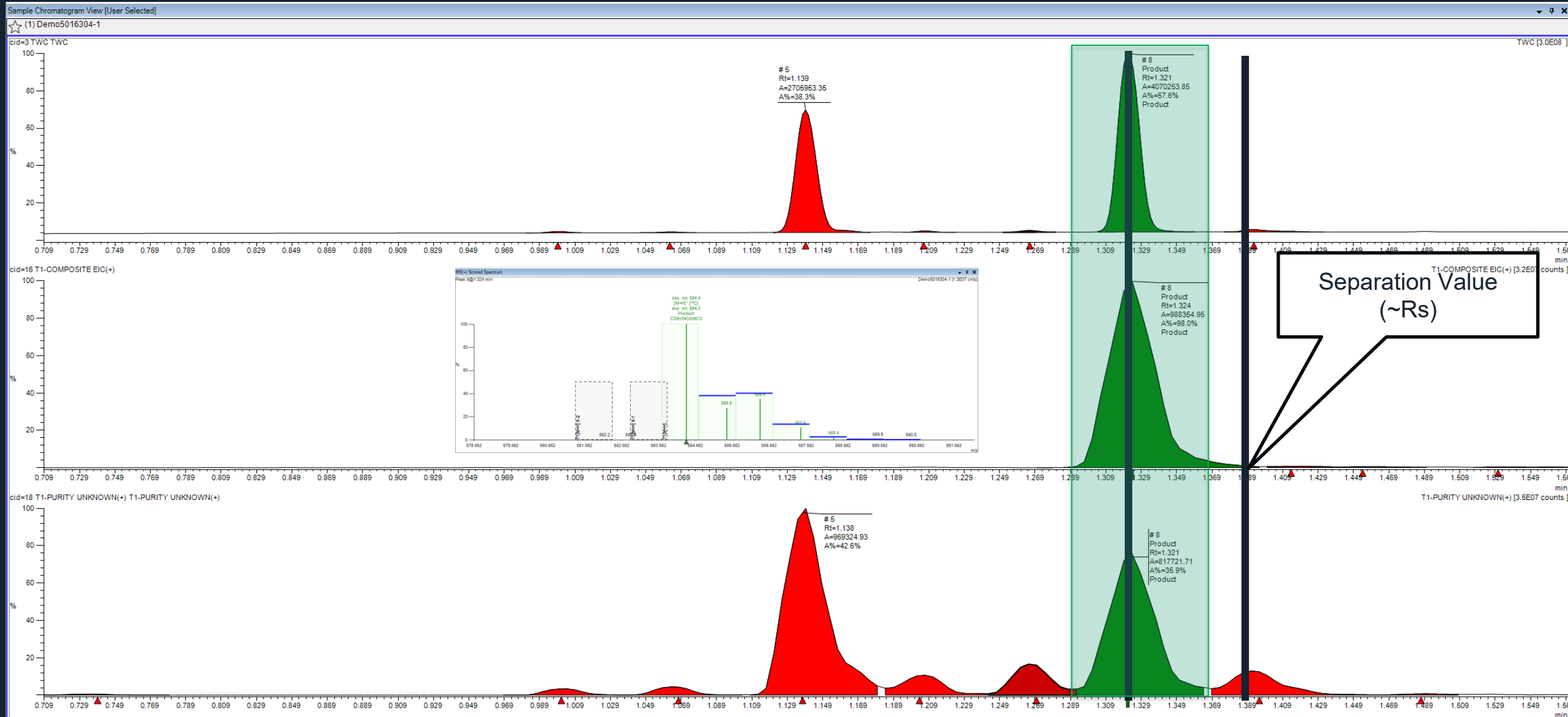
COI-EIC



Non-COI-EIC



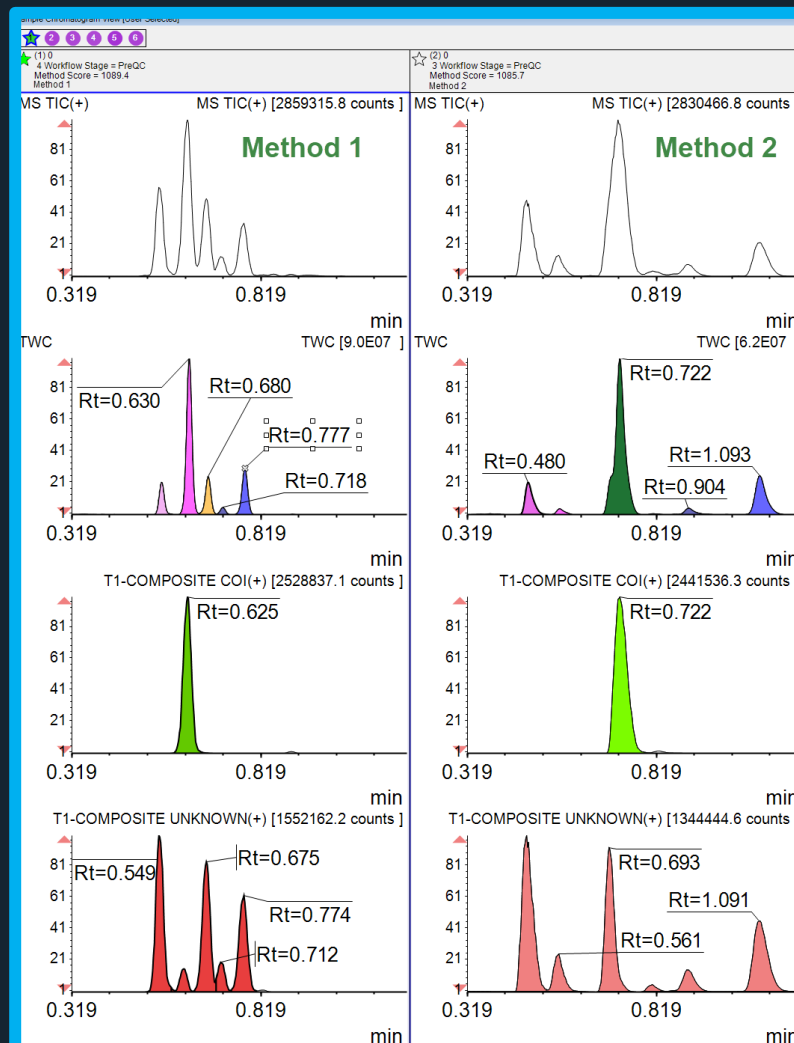
The goal of the **Method Selection** approach was to quickly identify conditions that could be used to obtain suitable purity



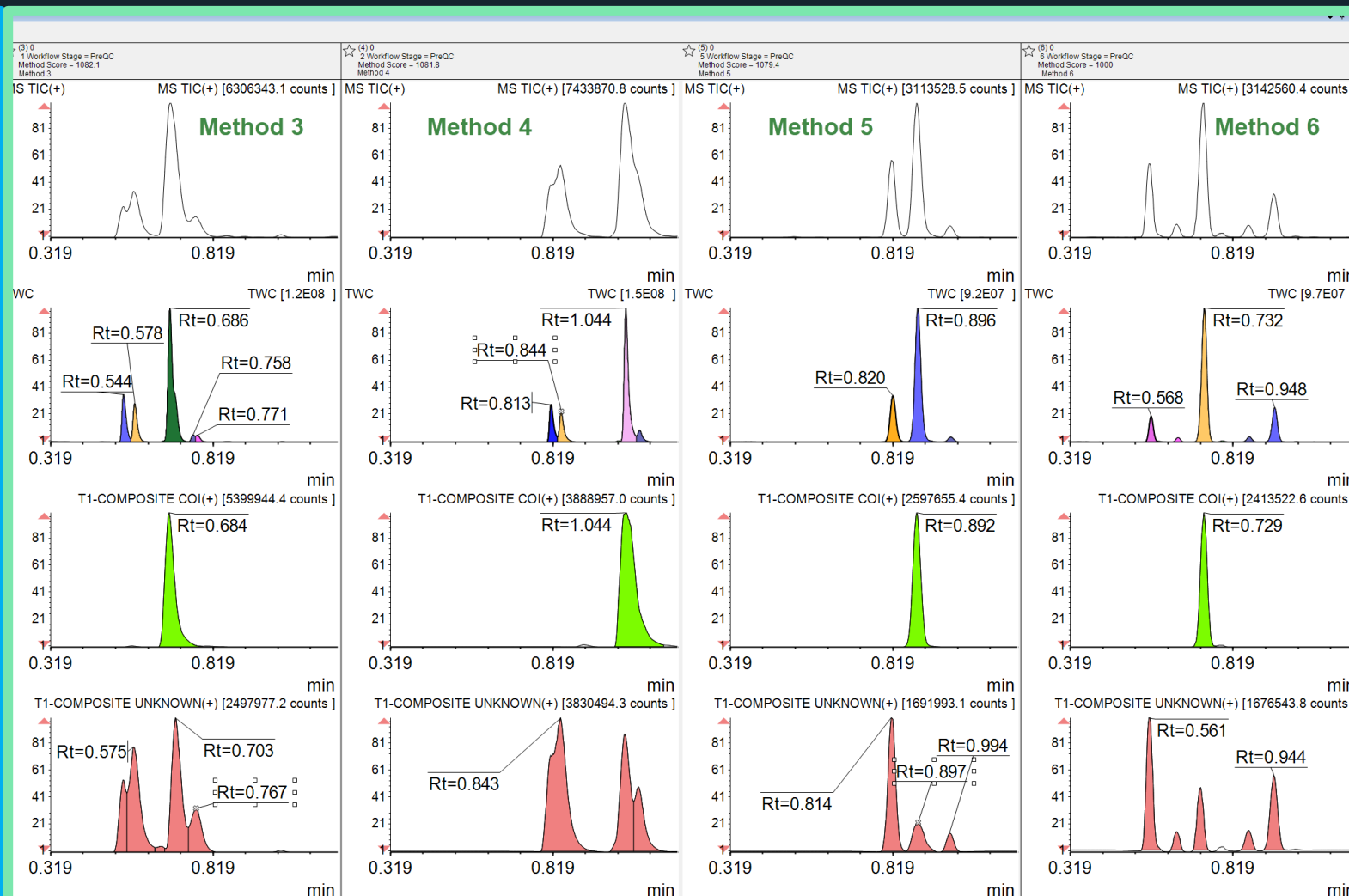
The resulting **Method Scores** were a best attempt to quantify the “best” method



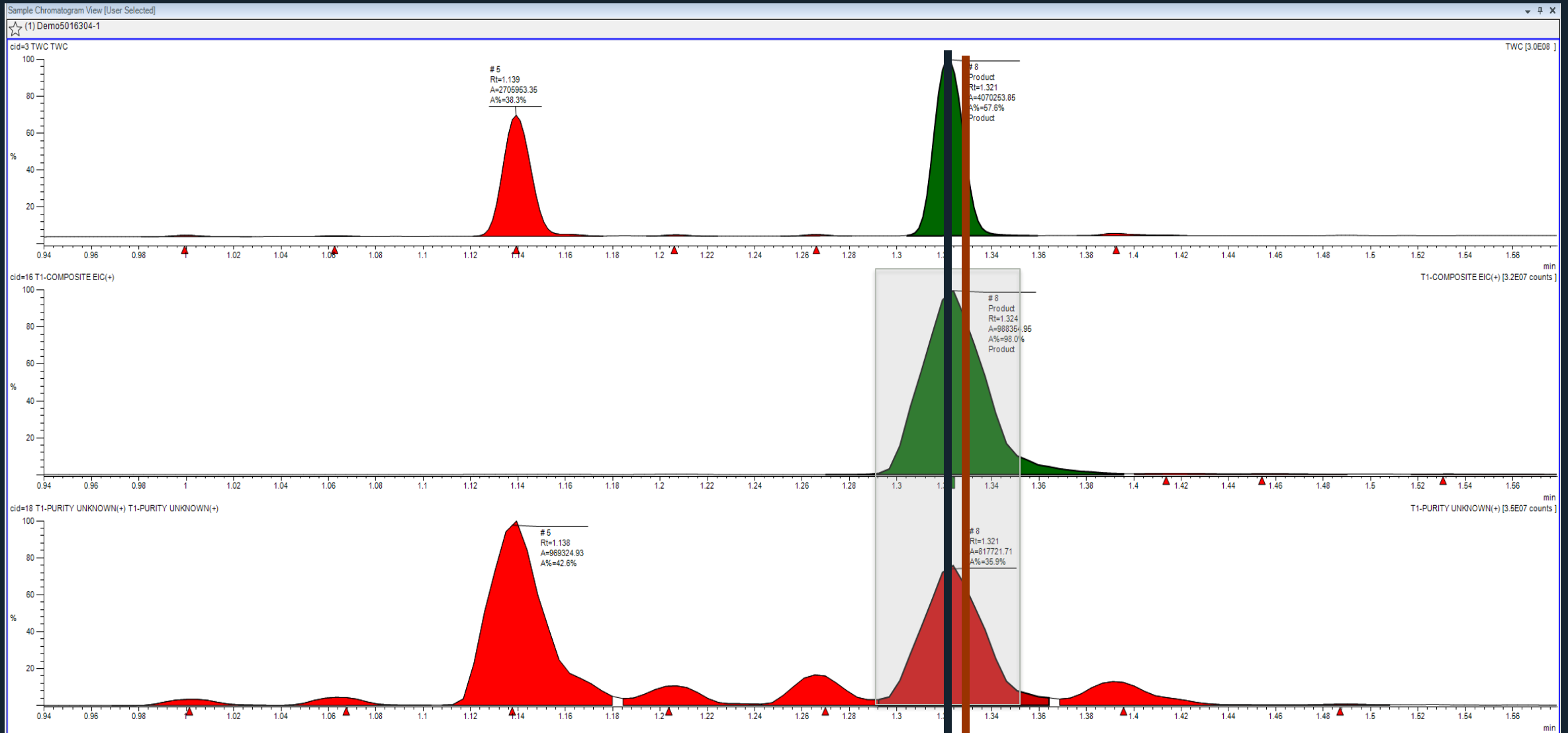
HPLC Methods



SFC Methods



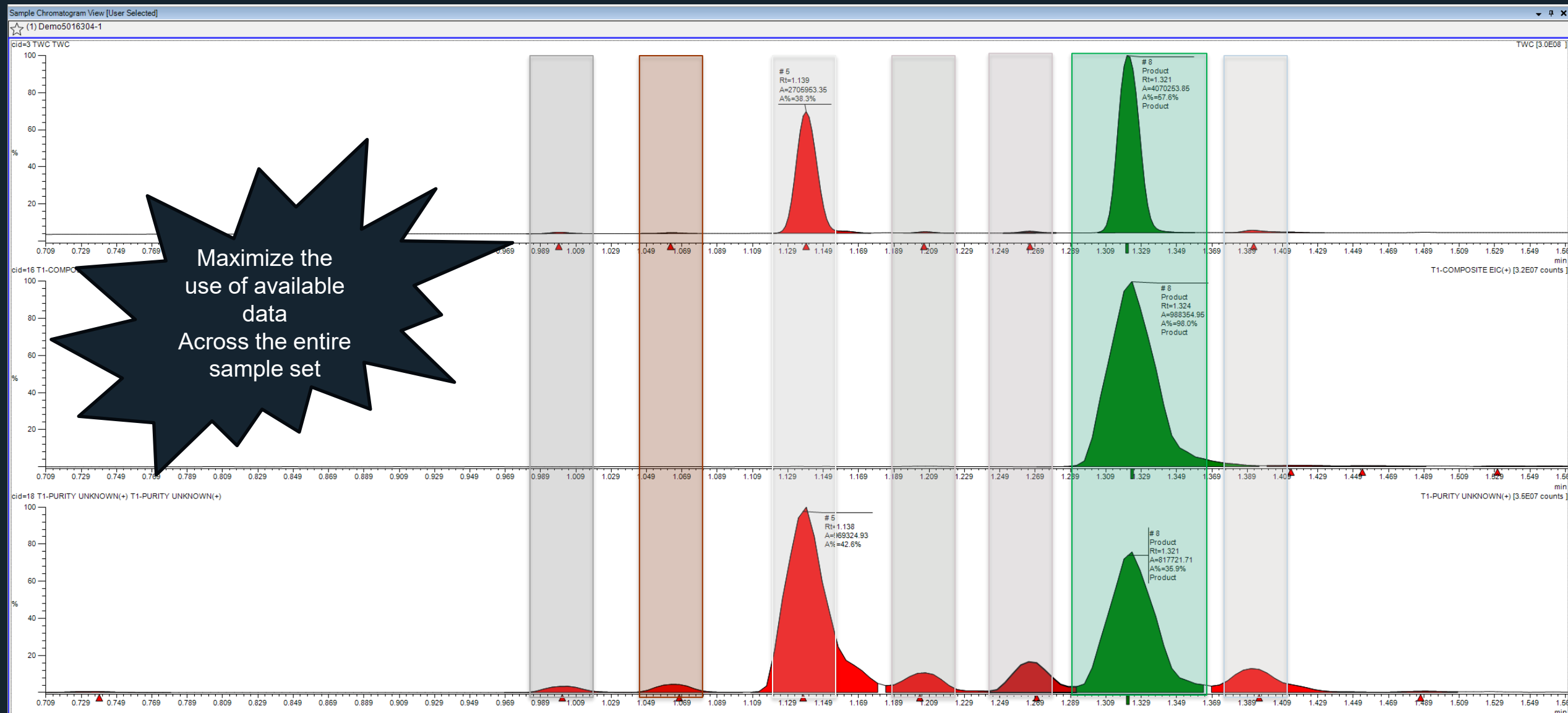
Method Selection approach ignored the magnitude of any co-elution



Virscidian's latest **Advanced Automated Impurity Analysis** provides a more comprehensive analysis



Maximize the
use of available
data
Across the entire
sample set



Analytical Studio enhancements select the best separation method from preliminary analysis and then...



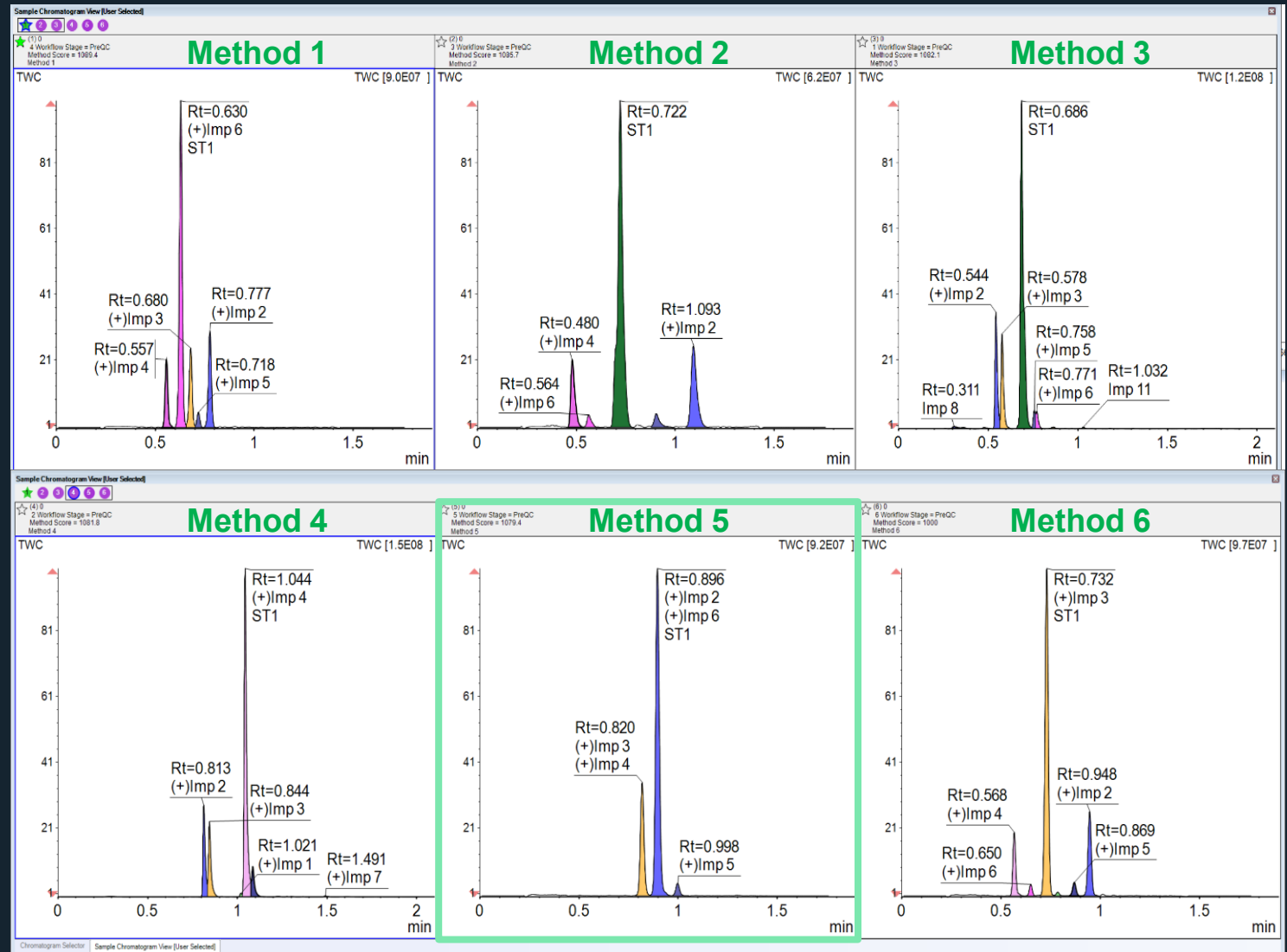
Uniquely identify
impurities in any
given sample



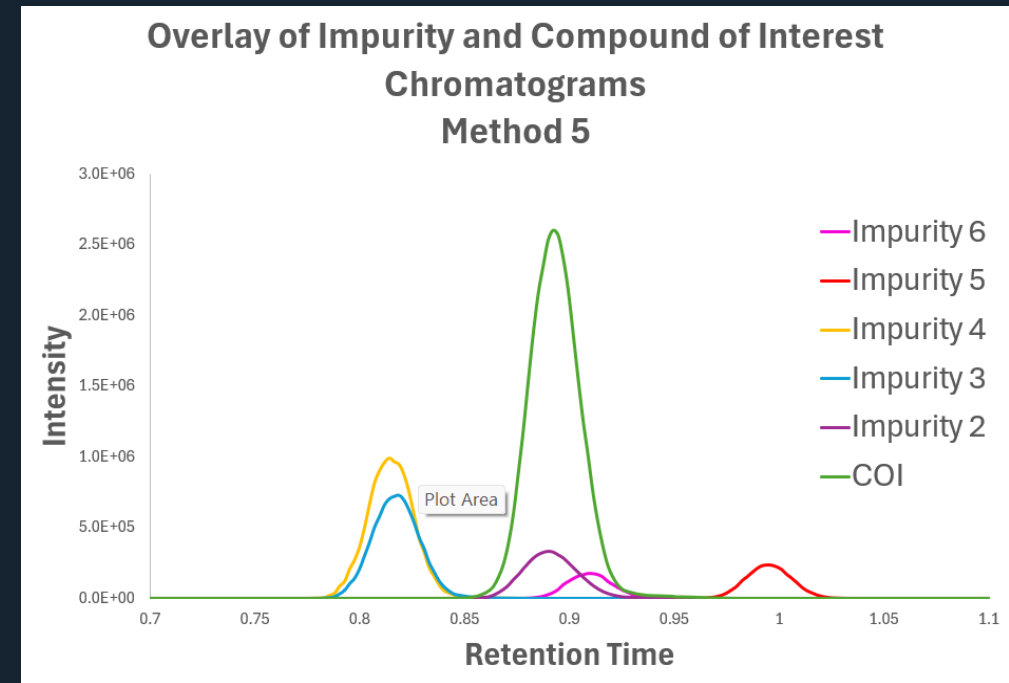
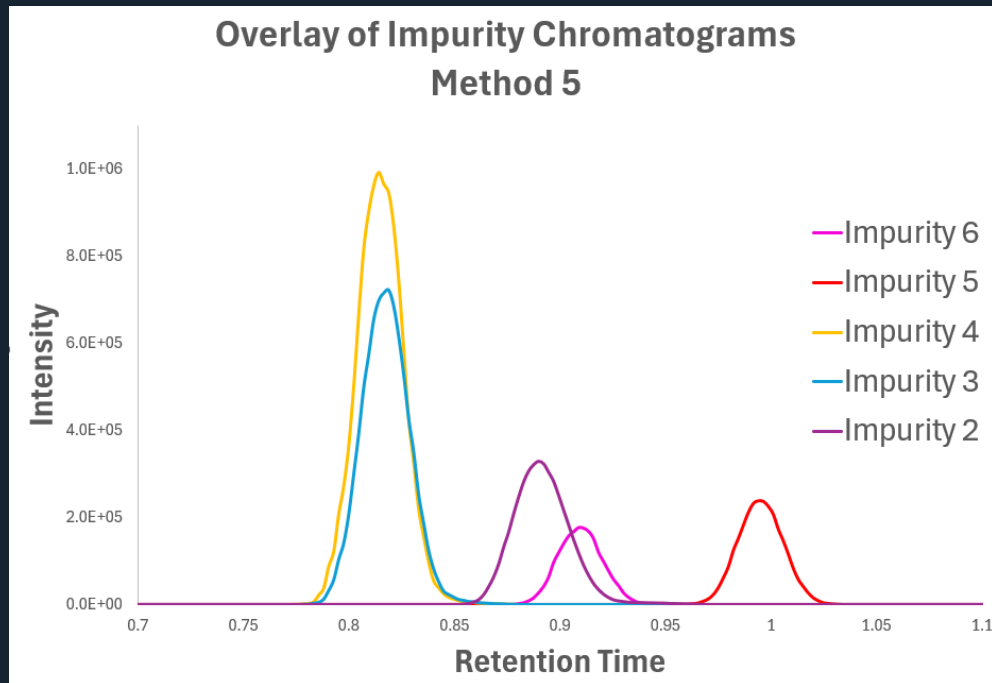
Automatically track
impurities across
the different
methods



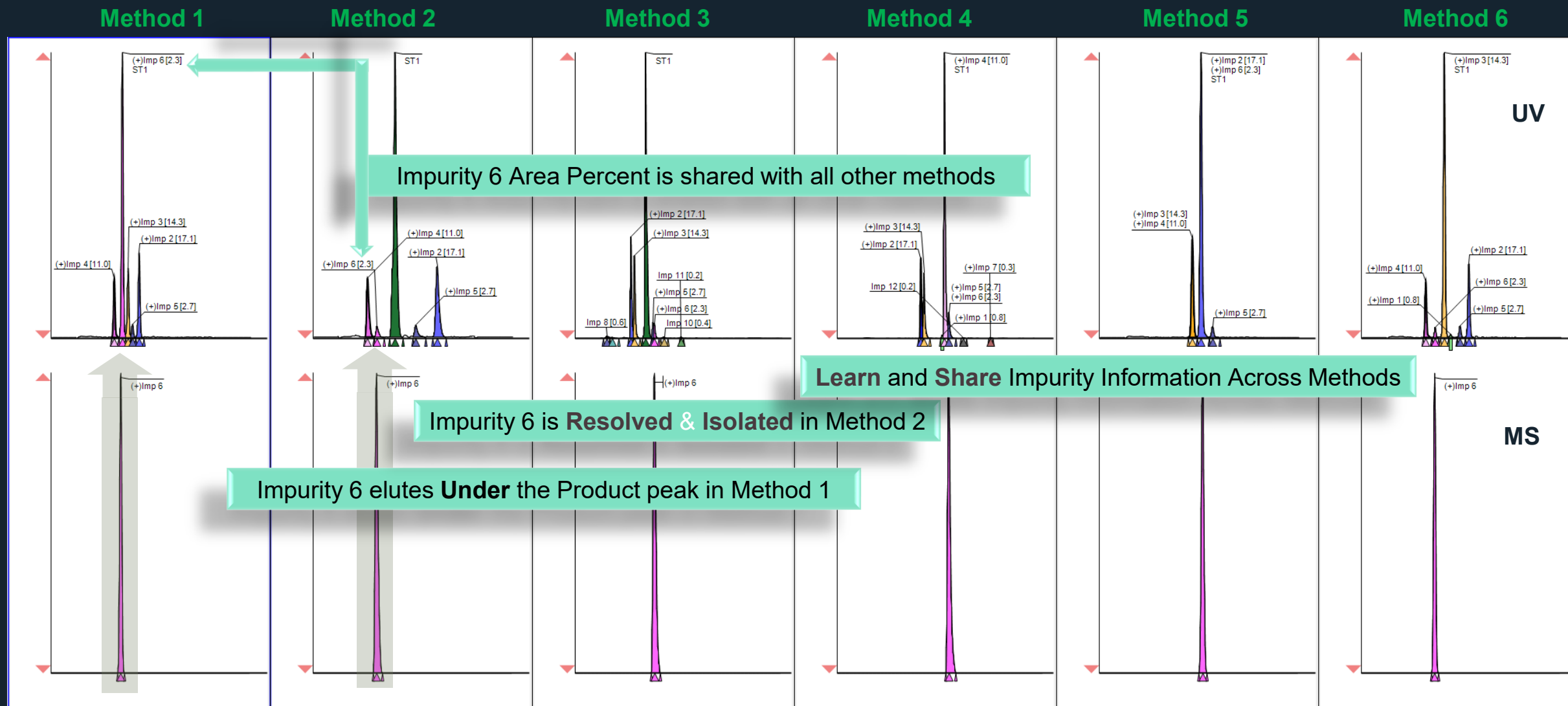
Quantitate
impurities impact
during co-elution



Advanced Automated Impurity Analysis translates MS learnings to UV data



There are coeluting Impurities in ALL Methods – So which is the best one with the lowest Impurity Impact?



The new impurities are captured and applied across the dataset



New substances are created
in the **Substance Editor**...

Substance Editor

Options

☒ Starts with
☐ Contains

☐ Populate identity signal list

General

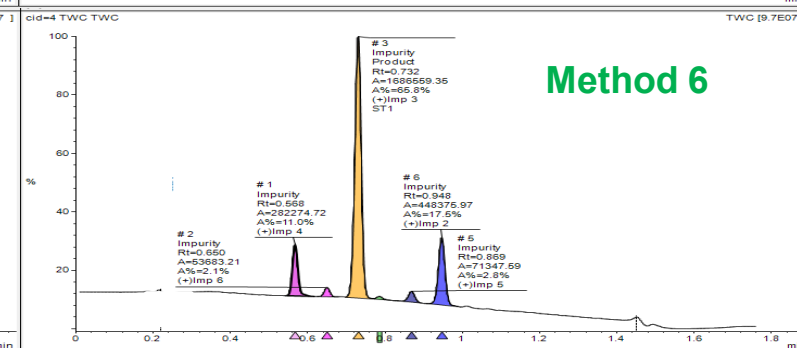
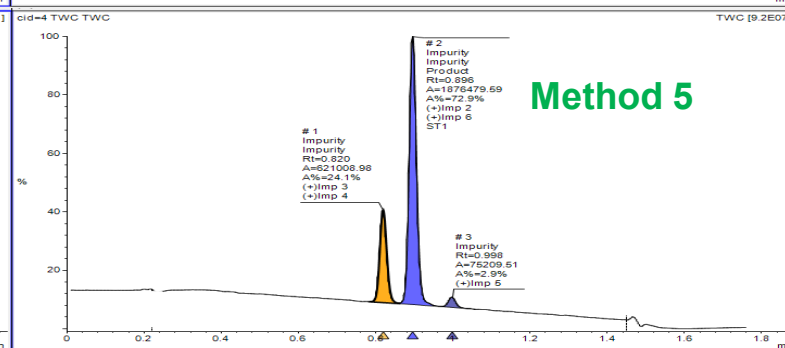
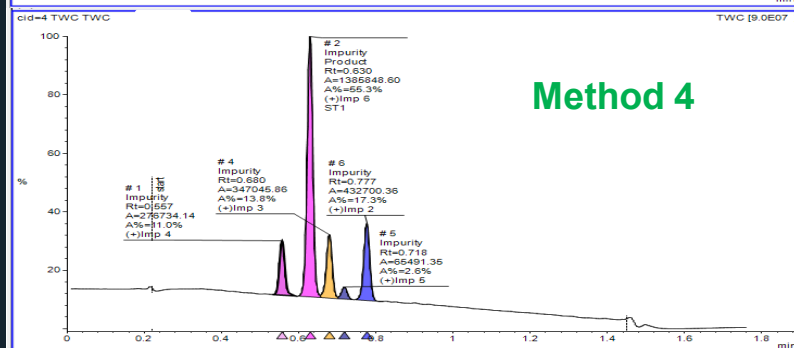
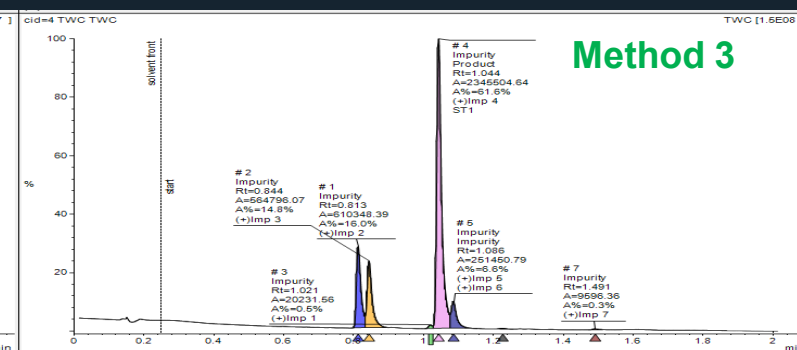
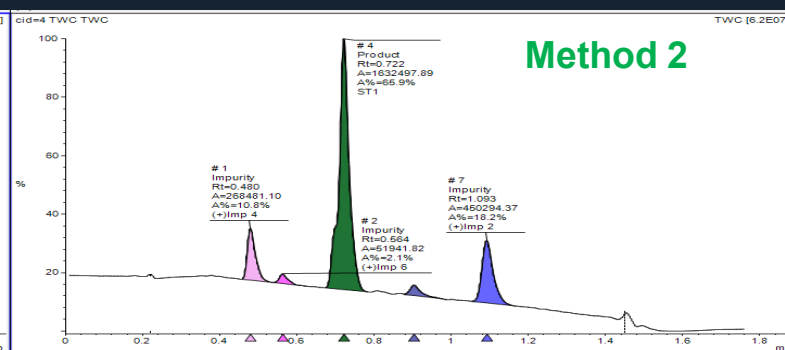
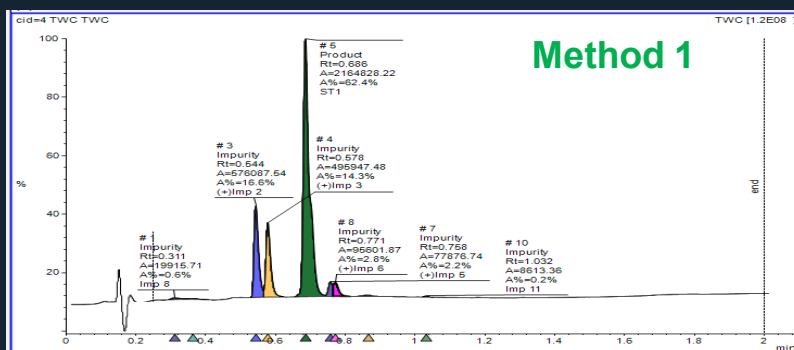
Name	Color	Description	Class	Substance Type	Target	Formula	Confirmation Mode	Signal Assignment Mode	Identity Signal	Rt Criteria	Peak Selection	#Peaks
(+)Imp 1		319.2_333.0	Impurity	Impurity	2	319.2,92481	Rt Only	Identity and Non-MS	(+)Imp 1 EIC(+)	Full Time Range	Largest	2
(+)Imp 2		337.1_338.2	Impurity	Impurity	3	337.1,1069116	Rt Only	Identity and Non-MS	(+)Imp 2 EIC(+)	Full Time Range	Largest	2
(+)Imp 3		351.1_352.2	Impurity	Impurity	4	351.1,1377810	Rt Only	Identity and Non-MS	(+)Imp 3 EIC(+)	Full Time Range	Largest	2
(+)Imp 4		378.1_379.2_38...	Impurity	Impurity	5	378.1,57993	Rt Only	Identity and Non-MS	(+)Imp 4 EIC(+)	Full Time Range	Largest	2
(+)Imp 5		399.1_401.0	Impurity	Impurity	6	399.1,154179	Rt Only	Identity and Non-MS	(+)Imp 5 EIC(+)	Full Time Range	Largest	2
(+)Imp 6		413.1_415.0	Impurity	Impurity	7	413.1,187192	Rt Only	Identity and Non-MS	(+)Imp 6 EIC(+)	Full Time Range	Largest	2
(+)Imp 7		683.3	Impurity	Impurity	8	683.3,116625	Rt Only	Identity and Non-MS	(+)Imp 7 EIC(+)	Full Time Range	Largest	2
ST1			Analyte	Product	1		MS Only	MS Only and Other				

ST1

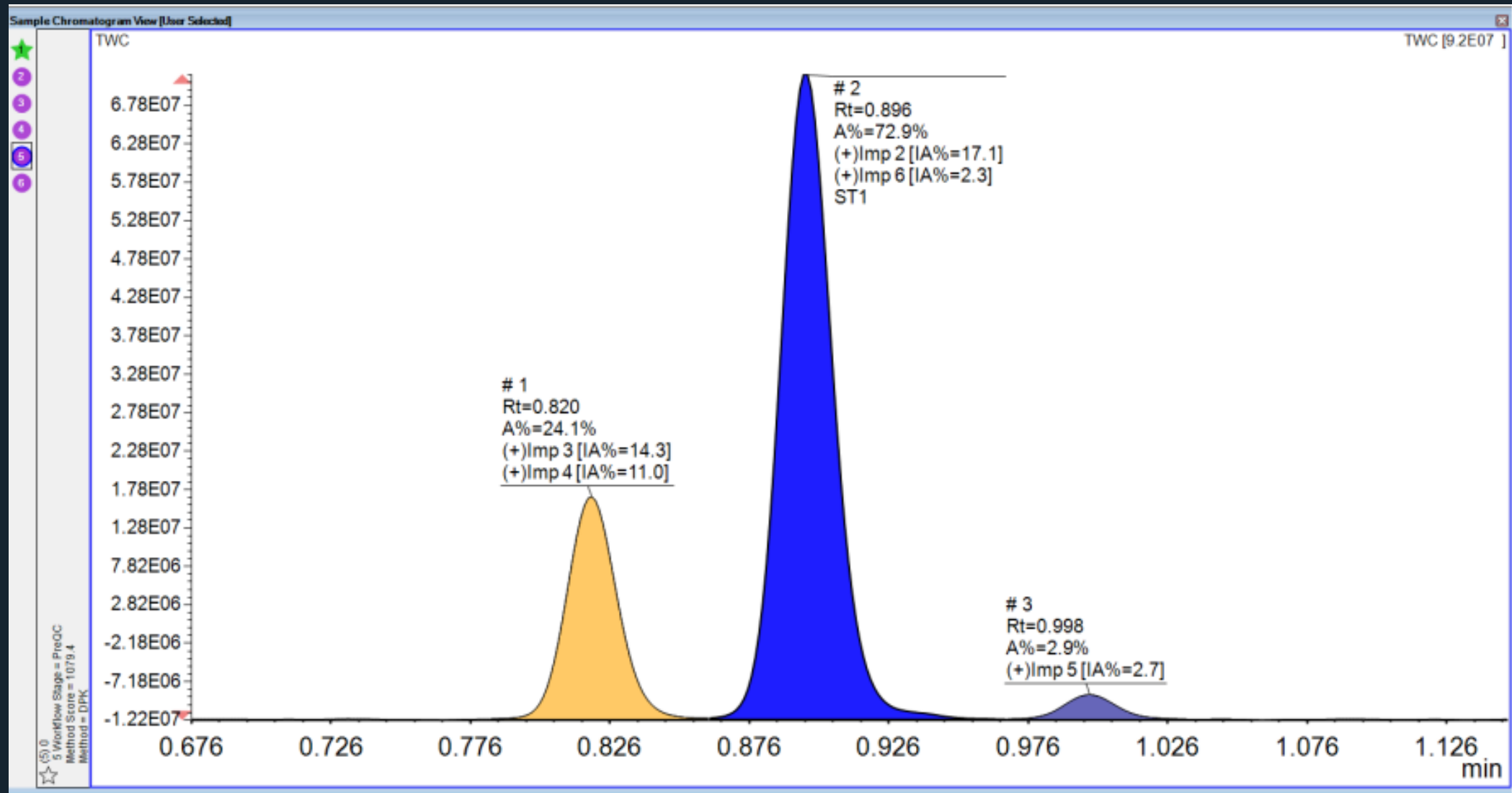
Current Selected All Linked

Replace Modify... Rename... Redefine... Delete... Append... Load... Save As...

... and peak annotations
updated accordingly



Peak results can be displayed & customized to match preference  Virscidian



The new impurities are captured and applied across the dataset



A new **Impurity Results** panel is introduced...

Impurity Results

Controls

Open/Close Panes

☒ Impurity Details

☒ Impact Values

☐ Composite Values

Show Impurity Results

☐ Show/Hide Impurity EIC

(+)Imp 1 319.2_333.0

(+)Imp 2 337.1_338.2

(+)Imp 3 351.1_352.2

(+)Imp 4 378.1_379.2_380.3_757...

(+)Imp 5 399.1_401.0

(+)Imp 6 413.1_415.0

(+)Imp 7 683.3

Impurity Details

No errors

oJ0ie4kq

Method

Inlet Method

Location

LOW

1

Impurity

Impurity Number

Masses

EIC Rt

EIC Area

EIC Height

(+)Imp 2

2

337.1_338.2

0.55

2620374.68

1341383.94

Impurity Number

Signal

Quality (1-5)

Resolved

Isolated

COI Resolved

COI Coelution

Rs Min.

Peak

F

2

TWC

4

1.18

3

0

Method

Inlet Method

Location

HIGH

2

Impurity

Impurity Number

Masses

EIC Rt

EIC Area

EIC Height

(+)Imp 2

2

337.1_338.2

0.82

5828894.51

2753345.28

Impurity Number

Signal

Quality (1-5)

Resolved

Isolated

COI Resolved

COI Coelution

Rs Min.

Peak

F

2

TWC

4

1.00

1

0

Method

Inlet Method

Location

PEI

3

Impurity

Impurity Number

Masses

EIC Rt

EIC Area

EIC Height

(+)Imp 2

2

337.1_338.2

1.09

1622403.81

606550.11

Impurity Number

Signal

Quality (1-5)

Resolved

Isolated

COI Resolved

COI Coelution

Rs Min.

Peak

F

2

TWC

4

Method

Inlet Method

Location

DIOL

4

Impurity

Impurity Number

Masses

EIC Rt

EIC Area

EIC Height

(+)Imp 2

2

337.1_338.2

0.77

1515547.37

957494.44

Impurity Number

Signal

Quality (1-5)

Resolved

Isolated

COI Resolved

COI Coelution

Rs Min.

Peak

F

2

TWC

4

Impurity Details

Impact Values

...that estimates the **Impact Values** for the impurities

Method	Inlet Method	Location													
Method 5		5													
Impurity	Impurity Number	Masses	EIC Rt	EIC Area	EIC Height										
(+)Imp 6	6	413.1_415.0	0.91	280875.01	177176.00										
Impurity	Impurity Number	Signal	Quality (0-4)	Resolved	Isolated	C	COI Coelution	Δ	Rs Min.	Peak	Rt	Area	Area %	Height	Shared Impurities
6	TWC	1								2	0.90	1876479.59	72.94	83997256.94	(+)Imp 2
Impurity	Impurity Number	Masses	EIC Rt	EIC Area	EIC Height										
(+)Imp 5	5	399.1_401.0	1.00	383723.13	236660.67										
Impurity	Impurity Number	Signal	Quality (0-4)	Resolved	Isolated	C	COI Coelution	Δ	Rs Min.	Peak	Rt	Area	Area %	Height	Shared Impurities
5	TWC	4							2.39	3	1.00	75209.51	2.92	3241454.94	
Impurity	Impurity Number	Masses	EIC Rt	EIC Area	EIC Height										
(+)Imp 2	2	337.1_338.2	0.89	624682.50	328400.44										
Impurity	Impurity Number	Signal	Quality (0-4)	Resolved	Isolated	C	COI Coelution	Δ	Rs Min.	Peak	Rt	Area	Area %	Height	Shared Impurities
2	TWC	1								2	0.90	1876479.59	72.94	83997256.94	(+)Imp 6
Impurity	Impurity Number	Masses	EIC Rt	EIC Area	EIC Height										
(+)Imp 3	3	351.1_352.2	0.82	1214189.20	722823.11										
Impurity	Impurity Number	Signal	Quality (0-4)	Resolved	Isolated	C	COI Coelution	Δ	Rs Min.	Peak	Rt	Area	Area %	Height	Shared Impurities
3	TWC	0							2.02	1	0.82	621008.98	24.14	29028291.05	(+)Imp 4
Impurity	Impurity Number	Masses	EIC Rt	EIC Area	EIC Height										
(+)Imp 4	4	378.1_379.2_380.3_757.2_758.2	0.82	1631305.43	992148.00										
Impurity	Impurity Number	Signal	Quality (0-4)	Resolved	Isolated	C	COI Coelution	Δ	Rs Min.	Peak	Rt	Area	Area %	Height	Shared Impurities
4	TWC	0							2.02	1	0.82	621008.98	24.14	29028291.05	(+)Imp 3

Advanced Automated Impurity Analysis can be combined with existing Analytical Studio features



Edit Method

File

Description: 1_CrudeQC_SFC_Method

Peak Picking

MS Processing

*UV Processing

Spectrum Scoring

Detector Time Alignment

Purity

Search Adducts

Detector Names

*Filter Detectors

Expressions

Custom Fields

Prep Gradients

Fraction Settings

Automatic selection settings

Assign Unassign

Column

Any Specified

Add column:

Selected column:

COI Intensity pH Method Score

Any Any Any Any

Single Weak Low Medium

Multiple Average High High

Strong

Method Score Range

Expression:

Low > 0 and < 0.0 Medium >= 0.0 High >= 0.0

Signal Intensity Category Settings

Signal alias:

COI SIM(-)

COI SIM(+)

TWC

COI SIM(-)

Weak > 0 and < 0

Average >= 0

Strong >= 0

Save

Load Save As

Expression: Sample metadata - Chemical Stability

Substance Type Product

Gradient Signal: TWC

Secondary Signal: Use other assigned peaks if substance not confirmed in Gradient Signal

Default Strategy: 2EP-NH3

New Strategy: Strategy 5

Methods Folder:

Select multi-COI gradients using overlapping time zones

Gradient window selection settings

Peak attribute to define start and end of window Start and end at 10% height

Define start and end window using substance peaks >= 0 Rel. Area %

Start window versus end window weighting factor 0 0-100%

Import... Append... Rename... Copy...

Create

Validate

Copy and paste to strategies with: Ctrl+V Ctrl+C or Right Click Copy and Paste

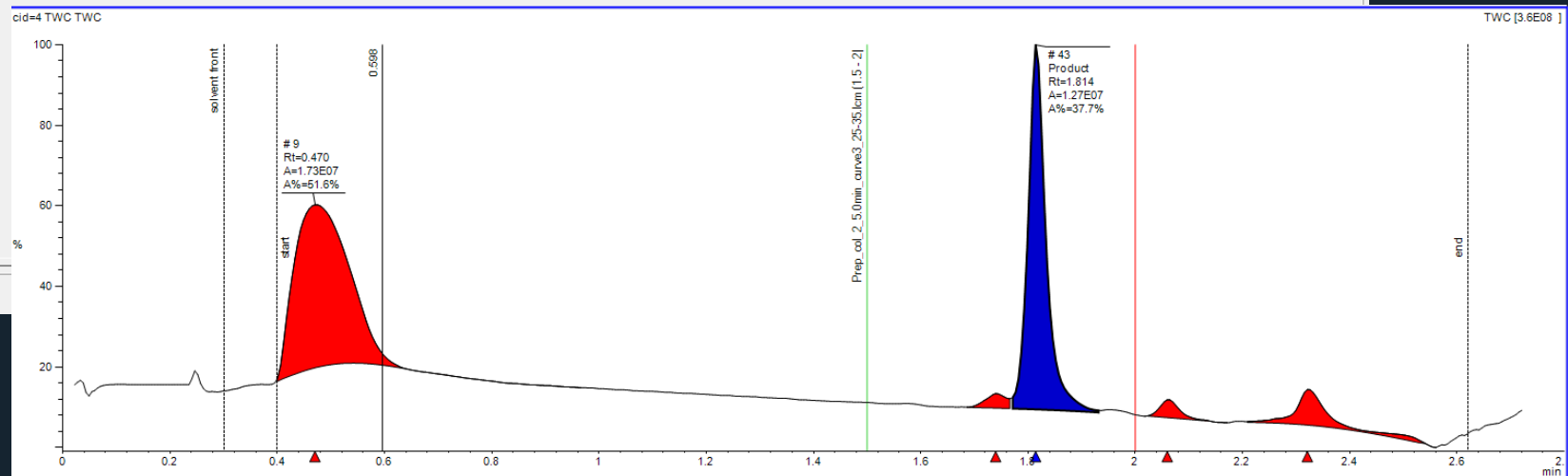
Auto Fill Validate Strategies

Gradient	Method	% B	Pre-Method	MS-Method	Start(min)
Prep_col_1_5.0min_curve1_5-15.lcm (0 - 1.25)	Prep_col_1_5.0min_curve1_5-15.lcm	0			0.00
Prep_col_1_5.0min_curve2_15-25.lcm (1.25 - 1.5)	Prep_col_1_5.0min_curve2_15-25.lcm	0			1.25
Prep_col_1_5.0min_curve3_25-35.lcm (1.5 - 2)	Prep_col_1_5.0min_curve3_25-35.lcm	0			1.50
Prep_col_1_5.0min_curve4_35-50.lcm (2 - 3)	Prep_col_1_5.0min_curve4_35-50.lcm	0			2.00

Multi-column Method selection

Focused Gradients

Review-by-Exception Expression Logic



Concluding Remarks



Analytical Studio Professional method selection capabilities have evolved

- Moved from simplistic to comprehensive analysis
- Enable better informed decision making

Advanced Automated Impurity Analysis

- Utilizes all available data
- Assessments shared across samples to estimate impurity impacts
- Integrates seamlessly into HTP workflow

Virscidian continues to work to deliver cutting edge solutions

- Partner with customers and vendors
- Quickly move from idea to implementation



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