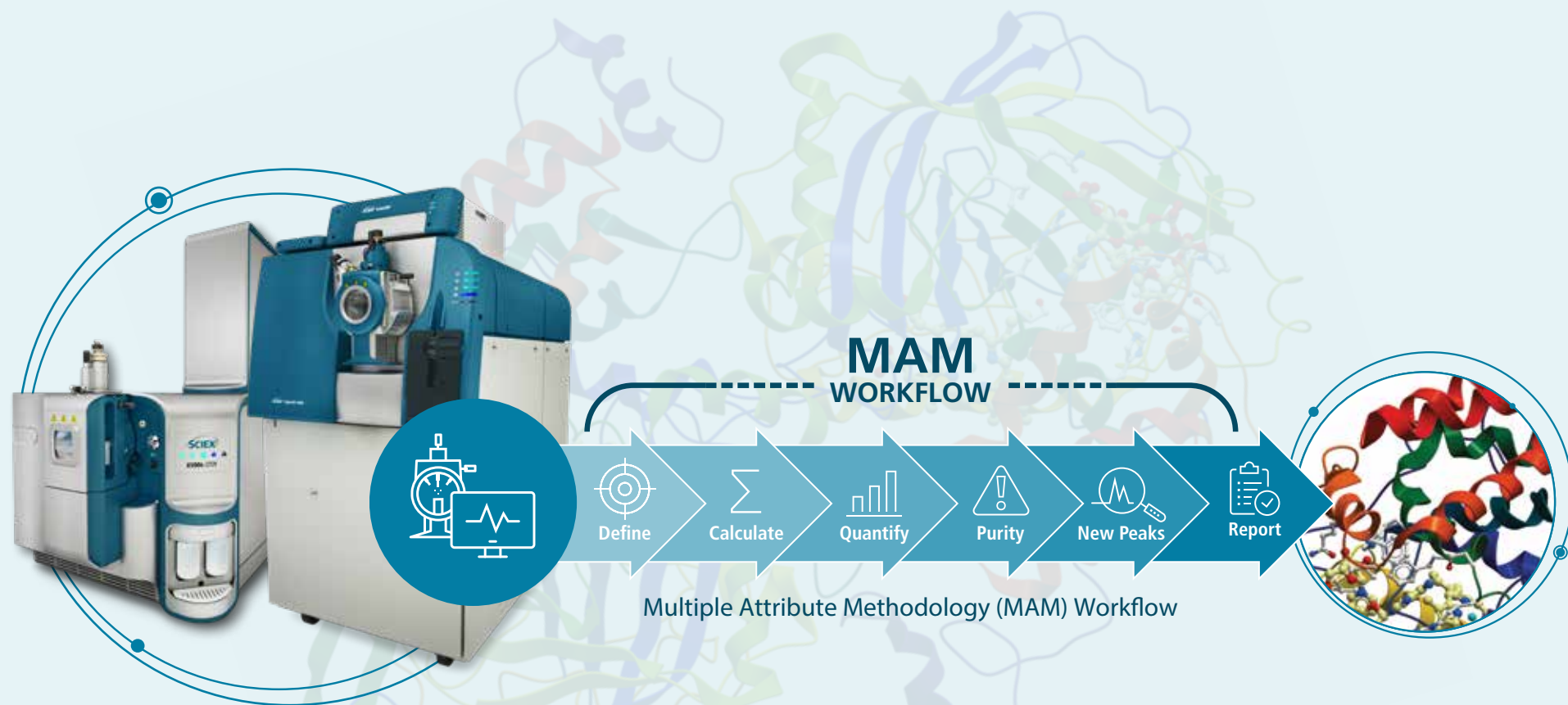


The Compliant-Ready LC-MS Workflow for MAM

Multiple attribute methodology (MAM) for biotherapeutic attribute monitoring and purity testing





Multiple attribute methodology (MAM) by accurate mass LC-MS

MAM with confidence and compliance

In biotherapeutic process development, evaluating and tracking potential product quality attributes (PQAs) is crucial to ensure quality, safety, and efficacy. Currently, multiple analytical assays are used for PQA monitoring throughout biologic development and production, which is resource intensive.

You can streamline your workflows with a faster, more in depth view of your biologic with Multiple Attribute Methodology (MAM) using Accurate Mass LC-MS:

- ✓ Directly detect and measure biologically relevant attributes
- ✓ Track known variants and contaminants
- ✓ Detect and flag the presence of unspecified impurities
- ✓ Use the same workflow for intact or peptide-level analysis.

The powerful, yet straightforward SCIEX Workflow for MAM offers a compliant and flexible solution for simplified PQA definition, monitoring, quantification and reporting.

Biologic PQA Assessments	LC-MS MAM Workflow	SEC	CEX	CE-SDS	HILIC	ELISA
Deamidation	Green	Red	Green	Red	Red	Red
Glycation	Green	Red	Red	Green	Red	Red
High Mannose	Green	Red	Red	Red	Green	Red
Methionine Oxidation	Green	Red	Red	Red	Red	Red
Signal Peptide	Green	Red	Red	Red	Red	Red
Glycosylation	Green	Red	Green	Yellow	Green	Red
CDR Tryptophan Degradation	Green	Red	Red	Red	Red	Red
C-terminal Lysine	Green	Red	Green	Red	Red	Red
Misincorporations	Green	Red	Red	Red	Red	Red
C-terminal amidation	Green	Red	Green	Red	Red	Red
Fucosylation	Green	Red	Red	Red	Red	Red
Residual Protein A	Green	Red	Red	Red	Red	Red
Host Cell Protein	Green	Red	Red	Red	Red	Green
Aggregate	Red	Green	Green	Green	Red	Red
Cysteine Adduct Assessment	Yellow	Red	Yellow	Red	Red	Red

In a single LC-MS/MS assay, get direct physical information about many of your most important product quality attributes

The SCIEX flexible solution for MAM

Complete solution for accelerating biotherapeutic analysis throughout development



Ultimate workflow flexibility in a powerful accurate mass platform

Gain the flexibility to do comprehensive characterization, MAM method development, quantification and high throughput comparability studies on the powerhouse TripleTOF® 6600 System.



Unparalleled robustness with ultra-low downtime

The ExionLC™ AD delivers excellent accuracy, reliability and repeatability across thousands of injections, with maximum uptime

Simplified set-up for accelerated results in a compact footprint

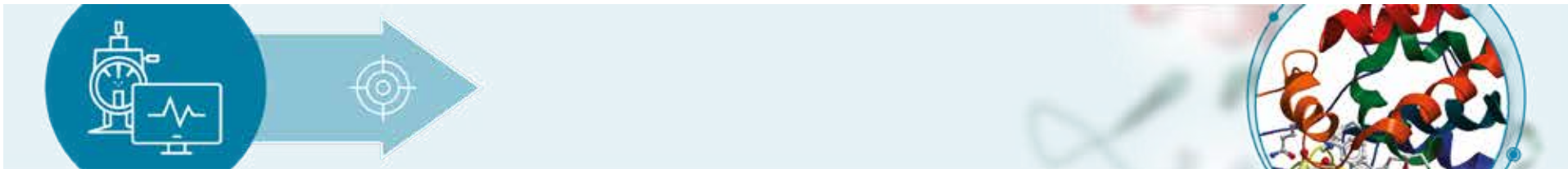
The X500B QTOF system is an easy-to-use, robust platform for streamlining your biologics characterization studies. Create, save and run methods easier with the intuitive SCIEX OS user interface.

Compliant-ready acquisition and decision making

SCIEX OS automates key steps of analysis, streamlines all your workflows, and enables you to make informed decisions quickly. Enables MAM workflows at the peptide, subunit or intact level.



Explore the complete workflow and learn how to accelerate your biotherapeutic development.



Attribute discovery

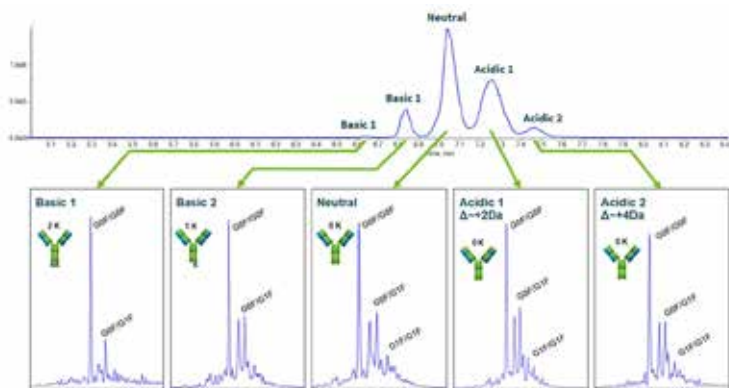
Expedite attribute characterization and simplify MAM method development:

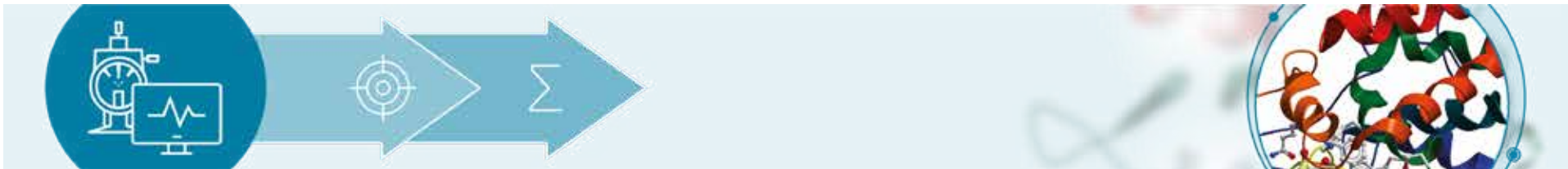
Comprehensive Characterization with Complete Detection

- Simple and comprehensive detection of attributes
- Attributes can be at the level of peptide, subunit or even intact
- Easily acquire high resolution TOF MS, high resolution MS/MS with IDA or comprehensive and unbiased high resolution MS/MS with SWATH Acquisition
- Intuitive and easy-to-use viewing and filtering options in BPV Flex allow you to quickly dig into the attributes of most interest

The flexibility to work with other software

If you prefer to do your attribute definition in another software, no problem. SCIEX OS supports the import of attribute definitions from several other software vendors including Protein Metrics and GeneData.





Attribute calculation

Customize how you calculate and quantify your attributes

Full control of quantification

- Adjustable reconstruction and quantification parameters
- Parameters can be optimized per attribute and changes can be applied in real time

Full control of calculation

- Customize how and what peak areas you use
- Customize the statistics of your peak areas (sum, max, mean, etc.)
- Customize how you calculate your percentages

Reconstruction (new 3C)

Expected RT: 5.06 min
 XIC Gaussian Smooth Width: 0.0 points
 Reconstructed on the largest XIC Peak
 RT Half Window: 15.0 sec
 Numbers of Spectra to Average: 13

Reconstruction

Resolution: 5000
 Reconstruction Start Mass: 22000.00 Da
 Reconstruction Stop Mass: 25000.00 Da

Advanced Reconstruction

Number of Iterations: 20
 Signal to Noise Threshold: 10
 Step Mass: 1.00 Da
 Use input m/z Range
 Start m/z: Da
 Stop m/z: Da

Apply RT, Reconstruction and Adv. Reconstruction parameters to: Component

Mass Peak Selection

Expected MW: 23127.20 Da
 Mass Half Window: 2 Da

Apply peak parameters to all of the components

Chromatogram: XIC, XIC from 20180828_Non-24h-idea-top-60n-off-w..._Non-24h-idea-top-60n-off-w... + TOP MS (900 - 3000) m/z: 700.0000 - 2500.0000 Da, RT: 5.13 min. Peak at 5.70 min.

Mass Spectrum: Spectrum from 20180828_Non-24h-idea-top-60n-off-w..._off... + TOP MS (800 - 3000) from 5.045 to 5.151 min. Peaks at 926.16, 925.98, 926.90, 927.81, 927.09, 798.60, 1000.54, 1132.26, 1157.17, 1285.85, 1364.25, 1779.79, 1908.29, 1908.01, 1925.16, 1927.54, 2109.48, 2109.22, 2317.45.

Reconstruction: XIC, Reconstruction from 20180828_Non-24h-idea-top-60n-off-w..._off... + TOP MS (900 - 3000) from 5.045 to 5.151 min. MW: 23127.23 Da, Area: 7.418e5, Height: 7.280e4. Peaks at 23109.49, 23144.50, 23190.55, 23280.04, 23374.88.

Use the calculator to create a new formula.

Formula name:

= GETGROUP([Area];1)+GETGROUP([Area];2)+GETGROUP([Area];3)+GETGROUP([Area];4)

COUNT	MAX	STDEV	Clear
SUM	MIN	MEDIAN	←
MEAN	ABS	MAD	↓
/	*	-	+

▼ Regression parameters

- + r^2
- Slope
- Intercept
- Quadratic coefficient
- Linear coefficient
- Constant term

▼ Column

- Accuracy
- Accuracy Acceptance

Test "NA" values as: Zero

Use the calculator to create a new formula.

Formula name: AttributeArea

= [Area]

COUNT	MAX	STDEV	Clear
SUM	MIN	MEDIAN	←
MEAN	ABS	MAD	↓
/	*	-	+

Test "NA" values as: Zero

Use the calculator to create a new formula.

Formula name:

= [Area]/[SumArea]*100

COUNT	MAX	STDEV	Clear
SUM	MIN	MEDIAN	←
MEAN	ABS	MAD	↓
/	*	-	+

Test "NA" values as: Zero



Attribute review

Easily make insights about your MAM results

Easily set acceptance criteria

Define pass/fail criteria based on upper limit, lower limit, ranges or % deviation from reference values.

One click leads to the information you need

A live interface ties together attributes, visualizations, MS and MS/MS data.



Impurity detection

Built-in unspecified impurity testing to discover new species or contaminants

Use chromatographic (ie retention time) or spectral (ie area ratio) information to easily identify new species.

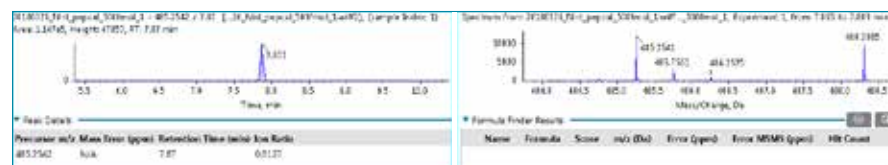
Reliably and automatically find new peaks.

Rule name	AreaControl
Flag a results column	Area Ratio Control
Flagging criteria	Range

Rule name	RTDelta
Flag a results column	RTDelta
Flagging criteria	Upper limit

Component	Found At Mass	Adduct / C...	Area	Outlier Reasons	Retention Time	'RTDelta	Height	'Area Ratio Cont...
495.2542 / 7.87...	495.2542	[M+2H] ²⁺	1.147e5	AreaControl, ControlHeight, ControlQu...	7.87	0.001	47851	114718.978
491.2658 / 8.42...	491.2659	[M+2H] ²⁺	5.977e4	AreaControl, ControlHeight, ControlQu...	9.39	0.025	8291	58771.478
488.5580 / 18.7...	488.5582	[M+2H] ³⁺	1.503e5	AreaControl, ControlHeight, ControlQu...	10.70	0.011	34827	150294.998
473.2682 / 18.8...	473.2682	[M+2H] ²⁺	1.823e5	AreaControl, ControlHeight, ControlQu...	10.94	0.004	42654	182305.468
583.3138 / 12.2...	583.3143	[M+2H] ²⁺	1.189e5	AreaControl, ControlHeight, ControlQu...	12.29	0.049	11596	118872.263
593.8087 / 14.1...	593.8087	[M+2H] ²⁺	1.811e5	AreaControl, ControlHeight, ControlQu...	14.10	0.014	18500	181183.845
739.3619 / 16.4...	739.3622	[M+2H] ²⁺	6.758e4	AreaControl, ControlHeight, ControlQu...	16.44	0.020	13362	67582.376
493.2437 / 16.4...	493.2438	[M+2H] ³⁺	2.594e4	AreaControl, ControlHeight, ControlQu...	16.44	0.009	5878	25943.519
533.3226 / 17.8...	533.3237	[M+2H] ²⁺	2.917e5	AreaControl, ControlHeight, ControlQu...	17.83	0.022	56748	291997.897

All new species have live links back to their chromatographic, MS and MS/MS information.





Compliance ready

Achieve all of your MAM functionality in a fully compliant-ready environment

Full complement of compliance features

- Customizable user roles and security
- Password-protected method locks and recorded events

A detailed audit trail

- Changes can be tracked in detail
- Before and after states can be viewed from changes
- All user changes are recorded

Confirm Change Events

Change Events

Timestamp	Event Name	Event Description
5/26/2020 1:19:24 PM	Integration parameters changed	20191015 Adalimumab lot 3 of Q01/Man3 (C:\Users\zoe.zheng\Documents\Data\Adalimumab-intact\20191015-Adalimumab lot 3.mf12_sample TL. Expected RT was changed from 4 to 6.54. Reconstructed Area changed to "48912.212" counts. MW changed to 147654.537 Da.

E-Signature

Timestamp: 5/26/2020 1:19:24 PM
 User Name: NETADDS\Zoe.Zhang
 Full User Name: Zhang, Zoe (Yuzhuo)

Reason:

Password:

Timestamp	Event Name	Description	Reason	E-Signature	Full User Name	User	Category
5/26/2020 1:19:24 PM	Integration parameters changed	20191015 Adalimumab lot 3 of Q01/Man3 (C:\Users\zoe.zheng\Documents\Data\Adalimumab-intact\20191015-Adalimumab lot 3.mf12_sample TL. Expected RT was changed from 4 to 6.54. Reconstructed Area changed to "48912.212" counts. MW changed to 147654.537 Da.	Correct RT		Zhang, Zoe (Yuzhuo)	NETADDS\Zoe.Zhang	Analytics

Analytics Details | **General Details**

Results Table Comparison

C:\SQE\05 Data\Default\Quantitative Results\compliance testing-qa-test: Results Table of the selected Event (5/26/2020...

Index	Sample Name	Sample Type	Component Name	Component Type	Component Group Name	Peak RT	Area	Reten. Time	Reten. Time E.	Reten. Time S.
1	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678
2	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678
3	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678
4	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678

C:\SQE\05 Data\Default\Quantitative Results\compliance testing-qa-test: Previous version of the Results Table of the selected...

Index	Sample Name	Sample Type	Component Name	Component Type	Component Group Name	Peak RT	Area	Reten. Time	Reten. Time E.	Reten. Time S.
1	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	4.00	147654	3.97	3.874	4.026
2	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678
3	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678
4	20191015 Adalimumab	Unknown	Q01/Man3	Quantifier	Zyrosys	6.54	147654	6.57	6.402	6.678

Peak | **Cal. Curve**










Reporting

Reporting that's quick to set up and easy to interpret

Flexibility extends to reporting too

- Export to text files, PDFs or a variety of other formats.
- Use included templates or easily create your own
- Export all of the fields and parameters or just the ones you need
- Not just data – report trends and visualizations

 <ul style="list-style-type: none"> • A compliant-ready system • Easy to use acquisition software • Auto tune and calibration 	 <ul style="list-style-type: none"> • Characterize product • Define unlimited attributes, acceptance criteria and integration parameters 	 <ul style="list-style-type: none"> • Fully customizable calculation engine • Make your attributes how you like them 	 <ul style="list-style-type: none"> • Simplify review with automated quantification • Change quantification parameters on the fly 	 <ul style="list-style-type: none"> • Automatically flag deviations or fail attributes • Easily review with real time data investigation 	 <ul style="list-style-type: none"> • Find and flag impurities with new peak detection 	 <ul style="list-style-type: none"> • Streamline customizable reporting • Visualization and trend analysis tools
--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------



The SCIEX flexible solution for MAM

The flexibility to work across peptide level, subunit level or intact analysis of therapeutic proteins in a trusted, compliant-ready environment. The SCIEX flexible solution for MAM will accelerate your protein therapeutic development.

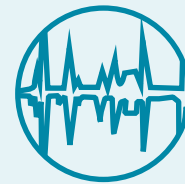
Learn how your lab can stay at the forefront and leverage powerful LC-MS methodologies to support faster, more confident biotherapeutic development. Explore more at: sciex.com/content/SCIEX/na/us/en/applications/pharma-and-biopharma/protein-therapeutics/multiple-attribute-methodology-workflow

20
out of the top
20

Pharma and BioPharma companies use SCIEX compliant LC-MS software solutions.



21 CFR Part 11 compliant-ready



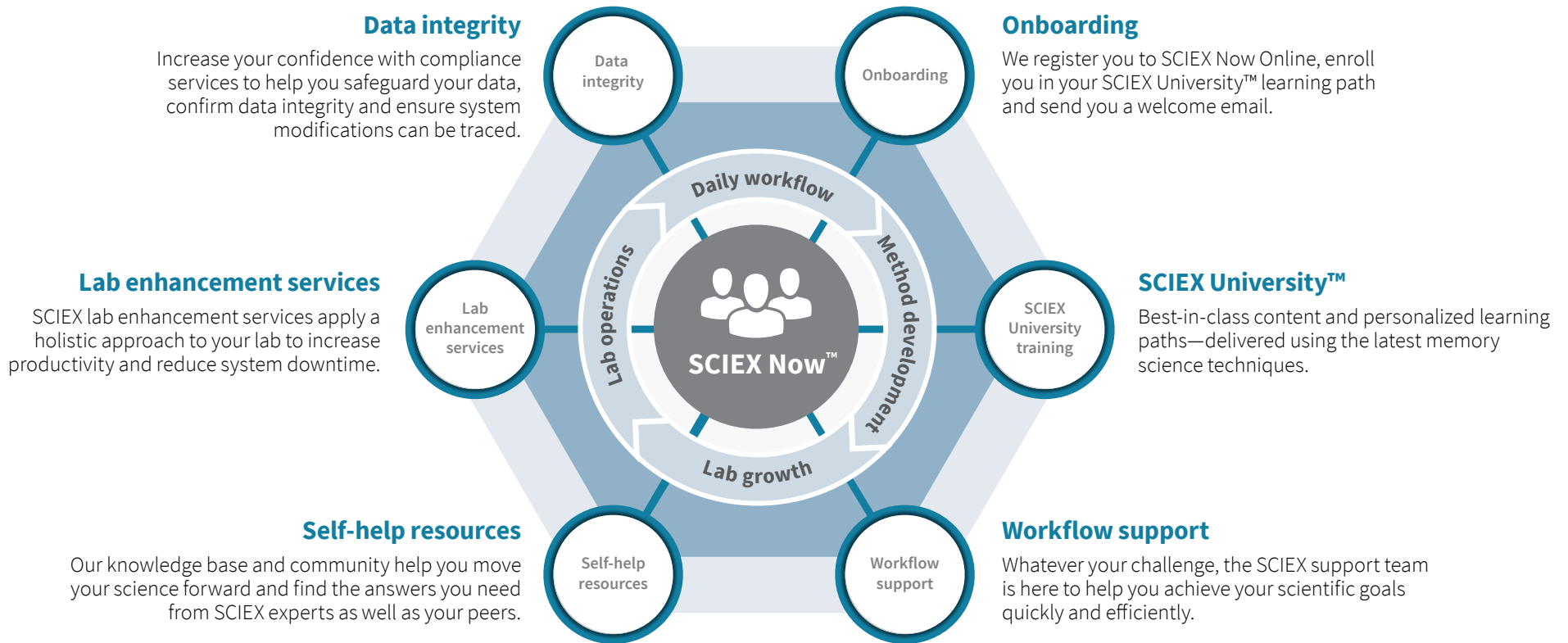
Intact MAM capable



Peptide level MAM capable

SCIEX Now™ Support Network

The destination for all your support needs



Start your path to success now: sciex.com/sciexnow

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Headquarters

500 Old Connecticut Path
Framingham, MA 01701 USA
Phone 508-383-7700
sciex.com

International Sales

For our office locations please call the division headquarters or refer to our website at sciex.com/offices

