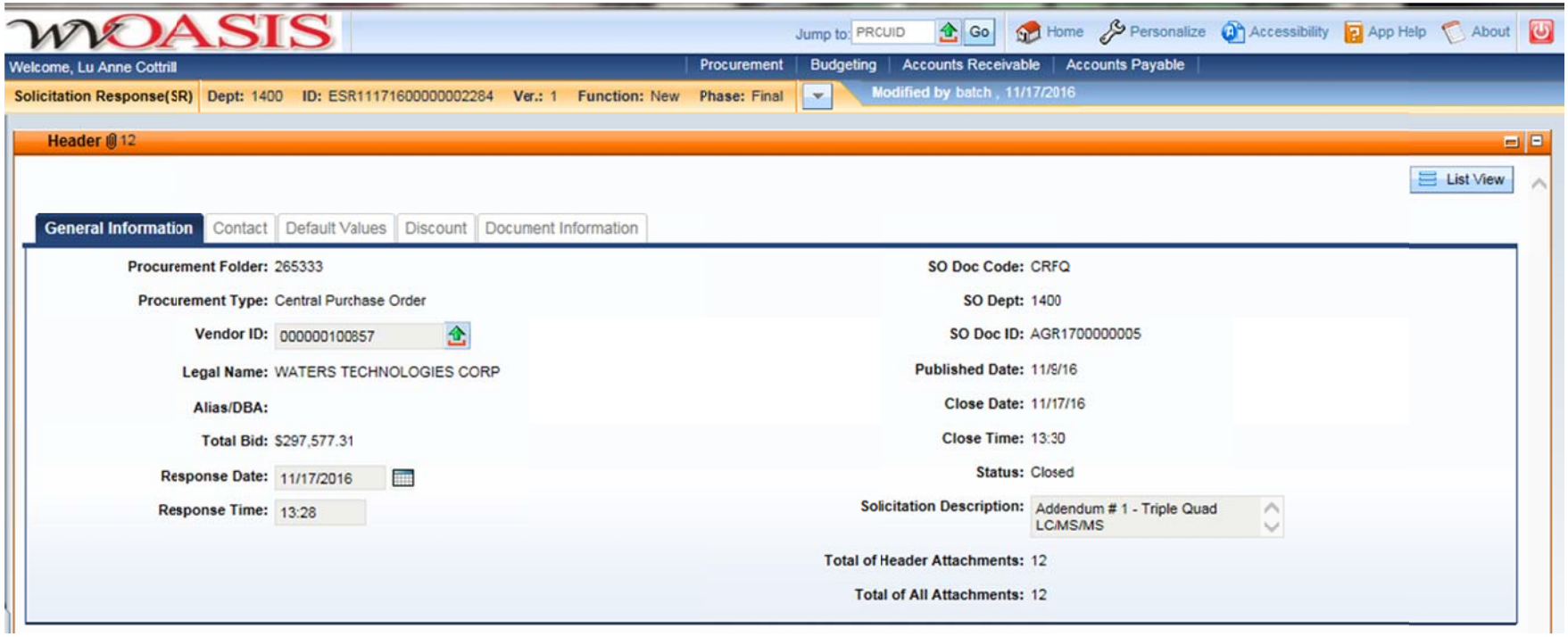
The following documentation is an electronically-submitted vendor response to an advertised solicitation from the *West Virginia Purchasing Bulletin* within the Vendor Self-Service portal at ***wvOASIS.gov***. As part of the State of West Virginia's procurement process, and to maintain the transparency of the bid-opening process, this documentation submitted online is publicly posted by the West Virginia Purchasing Division at ***WVPurchasing.gov*** with any other vendor responses to this solicitation submitted to the Purchasing Division in hard copy format.


WVOASIS
Jump to: PRCUID Go
Home
Personalize
Accessibility
App Help
About
Welcome, Lu Anne Cottrill
Procurement
Budgeting
Accounts Receivable
Accounts Payable
Solicitation Response(SR) Dept: 1400 ID: ESR11171600000002284 Ver.: 1 Function: New Phase: Final
Modified by batch , 11/17/2016
Header 12
List View
General Information
Contact
Default Values
Discount
Document Information
Procurement Folder: 265333
Procurement Type: Central Purchase Order
Vendor ID: 000000100857
Legal Name: WATERS TECHNOLOGIES CORP
Alias/DBA:
Total Bid: $297,577.31
Response Date: 11/17/2016
Response Time: 13:28
SO Doc Code: CRFQ
SO Dept: 1400
SO Doc ID: AGR1700000005
Published Date: 11/9/16
Close Date: 11/17/16
Close Time: 13:30
Status: Closed
Solicitation Description: Addendum # 1 - Triple Quad LC/MS/MS
Total of Header Attachments: 12
Total of All Attachments: 12

Purchasing Division
2019 Washington Street East
Post Office Box 50130
Charleston, WV 25305-0130

State of West Virginia
Solicitation Response

Proc Folder : 265333

Solicitation Description : Addendum # 1 - Triple Quad LC/MS/MS

Proc Type : Central Purchase Order

Date issued	Solicitation Closes	Solicitation Response	Version
	2016-11-17 13:30:00	SR 1400 ESR11171600000002284	1

VENDOR

000000100857

WATERS TECHNOLOGIES CORP

Solicitation Number: CRFQ 1400 AGR1700000005

Total Bid : $297,577.31 **Response Date:** 2016-11-17 **Response Time:** 13:28:58

Comments:

Dear Linda,
Please note I have to finalize the Exceptions document and will email it to you as soon as it is complete.
Please see attached for our response and contact me immediately with any questions.
We thank you for the opportunity and look forward to working with the State of West Virginia.
Thank you,
Alicia Shannon
bid_desk@waters.com

FOR INFORMATION CONTACT THE BUYER

Linda Harper

(304) 558-0468
linda.b.harper@wv.gov

Signature on File **FEIN #** **DATE**

All offers subject to all terms and conditions contained in this solicitation

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
1	LCMSMS, Workstation, software, printer	1.00000	EA	$296,428.850000	$296,428.85

Comm Code	Manufacturer	Specification	Model #
41100000			

Extended Description : LCMSMS, Workstation, software, printer per specification 3.1.1 & 3.1.2

Comments: Please refer to quotation 21332675 for detailed pricing information

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
2	Shipping Charges and inside delivery	1.00000	EA	$1,148.460000	$1,148.46

Comm Code	Manufacturer	Specification	Model #
78121603			

Extended Description : Shipping Charges and inside deliver per section 3.1.3

Comments: Please refer to quotation 21332675 for detailed pricing information

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
3	Installation/validation	1.00000	EA	$0.000000	$0.00

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description : Installation/validation per section 3.1.3

Comments: Included in item 3.1.1 & 3.1.2. Please refer to quotation 21332675 for detailed pricing information

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
4	Training/Warranty	1.00000	EA	$0.000000	$0.00

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description : Training/Warranty per section 3.1.3

Comments: Included in item 3.1.1 & 3.1.2. Please refer to quotation 21332675 for detailed pricing information

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
5	Service	1.00000	EA	$0.000000	$0.00

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description : Service per section 3.1.3

Comments: Included in item 3.1.1 & 3.1.2. Please refer to quotation 21332675 for detailed pricing information

Purchasing Divison
2019 Washington Street East
Post Office Box 50130
Charleston, WV 25305-0130

State of West Virginia
Request for Quotation
01 — Agricultural

Proc Folder: 265333
Doc Description: Triple Quad LC/MS/MS
Proc Type: Central Purchase Order

Date Issued	Solicitation Closes	Solicitation No	Version
2016-10-24	2016-11-17 13:30:00	CRFQ 1400 AGR1700000005	1

BID RECEIVING LOCATION

BID CLERK
DEPARTMENT OF ADMINISTRATION
PURCHASING DIVISION
2019 WASHINGTON ST E
CHARLESTON WV 25305
US

VENDOR

Vendor Name, Address and Telephone Number:

Waters Technologies Corporation
34 Maple St
Milford, MA 01757
800-252-4752

FOR INFORMATION CONTACT THE BUYER

Linda Harper
(304) 558-0468
linda.b.harper@wv.gov

Signature X Kristen A. Drakeley **FEIN #** 04-3234558 **DATE** 11/16/16

All offers subject to ~~all terms and conditions contained in this solicitation~~

Please refer to the attached document titled "Exceptions"

ADDITIONAL INFORMAITON:

The West Virginia Purchasing Division for the Agency, The West Virginia Department of Agriculture is soliciting bids from qualified vendors to establish a "One-Time" contract for the purchase of a Liquid Chromatography/Mass Spectrometer (LC/MS) Instrument per the Specifications, ~~Terms & Conditions~~ and bid requirements as attached.

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221	AUTHORIZED RECEIVER 304-558-2227
AGRICULTURE DEPARTMENT OF	AGRICULTURE DEPARTMENT OF
ADMINISTRATIVE SERVICES	REGULATORY PROTECTION DIVISION
1900 KANAWHA BLVD E	313 GUS R DOUGLAS LN, BLDG 11
CHARLESTON WV25305-0173	CHARLESTON WV 25312
US	US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
1	LCMSMS, Workstation, software, printer	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
41100000			

Extended Description :

LCMSMS, Workstation, software, printer per specification 3.1.1 & 3.1.2

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221	AUTHORIZED RECEIVER 304-558-2227
AGRICULTURE DEPARTMENT OF	AGRICULTURE DEPARTMENT OF
ADMINISTRATIVE SERVICES	REGULATORY PROTECTION DIVISION
1900 KANAWHA BLVD E	313 GUS R DOUGLAS LN, BLDG 11
CHARLESTON WV25305-0173	CHARLESTON WV 25312
US	US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
2	Shipping Charges and inside delivery	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
78121603			

Extended Description :

Shipping Charges and inside deliver per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221	AUTHORIZED RECEIVER 304-558-2227
AGRICULTURE DEPARTMENT OF	AGRICULTURE DEPARTMENT OF
ADMINISTRATIVE SERVICES	REGULATORY PROTECTION DIVISION
1900 KANAWHA BLVD E	313 GUS R DOUGLAS LN, BLDG 11
CHARLESTON WV25305-0173	CHARLESTON WV 25312
US	US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
3	Installation/validation	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :
Installation/validation per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
4	Training/Warranty	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :
Training/Warranty per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
5	Service	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :
Service per section 3.1.3

SCHEDULE OF EVENTS

Line	Event	Event Date
1	Question Deadline 3:00 p.m.	2016-11-04

INSTRUCTIONS TO VENDORS SUBMITTING BIDS

1. REVIEW DOCUMENTS THOROUGHLY: The attached documents contain a solicitation for bids. Please read these instructions and all documents attached in their entirety. These instructions provide critical information about requirements that if overlooked could lead to disqualification of a Vendor's bid. All bids must be submitted in accordance with the provisions contained in these instructions and the Solicitation. Failure to do so may result in disqualification of Vendor's bid.

2. MANDATORY TERMS: The Solicitation may contain mandatory provisions identified by the use of the words "must," "will," and "shall." Failure to comply with a mandatory term in the Solicitation will result in bid disqualification.

3. PREBID MEETING: The item identified below shall apply to this Solicitation.

☑ A pre-bid meeting will not be held prior to bid opening

☐ A **NON-MANDATORY PRE-BID** meeting will be held at the following place and time:

☐ A **MANDATORY PRE-BID** meeting will be held at the following place and time:

All Vendors submitting a bid must attend the mandatory pre-bid meeting. Failure to attend the mandatory pre-bid meeting shall result in disqualification of the Vendor's bid. No one person attending the pre-bid meeting may represent more than one Vendor.

An attendance sheet provided at the pre-bid meeting shall serve as the official document verifying attendance. The State will not accept any other form of proof or documentation to verify attendance. Any person attending the pre-bid meeting on behalf of a Vendor must list on the attendance sheet his or her name and the name of the Vendor he or she is representing.

Additionally, the person attending the pre-bid meeting should include the Vendor's E-Mail address, phone number, and Fax number on the attendance sheet. It is the Vendor's responsibility to locate the attendance sheet and provide the required information. Failure to complete the attendance sheet as required may result in disqualification of Vendor's bid.

All Vendors should arrive prior to the starting time for the pre-bid. Vendors who arrive after the starting time but prior to the end of the pre-bid will be permitted to sign in, but are charged with knowing all matters discussed at the pre-bid.

Questions submitted at least five business days prior to a scheduled pre-bid will be discussed at the pre-bid meeting if possible. Any discussions or answers to questions at the pre-bid meeting are preliminary in nature and are non-binding. Official and binding answers to questions will be published in a written addendum to the Solicitation prior to bid opening.

4. VENDOR QUESTION DEADLINE: Vendors may submit questions relating to this Solicitation to the Purchasing Division. Questions must be submitted in writing. All questions must be submitted on or before the date listed below and to the address listed below in order to be considered. A written response will be published in a Solicitation addendum if a response is possible and appropriate. Non-written discussions, conversations, or questions and answers regarding this Solicitation are preliminary in nature and are nonbinding.

Submitted e-mails should have solicitation number in the subject line.

Question Submission Deadline: Friday, November 4, 2016, 3:00 p.m.

Submit Questions to: Linda Harper, Senior Buyer
2019 Washington Street, East
Charleston, WV 25305
Fax: (304) 558-4115 (Vendors should not use this fax number for bid submission)
Email: Linda.B.Harper@wv.gov

5. VERBAL COMMUNICATION: Any verbal communication between the Vendor and any State personnel is not binding, including verbal communication at the mandatory pre-bid conference. Only information issued in writing and added to the Solicitation by an official written addendum by the Purchasing Division is binding.

6. BID SUBMISSION: All bids must be submitted electronically through wvOASIS or signed and delivered by the Vendor to the Purchasing Division at the address listed below on or before the date and time of the bid opening. Any bid received by the Purchasing Division staff is considered to be in the possession of the Purchasing Division and will not be returned for any reason. The Purchasing Division will not accept bids, modification of bids, or addendum acknowledgment forms via e-mail. Acceptable delivery methods include electronic submission via wvOASIS, hand delivery, delivery by courier, or facsimile.

The bid delivery address is:
Department of Administration, Purchasing Division
2019 Washington Street East
Charleston, WV 25305-0130

A bid that is not submitted electronically through wvOASIS should contain the information listed below on the face of the envelope or the bid may be rejected by the Purchasing Division.:

SEALED BID: Triple Quad LC/MS/MS
BUYER: Linda B. Harper
SOLICITATION NO.: CRFQ AGR1700000005
BID OPENING DATE: November 17, 2016
BID OPENING TIME: 1:30 p.m.
FAX NUMBER:

The Purchasing Division may prohibit the submission of bids electronically through wvOASIS at its sole discretion. Such a prohibition will be contained and communicated in the wvOASIS system resulting in the Vendor's inability to submit bids through wvOASIS. Submission of a response to an Expression or Interest or Request for Proposal is not permitted in wvOASIS.

For Request For Proposal ("RFP") Responses Only: In the event that Vendor is responding to a request for proposal, the Vendor shall submit one original technical and one original cost proposal plus N/A convenience copies of each to the Purchasing Division at the address shown above. Additionally, the Vendor should identify the bid type as either a technical or cost proposal on the face of each bid envelope submitted in response to a request for proposal as follows:

BID TYPE: (This only applies to CRFP)
☐ Technical
☐ Cost

7. BID OPENING: Bids submitted in response to this Solicitation will be opened at the location identified below on the date and time listed below. Delivery of a bid after the bid opening date and time will result in bid disqualification. For purposes of this Solicitation, a bid is considered delivered when confirmation of delivery is provided by wvOASIS (in the case of electronic submission) or when the bid is time stamped by the official Purchasing Division time clock (in the case of hand delivery).

Bid Opening Date and Time: November 17, 2016, 1:30 p.m.

Bid Opening Location: Department of Administration, Purchasing Division
2019 Washington Street East
Charleston, WV 25305-0130

8. ADDENDUM ACKNOWLEDGEMENT: Changes or revisions to this Solicitation will be made by an official written addendum issued by the Purchasing Division. Vendor should acknowledge receipt of all addenda issued with this Solicitation by completing an Addendum Acknowledgment Form, a copy of which is included herewith. Failure to acknowledge addenda may result in bid disqualification. The addendum acknowledgement should be submitted with the bid to expedite document processing.

9. BID FORMATTING: Vendor should type or electronically enter the information onto its bid to prevent errors in the evaluation. Failure to type or electronically enter the information may result in bid disqualification.

10. ALTERNATES: Any model, brand, or specification listed in this Solicitation establishes the acceptable level of quality only and is not intended to reflect a preference for, or in any way favor, a particular brand or vendor. Vendors may bid alternates to a listed model or brand provided that the alternate is at least equal to the model or brand and complies with the required specifications. The equality of any alternate being bid shall be determined by the State at its sole discretion. Any Vendor bidding an alternate model or brand should clearly identify the alternate items in its bid and should include manufacturer's specifications, industry literature, and/or any other relevant documentation demonstrating the equality of the alternate items. Failure to provide information for alternate items may be grounds for rejection of a Vendor's bid.

11. EXCEPTIONS AND CLARIFICATIONS: The Solicitation contains the specifications that shall form the basis of a contractual agreement. Vendor shall clearly mark any exceptions, clarifications, or other proposed modifications in its bid. Exceptions to, clarifications of, or modifications of a requirement or term and condition of the Solicitation may result in bid disqualification.

12. COMMUNICATION LIMITATIONS: In accordance with West Virginia Code of State Rules §148-1-6.6, communication with the State of West Virginia or any of its employees regarding this Solicitation during the solicitation, bid, evaluation or award periods, except through the Purchasing Division, is strictly prohibited without prior Purchasing Division approval. Purchasing Division approval for such communication is implied for all agency delegated and exempt purchases.

13. REGISTRATION: Prior to Contract award, the apparent successful Vendor must be properly registered with the West Virginia Purchasing Division and must have paid the $125 fee, if applicable.

14. UNIT PRICE: Unit prices shall prevail in cases of a discrepancy in the Vendor's bid.

15. PREFERENCE: Vendor Preference may only be granted upon written request and only in accordance with the West Virginia Code § 5A-3-37 and the West Virginia Code of State Rules. A Vendor Preference Certificate form has been attached hereto to allow Vendor to apply for the preference. Vendor's failure to submit the Vendor Preference Certificate form with its bid will result in denial of Vendor Preference. Vendor Preference does not apply to construction projects.

16. SMALL, WOMEN-OWNED, OR MINORITY-OWNED BUSINESSES: For any solicitations publicly advertised for bid, in accordance with West Virginia Code §5A-3-37(a)(7) and W. Va. CSR § 148-22-9, any non-resident vendor certified as a small, women-owned, or minority-owned business under W. Va. CSR § 148-22-9 shall be provided the same preference made available to any resident vendor. Any non-resident small, women-owned, or minority-owned business must identify itself as such in writing, must submit that writing to the Purchasing Division with its bid, and must be properly certified under W. Va. CSR § 148-22-9 prior to contract award to receive the preferences made available to resident vendors. Preference for a non-resident small, women-owned, or minority owned business shall be applied in accordance with W. Va. CSR § 148-22-9.

17. WAIVER OF MINOR IRREGULARITIES: The Director reserves the right to waive minor irregularities in bids or specifications in accordance with West Virginia Code of State Rules § 148-1-4.6.

18. ELECTRONIC FILE ACCESS RESTRICTIONS: Vendor must ensure that its submission in wvOASIS can be accessed by the Purchasing Division staff immediately upon bid opening. The Purchasing Division will consider any file that cannot be immediately opened and/or viewed at the time of the bid opening (such as, encrypted files, password protected files, or incompatible files) to be blank or incomplete as context requires, and are therefore unacceptable. A vendor will not be permitted to unencrypt files, remove password protections, or resubmit documents after bid opening if those documents are required with the bid.

19. NON-RESPONSIBLE: The Purchasing Division Director reserves the right to reject the bid of any vendor as Non-Responsible in accordance with W. Va. Code of State Rules § 148-1-5.3, when the Director determines that the vendor submitting the bid does not have the capability to fully perform, or lacks the integrity and reliability to assure good-faith performance."

20. ACCEPTANCE/REJECTION: The State may accept or reject any bid in whole, or in part in accordance with W. Va. Code of State Rules § 148-1-4.5. and § 148-1-6.4.b."

21. YOUR SUBMISSION IS A PUBLIC DOCUMENT: Vendor's entire response to the Solicitation and the resulting Contract are public documents. As public documents, they will be disclosed to the public following the bid/proposal opening or award of the contract, as required by the competitive bidding laws of West Virginia Code §§ 5A-3-1 et seq., 5-22-1 et seq., and 5G-1-1 et seq. and the Freedom of Information Act West Virginia Code §§ 29B-1-1 et seq.

DO NOT SUBMIT MATERIAL YOU CONSIDER TO BE CONFIDENTIAL, A TRADE SECRET, OR OTHERWISE NOT SUBJECT TO PUBLIC DISCLOSURE.

Submission of any bid, proposal, or other document to the Purchasing Division constitutes your explicit consent to the subsequent public disclosure of the bid, proposal, or document. The Purchasing Division will disclose any document labeled "confidential," "proprietary," "trade secret," "private," or labeled with any other claim against public disclosure of the documents, to include any "trade secrets" as defined by West Virginia Code § 47-22-1 et seq. All submissions are subject to public disclosure without notice.

Please refer to document titled "Exceptions" for all proposed exceptions to the terms and conditions contained in the bid documentation for the following marked pages.

GENERAL TERMS AND CONDITIONS:

1. CONTRACTUAL AGREEMENT: Issuance of a Award Document signed by the Purchasing Division Director, or his designee, and approved as to form by the Attorney General's office constitutes acceptance of this Contract made by and between the State of West Virginia and the Vendor. Vendor's signature on its bid signifies Vendor's agreement to be bound by and accept the terms and conditions contained in this Contract.

2. DEFINITIONS: As used in this Solicitation/Contract, the following terms shall have the meanings attributed to them below. Additional definitions may be found in the specifications included with this Solicitation/Contract.

2.1. "Agency" or **"Agencies"** means the agency, board, commission, or other entity of the State of West Virginia that is identified on the first page of the Solicitation or any other public entity seeking to procure goods or services under this Contract.

2.2. "Bid" or **"Proposal"** means the vendors submitted response to this solicitation.

2.3. "Contract" means the binding agreement that is entered into between the State and the Vendor to provide the goods or services requested in the Solicitation.

2.4. "Director" means the Director of the West Virginia Department of Administration, Purchasing Division.

2.5. "Purchasing Division" means the West Virginia Department of Administration, Purchasing Division.

2.6. "Award Document" means the document signed by the Agency and the Purchasing Division, and approved as to form by the Attorney General, that identifies the Vendor as the contract holder.

2.7. "Solicitation" means the official notice of an opportunity to supply the State with goods or services that is published by the Purchasing Division.

2.8. "State" means the State of West Virginia and/or any of its agencies, commissions, boards, etc. as context requires.

2.9. "Vendor" or **"Vendors"** means any entity submitting a bid in response to the Solicitation, the entity that has been selected as the lowest responsible bidder, or the entity that has been awarded the Contract as context requires.

3. CONTRACT TERM; RENEWAL; EXTENSION: The term of this Contract shall be determined in accordance with the category that has been identified as applicable to this Contract below:

☐ **Term Contract**

Initial Contract Term: This Contract becomes effective on _____ and extends for a period of _____ year(s).
Renewal Term: This Contract may be renewed upon the mutual written consent of the Agency, and the Vendor, with approval of the Purchasing Division and the Attorney General's office (Attorney General approval is as to form only). Any request for renewal should be submitted to the Purchasing Division thirty (30) days prior to the expiration date of the initial contract term or appropriate renewal term. A Contract renewal shall be in accordance with the terms and conditions of the original contract. Renewal of this Contract is limited to _____ successive one (1) year periods or multiple renewal periods of less than one year, provided that the multiple renewal periods do not exceed _____ months in total. Automatic renewal of this Contract is prohibited. Notwithstanding the foregoing, Purchasing Division approval is not required on agency delegated or exempt purchases. Attorney General approval may be required for vendor terms and conditions.

Delivery Order Limitations: In the event that this contract permits delivery orders, a delivery order may only be issued during the time this Contract is in effect. Any delivery order issued within one year of the expiration of this Contract shall be effective for one year from the date the delivery order is issued. No delivery order may be extended beyond one year after this Contract has expired.

☐ **Fixed Period Contract:** This Contract becomes effective upon Vendor's receipt of the notice to proceed and must be completed within _____ days.

☐ **Fixed Period Contract with Renewals:** This Contract becomes effective upon Vendor's receipt of the notice to proceed and part of the Contract more fully described in the attached specifications must be completed within _____ days.

Upon completion, the vendor agrees that maintenance, monitoring, or warranty services will be provided for one year thereafter with an additional _____ successive one year renewal periods or multiple renewal periods of less than one year provided that the multiple renewal periods do not exceed _____ months in total. Automatic renewal of this Contract is prohibited.

☑ **One Time Purchase:** The term of this Contract shall run from the issuance of the Award Document until all of the goods contracted for have been delivered, but in no event will this Contract extend for more than one fiscal year.

☐ **Other:** See attached.

4. NOTICE TO PROCEED: Vendor shall begin performance of this Contract immediately upon receiving notice to proceed unless otherwise instructed by the Agency. Unless otherwise specified, the fully executed Award Document will be considered notice to proceed.

5. QUANTITIES: The quantities required under this Contract shall be determined in accordance with the category that has been identified as applicable to this Contract below.

☐ **Open End Contract:** Quantities listed in this Solicitation are approximations only, based on estimates supplied by the Agency. It is understood and agreed that the Contract shall cover the quantities actually ordered for delivery during the term of the Contract, whether more or less than the quantities shown.

☐ **Service:** The scope of the service to be provided will be more clearly defined in the specifications included herewith.

☑ **Combined Service and Goods:** The scope of the service and deliverable goods to be provided will be more clearly defined in the specifications included herewith.

☐ **One Time Purchase:** This Contract is for the purchase of a set quantity of goods that are identified in the specifications included herewith. Once those items have been delivered, no additional goods may be procured under this Contract without an appropriate change order approved by the Vendor, Agency, Purchasing Division, and Attorney General's office.

6. EMERGENCY PURCHASES: The Purchasing Division Director may authorize the Agency to purchase goods or services in the open market that Vendor would otherwise provide under this Contract if those goods or services are for immediate or expedited delivery in an emergency. Emergencies shall include, but are not limited to, delays in transportation or an unanticipated increase in the volume of work. An emergency purchase in the open market, approved by the Purchasing Division Director, shall not constitute of breach of this Contract and shall not entitle the Vendor to any form of compensation or damages. This provision does not excuse the State from fulfilling its obligations under a One Time Purchase contract.

7. REQUIRED DOCUMENTS: All of the items checked below must be provided to the Purchasing Division by the Vendor as specified below.

☐ **BID BOND (Construction Only):** Pursuant to the requirements contained in W. Va. Code § 5-22-1(c), All Vendors submitting a bid on a construction project shall furnish a valid bid bond in the amount of five percent (5%) of the total amount of the bid protecting the State of West Virginia. The bid bond must be submitted with the bid.

☐ **PERFORMANCE BOND:** The apparent successful Vendor shall provide a performance bond in the amount of _____. The performance bond must be received by the Purchasing Division prior to Contract award. On construction contracts, the performance bond must be 100% of the Contract value.

☐ **LABOR/MATERIAL PAYMENT BOND:** The apparent successful Vendor shall provide a labor/material payment bond in the amount of 100% of the Contract value. The labor/material payment bond must be delivered to the Purchasing Division prior to Contract award.
In lieu of the Bid Bond, Performance Bond, and Labor/Material Payment Bond, the Vendor may provide certified checks, cashier's checks, or irrevocable letters of credit. Any certified check, cashier's check, or irrevocable letter of credit provided in lieu of a bond must be of the same amount and delivered on the same schedule as the bond it replaces. A letter of credit submitted in lieu of a performance and labor/material payment bond will only be allowed for projects under $100,000. Personal or business checks are not acceptable.

☐ **MAINTENANCE BOND:** The apparent successful Vendor shall provide a two (2) year maintenance bond covering the roofing system. The maintenance bond must be issued and delivered to the Purchasing Division prior to Contract award.

☐ **INSURANCE:** The apparent successful Vendor shall furnish proof of the following insurance prior to Contract award and shall list the state as a certificate holder:

☐ **Commercial General Liability Insurance:** In the amount of _____ _____ or more.

☐ **Builders Risk Insurance:** In an amount equal to 100% of the amount of the Contract.

☐

☐

☐

☐

☐

The apparent successful Vendor shall also furnish proof of any additional insurance requirements contained in the specifications prior to Contract award regardless of whether or not that insurance requirement is listed above.

☐ **LICENSE(S) / CERTIFICATIONS / PERMITS:** In addition to anything required under the Section entitled Licensing, of the General Terms and Conditions, the apparent successful Vendor shall furnish proof of the following licenses, certifications, and/or permits prior to Contract award, in a form acceptable to the Purchasing Division.

☐

☐

☐

☐

The apparent successful Vendor shall also furnish proof of any additional licenses or certifications contained in the specifications prior to Contract award regardless of whether or not that requirement is listed above.

8. WORKERS' COMPENSATION INSURANCE: The apparent successful Vendor shall comply with laws relating to workers compensation, shall maintain workers' compensation insurance when required, and shall furnish proof of workers' compensation insurance upon request.

9. LITIGATION BOND: The Director reserves the right to require any Vendor that files a protest of an award to submit a litigation bond in the amount equal to one percent of the lowest bid submitted or $5,000, whichever is greater. The entire amount of the bond shall be forfeited if the hearing officer determines that the protest was filed for frivolous or improper purpose, including but not limited to, the purpose of harassing, causing unnecessary delay, or needless expense for the Agency. All litigation bonds shall be made payable to the Purchasing Division. In lieu of a bond, the protester may submit a cashier's check or certified check payable to the Purchasing Division. Cashier's or certified checks will be deposited with and held by the State Treasurer's office. If it is determined that the protest has not been filed for frivolous or improper purpose, the bond or deposit shall be returned in its entirety.

10. LIQUIDATED DAMAGES: Vendor shall pay liquidated damages in the amount of

_____

for _____.

This clause shall in no way be considered exclusive and shall not limit the State or Agency's right to pursue any other available remedy.

11. ACCEPTANCE: Vendor's signature on its bid, or on the certification and signature page, constitutes an offer to the State that cannot be unilaterally withdrawn, signifies that the product or service proposed by vendor meets the mandatory requirements contained in the Solicitation for that product or service, unless otherwise indicated, and signifies acceptance of the terms and conditions contained in the Solicitation unless otherwise indicated.

12. PRICING: The pricing set forth herein is firm for the life of the Contract, unless specified elsewhere within this Solicitation/Contract by the State. A Vendor's inclusion of price adjustment provisions in its bid, without an express authorization from the State in the Solicitation to do so, may result in bid disqualification.

13. PAYMENT: Payment in advance is prohibited under this Contract. Payment may only be made after the delivery and acceptance of goods or services. The Vendor shall submit invoices, in arrears.

14. PURCHASING CARD ACCEPTANCE: The State of West Virginia currently utilizes a Purchasing Card program, administered under contract by a banking institution, to process payment for goods and services. The Vendor must accept the State of West Virginia's Purchasing Card for payment of all orders under this Contract unless the box below is checked.

☐ Vendor is not required to accept the State of West Virginia's Purchasing Card as payment for all goods and services.

15. TAXES: The Vendor shall pay any applicable sales, use, personal property or any other taxes arising out of this Contract and the transactions contemplated thereby. The State of West Virginia is exempt from federal and state taxes and will not pay or reimburse such taxes.

16. ADDITIONAL FEES: Vendor is not permitted to charge additional fees or assess additional charges that were not either expressly provided for in the solicitation published by the State of West Virginia or included in the unit price or lump sum bid amount that Vendor is required by the solicitation to provide. Including such fees or charges as notes to the solicitation may result in rejection of vendor's bid. Requesting such fees or charges be paid after the contract has been awarded may result in cancellation of the contract.

17. FUNDING: This Contract shall continue for the term stated herein, contingent upon funds being appropriated by the Legislature or otherwise being made available. In the event funds are not appropriated or otherwise made available, this Contract becomes void and of no effect beginning on July 1 of the fiscal year for which funding has not been appropriated or otherwise made available.

18. CANCELLATION: The Purchasing Division Director reserves the right to cancel this Contract immediately upon written notice to the vendor if the materials or workmanship supplied do not conform to the specifications contained in the Contract. The Purchasing Division Director may also cancel any purchase or Contract upon 30 days written notice to the Vendor in accordance with West Virginia Code of State Rules § 148-1-6.1.e.

19. TIME: Time is of the essence with regard to all matters of time and performance in this Contract.

20. APPLICABLE LAW: This Contract is governed by and interpreted under West Virginia law without giving effect to its choice of law principles. Any information provided in specification manuals, or any other source, verbal or written, which contradicts or violates the West Virginia Constitution, West Virginia Code or West Virginia Code of State Rules is void and of no effect.

21. COMPLIANCE: Vendor shall comply with all applicable federal, state, and local laws, regulations and ordinances. By submitting a bid, Vendor acknowledges that it has reviewed, understands, and will comply with all applicable laws, regulations, and ordinances.

22. ARBITRATION: Any references made to arbitration contained in this Contract, Vendor's bid, or in any American Institute of Architects documents pertaining to this Contract are hereby deleted, void, and of no effect.

23. MODIFICATIONS: This writing is the parties' final expression of intent. Notwithstanding anything contained in this Contract to the contrary no modification of this Contract shall be binding without mutual written consent of the Agency, and the Vendor, with approval of the Purchasing Division and the Attorney General's office (Attorney General approval is as to form only). Any change to existing contracts that adds work or changes contract cost, and were not included in the original contract, must be approved by the Purchasing Division and the Attorney General's Office (as to form) prior to the implementation of the change or commencement of work affected by the change.

24. WAIVER: The failure of either party to insist upon a strict performance of any of the terms or provision of this Contract, or to exercise any option, right, or remedy herein contained, shall not be construed as a waiver or a relinquishment for the future of such term, provision, option, right, or remedy, but the same shall continue in full force and effect. Any waiver must be expressly stated in writing and signed by the waiving party.

25. SUBSEQUENT FORMS: The terms and conditions contained in this Contract shall supersede any and all subsequent terms and conditions which may appear on any form documents submitted by Vendor to the Agency or Purchasing Division such as price lists, order forms, invoices, sales agreements, or maintenance agreements, and includes internet websites or other electronic documents. Acceptance or use of Vendor's forms does not constitute acceptance of the terms and conditions contained thereon.

26. ASSIGNMENT: Neither this Contract nor any monies due, or to become due hereunder, may be assigned by the Vendor without the express written consent of the Agency, the Purchasing Division, the Attorney General's office (as to form only), and any other government agency or office that may be required to approve such assignments. Notwithstanding the foregoing, Purchasing Division approval may or may not be required on certain agency delegated or exempt purchases.

27. WARRANTY: The Vendor expressly warrants that the goods and/or services covered by this Contract will: (a) conform to the specifications, drawings, samples, or other description furnished or specified by the Agency; (b) be merchantable and fit for the purpose intended; and (c) be free from defect in material and workmanship.

28. STATE EMPLOYEES: State employees are not permitted to utilize this Contract for personal use and the Vendor is prohibited from permitting or facilitating the same.

29. BANKRUPTCY: In the event the Vendor files for bankruptcy protection, the State of West Virginia may deem this Contract null and void, and terminate this Contract without notice.

30. PRIVACY, SECURITY, AND CONFIDENTIALITY: The Vendor agrees that it will not disclose to anyone, directly or indirectly, any such personally identifiable information or other confidential information gained from the Agency, unless the individual who is the subject of the information consents to the disclosure in writing or the disclosure is made pursuant to the Agency's policies, procedures, and rules. Vendor further agrees to comply with the Confidentiality Policies and Information Security Accountability Requirements, set forth in http://www.state.wv.us/admin/purchase/privacy/default.html.

31. YOUR SUBMISSION IS A PUBLIC DOCUMENT: Vendor's entire response to the Solicitation and the resulting Contract are public documents. As public documents, they will be disclosed to the public following the bid/proposal opening or award of the contract, as required by the competitive bidding laws of West Virginia Code §§ 5A-3-1 et seq., 5-22-1 et seq., and 5G-1-1 et seq. and the Freedom of Information Act West Virginia Code §§ 29B-1-1 et seq.

DO NOT SUBMIT MATERIAL YOU CONSIDER TO BE CONFIDENTIAL, A TRADE SECRET, OR OTHERWISE NOT SUBJECT TO PUBLIC DISCLOSURE.

Submission of any bid, proposal, or other document to the Purchasing Division constitutes your explicit consent to the subsequent public disclosure of the bid, proposal, or document. The Purchasing Division will disclose any document labeled "confidential," "proprietary," "trade secret," "private," or labeled with any other claim against public disclosure of the documents, to include any "trade secrets" as defined by West Virginia Code § 47-22-1 et seq. All submissions are subject to public disclosure without notice.

32. LICENSING: In accordance with West Virginia Code of State Rules § 148-1-6.1.e, Vendor must be licensed and in good standing in accordance with any and all state and local laws and requirements by any state or local agency of West Virginia, including, but not limited to, the West Virginia Secretary of State's Office, the West Virginia Tax Department, West Virginia Insurance Commission, or any other state agency or political subdivision. Upon request, the Vendor must provide all necessary releases to obtain information to enable the Purchasing Division Director or the Agency to verify that the Vendor is licensed and in good standing with the above entities.

33. ANTITRUST: In submitting a bid to, signing a contract with, or accepting a Award Document from any agency of the State of West Virginia, the Vendor agrees to convey, sell, assign, or transfer to the State of West Virginia all rights, title, and interest in and to all causes of action it may now or hereafter acquire under the antitrust laws of the United States and the State of West Virginia for price fixing and/or unreasonable restraints of trade relating to the particular commodities or services purchased or acquired by the State of West Virginia. Such assignment shall be made and become effective at the time the purchasing agency tenders the initial payment to Vendor.

34. VENDOR CERTIFICATIONS: By signing its bid or entering into this Contract, Vendor certifies (1) that its bid or offer was made without prior understanding, agreement, or connection with any corporation, firm, limited liability company, partnership, person or entity submitting a bid or offer for the same material, supplies, equipment or services; (2) that its bid or offer is in all respects fair and without collusion or fraud; (3) that this Contract is accepted or entered into without any prior understanding, agreement, or connection to any other entity that could be considered a violation of law; and (4) that it has reviewed this Solicitation in its entirety; understands the requirements, terms and conditions, and other information contained herein.

Vendor's signature on its bid or offer also affirms that neither it nor its representatives have any interest, nor shall acquire any interest, direct or indirect, which would compromise the performance of its services hereunder. Any such interests shall be promptly presented in detail to the Agency. The individual signing this bid or offer on behalf of Vendor certifies that he or she is authorized by the Vendor to execute this bid or offer or any documents related thereto on Vendor's behalf; that he or she is authorized to bind the Vendor in a contractual relationship; and that, to the best of his or her knowledge, the Vendor has properly registered with any State agency that may require registration.

35. VENDOR RELATIONSHIP: The relationship of the Vendor to the State shall be that of an independent contractor and no principal-agent relationship or employer-employee relationship is contemplated or created by this Contract. The Vendor as an independent contractor is solely liable for the acts and omissions of its employees and agents. Vendor shall be responsible for selecting, supervising, and compensating any and all individuals employed pursuant to the terms of this Solicitation and resulting contract. Neither the Vendor, nor any employees or subcontractors of the Vendor, shall be deemed to be employees of the State for any purpose whatsoever. Vendor shall be exclusively responsible for payment of employees and contractors for all wages and salaries, taxes, withholding payments, penalties, fees, fringe benefits, professional liability insurance premiums, contributions to insurance and pension, or other deferred compensation plans, including but not limited to, Workers' Compensation and Social Security obligations, licensing fees, etc. and the filing of all necessary documents, forms, and returns pertinent to all of the foregoing.

Vendor shall hold harmless the State, and shall provide the State and Agency with a defense against any and all claims including, but not limited to, the foregoing payments, withholdings, contributions, taxes, Social Security taxes, and employer income tax returns.

36. INDEMNIFICATION: The Vendor agrees to indemnify, defend, and hold harmless the State and the Agency, their officers, and employees from and against: (1) Any claims or losses for services rendered by any subcontractor, person, or firm performing or supplying services, materials, or supplies in connection with the performance of the Contract; (2) Any claims or losses resulting to any person or entity injured or damaged by the Vendor, its officers, employees, or subcontractors by the publication, translation, reproduction, delivery, performance, use, or disposition of any data used under the Contract in a manner not authorized by the Contract, or by Federal or State statutes or regulations; and (3) Any failure of the Vendor, its officers, employees, or subcontractors to observe State and Federal laws including, but not limited to, labor and wage and hour laws.

37. PURCHASING AFFIDAVIT: In accordance with West Virginia Code § 5A-3-10a, all Vendors are required to sign, notarize, and submit the Purchasing Affidavit stating that neither the Vendor nor a related party owe a debt to the State in excess of $1,000. The affidavit must be submitted prior to award, but should be submitted with the Vendor's bid. A copy of the Purchasing Affidavit is included herewith.

38. ADDITIONAL AGENCY AND LOCAL GOVERNMENT USE: This Contract may be utilized by other agencies, spending units, and political subdivisions of the State of West Virginia; county, municipal, and other local government bodies; and school districts ("Other Government Entities"). Any extension of this Contract to the aforementioned Other Government Entities must be on the same prices, terms, and conditions as those offered and agreed to in this Contract, provided that such extension is in compliance with the applicable laws, rules, and ordinances of the Other Government Entity. If the Vendor does not wish to extend the prices, terms, and conditions of its bid and subsequent contract to the Other Government Entities, the Vendor must clearly indicate such refusal in its bid. A refusal to extend this Contract to the Other Government Entities shall not impact or influence the award of this Contract in any manner.

39. CONFLICT OF INTEREST: Vendor, its officers or members or employees, shall not presently have or acquire an interest, direct or indirect, which would conflict with or compromise the performance of its obligations hereunder. Vendor shall periodically inquire of its officers, members and employees to ensure that a conflict of interest does not arise. Any conflict of interest discovered shall be promptly presented in detail to the Agency.

40. REPORTS: Vendor shall provide the Agency and/or the Purchasing Division with the following reports identified by a checked box below:

☐ Such reports as the Agency and/or the Purchasing Division may request. Requested reports may include, but are not limited to, quantities purchased, agencies utilizing the contract, total contract expenditures by agency, etc.

☐ Quarterly reports detailing the total quantity of purchases in units and dollars, along with a listing of purchases by agency. Quarterly reports should be delivered to the Purchasing Division via email at purchasing.requisitions@wv.gov.

41. BACKGROUND CHECK: In accordance with W. Va. Code § 15-2D-3, the Director of the Division of Protective Services shall require any service provider whose employees are regularly employed on the grounds or in the buildings of the Capitol complex or who have access to sensitive or critical information to submit to a fingerprint-based state and federal background inquiry through the state repository. The service provider is responsible for any costs associated with the fingerprint-based state and federal background inquiry.

After the contract for such services has been approved, but before any such employees are permitted to be on the grounds or in the buildings of the Capitol complex or have access to sensitive or critical information, the service provider shall submit a list of all persons who will be physically present and working at the Capitol complex to the Director of the Division of Protective Services for purposes of verifying compliance with this provision. The State reserves the right to prohibit a service provider's employees from accessing sensitive or critical information or to be present at the Capitol complex based upon results addressed from a criminal background check.

Service providers should contact the West Virginia Division of Protective Services by phone at (304) 558-9911 for more information.

42. PREFERENCE FOR USE OF DOMESTIC STEEL PRODUCTS: Except when authorized by the Director of the Purchasing Division pursuant to W. Va. Code § 5A-3-56, no contractor may use or supply steel products for a State Contract Project other than those steel products made in the United States. A contractor who uses steel products in violation of this section may be subject to civil penalties pursuant to W. Va. Code § 5A-3-56. As used in this section:

a. "State Contract Project" means any erection or construction of, or any addition to, alteration of or other improvement to any building or structure, including, but not limited to, roads or highways, or the installation of any heating or cooling or ventilating plants or other equipment, or the supply of and materials for such projects, pursuant to a contract with the State of West Virginia for which bids were solicited on or after June 6, 2001.
b. "Steel Products" means products rolled, formed, shaped, drawn, extruded, forged, cast, fabricated or otherwise similarly processed, or processed by a combination of two or more or such operations, from steel made by the open heath, basic oxygen, electric furnace, Bessemer or other steel making process. The Purchasing Division Director may, in writing, authorize the use of foreign steel products if:
c. The cost for each contract item used does not exceed one tenth of one percent (.1%) of the total contract cost or two thousand five hundred dollars ($2,500.00), whichever is greater. For the purposes of this section, the cost is the value of the steel product as delivered to the project; or
d. The Director of the Purchasing Division determines that specified steel materials are not produced in the United States in sufficient quantity or otherwise are not reasonably available to meet contract requirements.

43. PREFERENCE FOR USE OF DOMESTIC ALUMINUM, GLASS, AND STEEL: In Accordance with W. Va. Code § 5-19-1 et seq., and W. Va. CSR § 148-10-1 et seq., for every contract or subcontract, subject to the limitations contained herein, for the construction, reconstruction, alteration, repair, improvement or maintenance of public works or for the purchase of any item of machinery or equipment to be used at sites of public works, only domestic aluminum, glass or steel products shall be supplied unless the spending officer determines, in writing, after the receipt of offers or bids, (1) that the cost of domestic aluminum, glass or steel products is unreasonable or inconsistent with the public interest of the State of West Virginia, (2) that domestic aluminum, glass or steel products are not produced in sufficient quantities to meet the contract requirements, or (3) the available domestic aluminum, glass, or steel do not meet the contract specifications. This provision only applies to public works contracts awarded in an amount more than fifty thousand dollars ($50,000) or public works contracts that require more than ten thousand pounds of steel products.

The cost of domestic aluminum, glass, or steel products may be unreasonable if the cost is more than twenty percent (20%) of the bid or offered price for foreign made aluminum, glass, or steel products. If the domestic aluminum, glass or steel products to be supplied or produced in a "substantial labor surplus area", as defined by the United States Department of Labor, the cost of domestic aluminum, glass, or steel products may be unreasonable if the cost is more than thirty percent (30%) of the bid or offered price for foreign made aluminum, glass, or steel products. This preference shall be applied to an item of machinery or equipment, as indicated above, when the item is a single unit of equipment or machinery manufactured primarily of aluminum, glass or steel, is part of a public works contract and has the sole purpose or of being a permanent part of a single public works project. This provision does not apply to equipment or machinery purchased by a spending unit for use by that spending unit and not as part of a single public works project.

All bids and offers including domestic aluminum, glass or steel products that exceed bid or offer prices including foreign aluminum, glass or steel products after application of the preferences provided in this provision may be reduced to a price equal to or lower than the lowest bid or offer price for foreign aluminum, glass or steel products plus the applicable preference. If the reduced bid or offer prices are made in writing and supersede the prior bid or offer prices, all bids or offers, including the reduced bid or offer prices, will be reevaluated in accordance with this rule.

DESIGNATED CONTACT: Vendor appoints the individual identified in this Section as the Contract Administrator and the initial point of contact for matters relating to this Contract.

Contract Administration

(Name, Title)

POC: Alicia Shannon, Bid Specialist

(Printed Name and Title)

34 Maple St, Milford, MA 01757

(Address)

800-252-4752 / 508-482-8532

(Phone Number) / (Fax Number)

americas_contracts@waters.com

(email address)

CERTIFICATION AND SIGNATURE: By signing below, or submitting documentation through wvOASIS, I certify that I have reviewed this Solicitation in its entirety; that I understand the requirements, terms and conditions, and other information contained herein; that this bid, offer or proposal constitutes an offer to the State that cannot be unilaterally withdrawn; that the product or service proposed meets the mandatory requirements contained in the Solicitation for that product or service, unless otherwise stated herein; ~~that the Vendor accepts the terms and conditions contained in the Solicitation~~, unless otherwise stated herein; that I am submitting this bid, offer or proposal for review and consideration; that I am authorized by the vendor to execute and submit this bid, offer, or proposal, or any documents related thereto on vendor's behalf; that I am authorized to bind the vendor in a contractual relationship; and that to the best of my knowledge, the vendor has properly registered with any State agency that may require registration.

Waters Technologies Corporation

(Company)

Kristen A. Arakelian

(Authorized Signature) (Representative Name, Title)

Kristen Arakelian, Manager Contract Administration

(Printed Name and Title of Authorized Representative)

11/16/16

(Date)

800-252-4752 / 508-482-8532

(Phone Number) (Fax Number)

Please refer to document titled "Exceptions"

Waters meets or exceed all specifications. Please refer to attached literature for details.

SPECIFICATIONS

1. **PURPOSE AND SCOPE:** The West Virginia Purchasing Division is soliciting bids on behalf of West Virginia Department of Agriculture to establish a contract for the one time purchase of a **Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS), workstation PC, software, printer, shipping, installation, validation, warranty, training, and service.**

2. **DEFINITIONS:** The terms listed below shall have the meanings assigned to them below. Additional definitions can be found in section 2 of the General Terms and Conditions.

   2.1 **"APCI"** means atmospheric pressure chemical ionization.

   2.2 **"Contract Services"** means the LC/MS/MS with inside delivery, installation, validation, warranty, and training.

   2.3 **"ESI"** means electrospray ionization.

   2.4 **"FG"** means femtogram.

   2.5 **"Installation"** means unpacking and setting instrumentation in place with all connections secured for the instrument(s) to be in working order including software installation on the computer connected to the instrument.

   2.6 **"LC/MS/MS"** means Liquid Chromatography Triple Quadrupole Mass Spectrometer.

   2.7 **"MRM"** means multiple reactions monitoring.

   2.8 **"MSMS"** means tandem mass spectrometry.

   2.9 **"Pricing Page"** means the pages, contained in wvOASIS or attached as Exhibit A, upon which Vendor should list its proposed price for the Contract Items.

   2.10 **"Service"** means performing routine maintenance work or repair to the instrument or software.

   2.11 **"SIM"** means selected ion monitoring

   2.12 **"S/N"** means signal noise.

2.13 "Solicitation" means the official notice of an opportunity to supply the State with goods or services that is published by the Purchasing Division.

2.14 "Training" means teaching staff how to use and maintain the instrument and software.

2.15 "Validation" means is the process used to confirm that the analytical procedure employed for a specific test or matrices is suitable for its intended use.

2.16 "Warranty" means the written warranty of the manufacturer of a new instrument of its condition and fitness for use, including any terms or conditions precedent to the enforcement of obligations under that warranty.

3. GENERAL REQUIREMENTS:

3.1 Mandatory Contract Item Requirements: Contract Item must meet or exceed the mandatory requirements listed below for the **Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS).**

3.1.1 Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS)

3.1.1.1 Must be capable of detecting a variety of analytes including pesticides, herbicides, toxins, and drugs in matrices such as foods, soil, vegetation, animal feed, and water.

3.1.1.2 MSMS must have two ion sources that operate independently which can be set to electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI). The instrument must enable combinations such as ESI/APCI, ESI/ESI, APCI/APCI with the same or opposite polarities without having to remove the sources to switch modes.

3.1.1.3 Minimum sensitivity requirement for positive ion mode: signal/noise (S/N) 2000:1 25 femtograms (fg) of reserpine on column. Minimum sensitivity requirement for negative ion mode: signal/noise (S/N)>2000:1, 25 femtograms (fg) of chloramphenicol on column.

3.1.1.4 The source probes must be easy to remove without the use of tools.

3.1.1.5 Ion source must have flat response across flow rate up to 3 milliliters per minute without loss of sensitivity.

3.1.1.6 Capable of switching between rapidly between positive and negative ion detection without high voltage switching.

3.1.1.7 Acquisition modes: Q1 scan, Q2 scan, multiple reactions monitoring (MRM), selected ion monitoring (SIM), Neutral Loss scans, Product Ion, Precursor Ion, Time managed MRM

3.1.1.8 Minimum mass range requirement: 5-1500 mass to charge ratio (m/z)

3.1.1.9 Mass stability required: 0.05 atomic mass unit (amu) in 24 hours

3.1.1.10 Mass accuracy needed: minimum 0.1 unit across mass range

3.1.1.11 Scan speed: ≤30,000 daltons per second (da/s)

3.1.1.12 Quad resolution: unit, low and high, minimal sensitivity loss at 0.1 Daltons resolutions

3.1.1.13 Polarity switching time: ≤15 milliseconds

3.1.1.14 Dynamic range: 6 orders

3.1.1.15 Dual source switching speed: <20 milliseconds

3.1.1.16 Minimum multiple reactions monitoring (MRM) Dwell Time: 1 millisecond

3.1.1.17 MRM transitions: 450 per time segment > 40,000 ion transactions per method

3.1.1.18 Must have high selectivity mass filter at 0.3 Daltons. Signal loss must not be more than 10%.

3.1.1.19 For minimal tuning during method development and minimal maintenance of the ion path, the LC/MS/MS utilizes Hot Source Induced Desolvation interface to the mass analyzer by patented Laminar Flow Ion Guide using gas flow

3.1.1.20 High performance liquid chromatograph capable of solvent and column switching without user intervention

3.1.1.21 High performance liquid chromatograph capable of regulating column temperature of at least 2 different columns

3.1.1.22 High performance liquid chromatograph with an autosampler

3.1.1.23 The LC/MS/MS instrument must be fully automated for analysis with a system controller that is loaded with the necessary software.

3.1.1.24 The LC/MS/MS must include a maintenance kit.

3.1.1.25 Vendor must provide documentation for recommended environmental conditions, electrical requirements, gas requirements, or any other factor that would affect instrument performance.

3.1.2 Workstation and software

3.1.2.1 Data station with windows based operating system capable of multitasking allowing data processing and data acquisition simultaneously.

3.1.2.2 Operating system must be fully integrated to control LS/MS/MS.

3.1.3 Shipping, Installation, Validation, Warranty, Training and Service

3.1.3.1 Vendor must be on-site for delivery and perform the installation (labor and supplies included) of the LCMSMS.

3.1.3.2 The vendor must provide a written validation of the instrument's performance after installation.

3.1.3.3 Vendor will provide a full one-year parts and labor warranty on all items, including 2 preventative maintenances.

3.1.3.4 Vendor must be able to perform resolutions to service requests within 72 hours which includes on-site resolutions.

3.1.3.5 Vendor will provide on-site training (labor and non-consumable supplies included) for all instruments and software.

3.1.3.6 Vendor will provide copies of all system manuals (operations, training, technical, service, maintenance).

4. CONTRACT AWARD:

4.1 Contract Award: The Contract is intended to provide Agencies with a purchase price for the Contract Items. The Contract shall be awarded to the Vendor that provides the Contract Items meeting the required specifications for the lowest overall total cost as shown on the Pricing Pages.

4.2 Pricing Page: Vendor should complete the Pricing Page by placing all inclusive information in each column for item number, model/brand name, unit price and extended amount. There should be a price for the LCMSMS, workstation, software, printer, shipping/inside delivery, installation, validation, warranty, training and service. If there is no charge for any deliverable, indicate in the cell with "no charge". The bidder/vendor information must be completed and include an authorize signature. Vendor should complete the Pricing Page in full as failure to complete the Pricing Page in its entirety may result in Vendor's bid being disqualified.

Vendor should type or electronically enter the information into the Pricing Page to prevent errors in the evaluation.

5. PAYMENT:

5.1 Payment: Vendor shall accept payment in accordance with the payment procedures of the State of West Virginia.

6. DELIVERY AND RETURN:

6.1 Shipment and Delivery: Vendor should ship the Contract Items immediately after being awarded this Contract and receiving a purchase order or notice to proceed. Contract Items must be delivered to Agency at 313 Gus R. Douglass Lane, Charleston, WV 25312.

6.2 Late Delivery: The Agency placing the order under this Contract must be notified in writing if the shipment of the Contract Items will be delayed for any reason. Any delay in delivery that could cause harm to an Agency will be grounds for cancellation of the Contract, and/or obtaining the Contract Items from a third party.

Any Agency seeking to obtain the Contract Items from a third party under this provision must first obtain approval of the Purchasing Division.

6.3 Delivery Payment/Risk of Loss: Vendor shall deliver the Contract Items F.O.B. destination to the Agency's location.

6.4 Return of Unacceptable Items: If the Agency deems the Contract Items to be unacceptable, the Contract Items shall be returned to Vendor at Vendor's expense and with no restocking charge. Vendor shall either make arrangements for the return within five (5) days of being notified that items are unacceptable, or permit the Agency to arrange for the return and reimburse Agency for delivery expenses. If the original packaging cannot be utilized for the return, Vendor will supply the Agency with appropriate return packaging upon request. All returns of unacceptable items shall be F.O.B. the Agency's location. The returned product shall either be replaced, or the Agency shall receive a full credit or refund for the purchase price, at the Agency's discretion.

Please refer to document titled "Exceptions"

6.5 Return Due to Agency Error: Items ordered in error by the Agency will be returned for credit within 30 days of receipt, F.O.B. Vendor's location. Vendor shall not charge a restocking fee if returned products are in a resalable condition. Items shall be deemed to be in a resalable condition if they are unused and in the original packaging. Any restocking fee for items not in a resalable condition shall

be the lower of the Vendor's customary restocking fee or 5% of the total invoiced value of the returned items.

7 VENDOR DEFAULT:

7.1 The following shall be considered a vendor default under this Contract.

7.1.1 Failure to provide Contract Items in accordance with the requirements contained herein.

7.1.2 Failure to comply with other specifications and requirements contained herein.

7.1.3 Failure to comply with any laws, rules, and ordinances applicable to the Contract Services provided under this Contract.

7.1.4 Failure to remedy deficient performance upon request.

7.2 The following remedies shall be available to Agency upon default.

7.2.1 Immediate cancellation of the Contract.

7.2.2 Immediate cancellation of one or more release orders issued under this Contract.

7.2.3 Any other remedies available in law or equity.

8 **FACILITIES ACCESS:** Performance of Services will require access to the facility.

8.1 Vendor must identify principal service personnel who will be asked for identification upon entrance to the facility.

8.2 Anyone performing under this Contract will be subject to Agency's security protocol and procedures.

8.3 Vendor shall inform all staff of Agency's security protocol and procedures.

	PRICING PAGE				
Item No.	Description	Model No/Brand Name	Quanity	Unit Price	Extended Amount
3.1.1 & 3.1.2	LCMSMS, workstation, software, printer	Waters Xevo TQ-S micro/Acquity UPLC H-Class and Masslynx software	1	$493,975	$296,428.85
3.1.3	Shipping charges and inside delivery	Fed Ex Express Saver	1	N/A	$1,148.46
3.1.3	Installation/validation	included in item 3.1.1 & 3.1.2	1	N/A	$0
3.1.3	Training/warranty	included in item 3.1.1 & 3.1.2	1	N/A	$0
3.1.3	Service	included in item 3.1.1 & 3.1.2	1	N/A	$0
	Failure to use this form may result in disqualification			GRAND TOTAL	$297,577.31
	Bidder / Vendor Information				
Name:	Waters Technologies Corporation				
Address:	34 Maple St				
	Milford, MA 01757				
Phone:	800-252-4752				
Email Address:	bid_desk@waters.com				
Signature:	Kristen A. Arakelian				

Please refer to Waters Quotation #21332675 included for detailed pricing information

STATE OF WEST VIRGINIA
Purchasing Division

PURCHASING AFFIDAVIT

MANDATE: Under W. Va. Code §5A-3-10a, no contract or renewal of any contract may be awarded by the state or any of its political subdivisions to any vendor or prospective vendor when the vendor or prospective vendor or a related party to the vendor or prospective vendor is a debtor and: (1) the debt owed is an amount greater than one thousand dollars in the aggregate; or (2) the debtor is in employer default.

EXCEPTION: The prohibition listed above does not apply where a vendor has contested any tax administered pursuant to chapter eleven of the W. Va. Code, workers' compensation premium, permit fee or environmental fee or assessment and the matter has not become final or where the vendor has entered into a payment plan or agreement and the vendor is not in default of any of the provisions of such plan or agreement.

DEFINITIONS:

"**Debt**" means any assessment, premium, penalty, fine, tax or other amount of money owed to the state or any of its political subdivisions because of a judgment, fine, permit violation, license assessment, defaulted workers' compensation premium, penalty or other assessment presently delinquent or due and required to be paid to the state or any of its political subdivisions, including any interest or additional penalties accrued thereon.

"**Employer default**" means having an outstanding balance or liability to the old fund or to the uninsured employers' fund or being in policy default, as defined in W. Va. Code § 23-2c-2, failure to maintain mandatory workers' compensation coverage, or failure to fully meet its obligations as a workers' compensation self-insured employer. An employer is not in employer default if it has entered into a repayment agreement with the Insurance Commissioner and remains in compliance with the obligations under the repayment agreement.

"**Related party**" means a party, whether an individual, corporation, partnership, association, limited liability company or any other form or business association or other entity whatsoever, related to any vendor by blood, marriage, ownership or contract through which the party has a relationship of ownership or other interest with the vendor so that the party will actually or by effect receive or control a portion of the benefit, profit or other consideration from performance of a vendor contract with the party receiving an amount that meets or exceed five percent of the total contract amount.

AFFIRMATION: By signing this form, the vendor's authorized signer affirms and acknowledges under penalty of law for false swearing (*W. Va. Code* §61-5-3) that neither vendor nor any related party owe a debt as defined above and that neither vendor nor any related party are in employer default as defined above, unless the debt or employer default is permitted under the exception above.

WITNESS THE FOLLOWING SIGNATURE:

Vendor's Name: Waters Technologies Corporation

Authorized Signature: Kristen A. Arakelian Date: 11/17/16

State of Massachusetts

County of Worcester, to-wit:

Taken, subscribed, and sworn to before me this 17 day of November, 2016.

My Commission expires March 13, 2020.

AFFIX SEAL HERE

NOTARY PUBLIC Robin Friberg

ROBIN M. FRIBERG
Notary Public
COMMONWEALTH OF MASSACHUSETTS
My Commission Expires
March 13, 2020

Waters
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Linda Harper
State of West Virginia
Dept of Agriculture
1900 Kanawha Blvd E
CHARLESTON,WV,25305-0170
US

Telephone : 304 558 0468
Email : linda.b.harper@wv.gov

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Quotation No: 21332675 - Expiration Date: 12/30/2016

RE: RFQ #AGRI 700000005 Due 11/17/16

Dear Linda Harper,

Thank you for your interest in Waters! Please find the enclosed Sales Quotation for the products you inquired about. We look forward to working with you and your team for all of your laboratory needs.

To place an order for products and services on this quotation, you may send your hard copy purchase order via email to waters_quotes@waters.com

You may also contact Waters Sales Support to place your order via telephone at 800-252-4752 Ext.8023, fax your purchase order to 508-482-8532 or 508-482-8834.

If you have any questions regarding this quotation, please contact your local Account Representative: Matthew Welsh. Matthew may be reached by telephone at 800-252-4752 , or via Email at MATTHEW_WELSH@WATERS.COM, or visit us online at www.waters.com.

Waters Sales Support
Tel: 800-252-4752 Ext.8023
Email: waters_quotes@waters.com

EHS

Waters
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Account	: State of West Virginia
Quotation number	: 21332675
Creation date	: 11/11/2016
Expiration date	: 12/30/2016

Sales Proposal
Please reference this Quotation when Purchase Order is issued

When placing your purchase order, please provide your Holiday hours of operation.

Item	Product#	Qty	Description	Unit Price	Discount	Net Price
1	**176850043**	1	**Xevo TQ-S micro System**	476,455.00	- 195,084.15	281,370.85
			With the following configuration:			
	176003468	1	Xevo TQ-S micro			
	176002526	1	MassLynx Workstation with TL			
	668000273	1	MONITOR, Lenovo ThinkVision Flat Panel			
	176002685	1	Vac Rough Pump + Freq Conv			
	176003469	1	MS Ref Stds Xevo TQ-S micro			
	176002088	1	APCI			
	700004318	1	SOURCE SPARES KIT			
			ACQUITY UPLC H-Class System			
	176015008	1	ACQUITY UPLC H-Class CM Core System			
	176015028	1	ACQUITY UPLC TUV Detector			
			Installation, Training and Plans			
	741000321	1	TQD SYSTEM INSTALLATION CERT			
2	**176003850**	2	**XEVO TQ-S Micro (Rotary) PM Kit W/CHEM**	3,178.00	- 476.70	5,402.60
	201000294	2	XEVO TQ-S MICRO (ROTARY) PERF MAINT KIT			
	186007976	2	Xevo TQ-S micro Set Up Solution			
	186006846	2	MS Cleaning Solution			
3	201000233	2	H-Class QSM w/i2V PERFORMANCE MAINT KIT	1,605.00	- 240.75	2,728.50
4	201000234	2	H-CLASS SAMPLE MANAGER-FTN PM KIT	2,590.00	- 388.50	4,403.00
5	201000207	2	H-CLASS CM-A / CM-AUX & BIO PM KIT	17.00	- 2.55	28.90
6	700005269	2	PERFORMANCE PLUS HB DEUTERIUM LAMP ASSY	820.00	- 123.00	1,394.00
7	668000275	1	Printer, HP Laser Jet, P3015dn, 110 Volt	1,100.00		1,100.00
8	720002242EN	1	Implementation Kit	1.00		1.00

Sub Total	**296,428.85**
Estimated Freight Charges	**1,148.46**
Total Quotation in USD (Excludes Applicable Taxes)	**297,577.31**

Waters
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Account	: State of West Virginia
Quotation number	: 21332675
Creation date	: 11/11/2016
Expiration date	: 12/30/2016

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Waters Standard Terms and Conditions

Delivery:	60 Days
Freight Terms:	FOB Shipping Point
	Prepaid & Added
Payment Terms:	NET 30 DAYS
	Payment Terms Subject to Credit Review

Additional notes:

For Finance and Leasing Options - Contact Director of Instrument Leasing, Alex Johnson at 1-800-252-4752 Ext. 2307.

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Account	: State of West Virginia
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Optional Items

Product#	Qty	Description	Unit Price	Discount	Net Price
OPTIONAL ITEMS					
186007574	1	LC Multiresidue Pesticide Standards Kit	4,988.00	- 2,045.08	2,942.92
		Optional item is a special sale item and must be purchased with item 1 on one purchase order for the discount to be applicable.			

SUBTOTAL	USD	**2,942.92**

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Account	: State of West Virginia
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Expiration date	: 12/30/2016

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Detail Product Description(s)

Product# Description

176003468 Xevo TQ-S micro

The Xevo® TQ-S micro is a sensitive but compact tandem quadrupole mass spectrometer featuring reliable performance with a wide dynamic range and high rates of data acquisition. Robust sensitivity is enabled by proven ZSpray" and StepWave" which facilitate the detection of analytes at low concentrations in complex matrices and enable low volume injections with consistent, precise and accurate results. Xtended dynamic range" (XDR) technology provides accessible sensitivity and method transfer. The Xevo® TQ-S micro makes it easier to confidently quantify more analytes using reproducible high acquisition rates with Xcellerated Ion Transfer" (XIT). Using RADAR, which enables rapid switching between MS full scan and MS/MS acquisition modes, analysts can understand sample complexity and improve method development.

The following items are included as part of the standard system:
Z SPRAY" API interface#Dual orthogonal interface for robust LC/MS
Electrospray (ESI) inlet probe#for efficient ionisation of a wide range of compounds
ESCi" ionisation capability#rapid switching source for both ESI and APCI in the same run
IntelliStart" fluidics#Automated tuning, calibration and method development
TargetLynx XS" #Application manager (requires license as provided with PC, below)
OpenLynx" #Application manager (requires license as provided with PC, below)

The standard system does not include the following items, which must be specified separately:
Additional inlet probes and ion source options (detailed below).
Acquisition PC data system and monitor
Additional Workstation data system terminals.
Printers.
Additional MassLynx" options (detailed below).
Vacuum backing pump options (rotary or oil-free combinations)
HPLC systems or other inlet options.

1. Z SPRAY" API INTERFACE
This instrument is equipped with an atmospheric pressure ionisation (API) LC interface. The source and spraying elements are visible through a transparent window in the enclosure and are easily accessible via a quick-release mechanism. The source elements may be wiped clean in situ or removed for cleaning without the need for tools and without breaking vacuum. The nebulized spray is orientated orthogonally and positioned off axis for maximum source longevity and analyser protection against 'dirty' samples. The source also includes facilities for de-clustering ions formed at atmospheric pressure. Positive and negative capability is included. Positive ion, negative ion and ESCi" capability is available as standard (allowing rapid switching between ESI and APCI, positive and negative in the same run). All source voltages and gases are under data system control.

2. INTELLISTART" FLUIDICS
The instrument is equipped with an on-board infusion system capable of delivering reference solutions from 3 built-in vial locations. The on-board fluidics system is controlled by the IntelliStart software to provide automated instrument setup, mass calibration and method development. The reference solutions are delivered via switching valves for either direct or combined (into an LC flow) infusion into the API source. The valves can in addition be programmed from the software to function as an LC flow divert. If required, the fluidics can be controlled manually via the system Console.

3. TANDEM QUADRUPOLE ANALYSER

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Detail Product Description(s)

Product# Description

176003468 Xevo TQ-S micro - Continued

The instrument is equipped with two high performance quadrupole mass analysers with inter-element beam focusing and a mass range of 2-2000 amu. Pre-filters are fitted to the mass analysers to maximise resolution and transmission. The pre-filters also eliminate the need for cleaning of the quadrupole mass analysers. All lens and analyser voltages are digitally controlled. Analyser parameters may be programmed with respect to mass for optimal performance. Analyser parameters used for data acquisition are automatically recorded and appended to the relevant data file.

3. StepWave" ION TRANSFER OPTICS
This instrument is equipped with patented, off-axis StepWave " ion transfer optics. Uniquely the StepWave technology both dramatically increases the efficiency of ion transfer from the ion source to the quadrupole MS analyser at the same time as efficiently eliminating undesirable neutral contaminants. The technology employed allows Xevo TQ-S micro to deliver unprecedented levels of sensitivity, speed, and selectivity.

4. COLLISION CELL
The collision cell can be operated as a high efficiency travelling wave (T-Wave) device for collision induced dissociation. The travelling wave enables rapid cell clearance and refill for fast MRM transition switching while maintaining optimum signal to noise.

T-Wave" :
The cell can be operated as a high efficiency travelling wave (T-Wave) device for collision induced dissociation. The travelling wave enables rapid cell clearance and refill for fast MRM transition switching while maintaining optimum signal to noise.

RADAR" :
An information-rich acquisition approach that allows you to collect highly specific quantitative MRM data for target compounds while providing additional spectral data to help visualize all other components in the sample.

5. VACUUM SYSTEM
Clean, differentially pumped, automated vacuum system comprising:
Air-cooled Pfeiffer splitflow turbomolecular drag pump evacuating both the source & analyser.
Vacuum read backs and system vent/pump cycles are digitally monitored and controlled, to provide total software control and ensure fail-safe operation in the event of power failure.
The backing option must be ordered separately (See Backing Pump Options for part numbers and descriptions)

6. DETECTOR - Xtended Dynamic Range" (XDR)
The instrument is equipped with a low noise dynolite photomultiplier detector. The detector is positioned after the second analyzer. A High Voltage conversion dynode and phosphor are positioned at 90° off-axis to the analyser for the elimination of neutral noise. The detector features novel, integral focusing optics, which provides a detection efficiency approaching 100% for single ions. New XDR electronics incorporate 40 MS/s and 16 bit ADC to increase the dynamic range. The photomultiplier is enclosed in its own vacuum envelope for long life. The detector operates in both positive and negative ion mode, which can be switched rapidly under software digital control.

7. MASSLYNX" SOFTWARE / MS Workstation
The MS Workstation and MassLynx" 4.1 License for the application software for instrument control, data acquisition and processing must be ordered separately (See MS Workstation Variant Configurator section for part numbers and descriptions)

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Detail Product Description(s)

Product# Description

176003468 Xevo TQ-S micro - Continued

Post acquisition processing and general data manipulation can be carried out by an additional computer workstation and software installation (See the MassLynx" Process-only Workstations section of the MassLynx Variant configurator 176706000).

176002526 MassLynx Workstation with TL

MassLynx" Workstation with License
MassLynx 4.1 Application Software License includes key discs for TargetLynx" and OpenLynx"
Lenovo ThinkStation C20 with Windows 7 Professional 64
Intel® Xeon® E5620 Processor (2.40GHz 1066MHz 12MB Turbo SMT) - 80W, Windows 7 Professional 64 - bit (US English), Tower 6x4 Mechanical with Intel 5520 Motherboard, Intel 5520 Motherboard (C20X) - TPM Enabled, DDR3 ECC uDIMM PC3-10600 1333MHZ, 3 x 2GB ECC DDR3 PC3-10600 SDRAM (1333MHz uDIMM)
NVIDIA Quadro 400 (512MB DVI+DP), DVI -To - VGA Video Converter, Integrated Audio, Internal RAID - Not Enabled, 500GB SATA 3.5" Hard Drive - 7200 rpm, Lenovo 16x DVD +/- RW Dual Layer (Windows 7), Dual Integrated Ethernet 10/100/1000, Lenovo USB Preferred Pro Full Size Keyboard - US Euro, Lenovo Optical Wheel Mouse - USB Primax 400 DPI, Line Cord # US, Language Pack # English, Non-Return HDD - 3 Year Warranty US/EMEA, Three year on-site warranty (parts and labour)
Monitor: None; Printer: None

668000273 MONITOR, Lenovo ThinkVision Flat Panel

22" Flat Panel Monitor
Lenovo ThinkVision L2250p - LCD display - TFT - 22" - Widescreen - 1680 x 1050 / 75 Hz - 250 cd/m2 - 1000:1 - 5 ms -0.282 mm DVI-D, VGA - business black

176002088 APCI

APCI IonSABRE II
Dedicated probe option for atmospheric pressure chemical ionisation (APCI). The interface can be used at up to 2 ml/min without the need for flow splitting (not recomended APCI probe option for Xevo TQ).

176015008 ACQUITY UPLC H-Class CM Core System

ACQUITY UPLC H-Class Column Manager Core System- 2 Columns

176015028 ACQUITY UPLC TUV Detector

ACQUITY UPLC TUV Detector
The Waters ACQUITY UPLC Tunable UV (TUV) detector is a dual-wavelength Ultraviolet/Visible (UV/Vis) detector for use in the ACQUITY UPLC H-Class system. Optimized for Ultra Performance Liquid Chromatography, the TUV detector#s innovative light-guided flow cell and low-noise electronics result in a detector that delivers the utmost in UPLC sensitivity.
Detector wavelength range is 190-700nm. Detector response is linear up to 2.5 AU; dynamic range extends to 4.0 AU. Either single or dual wavelength operating modes are supported. Wavelength spectral scanning, including automatic blank subtraction can be stored in memory. Wavelength ratios, with absorbance threshold control, may be utilized for real time peak purity assessment.
Access to detector status # wavelength, lamp on/off # and diagnostic information is supported through the ACQUITY UPLC System Instrument Console. Instrument communications with the host computer are through Ethernet communications

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Detail Product Description(s)

Product# Description

176015028 ACQUITY UPLC TUV Detector - Continued

protocols.
Lamp optimization software and low-noise electronics guarantee low noise performance in the visible wavelength range and compensates for lamp degradation over time to ensure consistent response. The combination of lamp optimization software and an automatic second order filter enables operation in the visible wavelength range without requiring a lamp change. The lamp is warranted for 2000 hours.
The 10mm analytical light-guided flow cell delivers sensitivity and resolution to ACQUITY UPLC applications. Low dispersion performance is achieved with a 500 nL internal volume and 62.5 ¼m PEEK interconnectinlet/outlet tubing.

741000321 TQD SYSTEM INSTALLATION CERT

Waters TQ Detector MS System Installation
Includes:
-System Set up and Specification Testing
-Product Familiarization Training
-1 Year Manufacturers Warranty
- Insight Remote Intelligent Services

201000233 H-Class QSM w/i2V PERFORMANCE MAINT KIT

ACQUITY H QSM PERFORMANCE MAINTENANCE KIT

201000234 H-CLASS SAMPLE MANAGER-FTN PM KIT

ACQUITY H SM-FTN PERFORMANCE MAINT KIT

668000275 Printer, HP Laser Jet, P3015dn, 110 Volt

HP LaserJet P3015DN Laser 42ppm, 110V, 1200x1200DPI LTR USB 128MB Duplex / Has Network Connection.

Waters

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Account	: State of West Virginia
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Creation date	: 11/11/2016
Expiration date	: 12/30/2016

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Waters General Sales Terms and Conditions

THIS TRANSACTION IS EXPRESSLY CONDITIONED UPON AND SUBJECT TO ALL OF THE FOLLOWING TERMS AND CONDITIONS:

1. Acceptance - Buyer's acceptance of the offer to purchase the products and/or services set forth on the front page made by Waters Technologies Corporation d/b/a Waters Corporation (Waters) of this quotation shall create a contract subject to and expressly limited by the terms and conditions contained on this form. Acceptance of this quotation may only be made on the exact terms and conditions set forth on this quotation; if additional or different terms are proposed by Buyer, such additional or different terms shall not become a part of the contract formed by Buyer's acceptance of the quotation. Receipt of the products sold hereunder or commencement of the services provided hereunder shall be deemed acceptance of the terms and conditions of this quotation.
2. Taxes and Payment - Any tax, duty, custom or other fee of any nature imposed upon this transaction by any federal, state or local governmental authority shall be paid by Buyer in addition to the price quoted. In the event Waters is required to prepay any such tax or fee, Buyer will reimburse Waters. Payment terms shall be net thirty (30) days after shipment and are subject to credit approval. An interest charge equal to 1 1/2% per month (18% per year) will be added to quotations outstanding beyond 30 days after shipment. In addition, Waters reserves the right, in its sole discretion, to require C.O.D. payment terms from any Buyer. Waters may also refuse to sell to any person until all prior overdue accounts are paid in full.
3. Delivery and Shipment - Delivery terms shall be F.O.B. Waters shipping point; identification of the products shall occur when they leave Waters shipping point at which time title and risk of loss shall pass to Buyer. All shipment costs shall be paid by Buyer and if prepaid by Waters the amount thereof shall be reimbursed to Waters. Waters will make reasonable commercial efforts to ship the products or provide the services hereunder in accordance with the delivery date set forth on the reverse side hereof provided, that Waters accepts no liability for any losses or for general, indirect special or consequential damages arising out of delays in delivery.
4. Warranty - The products and/or services shall be covered by the applicable Waters standard warranty, a copy of which is supplied with the products and/or services or upon request. NO OTHER WARRANTY, WHETHER EXPRESS OR IMPLIED, IS MADE WITH RESPECT TO THE PRODUCTS AND/OR SERVICES. WATERS EXPRESSLY EXCLUDES THE IMPLIED WARRANTIES OF MERCHANTABILITY AND OF FITNESS FOR A PARTICULAR PURPOSE. Any model or sample furnished to the Buyer is merely illustrative of the general types and quality of goods and does not represent that the products will conform to the model or sample. Buyer's remedies under Waters warranty shall be limited to repair or replacement of the product or component which failed to conform to Waters applicable standard warranty. WATERS SHALL NOT BE LIABLE FOR CONSEQUENTIAL, INCIDENTAL, SPECIAL OR ANY OTHER INDIRECT DAMAGES RESULTING FROM ECONOMIC LOSS OR PROPERTY DAMAGE SUSTAINED BY BUYER FROM THE USE OF ITS PRODUCTS OR SERVICES.
5. Returned Goods - Waters may, in its sole discretion, authorizeproduct returns in appropriate circumstances, subject to such conditions as Waters may specify. Any such return shall be subject to the express prior authorization of Waters and payment by Buyer of a restocking charge. No returns will be authorized after one hundred twenty (120) days following shipment to Buyer.
6. Technical Advice - Waters may, at Buyer's request furnish technical assistance, advice and information with respect to the products if and to the extent that such advice, assistance and information is conveniently available. It is expressly agreed that there is no obligation to provide such information, which is provided without charge at the Buyer's risk, and which is PROVIDED WITHOUT WARRANTY OF ANY KIND AND IS SUBJECT TO THE WARRANTY DISCLAIMERS AND LIMITATION OF LIABILITY SET FORTH IN PARAGRAPH 4.
7. Waters Right of Possession, etc. - Buyer hereby grants Waters a purchase money security interest in the goods offered by this quotation to secure the due and punctual payment of the purchase price specified in this quotation. In the event of default by Buyer in any payment due Waters, Waters shall have the right, in addition to any other remedies it may have at law or in equity, to withhold shipment, to recall goods in transit and retake the same, to repossess any goods which may be stored with Waters for Buyer's account without the necessity of Waters initiating any other proceedings. In addition, Waters shall have all of the rights and remedies of a secured party under the Massachusetts Uniform Commercial Code and may exercise all such rights and remedies in accordance therewith. Buyer shall execute such documents as Waters may request to effectuate the foregoing security interest.
8. Agents, etc. - No agent, employee or other representative has the right to modify or expand Waters standard warranty applicable to the products and/or services or to make any representations as to the products other than those set forth in the applicable user or operator's guide delivered with the products, and any such affirmation, representation or warranty, if made, should not be relied upon by Buyer and shall not form a part of contract between Waters and Buyer for the purchase of the products or services.
9. Fair Labor Standards - The products or services provided hereunder were produced and/or performed in compliance with the requirements of all sections of the Fair Labor Standards Act of 1938 as amended.
10. Equal Employment - Waters is an Equal Opportunity Employer. It does not discriminate in any phase of the employment process against any person because of race, color, creed, religion, national origin, sex, age, veteran or handicapped status.
11. Modifications, Waiver, Termination - The contract formed by Buyer's acceptance of this quotation may be modified and any breach thereunder may be waived only by a written and signed document by the party against whom enforcement thereof is sought.
12. Governing Law - The contract formed by Buyer's acceptance of this quotation shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts, U.S.A.
13. Compliance with Laws - Buyer shall at all times comply with all applicable federal, state and local laws and regulations, including, without limitation, the provisions of the United States Export Control Laws as may be in effect for any of the products or services, and, if products or services hereunder are used in clinical applications, all applicable rules and regulations of the United States Food andDrug Administration and/or other domestic or international agencies with respect to the application of, as the case may be, Good Clinical Practices ("GCP"), Good Laboratory Practices ("GLP") or good Manufacturing Practices ("GMP").
14. Additional Terms and Conditions - This quotation is also subject to any Waters Special Terms and Conditions applicable to the products or services offered by this quotation, which appear on the front of this quotation. Any variance from the terms and conditions of this quotation in any order or other written notification from Buyer, will be of no effect. Should Buyer order products or services through a Waters office located outside of the United States, the terms and conditions of the quotation issued by the office outside of the United States shall govern such order.
15. Arbitration - Any and all disputes or controversies arising in connection with the contract formed by Buyer's acceptance of this quotation or the sale of products and/or performance of the services shall be resolved by final and binding arbitration in Boston, Massachusetts, under the rules of the American Arbitration Association then obtaining. The arbitrators shall have no power to add to, subtract from or modify any of these terms or conditions of this contract. Any award rendered in such arbitration may be enforced by either party in either the courts of the Commonwealth of Massachusetts or in the United States District Court for the District of Massachusetts, to whose jurisdiction for such purposes Waters and Buyer each hereby irrevocably consents and submits.
16. Software - To the extent there is any software included with the products, the software is being licensed, not sold and all rights, title and interest therein shall remain with Waters. Use of the software shall be in accordance with the applicable software license delivered with the products. U.S. Government Restricted Rights - RESTRICTED RIGHTS LEGEND. Use, duplication or disclosure by the Government is subject to restrictions as set forth in subparagraph (c)(1)(ii) of the Rights in Technical Data and Computer Software clause at DFARS 252.227-7013 or subparagraphs (c)(1) and (2) of the Commercial Computer Software - Restricted Rights clause at 48 CFR 52.227-19, as applicable.
17. Force Majeure - Waters shall have no liability for failure toperform, or delay in performance, in the delivery of any and all equipment manufactured or sold by Waters including instruments, supplies, components, systems, chemistry, accessories, replacement spare parts, or any and all services provided by Waters, caused by circumstances beyond its reasonable control including, but not limited to, acts of God, acts of nature, floods, fire, explosions, war or military mobilization, United States governmental action or inaction, request of governmental authority, delays of any kind in transportation or inability to obtain material or equipment, acts of other governments, strikes, or labor disturbances.
18. Diagnostic Products - Buyer acknowledges and agrees that only those products which are labeled and identified as in vitro diagnostic (#IVD#)

Sales Proposal
Please reference this Quotation when Purchase Order is issued

Waters General Sales Terms and Conditions

devices are intended to be used for IVD purposes. Buyer acknowledges and agrees that any products that are not labeled and identified as IVDs are general laboratory products intended for research and other general scientific uses and are not for use in IVD procedures.

Purchasing Divison
2019 Washington Street East
Post Office Box 50130
Charleston, WV 25305-0130

State of West Virginia
Request for Quotation
01 — Agricultural

Proc Folder: 265333
Doc Description: Addendum # 1 - Triple Quad LC/MS/MS
Proc Type: Central Purchase Order

Date Issued	Solicitation Closes	Solicitation No	Version
2016-11-09	2016-11-17 13:30:00	CRFQ 1400 AGR1700000005	2

BID RECEIVING LOCATION

BID CLERK
DEPARTMENT OF ADMINISTRATION
PURCHASING DIVISION
2019 WASHINGTON ST E
CHARLESTON WV 25305
US

VENDOR

Vendor Name, Address and Telephone Number:

Waters Technologies Corporation
34 Maple St
Milford, MA 01757
800-252-4752

FOR INFORMATION CONTACT THE BUYER

Linda Harper
(304) 558-0468
linda.b.harper@wv.gov

Signature X Kristen A. Rukala FEIN # 04-3234558 DATE 11/16/16

All offers subject to ~~all terms and conditions contained in this solicitation~~

Please refer to the attached document titled "Exceptions"

ADDITIONAL INFORMAITON:

Addendum 1 issued for the following reasons:

1. To modify Section 3.1.1.2 of the specifications based on Q.A./14. of vendor questions. Revised specifications attached.
2. To publish the vendor questions with responses.

No other changes.

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
1	LCMSMS, Workstation, software, printer	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
41100000			

Extended Description :

LCMSMS, Workstation, software, printer per specification 3.1.1 & 3.1.2

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
2	Shipping Charges and inside delivery	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
78121603			

Extended Description :

Shipping Charges and inside deliver per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
3	Installation/validation	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :
Installation/validation per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
4	Training/Warranty	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :
Training/Warranty per section 3.1.3

INVOICE TO	SHIP TO
PROCUREMENT OFFICER 304-558-2221 AGRICULTURE DEPARTMENT OF ADMINISTRATIVE SERVICES 1900 KANAWHA BLVD E CHARLESTON WV25305-0173 US	AUTHORIZED RECEIVER 304-558-2227 AGRICULTURE DEPARTMENT OF REGULATORY PROTECTION DIVISION 313 GUS R DOUGLAS LN, BLDG 11 CHARLESTON WV 25312 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
5	Service	1.00000	EA		

Comm Code	Manufacturer	Specification	Model #
73171605			

Extended Description :

Service per section 3.1.3

SCHEDULE OF EVENTS

Line	Event	Event Date
1	Question Deadline 3:00 p.m.	2016-11-04

SOLICITATION NUMBER: AGR1700000005
Addendum Number: 1

The purpose of this addendum is to modify the solicitation identified as ("Solicitation") to reflect the change(s) identified and described below.

Applicable Addendum Category:

[ ] Modify bid opening date and time

[✓] Modify specifications of product or service being sought

[✓] Attachment of vendor questions and responses

[ ] Attachment of pre-bid sign-in sheet

[ ] Correction of error

[ ] Other

Description of Modification to Solicitation:

Addendum 1 issued for the following reasons:

1. To modify Section 3.1.1.2 of the specifications based on Q.A./14. of vendor questions. Revised specifications attached.

2. To publish the vendor questions with responses.

No other changes.

Additional Documentation: Documentation related to this Addendum (if any) has been included herewith as Attachment A and is specifically incorporated herein by reference.

Terms and Conditions:

1. All provisions of the Solicitation and other addenda not modified herein shall remain in full force and effect.

2. Vendor should acknowledge receipt of all addenda issued for this Solicitation by completing an Addendum Acknowledgment, a copy of which is included herewith. Failure to acknowledge addenda may result in bid disqualification. The addendum acknowledgement should be submitted with the bid to expedite document processing.

ATTACHMENT A

CRFQ AGR1700000005

Vendor Questions

Q.1. Specification 3.1.1.20 says that the system should come with solvent and column selection. Can you please clarify how many solvents per pump (2, 3, 4, etc.) and how many columns (2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12? Specification 3.1.1.21 mentioned 2 columns, but we want to be certain.

A.1. 4 solvents per pump preferred and 2 columns

Q.2. Specification 3.1.1.21 mentioned a column temperature, but no temperature range on the column oven is provided. We offer a heating oven and a heating (ambient up to 85 degrees) and cooling oven (10 degrees below ambient up to 85 degrees). Can you please clarify which you need?

A.2. 4-90°

Q.3. Specification 3.1.1.22 mentions a High Performance Liquid Chromatograph with an autosampler. This leads to a series of questions on the configuration:

a. I assume you want a binary high pressure pump? Or, did you want a quaternary low pressure pump?

3a. quaternary low pressure pump

b. What pressure range do you want on the system? We offer standard (6000 psi), mid (9000 psi) and UHPLC (19000 psi).

3b. since systems vary 15,000 to 19,000 psi is acceptable

c. Should the autosampler be ambient or Peltier-cooled?

3c. cooled

d. Will you be sampling from 2 mL vials, which is typically standard, or do you want to sample from microtitre plates, etc..?

3d. possibly both

e. How many vials do you want your autosampler to hold? Shimadzu offers 100 and 324 2 mL vial options.

3e. 48 vials or more

f. Do you want the HPLC to include a traditional HPLC detector (such as a photo diode array) inline to help with troubleshooting and method development?

g. 3f. yes

Q.4. There is no mention of a Nitrogen or Air generator, and this will be necessary to run any LC/MS/MS. Should this be included on the bid, or should just the specifications be included as per 3.1.1.25?

A.4. Do not include in bid

Q.5. There is no mention of a UPS on the bid. This is highly recommended to protect the turbomolecular pump and deliver a stable source of power to the instrument. Should this be added?

A.5. Do not include in bid

Q.6. Section 3.1.3.4 refers to response time for service requests. Does this refer to requests under warranty or post warranty? Also, is there a requirement for post warranty contractual support pricing for this solicitation?

A.6 This refers to any service when the instrument has failed and the laboratory cannot process samples. The best response time is critical to the laboratory to maintain production, therefore, a 72 hour resolution to service requests is critical.

Q.7. Is the lab that is interested in purchasing an LCMS system interested or currently running any regulated EPA, FDA, or USDA LCMS Methods and if so which method numbers are being analyzed?

A.7. Multiple methods from the EPA, FDA, USDA, FERN, AOAC are being ran or are intended to be ran.

Q.8. Would they be able to outline which pesticides, herbicides, toxins, and drugs they would like analyze with the LCMS/MS system and what limits of detection and quantification they need for their work?

A.8. The laboratory will test an array of substances that are of concern under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In addition, two specific methods are of current interest – USDA FSIS CLG.TOX 001 and TOX 002 which screen for drugs, pesticides and poisons.

Q.9. Would they be able to outline a specific LCMS method that requires a flow rate of 3 mL/min and why this would be more advantegous than a lower flow rate method?

A.9. No specific LCMS method is referenced. The specification was referring to a loss in sensitivity at different flow rates and anything that meets that requirement or is more sensitive is required.

Q.10. Are they currently using any sample preparation for the analysis of these components and if they could optimize or potentially eliminate sample prep would that be something they would be interested in doing?

A.10. It is dependent upon the official method. If the method dictates the sample preparation, then the laboratory will have to follow it. Some preparations can be eliminated if the laboratory validates

the method. Also changes is methods that are validated will have to be approved by our customers before a validation is performed.

Q.11. Would they be able to outline a specific LCMS method that requires a scan rate of 30,000 Da/sec and how is this advantegous?

A.11 No specific LCMS method is referenced, however the laboratory will be performing method development and will be comparing if the chromatographic resolution is better with the higher scan rates.

Q.12. How does size of the LCMS solution they are looking to obtain affect their decision? If they could get a small footprint LCMS system would that add value to the work they do?

A.12. If all the specifications are met in the RFQ, the size could be something that would determine an award of the bid.

Q.13. We would like to be able to propose suggestion exceptions to terms and conditions with a mutual negotiation and agreement. Will you allow this should we be awarded the bid or will you disqualify us? Bid states "may" result in disqualification but we would like to attempt to negotiate if possible.

A.13. Suggested exceptions should be submitted and will be reviewed for acceptance. Certain State of West Virginia terms and conditions are non-negotiable.

Q.14. Can you clarify the need and importance for the spec listed in 3.1.1.2? I don't see how it applies to the real world applications. We have canned methods for all of the applications in question and none require this functionality.

A.14. There is an error in the specification 3.1.1.2. It should state "dual ion sources that operate independently which can be set to electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI). A copy of the revised specifications attached.

SPECIFICATIONS

1. **PURPOSE AND SCOPE:** The West Virginia Purchasing Division is soliciting bids on behalf of West Virginia Department of Agriculture to establish a contract for the one time purchase of a **Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS), workstation PC, software, printer, shipping, installation, validation, warranty, training, and service.**

2. **DEFINITIONS:** The terms listed below shall have the meanings assigned to them below. Additional definitions can be found in section 2 of the General Terms and Conditions.

   2.1 **"APCI"** means atmospheric pressure chemical ionization.

   2.2 **"Contract Services"** means the LC/MS/MS with inside delivery, installation, validation, warranty, and training.

   2.3 **"ESI"** means electrospray ionization.

   2.4 **"FG"** means femtogram.

   2.5 **"Installation"** means unpacking and setting instrumentation in place with all connections secured for the instrument(s) to be in working order including software installation on the computer connected to the instrument.

   2.6 **"LC/MS/MS"** means Liquid Chromatography Triple Quadrupole Mass Spectrometer.

   2.7 **"MRM"** means multiple reactions monitoring.

   2.8 **"MSMS"** means tandem mass spectrometry.

   2.9 **"Pricing Page"** means the pages, contained in wvOASIS or attached as Exhibit A, upon which Vendor should list its proposed price for the Contract Items.

   2.10 **"Service"** means performing routine maintenance work or repair to the instrument or software.

   2.11 **"SIM"** means selected ion monitoring

   2.12 **"S/N"** means signal noise.

2.13 "Solicitation" means the official notice of an opportunity to supply the State with goods or services that is published by the Purchasing Division.

2.14 "Training" means teaching staff how to use and maintain the instrument and software.

2.15 "Validation" means is the process used to confirm that the analytical procedure employed for a specific test or matrices is suitable for its intended use.

2.16 "Warranty" means the written warranty of the manufacturer of a new instrument of its condition and fitness for use, including any terms or conditions precedent to the enforcement of obligations under that warranty.

3. GENERAL REQUIREMENTS:

3.1 Mandatory Contract Item Requirements: Contract Item must meet or exceed the mandatory requirements listed below for the **Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS).**

3.1.1 Liquid Chromatography Triple Quadrupole Mass Spectrometer (LC/MS/MS)

3.1.1.1 Must be capable of detecting a variety of analytes including pesticides, herbicides, toxins, and drugs in matrices such as foods, soil, vegetation, animal feed, and water.

3.1.1.2 MSMS must have dual ion sources that operate independently which can be set to electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI). The instrument must enable combinations such as ESI/APCI, ESI/ESI, APCI/APCI with the same or opposite polarities without having to remove the sources to switch modes.

3.1.1.3 Minimum sensitivity requirement for positive ion mode: signal/noise (S/N) 2000:1 25 femtograms (fg) of reserpine on column. Minimum sensitivity requirement for negative ion mode: signal/noise (S/N)>2000:1, 25 femtograms (fg) of chloramphenicol on column.

3.1.1.4 The source probes must be easy to remove without the use of tools.

3.1.1.5 Ion source must have flat response across flow rate up to 3 milliliters per minute without loss of sensitivity.

3.1.1.6 Capable of switching between rapidly between positive and negative ion detection without high voltage switching.

3.1.1.7 Acquisition modes: Q1 scan, Q2 scan, multiple reactions monitoring (MRM), selected ion monitoring (SIM), Neutral Loss scans, Product Ion, Precursor Ion, Time managed MRM

3.1.1.8 Minimum mass range requirement: 5-1500 mass to charge ratio (m/z)

3.1.1.9 Mass stability required: 0.05 atomic mass unit (amu) in 24 hours

3.1.1.10 Mass accuracy needed: minimum 0.1 unit across mass range

3.1.1.11 Scan speed: ≤30,000 daltons per second (da/s)

3.1.1.12 Quad resolution: unit, low and high, minimal sensitivity loss at 0.1 Daltons resolutions

3.1.1.13 Polarity switching time: ≤15 milliseconds

3.1.1.14 Dynamic range: 6 orders

3.1.1.15 Dual source switching speed: <20 milliseconds

3.1.1.16 Minimum multiple reactions monitoring (MRM) Dwell Time: 1 millisecond

3.1.1.17 MRM transitions: 450 per time segment > 40,000 ion transactions per method

3.1.1.18 Must have high selectivity mass filter at 0.3 Daltons. Signal loss must not be more than 10%.

3.1.1.19 For minimal tuning during method development and minimal maintenance of the ion path, the LC/MS/MS utilizes Hot Source Induced Desolvation interface to the mass analyzer by patented Laminar Flow Ion Guide using gas flow

3.1.1.20 High performance liquid chromatograph capable of solvent and column switching without user intervention

3.1.1.21 High performance liquid chromatograph capable of regulating column temperature of at least 2 different columns

3.1.1.22 High performance liquid chromatograph with an autosampler

3.1.1.23 The LC/MS/MS instrument must be fully automated for analysis with a system controller that is loaded with the necessary software.

3.1.1.24 The LC/MS/MS must include a maintenance kit.

3.1.1.25 Vendor must provide documentation for recommended environmental conditions, electrical requirements, gas requirements, or any other factor that would affect instrument performance.

3.1.2 Workstation and software

3.1.2.1 Data station with windows based operating system capable of multitasking allowing data processing and data acquisition simultaneously.

3.1.2.2 Operating system must be fully integrated to control LS/MS/MS.

3.1.3 Shipping, Installation, Validation, Warranty, Training and Service

3.1.3.1 Vendor must be on-site for delivery and perform the installation (labor and supplies included) of the LCMSMS.

3.1.3.2 The vendor must provide a written validation of the instrument's performance after installation.

3.1.3.3 Vendor will provide a full one-year parts and labor warranty on all items, including 2 preventative maintenances.

3.1.3.4 Vendor must be able to perform resolutions to service requests within 72 hours which includes on-site resolutions.

3.1.3.5 Vendor will provide on-site training (labor and non-consumable supplies included) for all instruments and software.

3.1.3.6 Vendor will provide copies of all system manuals (operations, training, technical, service, maintenance).

4. CONTRACT AWARD:

4.1 Contract Award: The Contract is intended to provide Agencies with a purchase price for the Contract Items. The Contract shall be awarded to the Vendor that provides the Contract Items meeting the required specifications for the lowest overall total cost as shown on the Pricing Pages.

4.2 Pricing Page: Vendor should complete the Pricing Page by placing all inclusive information in each column for item number, model/brand name, unit price and extended amount. There should be a price for the LCMSMS, workstation, software, printer, shipping/inside delivery, installation, validation, warranty, training and service. If there is no charge for any deliverable, indicate in the cell with "no charge". The bidder/vendor information must be completed and include an authorize signature. Vendor should complete the Pricing Page in full as failure to complete the Pricing Page in its entirety may result in Vendor's bid being disqualified.

Vendor should type or electronically enter the information into the Pricing Page to prevent errors in the evaluation.

5. PAYMENT:

5.1 Payment: Vendor shall accept payment in accordance with the payment procedures of the State of West Virginia.

6. DELIVERY AND RETURN:

6.1 Shipment and Delivery: Vendor should ship the Contract Items immediately after being awarded this Contract and receiving a purchase order or notice to proceed. Contract Items must be delivered to Agency at 313 Gus R. Douglass Lane, Charleston, WV 25312.

6.2 Late Delivery: The Agency placing the order under this Contract must be notified in writing if the shipment of the Contract Items will be delayed for any reason. Any delay in delivery that could cause harm to an Agency will be grounds for cancellation of the Contract, and/or obtaining the Contract Items from a third party.

Any Agency seeking to obtain the Contract Items from a third party under this provision must first obtain approval of the Purchasing Division.

6.3 Delivery Payment/Risk of Loss: Vendor shall deliver the Contract Items F.O.B. destination to the Agency's location.

6.4 Return of Unacceptable Items: If the Agency deems the Contract Items to be unacceptable, the Contract Items shall be returned to Vendor at Vendor's expense and with no restocking charge. Vendor shall either make arrangements for the return within five (5) days of being notified that items are unacceptable, or permit the Agency to arrange for the return and reimburse Agency for delivery expenses. If the original packaging cannot be utilized for the return, Vendor will supply the Agency with appropriate return packaging upon request. All returns of unacceptable items shall be F.O.B. the Agency's location. The returned product shall either be replaced, or the Agency shall receive a full credit or refund for the purchase price, at the Agency's discretion.

6.5 Return Due to Agency Error: Items ordered in error by the Agency will be returned for credit within 30 days of receipt, F.O.B. Vendor's location. Vendor shall not charge a restocking fee if returned products are in a resalable condition. Items shall be deemed to be in a resalable condition if they are unused and in the original packaging. Any restocking fee for items not in a resalable condition shall

be the lower of the Vendor's customary restocking fee or 5% of the total invoiced value of the returned items.

7 VENDOR DEFAULT:

7.1 The following shall be considered a vendor default under this Contract.

7.1.1 Failure to provide Contract Items in accordance with the requirements contained herein.

7.1.2 Failure to comply with other specifications and requirements contained herein.

7.1.3 Failure to comply with any laws, rules, and ordinances applicable to the Contract Services provided under this Contract.

7.1.4 Failure to remedy deficient performance upon request.

7.2 The following remedies shall be available to Agency upon default.

7.2.1 Immediate cancellation of the Contract.

7.2.2 Immediate cancellation of one or more release orders issued under this Contract.

7.2.3 Any other remedies available in law or equity.

8 **FACILITIES ACCESS:** Performance of Services will require access to the facility.

8.1 Vendor must identify principal service personnel who will be asked for identification upon entrance to the facility.

8.2 Anyone performing under this Contract will be subject to Agency's security protocol and procedures.

8.3 Vendor shall inform all staff of Agency's security protocol and procedures.

ADDENDUM ACKNOWLEDGEMENT FORM
SOLICITATION NO.: AGR1700000005

Instructions: Please acknowledge receipt of all addenda issued with this solicitation by completing this addendum acknowledgment form. Check the box next to each addendum received and sign below. Failure to acknowledge addenda may result in bid disqualification.

Acknowledgment: I hereby acknowledge receipt of the following addenda and have made the necessary revisions to my proposal, plans and/or specification, etc.

Addendum Numbers Received:
(Check the box next to each addendum received)

[X]	Addendum No. 1	[ ]	Addendum No. 6
[ ]	Addendum No. 2	[ ]	Addendum No. 7
[ ]	Addendum No. 3	[ ]	Addendum No. 8
[ ]	Addendum No. 4	[ ]	Addendum No. 9
[ ]	Addendum No. 5	[ ]	Addendum No. 10

I understand that failure to confirm the receipt of addenda may be cause for rejection of this bid. I further understand that any verbal representation made or assumed to be made during any oral discussion held between Vendor's representatives and any state personnel is not binding. Only the information issued in writing and added to the specifications by an official addendum is binding.

Waters Technologies Corporation
Company

Kristen A. Arakelian
Authorized Signature

11/16/16
Date

NOTE: This addendum acknowledgement should be submitted with the bid to expedite document processing.

Acquity H UPLC® CLASS

ACQUITY UPLC H-Class

PERFORMANCE THAT ADVANCES YOUR LAB

Waters

THE SCIENCE OF WHAT'S POSSIBLE.®

TRANSFORM STANDARD PROCEDURES INTO ULTIMATE PERFORMANCE

As an analytical laboratory, you solve problems and provide scientific information to other business units within your company. You require scientific tools that give you definitive results. You need flexibility to handle the diversity samples you support and you need your tools to fit within your existing laboratory workflows. What you don't need is to compromise the quality of data or timeliness of the result.

The ACQUITY UPLC® H-Class System is the only quaternary based liquid chromatographic system that was designed for *TRUE UPLC PERFORMANCE* without compromise. Whether you routinely develop new methods or you perform routine analysis and support large numbers of samples, the ACQUITY UPLC H-Class System can help you reach your laboratory's goals of decreasing the time to result, while increasing the depth and quality of the information about your samples.

SYSTEMS THAT MEET YOUR NEEDS FOR TODAY AND TOMORROW

- Improve laboratory efficiency by moving methods to UPLC® Technology
- Tools to simplify and streamline your method development workflow
- Increased resolution provides improved characterization of your complex samples
- Ideally suited to reproduce existing HPLC, UHPLC, and UPLC methods

Acquity H UPLC® CLASS

HIGHEST RESOLUTION OF ANY QUATERNARY LC SYSTEM

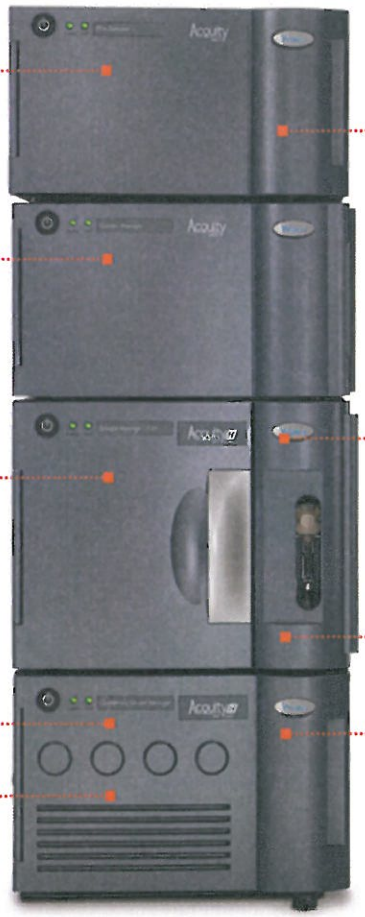
Low dispersion
True UPLC performance with band spread of less than 10 µL for highest chromatographic resolution.

Optional fraction collection
Temperature-controlled and compatible with narrow UPLC peaks.

Flexible sample support
Use either vials or ANSI well plate formats and with the sample organizer the sample capacity is extended for high-throughput and open access environments.

Gradient SmartStart
Easily manage system volume when transferring methods between different LC systems. Automate the timing of pre-injection steps for reduced inject-to-inject cycle times.

Auto•Blend Plus™ Technology
Automated online solvent blending at a specific pH and ionic strength that supports reversed phase, SEC, and IEX.



Wide range of detection capabilities
UPLC-optimized detectors to match your application needs, including photodiode array, UV/Vis, fluorescence, refractive index, evaporative light scattering, and mass spectrometry.

Versatile column management
Support for analytical LC column dimensions up to 300 mm with automated column switching between up to 6 analytical columns. Equipped with independently temperature controlled zones, active pre-heating, and eCord™ tracking for each column.

Flow-through-needle injector
Volume range of 0.1 to 1000 µL and ultra-low carryover performance compatible with your most sensitive LC-MS applications.

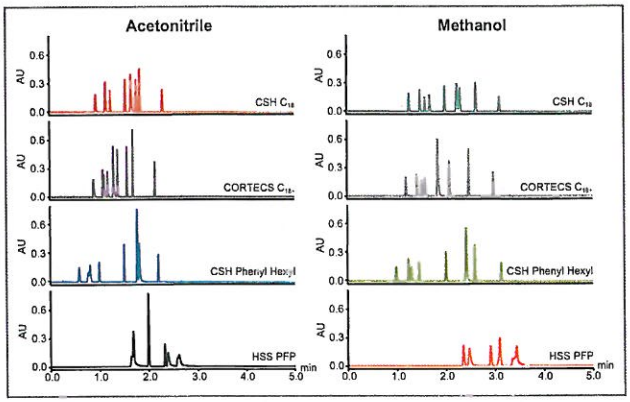
Quaternary solvent blending
Delivering repeatable gradient separations at pressures up to 15,000 psi. An optional solvent select valve adds access to an additional six solvents. Automated solvent compressibility, integrated solvent degassing, and programmable seal wash maximize flow accuracy, precision, and reliability.

DISCOVERING THE BEST METHOD GETS YOU THE BEST RESULTS

In method development, whether you use a step-wise approach, systematic screening, or a Quality by Design (QbD) protocol, you encounter the same obstacles.

- What conditions should I investigate?
- How do I track my peaks as conditions change?
- How can I reduce the time it takes to get a robust method?

The ACQUITY UPLC H-Class System gives you the flexibility to screen many method variables, quickly and automatically. Select between up to six columns, each in separate and independently controlled temperature zones. Eluents can be blended from four online from stock solutions to give you a wide range of selectivity, and this can be further expanded with addition of a six-solvent select valve. Combining these system capabilities with the Empower® Sample Set Generator can help you to completely automate your method development experiment. Adding the ACQUITY® QDa® Mass Detector allows you to track the peaks in the separation without needing to inject individual standards, decreasing the time it takes to run the experiment, process the results, and select the final conditions.

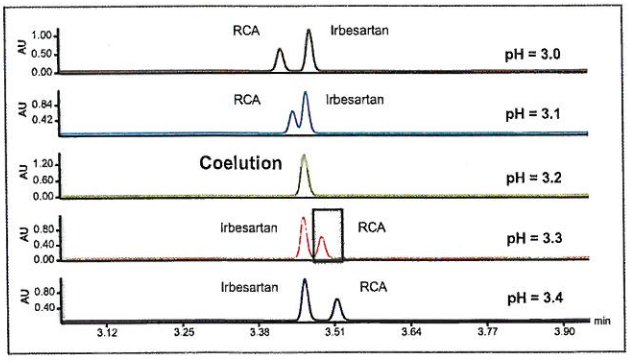


In developing a method for metoclopramide and its related components, the ACQUITY UPLC H-Class System was configured to automatically screen multiple column and eluent combinations to identify the separation conditions that provided the best chromatographic resolution.

ONLINE ELUENT BLENDING – ANY BUFFER, ANY SOLVENT, ANY pH

Auto•Blend Plus Technology automatically blends your mobile phase to a specified pH and ionic strength or organic modifier percentage, for any set of analytical conditions you need. By blending online to the desired pH and ionic strength conditions, you can significantly reduce the number of buffers you need to prepare every day. Also, having the system prepare the buffers for you can reduce day-to-day method variability.

Whether you are running biomolecules and require pH gradients for charge variant analysis, or you are doing small molecule method robustness testing and want to test small variations in pH, Auto•Blend Plus Software allows you to program an infinite set of conditions for any analytical method type.

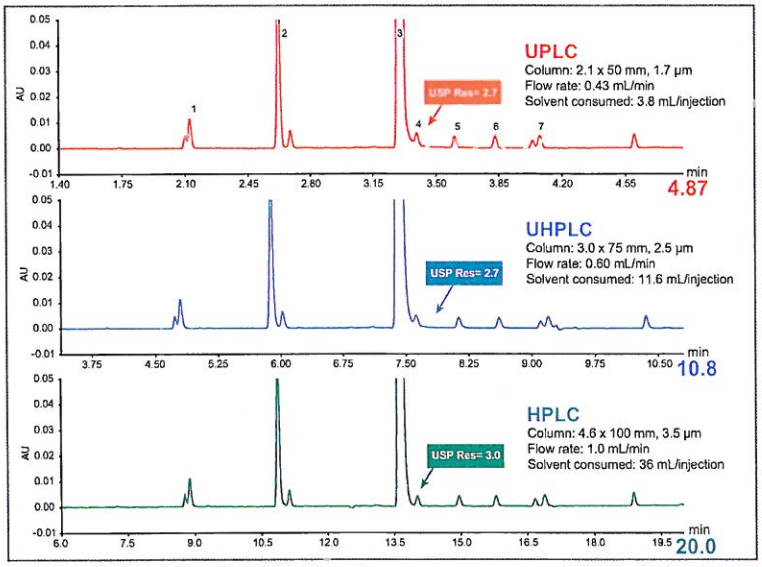


The USP assay for Irbesartan requires that the eluent be adjusted to pH 3.2, however this results in a co-elution of the API and its related compound. By making automated, online adjustments to the pH in 0.1 increments using Auto•Blend Plus, a more robust set of pH conditions can be found.

TAKE YOUR METHODS TO THE NEXT PERFORMANCE LEVEL

Leverage the benefits of UPLC Technology to improve your HPLC methods. By scaling your methods to UPLC, your applications will benefit from the combination of increased speed, resolution, and sensitivity that comes with modern small particle chemistries.

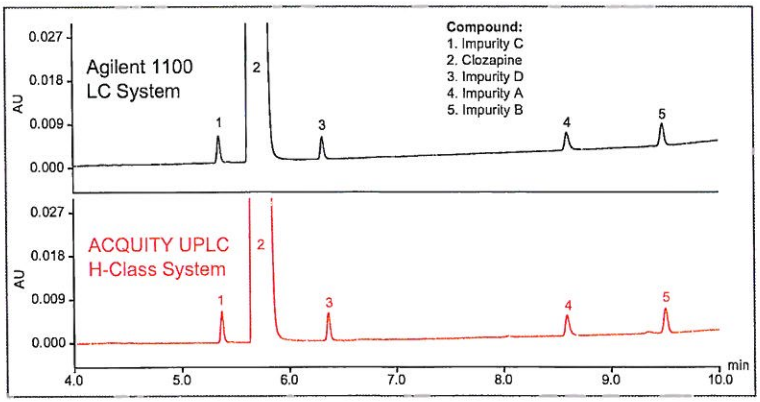
True UPLC performance comes by pairing a low-dispersion UPLC system with narrowbore columns packed with sub-2-µm particles. With a toolbox of simple and intuitive applications to help you systematically scale your methods, the process of converting your methods is simple. The result is improved laboratory efficiency, achieved with increased sample throughput, more information per injection, and a reduced cost per analysis.



The USP Analysis of Diclazuril and Organic Impurities was scaled from HPLC to UHPLC to UPLC. The UPLC method resulted in a 4x reduction in run time with a 10x reduction in solvent consumption resulting in improved sample throughput and reduced cost per analysis.

UPLC TOMORROW, BUT HPLC TODAY

Adopting a new analytical technology that improves laboratory efficiency is advantageous for supporting your new projects and products. However, there may still be a need to run existing analytical methods to support your existing products. Designed to reliably support your HPLC, UHPLC, and UPLC methods, the ACQUITY UPLC H-Class System is the ideal solution to future-proof your laboratory, enabling the transition to true UPLC performance when you are ready.



For the USP assay of Clozapine, the system suitability solution was run on both an Agilent 1100 LC System and the ACQUITY UPLC H-Class System. For this gradient method, equivalent chromatographic results were achieved on both systems.

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ACQUITY UPLC H-Class System

The Waters® ACQUITY UPLC® H-Class System delivers the flexibility of quaternary solvent blending with the advanced performance of UPLC® separations. The system's holistic design is targeted for routine analysis and method development use and is perfectly suited for running both HPLC and UPLC applications while still realizing the improved resolution and sensitivity of UPLC separations. The system is comprised of a Quaternary Solvent Manager (QSM), a Sample Manager with Flow-Through Needle (SM-FTN) design, and offers a choice of column compartment products.

ACQUITY UPLC H-CLASS SYSTEM FEATURES

Dwell volume (total system)	<400 µL (includes standard 100 µL mixer)
Integrated leak management	Leak sensors, as standard, and safe leak handling
Quantum synchronization	Injection synchronization between pump and sample manager enhances retention time reproducibility
Operating flow rate range	0.010 to 2.000 mL/min, in 0.001 mL increments
Maximum operating pressure	15,000 psi up to 1 mL/min, 9000 psi up to 2 mL/min
pH range	2 to 12
Unattended operation	Leak sensors, full 96-hour diagnostic data display through console software
Cycle time	<30 s inject-to-inject (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)

QUATERNARY SOLVENT MANAGER (QSM)

Number of solvents	One to four, in any combination as standard Expanded solvent choices with optional six-port solvent select valve
Solvent conditioning	Integrated vacuum degassing, four chambers One additional for the SM-FTN purge solvent
Gradient formation	Low-pressure mixing, quaternary gradient
Gradient profiles	11 gradient curves [including linear, step (2), concave (4), and convex (4)]
Primary check valve	Intelligent Intake Valve (i^2 Valve)
Flow accuracy	±1.0% at 0.5 to 2.0 mL/min using 100% A Back pressure 600 to 1000 psi with degassed H_2O
Flow precision	0.075% RSD or ±0.020 min SD, whichever is greater, based on six replicates 60:40 H_2O/MeOH via Auto•Blend Plus™ Technology, 0.5 mL/min, alkylphenone mix (5.0 µL injection volume), ACQUITY UPLC BEH C_{18}, 1.7 µm, 2.1 x 50 mm, 35 °C ± 0.3 °C, UV @ 254 nm

Composition ripple (baseline noise)	<1.0 mAu (<0.1 mAU with optional 250.0 µL mixer) A: H_2O + 0.1% TFA, B: ACN + 0.1% TFA, 0.5 mL/min, ACQUITY UPLC BEH C_{18} 1.7 µm, 2.1 x 50 mm UV @ 214 nm, 10 mm analytical flow cell
Composition accuracy	±0.5% absolute (full scale) from 5% to 90% from 0.5 to 2.0 mL/min Degassed ACN/H_2O (90:10), ACN/H_2O (90:10) with caffeine at 12 mg/L concentration, back pressure 2000 psi, step gradient method, UV at 273 nm
Composition precision	<0.15% RSD or ±0.04 min SD, whichever is greater, based on six replicate injections 60:40 H_2O/MeOH via Auto•Blend Plus Technology, 0.5 mL/min, alkylphenone mix (5.0 µL injection volume), ACQUITY UPLC BEH C_{18}, 1.7 µm, 2.1 x 50 mm, 35 °C ± 0.3 °C, UV @ 254 nm
Compressibility compensation	Automatic and continuous
Priming	Wet priming can run at flow rates up to 4 mL/min
Pump seal wash	Equipped with a wash system to flush the rear of the high pressure seal and the plunger
Flow ramping	Range: 0.01 to 30.00 min to reach 2.0 mL/min Default: 0.45 min to reach 2.0 mL/min
Primary wetted materials	316L stainless steel, PPS, fluoropolymer, fluoroelastomer, UHMWPE blend, sapphire, ruby, zirconia, Nitronic 60, DLC, PEEK and PEEK blend, titanium alloy

SAMPLE MANAGER-FTN (SM-FTN)

Injection volume range	0.1 to 10.0 µL as standard Up to 1000.0 µL with optional extension loops
Accuracy (aspiration)	±0.2 µL, measured by fluid weight removed from vial with 10.0 µL injections averaged over 20 injections using standard 100 µL syringe
Linearity	>0.999 (standard needle) caffeine 0.030 mg/mL, ACN/H_2O (10:90), isocratic 0.6 mL/min, 0.2 to 10.0 µL, 1 to 70% needle volume
Precision	<1% RSD 0.2 to 1.9 µL <0.5% RSD 2.0 to 10.0 µL (See ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Number of sample plates	Any two of the following: • 96 and 384 microtiter plates • 48 position 2.00-mL vial plates • 48 position 0.65-mL micro-centrifuge tube plates • 24 position 1.50-mL micro-centrifuge tube plates
Maximum sample capacity	768 in two 384-well plates or, 96 in 2-mL vial holders Additional positions for dilution functions
Sample compartment temperature range	4.0 to 40.0 °C, settable in 0.1 °C increments with a tolerance range between -2 and +4 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Temperature accuracy	±0.5 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Temperature stability	±1.0 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Injection needle wash	Integral, active, programmable
Minimum sample required	3 µL residual, using total recovery 2-mL vials (zero offset)

Sample carryover	<0.004% caffeine (UV) <0.005% sulphadimethoxine (MS)
Advanced Sample Manager capabilities	Auto-dilution and auto-addition
Primary wetted materials	316L stainless steel, gold plated stainless steel, Vespel SCP, PEEK blend, DLC

COLUMN HEATER (CH-A AND CH-30A)

Column capacity	CH-A: Single column, up to 4.6 mm internal diameter (I.D.), up to 150 mm in length with filter or guard column CH-30A: Single column, up to 4.6 mm internal diameter (I.D.), up to 300 mm length with filter or guard column
Column compartment temperature range	20.0 to 90.0 °C, settable in 0.1 °C increments (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Column compartment temperature accuracy	±0.5 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Column compartment temperature stability	±0.3 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Solvent conditioning	Active pre-heating as standard; passive pre-heating (also accommodated in CH-A only for legacy method support)
Column tracking	eCord™ Technology column information management tracks and archives column usage history

COLUMN MANAGEMENT (CM-A AND CM-AUX)

Column capacity	CM-A: Two columns, as standard (maximum length of 150 mm with filter or guard column) or four columns (maximum length of 50 mm) can be supported with optional tubing kit, up to 4.6 mm internal diameter (I.D.). CM-Aux: Two columns (maximum length of 150 mm, with filter or guard column). Up to two CM-Aux units can be configured with one CM-A for support of up to six columns.
Switching valves	Two injector-style, nine-port, eight-position valves (CM-A only); provides programmable, automatic, random access switching, waste and bypass positions for rapid solvent changeover
Column compartment(s) temperature range	4.0 to 90.0 °C, settable in 0.1 °C increments Two independent heat/cool zones per module, up to six zones in stacked configuration (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Column compartment(s) temperature accuracy	±0.5 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Column compartment(s) temperature stability	±0.3 °C (see ACQUITY UPLC H-Class and H-Class Bio System Specifications Guide for conditions)
Solvent conditioning	Active pre-heating as standard
Column tracking	eCord Technology column information management tracks and archives column usage history

SAMPLE ORGANIZER

Sample plate capacity	Sample plate capacity is configured based on the types and combinations of plates being used: • Maximum of 19 standard microtiter plates, up to 15.5 mm high, or, • Maximum of 9 intermediate height plates (or 2-mL vial holders), up to 40.0 mm high, or, • Maximum of 6 deep well plates (or 4-mL vial holders), up to 47.0 mm high
Maximum sample capacity	Maximum of 7296 samples in nineteen 384-well plates
Sample compartment temperature range	4.0 to 40.0 °C, settable in 0.1 °C increments with a tolerance range between -2 and +4 °C (See ACQUITY UPLC Sample Organizer Operator's Overview and Maintenance Guide for conditions)
Temperature accuracy	+/- 1 °C at the sensor
Temperature stability	+/- 1 °C at the sensor

ACQUITY UPLC H-CLASS INSTRUMENTAL CONTROL

External control	Empower™ Software, MassLynx™ Software, or standalone through console software
External communications	Ethernet interfacing via RJ45 connection to host PC
Event inputs/outputs	Rear panel contact closure and/or TTL inputs/outputs
Connections INSIGHT®	Provides real-time monitoring and automatic notification of instrument performance and diagnostic information allowing for quicker problem resolution
Local control	ACQUITY UPLC Local Console Controller (LCC)

ENVIRONMENTAL

Acoustic noise	<65 dBA, system
Operating temperature range	4.0 to 40.0 °C (39.2 to 104.0 °F)
Operating humidity range	20% to 80%, non-condensing

POWER REQUIREMENTS

Voltage	100 to 240 VAC
Frequency	50 to 60 Hz

PHYSICAL DIMENSIONS

ACQUITY UPLC H-Class System: Quaternary Solvent Manager, Sample Manager-FTN, Column Heater, and Solvents Tray	Width: Height: Depth:	34.3 cm (13.5 in.) 71.1 cm (28.0 in.) 71.2 cm (28.0 in.)
ACQUITY UPLC H-Class System: Quaternary Solvent Manager, Sample Manager-FTN, Column Manager, and Solvents Tray	Width: Height: Depth:	34.3 cm (13.5 in.) 79.6 cm (31.4 in.) 71.2 cm (28.0 in.)
Sample Organizer	Width: Height: Depth:	25.4 cm (10 in.) 96.5 cm (38.0 in.) 71.1 cm (28.0 in.)

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Waters ACQUITY UPLC®
H-Class System
and H-Class Bio System

Site Preparation Guide

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Notice

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Table of Contents

Introduction

This document serves as a guideline to help you prepare your laboratory facility for your Waters ACQUITY H-Class System. It describes the physical and environmental conditions, power, solvents, and sample preparation hardware required for the operation of the Waters ACQUITY H-Class System.

IMPORTANT: *References to the ACQUITY H-Class System (and its instruments) also pertain to the ACQUITY H-Class Bio System (and its instruments).*

System Description

The core ACQUITY H-Class System consists of a Quaternary Solvent Manager, Sample Manager – Flow Through Needle, and Solvent Tray Module. Available as options are the tunable UV (TUV), the photo-diode array (PDA) detector[1], the evaporative light scattering (ELS) detector, the fluorescence (FLR) detector, the Column Heater-A (CH-A), the 30-cm Column Heater-A (CH-30A), the Column Manager-A (CM-A), the 30-cm Column Heater/Cooler, and the Auxiliary Column Manager-A (CM-Aux). Several mass spectrometers are also available as options, as is a Flex Cart that includes casters for easy movement, adjustable table top, integrated power outlets, and storage space for the data system and waste container.

Responsibilities

A certified Waters engineer will be responsible for installing and commissioning the system to ensure that the instrument is properly installed and fully operational. Your laboratory must meet the requirements specified in this guide and be prepared in advance to allow the engineer to perform the installation. Only after you prepare your laboratory and complete and return the checklist at the end of this document can the installation be scheduled.

A major part of the system installation is a series of tests designed to evaluate the instrument performance under specific operating conditions. At the end of each test, the result is entered in the Installation Checklist.

To help train the intended operator in basic system operation, it is important that you schedule the installation so that the operator is present to assist with the installation performance tests.

If you require specific training on the ACQUITY H-Class System or Empower™ or MassLynx™ software, arrange for this separately from the startup through your local Waters office.

If you have any questions regarding the information in this document or any particular site problems, contact your local Waters sales representative. If necessary, we will arrange to conduct a site survey.

1. *The term "ACQUITY PDA Detector" refers to two detectors: the ACQUITY UPLC Photodiode Array (PDA) Detector, and ACQUITY UPLC PDA Extended Wavelength (eλ or eLambda) Detector.*

Space and Moving Requirements

Carefully review the following sections.

- Typical ACQUITY H-Class System Configurations
- Minimum Footprint
- Component Dimensions
- Component Weights
- Minimum Door Widths
- Lifting
- Additional Space Considerations

Typical ACQUITY H-Class System Configurations

A typical system (Figure 1) consists of the following components in a stacked position:

- Quaternary Solvent Manager (QSM)
- Sample Manager – Flow Through Needle (SM-FTN)
- Column Heater (CH-A)
- Tunable wavelength UV (TUV), photo-diode array (PDA), evaporative light scattering (ELS), or fluorescence (FLR) detectors (all optional)
- Solvent Tray Module

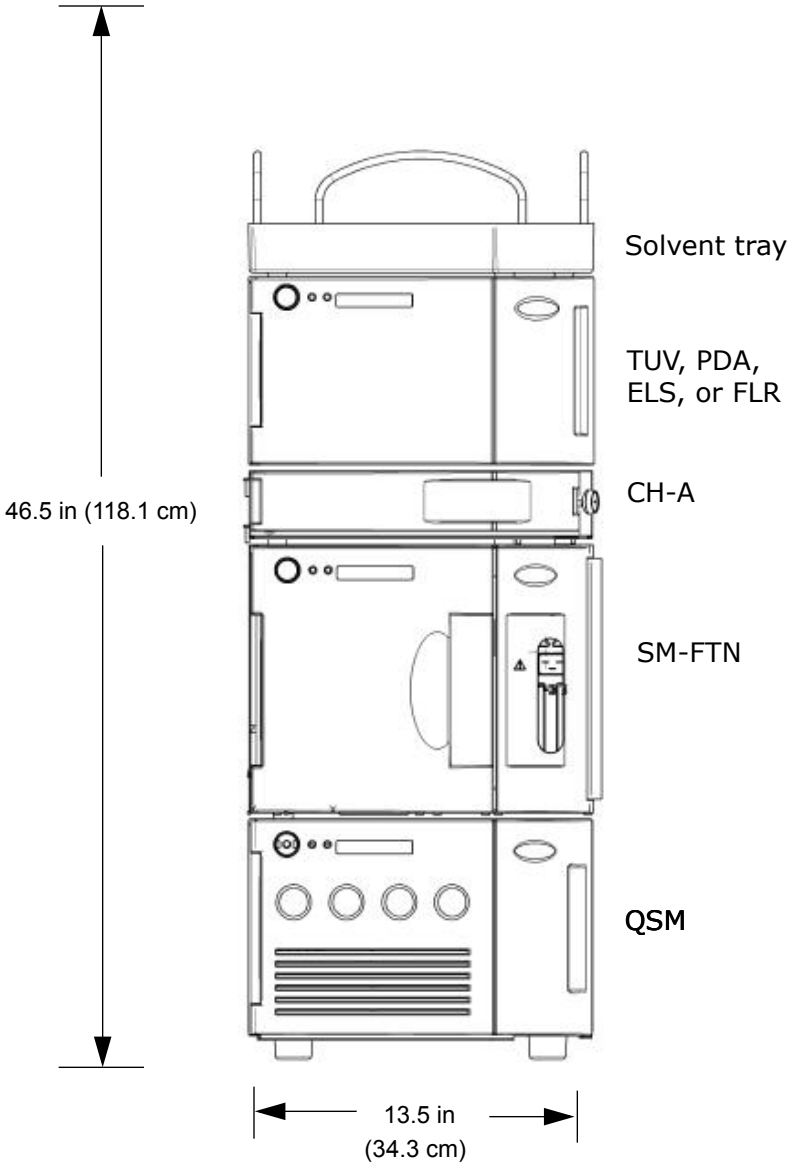


Figure 1 - ACQUITY H-Class System with Column Heater-A

NOTE: *The vertical dimension in Figure 1 includes extra 10-inch (25.4-cm) clearance for solvent tray access; see Table 2 for depth requirements.*

Figure 2 shows an ACQUITY H-Class System with an optional Column Manager (CM-A) positioned above the SM-FTN.

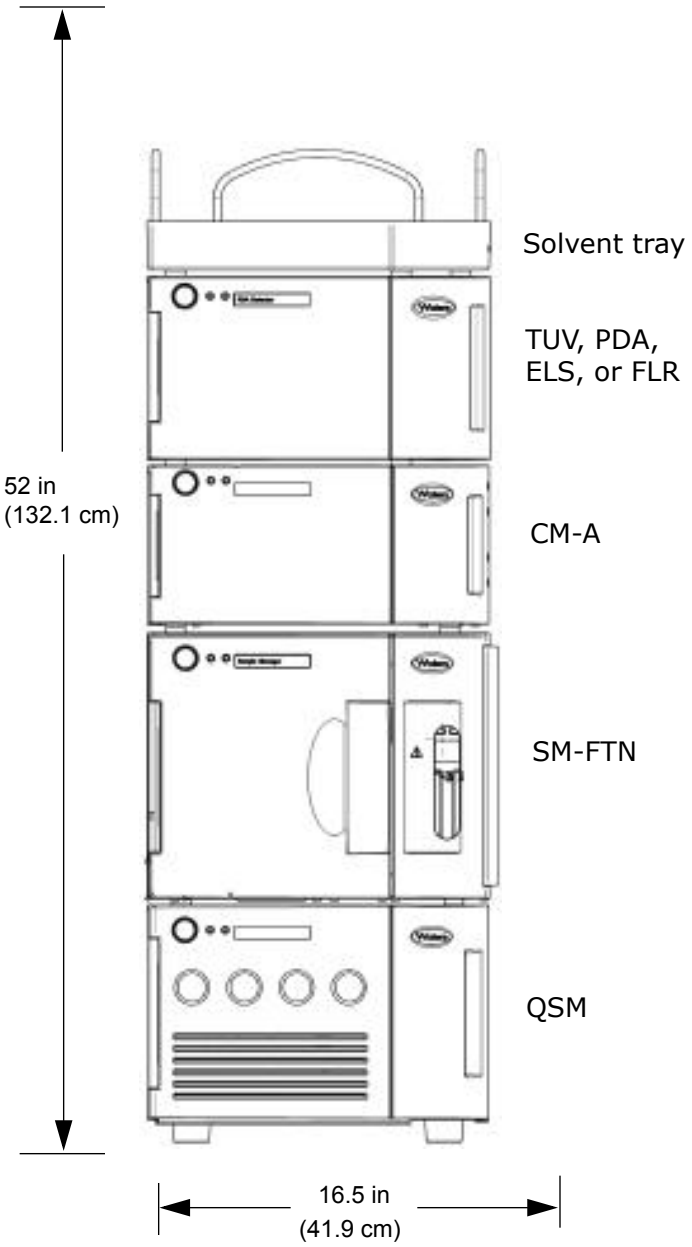


Figure 2 - ACQUITY H-Class System with Column Manager-A

NOTE: *The vertical dimension in Figure 2 includes an extra 10-inch (25.4-cm) clearance for solvent tray access; the horizontal dimension includes an extra 3-inch (7.6 cm) right-side clearance for SM-FTN, CM-A, CM-Aux ventilation. See Table 2 for depth requirements.*

Figure 3 provides overhead views for systems with SQD or TQD mass spectrometers. If your system uses another mass spectrometer, refer to its site preparation guide for dimensions and additional space requirements.

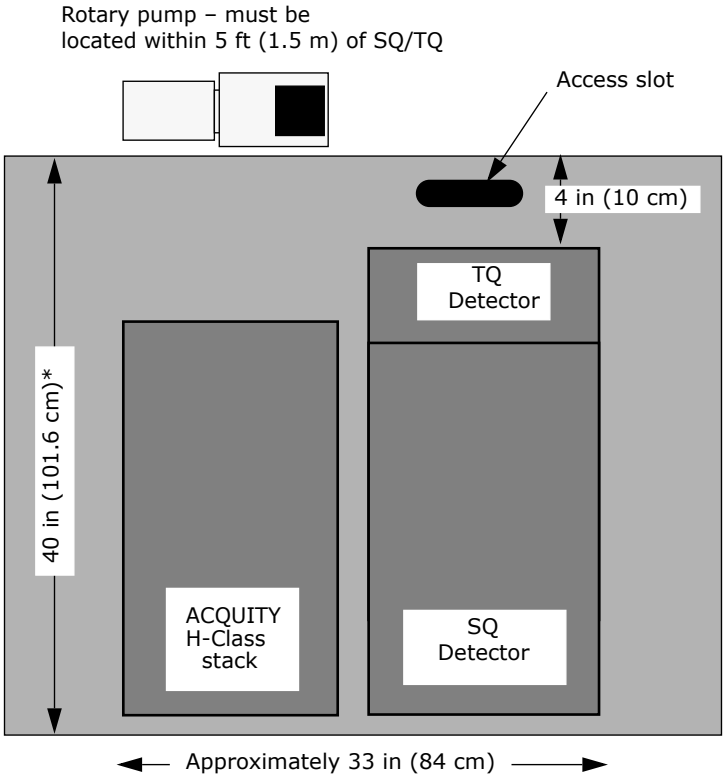


Figure 3 - Space requirements for systems with SQD or TQD mass spectrometers.

Minimum Footprint

There are several possible footprints for your ACQUITY H-Class System. Many configurations use a single-stack footprint; dual detector with a CM-A/CM-Aux configuration requires a dual-stack footprint; some configurations can require a triple-stack footprint.

Figure 4 shows *example* configurations for various single-, dual-, and triple-stack footprints.

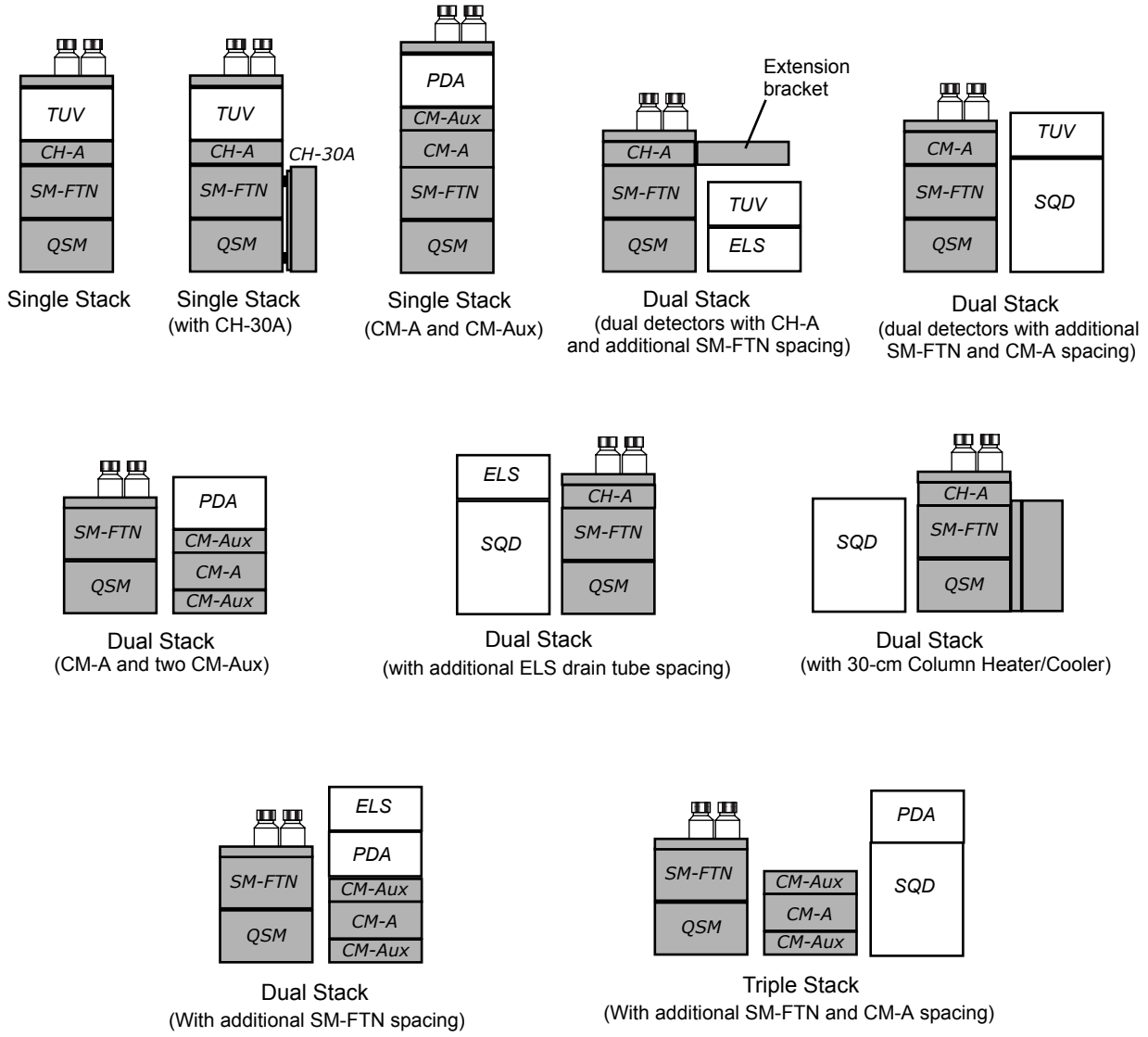


Figure 4 - Footprint Examples (Front View)

NOTE: *Table 1 provides the minimum required footprint dimensions for most single-stack, dual-stack, and triple-stack configurations. If your system includes a mass spectrometer, refer to the mass spectrometer site preparation guide for its specific footprint requirements. Use the dimensions in Table 2 to determine the actual footprint required for the components that comprise your system.*

Table 1: Minimum Footprint Dimension Examples

Configuration	Minimum Required Width	Minimum Required Depth[a]
Single stack	13.5 in (34.3 cm)	34.0 in (86.4 cm)
Single stack with additional 6.5-inch (16.5-cm) space on the right for a CH-30A	20 in (50.8 cm)	34.0 in (86.4 cm)
Dual stack with additional 3-inch (7.6-cm) ventilation space on the right of a SM-FTN, CM-A, or CM-Aux	30.0 in (76.2 cm)	34.0 in (86.4 cm)
Dual stack with additional 6.5-inch (16.5-cm) space on the right for a CH-30A	33.5 in (85.1 cm)	34.0 in (86.4 cm)
Dual stack with additional 1-inch (2.54-cm) drain tube space for the ELS detector	28.0 in (71.1 cm)	34.0 in (86.4 cm)
Multi-detector drip tray in a dual stack with additional 2-inch (5.1-cm) space to the right of any optical detector	29.0 in (73.7 cm)	34.0 in (86.4 cm)
Triple stack, as shown in Figure 4	47.0 in (119.4 cm)	34.0 in (86.4 cm)

a. Includes 6-inch (15.2-cm) rear clearance for ventilation and connections.

Component Dimensions

Table 2: Component Dimensions

System Component	Width	Depth	Height
Quaternary Solvent Manager	13.5 in (34.3 cm)	26.0 in (66.1 cm)	9.38 in (23.8 cm) with 0.875 in (2.2 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections.		
Isocratic Solvent Manager	13.5 in (34.3 cm)	26.0 in (66.1 cm)	9.38 in (23.8 cm) with 0.875 in (2.2 cm) feet[a]
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections.		
Sample Manager (SM-FTN)	13.5 in (34.3 cm)	28.0 in (71.2 cm)	10.7 in (27.1 cm) with 0.25 in (0.64 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear and 3 in. (7.6 cm) to the right for ventilation and connections. Additionally, the fluidics drawer of the sample manager slides outward 15.5 in (39.4 cm).		
Column Heater-A	13.5 in (34.3 cm)	22.0 in (56.0 cm)	2.95 in (7.5 cm) with 0.25 in (0.64 cm) feet*
	If using with a mass spectrometer, allow 13.25 in (33.6 cm) of clearance for the Column Heater bracket in the extended position to right of the stack.		
30-cm Column Heater-A	4.75 in (12.1 cm)	5.0 in (12.7 cm)	20 in (50.8 cm)
	Mounted width is 6.5 in (16.5 cm)		
Column Manager-A	13.5 in (34.3 cm)	24.0 in (61 cm)	7.8 in (20 cm)
	Allow at least 6 in. (15.2 cm) clearance at the rear and 3 in. (7.6 cm) to the right for ventilation and connections.		
Auxiliary Column Manager-A	13.5 in (34.3 cm)	24.0 in (61 cm)	5.4 in (13.7 cm)
	Allow at least 6 in. (15.2 cm) clearance at the rear and 3 in. (7.6 cm) to the right for ventilation and connections.		
30-cm Column Heater/ Cooler	8 in (20.3 cm)*	14.0 in (35.6 cm)	21.75 in (55.2 cm)
	*Width dimension includes 2-inch (5.1-cm) mounting bracket.		
TUV Detector	13.5 in (34.3 cm)	21.0 in (53.4 cm)	8.2 in (20.8 cm) with 0.25 in (0.64 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections. When the multi-detector drip tray option is used, allow for an additional 2 in. (5.1 cm) drain tube clearance to the right of the detector.		

Table 2: Component Dimensions (Continued)

PDA Detector	13.5 in (34.3 cm)	24.0 in (61 cm)	8.5 in (21.6 cm) with 0.25 in (0.64 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections. When the multi-detector drip tray option is used, allow for an additional 2 in. (5.1 cm) drain tube clearance to the right of the detector.		
ELS Detector	13.5 in (34.3 cm)	20.4 in (51.8 cm)	8.5 in (21.6 cm) with 0.25 in (0.64 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections. When positioned in the left stack, allow for an additional 1 in. (2.54 cm) drain tube clearance between the stacks.		
FLR Detector	13.5 in (34.3 cm)	20.4 in (51.8 cm)	8.5 in (21.6 cm) with 0.25 in (0.64 cm) feet*
	Allow at least 6 in. (15.2 cm) clearance at the rear for ventilation and connections. When the multi-detector drip tray option is used, allow for an additional 2 in. (5.1 cm) drain tube clearance to the right of the detector.		
Solvent Tray Module	13.5 in (34.3 cm)	20.5 in (52.1 cm)	5.0 in (12.7 cm)
	* All instruments are equipped with 0.25 in (0.64 cm) high feet. The Quaternary Solvent Manager is shipped with 0.875 in (2.2 cm) snap-in feet installed over the 0.25 in feet.		
QDa Detector	14 in (35.3 cm)	29.5 in (75 cm)	8 in (20 cm)
	Refer to the QDa Detector Site Preparation Guide, P/N 715002299, for rotary pump space requirements.		
SQ Detector	14.0 in. (35.6 cm)	25.0 in (63.5 cm)	21.0 in (53.4 cm)
TQ Detector	14.0 in. (35.6 cm)	33.5 in (85.1 cm)	21.0 in (53.4 cm)

Component Weights

Ensure that your bench top is able to support the total weight of the system components (Table 3). Note that the Waters ACQUITY Flex Cart (Figure 5) is rated to safely handle the weight of these components.

Table 3: Component Weights

System Component	Weight
Quaternary Solvent Manager	60.5 lb (27.5 kg)
Isocratic Solvent Manager	57 lb (25.9 kg)
Sample Manager - FTN	57.5 lb (26.1 kg)
Column Heater-A	12.5 lb (5.7 kg)
30-cm Column Heater-A	10 lb (4.5 kg)
Column Manager-A	46 lb (21 kg)
Auxiliary Column Manager-A	25 lb (11.4 kg)

Table 3: Component Weights

System Component	Weight
30-cm Column Heater/Cooler	30.0 lb (13.6 kg)
TUV Detector	20.5 lb (9.3 kg)
Photodiode Array Detector	34.3 lb (15.6 kg)
ELS Detector	32.5 lb (14.7 kg)
FLR Detector	30 lb (13.6 KG)
Solvent Tray Module	5 lb (2.3 kg)
QDa Detector (Standard) QDa Detector (Performance)	62 lb (28 kg) 55 lb (25 kg)
SQ Detector	127 lb (58 kg)
TQ Detector	189 lb (85.5 kg)

Minimum Door Widths

Doors through which the system will be moved must be a minimum of 25 in (63.5 cm) wide. If you are using the optional Waters ACQUITY Flex Cart, the minimum door width is 30 in (76.2 cm). Elevators and corridors must be wide enough to allow corners to be negotiated. Special arrangements may be required if you plan to move the system to the laboratory via a staircase.

Lifting

As a general guide before lifting, lowering, or moving the instruments:

- Assess the risk of injury
- Take action to eliminate risk
- Plan the operation in advance and in conjunction with our engineer when he/she arrives on site
- Adhere to appropriate country and/or company regulations

Additional Space Considerations

Consider the following when choosing and preparing your site:

- When choosing a location for the system, allow at least 6 inches (15.2 cm) behind the system for ventilation and rear panel connections. Also, allow enough space to remove the side panels for service access.
- The SM-FTN, CM-A, and CM-Aux require 3 inches (7.6 cm) of right-side ventilation clearance.
- All Waters instruments ship domestically with a 7.5-ft (2.3-m) power cord that must be plugged into the rear of the chassis. International power cords are 8.25 ft (2.5 m).
- The system may be placed either on a traditional laboratory bench or inside a fume hood. Ideally the system should be placed on a movable worktable (i.e. a laboratory bench on wheels).
- If installing the system inside a fume hood, you may need to carefully position the system on blocks to provide sufficient clearance for the Quaternary Solvent Manager

door to open (above the entry shelf of the hood) and allow for proper drainage of the drip management system.

- All of the power on/off switches for the ACQUITY H-Class System are located on the upper-left front panels of each instrument.
- The data system (computer CPU, monitor, keyboard, Ethernet switch, and mouse) must be placed on a laboratory bench close to the system. These components require approximately 24 in (61.0 cm) of bench space. Standard length cables are provided with the system. If necessary, extension cables for any of these cables may be sourced locally from a PC vendor.

  NOTE: *An internet connection is required in order to enable the optional Connections INSIGHT® (Intelligent Services).*

- If using the ACQUITY H-Class System with a mass spectrometer, the data system must be located within 16 ft (5 m) of the mass spectrometer to allow connection of the communication cables. Refer to the mass spectrometer site preparation guide for additional space requirements. Also, an access slot may need to be cut in the bench top to allow the vacuum tubes and gas lines to be passed to and from the mass spectrometer. Refer to the appropriate mass spectrometer site preparation guide for details.
- Solvent supply reservoir(s) must be located on the top of the ACQUITY H-Class System in the Solvent Tray Module. For installation and removal of solvent bottles, plan for an additional 10 in. (25.4 cm) of space above the top of the bottles.
- If using the optional Waters ACQUITY Flex Cart (Figure 5) to support the system, you need approximately 2.5 ft (0.77 m) of linear floor space (Figure 3). The Flex Cart has a footprint of 30 x 33 in (76.2 x 83.8 cm) and accommodates single-stack ACQUITY H-Class System configurations. You can set the Flex Cart tabletop height from 30 to 44 in (76.2 to 111.8 cm). The Flex Cart can also house the system waste containers and data system.

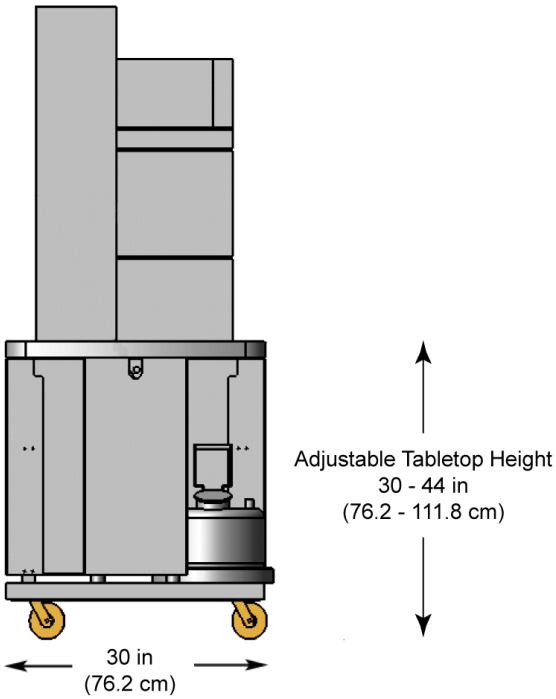


Figure 5 - ACQUITY System Flex Cart

Solvent Considerations

Depending on the solvent being used, suitable solvent containers may be placed on a magnetic stirrer/hotplate within the Solvent Tray Module on top of the system.

Due to the increased sensitivity that both the ACQUITY H-Class System and the new series of mass spectrometers offer, all solvents, including water and additives, must be of the highest chemical purity. Failure to use such solvents will result in high background contamination, low signal-to-noise, and loss of sensitivity. Waters recommends using clean, high-purity, submicron filtered solvents. Solvents that are submicron filtered by the manufacturer do not require any additional filtering.

Use ultrapure (i.e., particle-free, chemically clean, 18-megaohm cm resistivity) water. This will reduce the amount of impurities in the water that can collect on the column during equilibration with the weak solvent.

If your ACQUITY H-Class System includes a mass spectrometer, or is part of an application-based system, IPA will need to be supplied to perform a system flush. Refer to the mass spectrometer or application-based system site preparation guide for additional solvent requirements.

For further detail on controlling contamination, and information on solvent brands and mobile phase reservoirs, refer to the document *Controlling Contamination in UltraPerformance LC®/MS and HPLC/MS Systems*, part number 715001307, located in the Waters Support Center on the Web (www.waters.com).

Gas Supply

WARNING: IF USING ZERO GRADE AIR, CONSIDER THE COMBUSTIBILITY OF THE SOLVENTS.

Nitrogen Gas for Mass Spectrometers

For systems with an optional mass spectrometer, you must provide a supply of dry, oil-free nitrogen with a purity of at least 95%. The nitrogen must be regulated at 7 bar (100 psi) outlet pressure. Refer to the mass spectrometer site preparation guide that ships with your system for additional nitrogen gas supply requirements.

Collision Gas for Mass Spectrometers

Argon is required for the collision cell on systems that include some mass spectrometers. The argon must be dry, high purity (≥99.997%) and regulated at a pressure of 0.5 bar (7 psi). Refer to the mass spectrometer site preparation guide that ships with your system for additional collision gas supply requirements.

Gas for the ELS Detector

The ELS Detector requires a suitable supply of high purity nitrogen gas or zero grade air (e.g., oil-, moisture-, and particle-free gas). Gas cylinders are not recommended due to their limited capacity. Waters recommends using a gas flow of approximately 3 - 4 L/min. A constant gas supply (65 - 90 psi at the regulator) is required to operate the detector.

Waste Collection

The ACQUITY UPLC Drip Management System is a closed-architecture, gravity-driven drainage system that effectively collects and removes any solvent leaks and process waste from the needle and plunger seal washes. Each instrument uses a drip tray to collect and

route the waste from one module tray to the one beneath it, eventually exiting the system through the elbow drain located below the Quaternary Solvent Manager compartment door.

Follow these waste collection requirements when preparing your laboratory:

- To maintain proper drainage and leak control, the ACQUITY H-Class System must be level.
- A waste container, such as a large-capacity carboy or safely enclosed glass container, must be positioned below the bench top to collect the waste.
- All waste tubing must be routed in a manner that prevents the formation of traps in the tubing.
- The Solvent Tray Module located on top of the system is capable of holding up to two liters of spilled solvent. You will need to supply a separate waste container of sufficient capacity to collect any spill from the waste line at the rear of the tray.
- When an optical detector is positioned above another detector in the stack, the Waters Multi-detector Drip Tray option (P/N 205000355) must be installed on the upper detector.

Power Requirements

Refer to the following power requirements when preparing your laboratory:

- All ACQUITY H-Class System components require a dedicated, earthed (grounded) power source. The receptacles from this power source must be accessible to the ACQUITY H-Class System components, and must share a common ground.
- If your ACQUITY H-Class System has a mass spectrometer, refer to its site preparation guide for power requirements.
- The use of a line conditioner or an uninterruptible power supply (UPS) should also be considered for optimum long-term input voltage stability.

Refer to Table 4 for system component power requirements.

Table 4: Power Requirements by Component

System Component	Input Voltage/ Frequency	Fuse Rating	Max. Power Draw	Power Cord Supplied
Quaternary Solvent Manager	100 to 240 VAC 50/60 Hz	5.0 A	360 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
Isocratic Solvent Manager	100 to 240 VAC 50/60 Hz	5.0 A	200 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
Sample Manager - FTN (with a CH-A)	100 to 240 VAC 50/60 Hz	10.0 A	400 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
TUV Detector	100 to 240 VAC 50/60 Hz	3.15 A	185 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
PDA Detector	100 to 240 VAC 50/60 Hz	3.15 A	145 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
ELS Detector	100 to 240 VAC 50/60 Hz	5.0 A	200 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
FLR Detector	100 to 240 VAC 50/60 Hz	3.15 A	280 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international

Table 4: Power Requirements by Component (Continued)

QDa Detector - Diaphragm pump - Rotary pump	100 to 240 VAC 50/60 Hz	13 to 16 A	400 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
	24 VDC	N/A	64 VA	Connects to the QDa
	100 to 240 VAC 50/60 Hz	13 to 16 A	300 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
Column Manager-A	100 to 240 VAC 50/60 Hz	N/A	400 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
Auxiliary Column Manager-A	100 to 240 VAC 50/60 Hz	N/A	400 VA	N/A
30-cm Column Heater/ Cooler	100 to 240 VAC 50/60 Hz	3.15 A	240 VA	7.5 ft (2.3 m) domestic 8.25 ft (2.5 m) international
SQ Detector (including rotary pump)	200 to 240 VAC 50/60 Hz	13 –16 A	1430 VA	8.25 ft (2.5 m) – detector 6.5 ft (2 m) – pump
TQ Detector (including rotary pump)	200 to 240 VAC 50/60 Hz	13 –16 A	2000 VA	8.25 ft (2.5 m) – detector 6.5 ft (2 m) – pump

NOTE: *The Flex Cart includes a power strip on the back of the cart to which the ACQUITY H-Class System components connect, reducing the number of VAC receptacles required to one or two.*

Figure 6 shows the plug types supplied with the ACQUITY H-Class System

 US/Canada (125 V)	5-15P (UL817 and CSA C.22.2)
 US/Canada (250 V)	L6-15P (UL817 and CSA C.22.2)
 US/Canada (250 V)	6-15P (UL817 and CSA C.22.2)
 UK	3-pin (BS1363)
 Europe	2-pin (CEE7)
 Denmark	3-pin (Afsnit 107-2-D1)
 Australia	3-pin (AS/NZS 3112)
 China	3-pin (GB2099, 10A and 16A versions)

Figure 6 - Plug Types Supplied with the ACQUITY H-Class System

Environmental Requirements

General

Follow these general environmental requirements when preparing your laboratory:

- Waters recommends that the ACQUITY H-Class System be installed in an environmentally controlled laboratory, in a draft-free position away from excessive amounts of dust.
- The air-conditioning or heating ventilation must not be positioned directly above the system.
- The relative humidity must not exceed 80%, non-condensing.
- The ACQUITY H-Class System must be installed in an environment that complies with Pollution Category 1 and Installation Category 2.

Temperature

Follow these temperature requirements and considerations when preparing your laboratory:

- The ambient temperature in the laboratory must be from 4 to 40 °C (39.2 to 104 °F). When using the ACQUITY ELS Detector, the ambient temperature must be from 4 to 30 °C (39.2 to 86 °F). Failure to operate in these ranges will compromise the performance of the system and may result in instrument failure.

  CAUTION: *The CH-A is designed to accurately control the column temperature when the difference between the room and column temperatures is at least 5 °C (9 °F). Also, sample cooling in CM-A the will not reach 4 °C (39.2°F) if the ambient temperature is 25 °C (77 °F) or greater.*
- The optimum temperature range of the laboratory is 19 to 22 °C (66 to 72 °F). Short-term thermal variations should be no more than 2 °C (3.6 °F) per 1.5 hours.
- The ambient temperature range for normal operation for the computer workstation is 10°C to 35 °C (50 to 95°F).

Vibration

The Waters ACQUITY H-Class System must not be placed close to heavy machines such as compressors and generators which can create excessive floor vibration.

Magnetic Fields

If using the Waters ACQUITY H-Class System as an inlet for a mass spectrometer, position the system with mass spectrometer away from strong magnetic fields such as those generated by NMR systems or magnetic sector mass spectrometers.

Radio Emissions

The Waters ACQUITY H-Class System must be placed in an environment where Radio Frequency (RF) emission from surrounding sources is minimal.

Possible sources of RF emission include RF-linked alarm systems, mobile telephones, and hand-held transmitters.

Exhaust Outlets

An in-line degasser, integral to the Quaternary Solvent Manager, exhausts dissolved gases from the eluents and condensate from the exhaust system through a vent line on the front of the Quaternary Solvent Manager. To avoid exposure to solvent vapors, it is recommended that you route the exhaust to a laboratory fume hood using the supplied tubing. A 3.5-foot (1.06 m) length of 1/8-inch (0.32-cm) I.D. tubing is supplied in the Quaternary Solvent Manager Startup Kit.

To properly vent the exhaust vapor to waste in the ELS Detector, a drying gas exhaust bottle is provided to trap any condensate that forms from vented vapor exiting the detector. A 3-foot (0.9-m) and 5-foot (1.5-m) length of black exhaust hose is also supplied to route exhaust from the detector to the bottle, and from the bottle to a laboratory exhaust system that applies a slight negative pressure.

CAUTION: ***TO AVOID CONTACT WITH ELUENT GASES, CONNECT THE OUTLET VENT TO A SUITABLE EXHAUST, SUCH AS A PROPERLY FUNCTIONING HOOD.***

Test Samples

CAUTION: ***HAZARDOUS SAMPLES MUST BE HANDLED IN A MANNER THAT CONFORMS TO THE MANUFACTURER'S GUIDELINES AS DEFINED IN THE RELEVANT HAZARD DATA SHEETS.***

The Waters service engineer will use the samples supplied with the ACQUITY H-Class System to test a system that includes a mass spectrometer, TUV, PDA, ELS, or other ACQUITY H-Class System detector.

NOTE: *The Waters engineer will not carry test samples to the installation. If the test samples cannot be provided prior to the agreed installation date, the installation must be rescheduled. If the Waters engineer arrives on site and the necessary facilities are unavailable, the customer will be charged any costs incurred for the visit.*

If your laboratory practices require full sample certification documentation, Waters Analytical Standards and Reagents provide ready-to-use reference materials and reagents that are fully traceable and certified.

Supplies of high-purity water and acetonitrile are required to perform the tests. Refer to "Solvent Considerations" for more information.

Items Supplied by the Customer

The following items must be supplied by the customer:

- Three 1-liter wash bottles for strong needle wash, weak needle wash, and plunger wash
- Two solvent waste containers
- Two 2-liter or four 1-liter mobile phase bottles
- Appropriate glassware for sample and solvent preparation
- Solvents and solvent filtration apparatus

For systems that include a mass spectrometer, refer to the mass spectrometer site preparation guide for specific requirements.

Computer Requirements

If you are planning to provide your own computer for an Empower- or MassLynx-controlled ACQUITY H-Class System, contact your sales person for details on the required computer hardware and operating system specifications.

Connections INSIGHT® Installation Requirements

Installation of the Waters Connections INSIGHT® software (Intelligent Services that provide real-time, remote system monitoring and notification) requires the following:

- An active Internet connection
- This Internet connection can either be direct or through a firewall or proxy server

NOTE: *The outgoing-initiated connection from the Connections INSIGHT Service Agent to the Waters Connections Enterprise Server uses SSL (Secure Sockets Layer) port 443. Information sent includes only instrument usage counters, error message text, and instrument configuration data. The Connections INSIGHT Service Agent does not have access to nor does it transmit business-sensitive information, and connects only to the Waters Connections Enterprise Server.*

ACQUITY H-Class System Site Preparation Checklist

This checklist must be completed and returned to Waters when all the requirements are available.

NOTE: *It is the customer's responsibility to ensure that ALL the laboratory supplies are correct. Please attach any additional information to this document where necessary.*

Space Requirements (without bench) - see page 5

The available bench space is adequate for the system. ..... ❑

Floor Space Requirements (with bench) - see page 5

The available floor space is adequate for the system. ..... ❑

Lifting and Carrying - see page 13

Suitable equipment or personnel will be available to lift the instrument onto the laboratory bench. ..... ❑

Solvents and Samples - see page 15

Suitable solvent and solvent containers are available, and solvent and sample preparation facilities are in place. ..... ❑

Gases and Regulators – see **page 15**

For systems with a mass spectrometer, a regulated (0.5 bar [7 psi]), dry, oil-free nitrogen source with a purity of at least 95% is available..... ❑

For systems with a TQD or other mass spec, high purity (≥99.997%) argon gas regulated at 0.5 bar (7 psi) is available with a 3 mm (1/8 in.) adaptor ..... ❑

For systems with an ELS Detector, a supply of high purity nitrogen gas or zero grade air source (e.g., oil- and particle-free gas) is available..... ❑

Waste Collection - see page 15

Suitable waste containers are available. ..... ❑

Power Requirements - see page 16

The specified power source requirements are met, and an appropriate number of power receptacles are available. ..... ❑

Environmental Requirements - see page 19

The laboratory meets the temperature, humidity, vibration, magnetic fields, and radio emissions requirements. ..... ❑

Exhaust Outlets - see page 19

A suitable fume hood is available. ..... ❑

Ancillary Equipment

If you plan to use any other equipment with the system, provide details below.

Make/Type	Model	Already commissioned	To be commissioned

Test Samples - see page 20

The supplied test samples, required for installation, are available. ..... ❑

Customer-supplied Items - see page 21

All customer-supplied items, including wash and mobile phases bottles, waste containers, glassware, solvents, and filtration apparatus are available... ❑

Minimum Computer Requirements - see page 21

If not purchasing the computer from Waters Corporation, a computer that meets the specified requirements is available. ..... ❑

Waters Connections INSIGHT® Requirements - see page 21

If you are planning to install Waters Connections INSIGHT® software, an Internet connection is available. ..... ❑

I confirm that all supplies are now available and that all specified environmental conditions have been met. During the installation, the operator intends to be available for demonstration and training by the Waters engineer:

At all times. ..... ❑

Approximately _____% of the time. ..... ❑

Not at all. ..... ❑

During the likely period of installation, the following dates are NOT convenient:

_____

Signed: _____

NOTE: *If an authorized Waters service engineer arrives on site to begin installation work and cannot complete the installation due to lack of facilities (i.e. power, laboratory readiness), costs incurred will be charged.*

Please complete the following sections in block letters:

Position: _____

Name: _____

Organization: _____

Street: _____

City/State: _____

Zip/Postal Code: _____

Country: _____

Telephone: _____

Fax: _____

Email: _____

NOTE: *The installation of your system cannot begin until pages 22 through 24 of this document have been fully completed and returned to the Sales Support Representative at your local Waters office.*

[APPLICATION NOTE]

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

A RAPID METHOD FOR THE SCREENING AND CONFIRMATION OF OVER 400 PESTICIDE RESIDUES IN FOOD

James Morphet and Peter Hancock, Waters Corporation, Manchester, UK

AIM

To utilize the power of UltraPerformance Liquid Chromatography (UPLC®) combined with fast MS acquisition rates, to give a rapid method for the screening of 402 pesticide residues in a single 10 minute run. A second injection, for confirmatory purposes, will meet SANCO Analytical Quality Control procedures for pesticide residue analysis (SANCO/2007/3131[1]).

INTRODUCTION

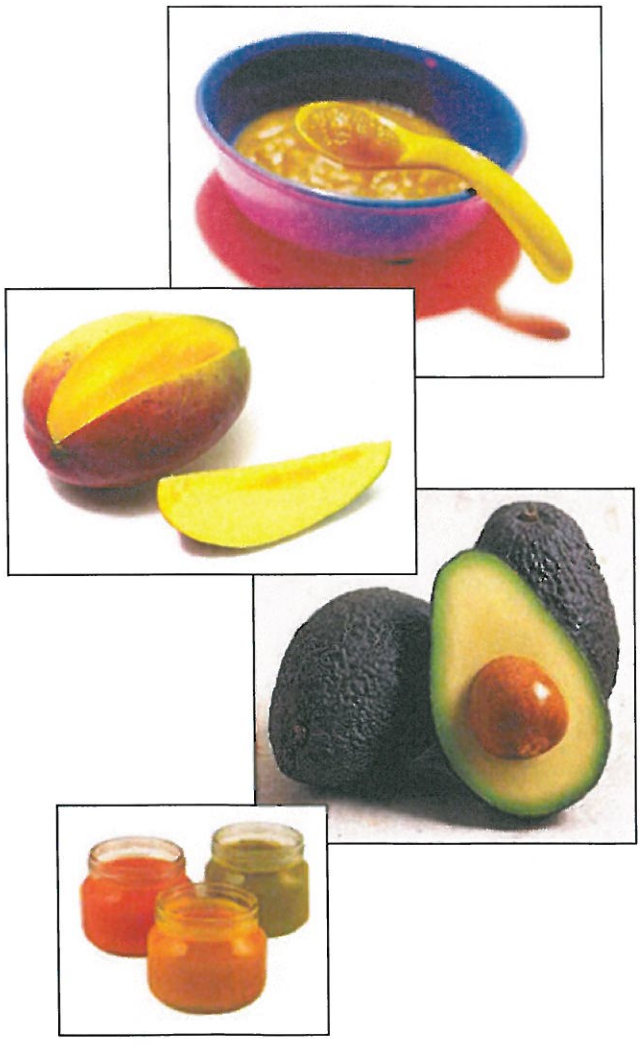
Pesticides are widely used in the production of foodstuffs to meet consumer demand for plentiful food at reasonable prices, all year round. However, continued growth in the use of pesticides, poor agricultural practices, and illegal use can pose significant risks to human health through the presence of pesticide and metabolite residues in food products. Most countries have strict regulations governing pesticides. Legislation imposes Maximum Residue Limits[2] (MRLs) for pesticide residues in food products requiring analytical techniques that are sensitive, selective, and robust.

Multi-residue pesticide analysis is challenging due to the low levels present, the wide variety of pesticides, and the very different chemical classes they represent. As there are currently well over 1,000 pesticides in use, laboratories are under increasing pressure to broaden the range of pesticides determined in a single analysis over a shortened run time.

The need to meet mandated detection limits, develop generic sample preparation techniques for complex matrices, and the desire to increase sample throughput are the main challenges facing food safety testing laboratories today. The use of a single multi-residue method per instrument can dramatically improve return on investment by removing the need to change method parameters. This is often the case when analyzing a wide variety of commodities with differing lists of legislated pesticides.

Advances in chromatographic separation and detection technologies have enabled analysts to increase the number of analytes determined in a single run. Tandem quadrupole mass spectrometry offers a highly specific and selective detection technique that has become the technique of choice within the laboratory.[3]

The following method describes a solution for the rapid analysis of pesticides in mango, avocado, and fruit-based baby food extracts that is able to exceed current worldwide legislation.



EXPERIMENTAL

Dispersive SPE, commonly referred to as "QuEChERS", is a simple and straightforward sample preparation technique suitable for multi-residue pesticide analysis in a wide variety of food and agricultural products.[4] The homogenized food samples were extracted with organic solvent using Waters® DisQuE™ dispersive sample preparation tubes. Once mixed, the pesticide residues were partitioned into the organic solvent, which was then subjected to further clean-up. The supernatant was collected, diluted, and injected onto the LC/MS/MS system as described below:

Extraction Procedure[4]:

1. Add 15 g homogenized sample to a 50-mL DisQuE extraction tube containing 1.5 g sodium acetate and 6 g magnesium sulfate. Add 15 mL 1% acetic acid in acetonitrile.
2. Add any pre-extraction internal standards.
3. Shake vigorously for one minute and centrifuge > 1500 rcf for one minute.
4. Transfer 1 mL of the acetonitrile extract in to the 2-mL DisQuE extraction tube containing 50 mg PSA and 150 mg of magnesium sulphate.
5. Shake for 30 seconds and centrifuge >1500 rcf for one minute.
6. Transfer 100 µL of final extract into an autosampler vial. Add any post-extraction internal standards. Dilute with 900 µL water.

Chromatographic conditions

LC system:	Waters ACQUITY UPLC® System	
Column:	ACQUITY UPLC BEH C_{18} 2.1 x 100 mm, 1.7 µm	
Column temp:	40 °C	
Sample temp:	4 °C	
Flow rate:	0.450 mL/min.	
Mobile phase A:	98:2 water: methanol + 0.1% formic acid	
Mobile phase B:	Methanol + 0.1% formic acid	
Gradient:	0.00 min	95% A
	0.25 min	95% A
	7.75 min	0% A
	8.50 min	0% A
	8.51 min	95% A
Weak needle wash:	98:2 water: methanol + 0.1% formic acid	
Strong needle wash:	Methanol + 0.1% formic acid	
Total run time:	10 min	
Injection volume:	20 µL, full loop injection	

MS conditions

MS system:	Waters ACQUITY® TQ Detector
Ionization mode:	ESI positive polarity
Capillary voltage:	1 kV
Desolvation gas:	Nitrogen, 800 L/Hr, 400 °C
Cone gas:	Nitrogen, 5 L/Hr
Source temp:	120 °C
Acquisition:	Multiple Reaction Monitoring (MRM)
Collision gas:	Argon at 3.5 x 10^{-3} mBar

Acquisition and Processing methods

The data were acquired using Waters MassLynx™ Software, v. 4.1. Incorporated into MassLynx, the IntelliStart™ technology automates optimization of MS parameters for the sample and also monitors the health of the MS system, reducing the time for operator-intensive troubleshooting and upkeep.

This data was processed using TargetLynx™ Application Manager. This quantification package enables automated data acquisition, processing, and reporting for quantitative data, incorporating a range of confirmatory checks that identify samples that fall outside user-specified or regulatory thresholds.

RESULTS AND DISCUSSION

The analysis of 402 pesticide residues (Appendix 1) in mango, avocado, and fruit-based baby food was achieved using ACQUITY TQD: liquid chromatography combined with tandem quadrupole mass spectrometry (UPLC/MS/MS) operated in Multiple Reaction Monitoring (MRM) mode.

The rapid determination and confirmation method was achieved in two parts. Part one was a single injection with one MRM transition per pesticide, ideal for screening purposes. Part 2, where compounds of interest can then be confirmed, was achieved by two separate injections with two MRM transitions per pesticide.

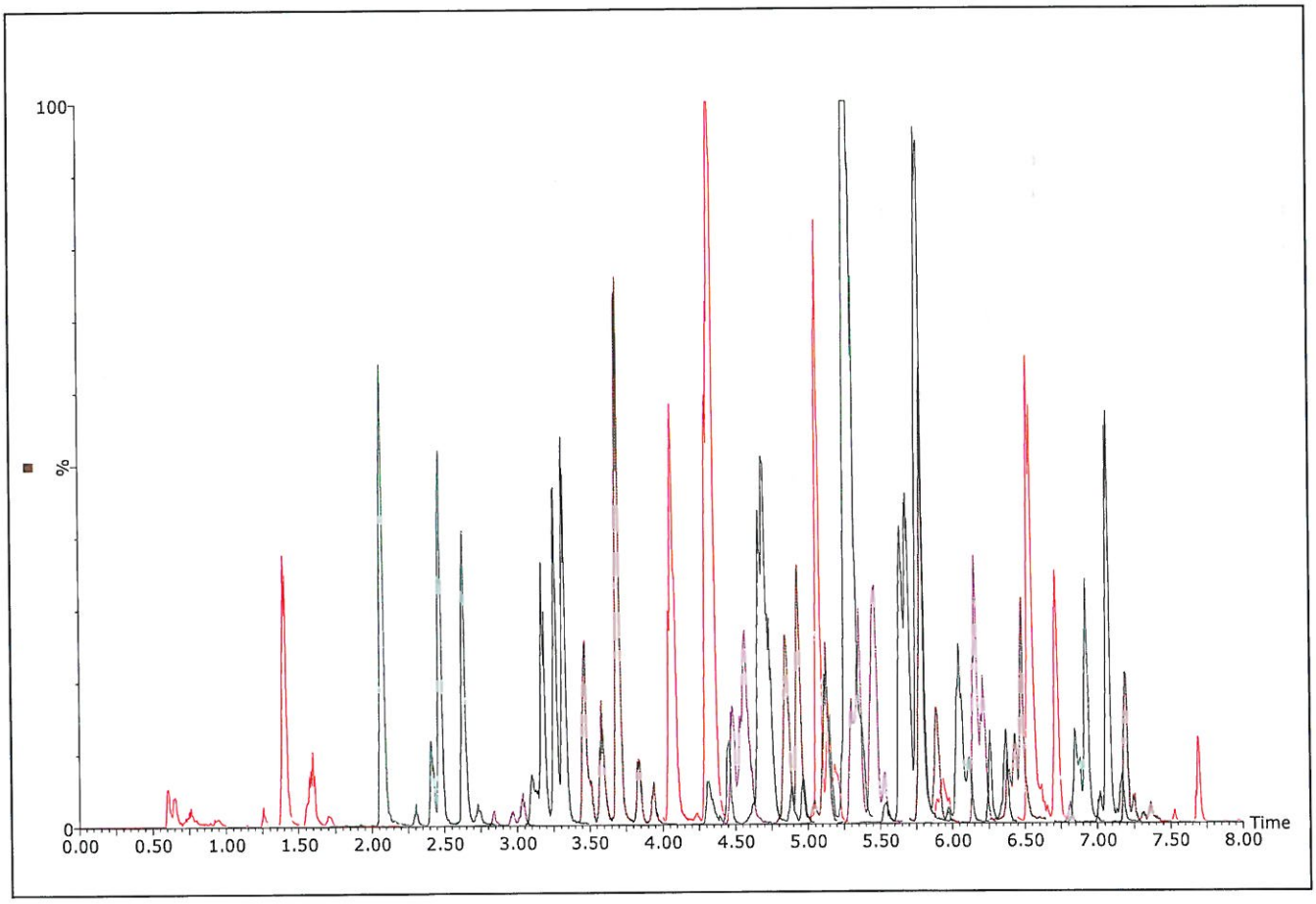


Figure 1. Chromatogram showing all 402 pesticide residues in one 10 minute run in injection solvent.

Figure 1 shows all 402 pesticide residues in one 10 minute run, fully utilizing the enhanced speed and resolution of UPLC.

For all injections, the same UPLC conditions were used saving analytical time and costs, thus maximizing return on investment. This single setup will allow analysts with less experience to run the method as the need for changes to be made in between batches is removed.

The IntelliStart technology provides simple instrument setup and MS method development and therefore easy access even for the most inexperienced MS user.

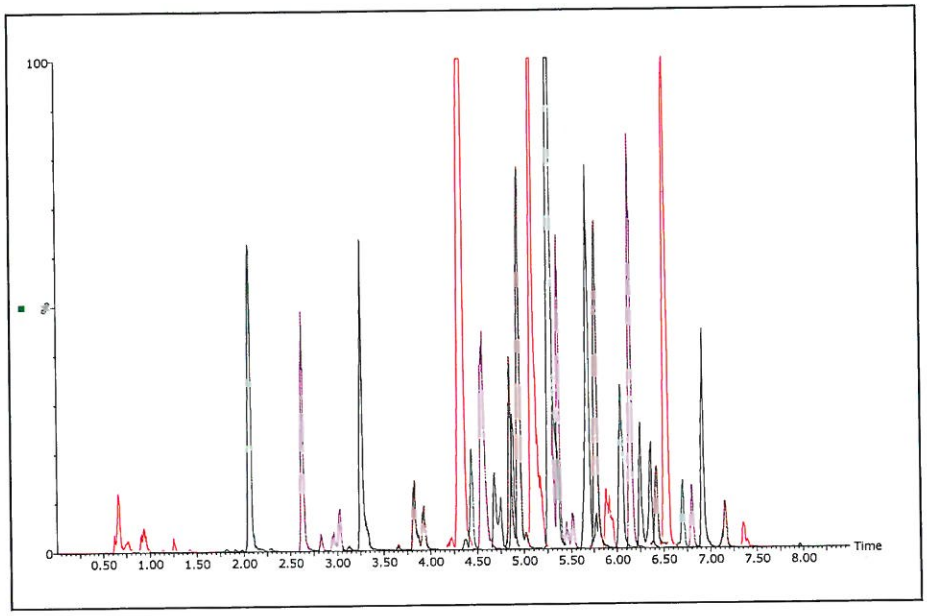


Figure 2. Chromatogram showing first 201 pesticide residues at 10 µg/kg in injection solvent.

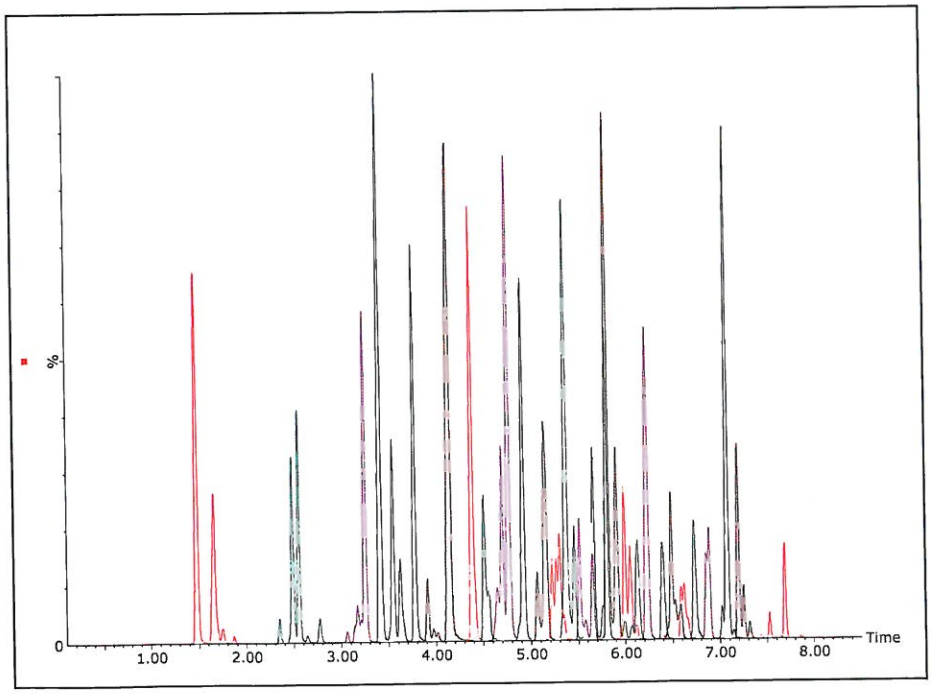


Figure 3. Chromatogram showing second 201 pesticide residues at 10 µg/kg in injection solvent.

Part 2, where compounds of interest can then be confirmed, was achieved by two separate injections with two MRM transitions per pesticide. Figures 2 and 3 show the separation of 201 pesticide residues across two run times of 10 minutes each.

The selectivity given using a tandem quadrupole mass spectrometer (ACQUITY TQD) shows an advantage over a single quadrupole instrument as it allows co-eluting compounds to be identified and quantified with confidence.

The enhanced speed and resolution of UPLC enabled all peaks to elute within eight minutes. Dwell times of 5 ms were used to achieve at least 12 data points across each peak for both quantification and confirmatory ions.

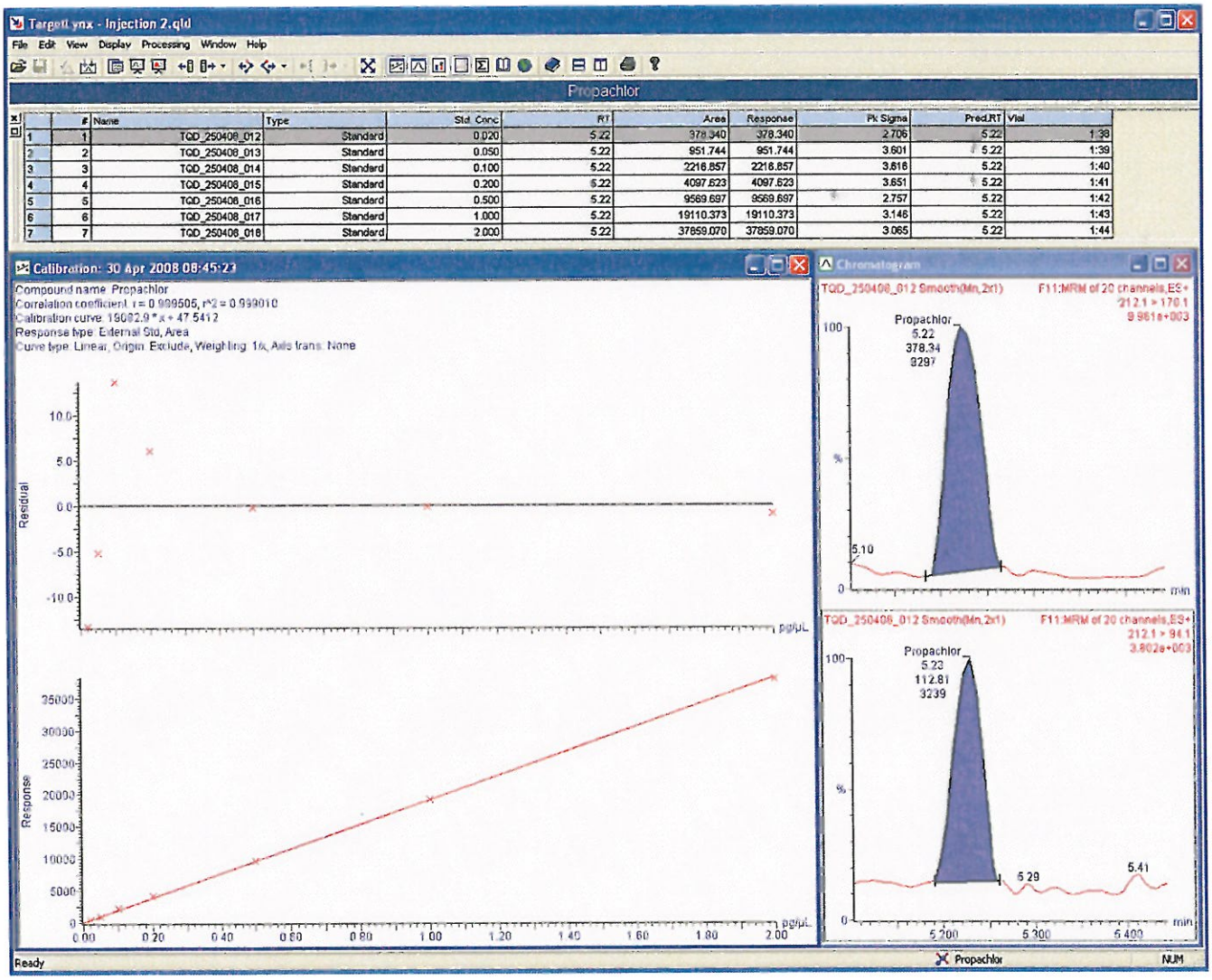


Figure 4. TargetLynx view showing a solvent standard calibration curve over a linear range from 0.02-2 pg/µL. The highlighted chromatogram is at 0.02 pg/µL.

A calibration curve was prepared in the injection solvent (water:methanol, 90:10 v/v) and injected. Excellent linearity was achieved using a weighting factor of 1/x with a high coefficient of determination achieved. This is shown in Figure 4.

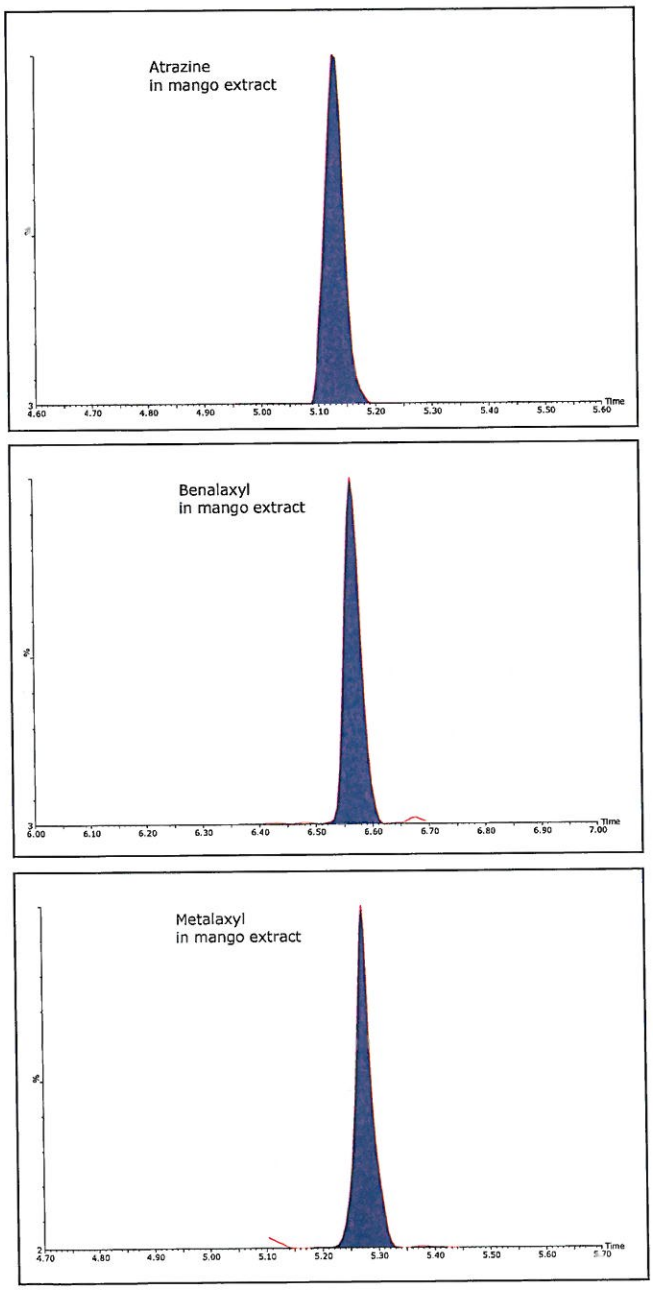
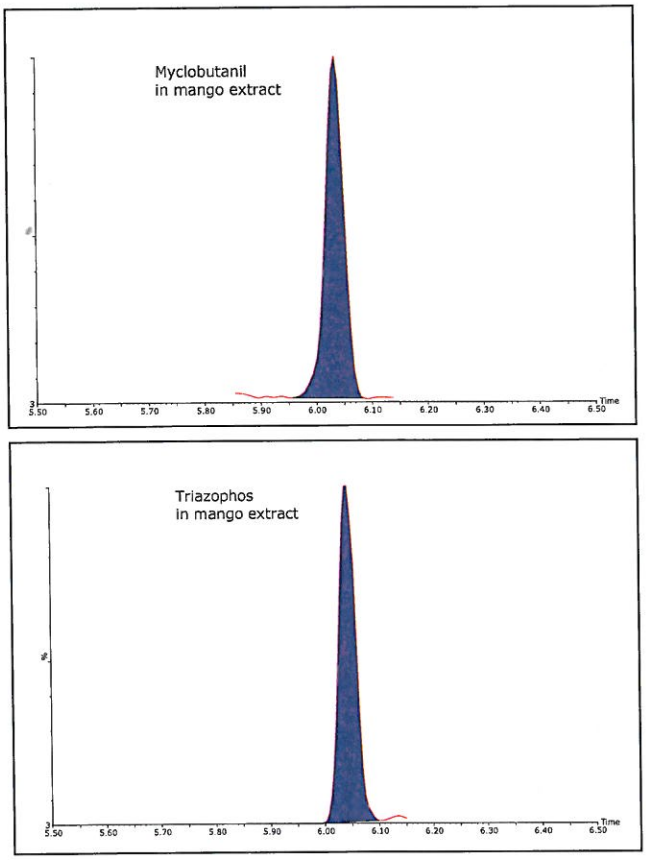


Figure 5. Five pesticides in mango extract at 10 µg/kg.



The 402 pesticide mix was spiked into the three matrices and the extracts analyzed. Figures 5, 6, and 7 show pesticides at 10 µg/kg, equivalent to the lowest worldwide (EU) legislation, in mango, avocado, and fruit-based baby food extracts respectively.

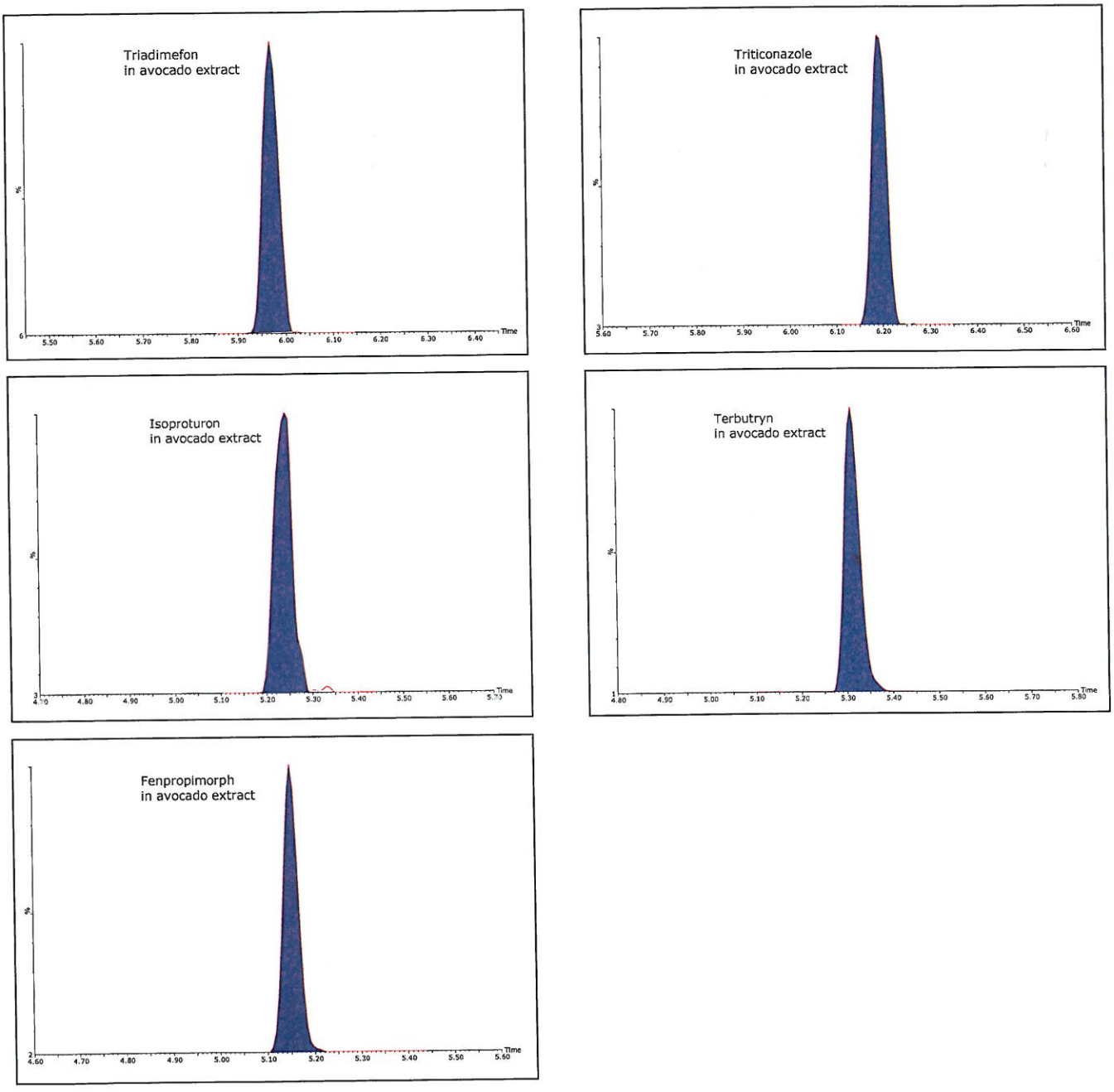


Figure 6. Five pesticides in avocado extract at 10 µg/kg.

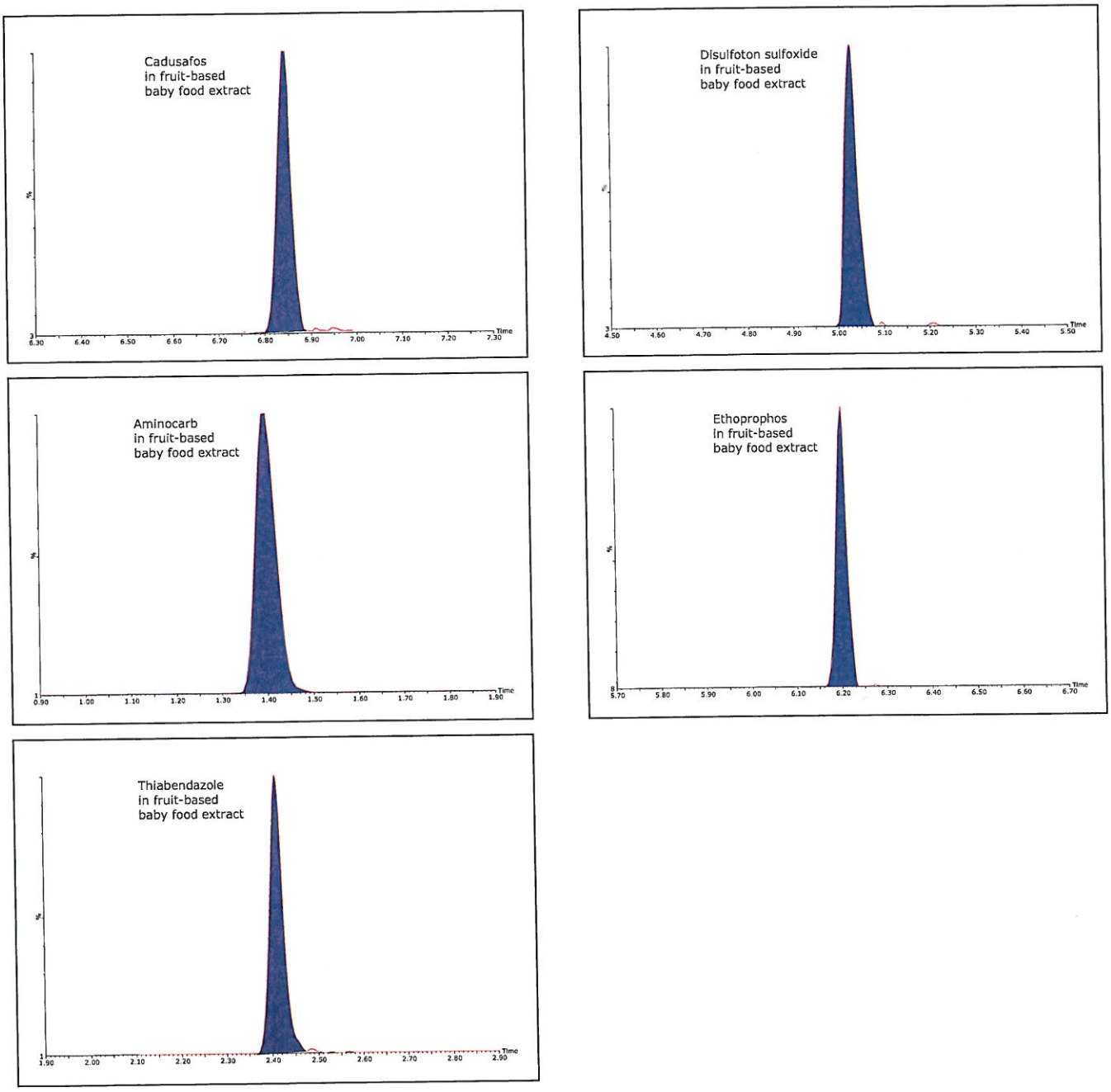


Figure 7. Five pesticides in fruit-based baby food extract at 10 µg/kg.

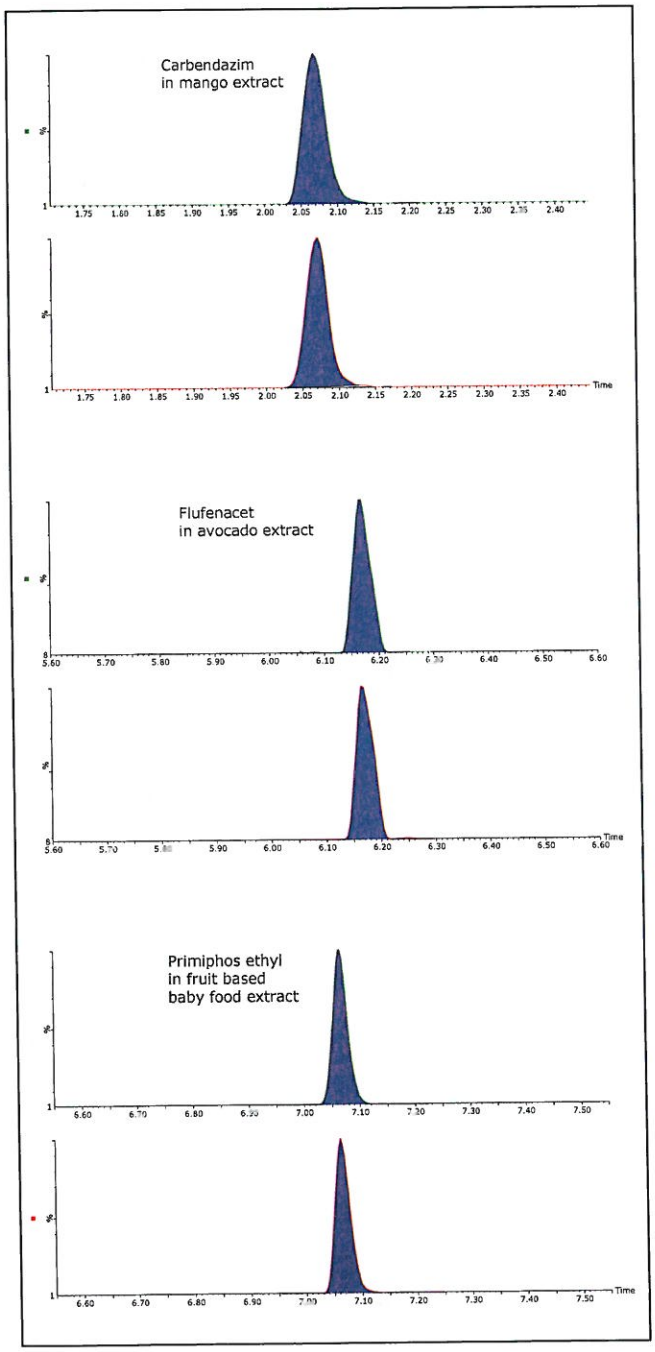


Figure 8. Confirmation through secondary MRM transition using ACQUITY TQD at 10 µg/kg in matrix. The ion ratios for carbendazim, primiphos ethyl, and flufenacet are 0.16, 0.18 and 0.61 respectively.

The advantage of using ACQUITY TQD is that ion ratio confirmation is also possible. This is used to confirm the identity of any pesticide that was presumptive positive from the screening method. Within the EU, ion ratio confirmation is important for pesticide analysis as documented in SANCO/2007/3131[1].

In Part 2, the confirmatory runs, all 402 pesticides were chromatographed with both primary (for quantitation) and secondary (for confirmation) MRM transitions present. Figure 8 shows three more compounds in the three matrices with both MRM transitions.

CONCLUSION

A rapid multi-residue method was developed for the screening of over 400 pesticides in one 10 minute run with one MRM transition per pesticide. For confirmation, two 10 minute runs were required with two MRM transitions per pesticide. The analysis of pesticides in mango, avocado and fruit-based baby food extracts was able to exceed current worldwide legislated limits.

Improved efficiency and increased sample throughput were realized through the combination of powerful UPLC and fast MS acquisition technologies. The Waters ACQUITY TQD as shown in Figure 9 offers:

- Enhanced chromatographic resolution and short analysis times
- Incorporation of confirmatory MRM traces
- Compliance with legislative regulations such as SANCO
- IntelliStart technology is designed to reduce the burden of complicated operation, training new users, time-intensive troubleshooting, and upkeep
- The small footprint of the ACQUITY TQD will give any laboratory an advantage as it removes the need for larger instrumentation.

The benefits of this Waters UPLC/MS/MS solution for a revenue conscious laboratory can be realized through increased efficiency through analytical time savings and decreased need for sample retesting, resulting in increased lab productivity. Cost savings can be made by lowering the use of lab consumables with the environmental impact of solvent usage also being reduced.

The sensitivity achieved for a large number of pesticide residues in real food matrices indicates this UPLC/MS/MS method is an ideal basis for the rapid analysis of pesticides in a wide range of food samples.

Figure 9. ACQUITY TQD.

Acknowledgements

The authors would like to thank Central Science Laboratory (CSL), Sand Hutton, York, UK and VWA, Amsterdam, The Netherlands for kindly supplying MRM transitions and standard solution mixes that were analyzed in this project. Furthermore, University of Jaume I Castellon, Spain, Waters UK, Waters US and Nihon Waters, Japan demonstration laboratories are all thanked for their contributions in supplying MRM transitions.

References

1. Website: http://ec.europa.eu/food/plant/protection/resources/qualcontrol_en.pdf
2. Commission of the European Communities EC 396/2005, OJ 2005; L70:1.
3. Leandro C.C., Hancock P., Fussell R.J., Keely B.J., J. Chrom A 2007; 1144:161.
4. Lehotay, J.AOAC Int. 90(2) 2007, 485-520.

Appendix

List of the 402 pesticides analyzed

3,4,5-Trimethacarb"
Acephate
Acetamiprid
Acibenzolar-S-methyl
Acitidone
Aldicarb
Aldicarb sulfone
Aldicarb sulfoxide
Ametryn
Amidosulfuron
Aminocarb
Amitrole
Anilazine
Anilofos
Asulam
Atraton
Atrazine
Atrazine-desethyl
Atrazine-desisopropyl
Azaconazole
Azamethiphos
Azinphos-ethyl
Azinphos-methyl
Aziprotryne
Azobenzene
Azoxystrobin
Benalaxyl
Benazolin
Bendiocarb
Benfuracarb
Benfuresate
Bensulfuron methyl
Bensulide
Bentazone
Benzoximate
Benzthiazuron
Bifenazate
Bitertanol
Boscalid
Bromacil
Bromuconazole
Bupirimate
Buprofezin
Butocarboxim
Butocarboxim sulfoxide
Butoxycarboxim
Buturon
Butylate
Cadusafos
Carbaryl
Carbendazim
Carbetamide
Carbofuran
Carbofuran-3-hydroxy
Carbofuran-3-keto
Carbosulfan
Carboxin
Carfentrazone-ethyl
Chlorbromuron
Dibrom
Dichlofluanid
Dichlorvos
Diclobutrazol
Dicrotophos
Diethofencarb
Difenoconazole
Difenoxuron
Diflubenzuron
Dimefuron
Dimepiperate
Dimethachlor
Dimethametryn
Dimethenamid
Dimethirimol
Dimethoate
Dimethomorph
Dimetilan
Dimoxystrobin
Diniconazole
Dioxacarb
Diphenamid
Diphenylamine
Disulfoton
Disulfoton-sulfone
Disulfoton-sulfoxide
Ditalimfos
Dithiopyr
Diuron
DMST
Dodemorph
Edifenphos
Epoxiconazole
EPTC
Esprocarb
Ethidimuron
Ethiofencarb
Ethiofencarb sulfone
Ethiofencarb sulfoxide
Ethirimol
Ethofumesate
Ethoprophos
Ethoxyquin
Ethoxysulfuron
Etofenprox
Famphur
Fenamidone
Fenamiphos
Fenamiphos sulphone
Fenamiphos sulphoxide
Fenarimol
Fenazaquin
Fenazox
Fenbuconazole
Fenfuram
Fenhexamid
Fenobucarb
Fenoxycarb
Fenpiclonil
Indoxacarb
Iodosulfuron methyl
Iprobenphos
Iprovalicarb
Isazophos
Isocarbamide
Isocarbofos
Isofenphos
Isomethiozin
Isonoruron
Isoprocarb
Isopropalin
Isoproturon
Isoxaben
Kresoxim-methyl
Lenacil
Linuron
Malaoxon
Malathion
Mecarbam
Mefenacet
Mepanipyrim
Mephosfolan
Mepronil
Mesosulfuron-methyl
Mesotrione
Metalaxyl
Metamitron
Metazachlor
Metconazole
Methabenzthiazuron
Methacrifos
Methamidophos
Methfuroxam
Methidathion
Methiocarb
Methiocarb sulfone
Methiocarb sulfoxide
Methomyl
Methoprotryne
Methoxyfenozide
Metobromuron
Metolachlor
Metolcarb
Metosulam
Metoxuron
Metrafenone
Metribuzin
Metsulfuron methyl
Mevinphos
Molinate
Monocrotophos
Monolinuron
Monuron
Myclobutanil
Napropamide
Naptalam
Neburon
Nicosulfuron
Propanil
Propaquizafop
Propazine
Propetamphos
Propham
Propiconazole
Propoxur
Propyzamide
Prosulfocarb
Prosulfuron
Pymetrozine
Pyracarbolid
Pyraclostrobin
Pyrazophos
Pyrazosulfuron-ethyl
Pyridaben
Pyridafol
Pyridaphenthion
Pyridate
Pyrifenox
Pyrimethanil
Pyriproxifen
Pyroquilon
Quinalphos
Quinmerac
Quinoxyfen
Quizalofop-ethyl
Quizalofop-methyl
Rabenzazol
Rotenone
Sebuthylazin
Sebuthylazin-desethyl
Secbumeton
Sethoxydim
Siduron
Simazine
Simeconazole
Simetryn
Spinosad A
Spinosad D
Spiromesifen
Spiroxamine
Sulcotrione
Sulfallate
Sulfaquinoxaline
Sulfometuron-methyl
Sulfosulfuron
Sulfotep
Tebuconazole
Tebufenozide
Tebufenpyrad
Tebupirimfos
Tebutam
Tebuthiuron
Temephos
Tepraloxydim
Terbufos
Terbufos-sulfone
Terbufos-sulfoxide

Appendix (continued)

Chlorfenvinphos
Chlorfluazuron
Chloridazon
Chloroxuron
Chlorpropham
Chlorpyrifos
Chlorpyriphos-methyl
Chlorsulfuron
Chlorthiophos
Chlortoluron
Cinidon-ethyl
Cinosulfuron
Clethodim
Clodinafop-propargyl
Clomazone
Clopyralid
Cloquintocet - mexyl
Clothianidin
Coumaphos
Cruformate
Cyanazine
Cyanofenphos
Cyazofamid
Cycloate
Cycloxydim
Cycluron
Cyflufenamid
Cymoxanil
Cyproconazole
Cyprodinil
Cyromazine
Daminozide
Demeton O
Demeton S
Demeton-S-methyl
Demeton-S-methyl-sulfon
Desmedipham
Desmethyl-formamido-pirimicarb
Desmethyl-pirimicarb
Desmetryn
Dialifos
Diallate
Fenpropathrin
Fenpropidin
Fenpropimorph
Fenpyroximat
Fensulfothion
Fenthion
Fenthion-sulfone
Fenthion-sulfoxide
Fenuron
Flamprop-isopropyl
Flamprop-methyl
Fluazafop-P-butyl
Fluazifop
Flucycloxuron
Flufenacet
Flufenoxuron
Fluomethuron
Fluoxastrobin
Fluroxypyr
Fluroxypyr-meptyl
Flurtamone
Flusilazole
Flutolanil
Flutriafol
Fonofos
Foramsulfuron
Formetanate
Fosthiazate
Fuberidazole
Furathiocarb
Halosulfuron methyl
Haloxyfop
Haloxyfop-2-ethoxyethyl
Haloxyfop-methyl
Heptenophos
Hexaconazole
Hexazinone
Hexythiazox
Imazalil
Imazapyr
Imazaquin
Imidacloprid
Nicotine
Nitenpyram
Nitralin
Nuarimol
Ofurace
Omethoate
Orbencarb
Oryzalin
Oxamyl
Oxasulfuron
Oxycarboxin
Oxydemeton-methyl
Paclobutrazol
Paraoxon-methyl
Parathion
Pebulat
Penconazole
Pencycuron
Pendimethalin
Phenmedipham
Phenthoate
Phorate
Phorate sulfone
Phorate sulfoxide
Phosalone
Phosphamidon
Phoxim
Picloram
Picolinafen
Picoxystrobin
Piperonyl butoxide
Piperophos
Pirimicarb
Pirimiphos-ethyl
Pirimiphos-methyl
Procloraz
Profenofos
Promecarb
Prometon
Prometryn
Propachlor
Propamocarb
Terbumeton
Terbumeton-desethyl
Terbuthylazine
Terbuthylazine-2-hydroxy
Terbuthylazine-desethyl
Terbutryn
Tetrachlorvinphos
Tetraconazole
Thiabendazole
Thiacloprid
Thiamethoxam
Thiazafluron
Thidiazuron
Thifensulfuron methyl
Thiodicarb
Thiofanox
Thiofanox-sulfone
Thiophanate
Thiophanate-methyl
Tolylfluanid
Topramezone
Tralkoxidym
Triadimefon
Triadimenol
Triallate
Triasulfuron
Triazophos
Triazoxid
Trichlorfon
Tricyclazole
Trietazine
Trifloxystrobin
Trifloxysulfuron
Triflumizole
Triflumuron
Triflusulfuron-methyl
Triticonazole
Vamidothion
Vernolat
Zoxamide

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[DIOXINS/POPs]

[PERFLUOROALKYL AND POLYFLUORALKYL SUBSTANCES (PFAS)]

[POLYCYCLIC AROMATIC HYDROCARBONS (PAHs)]

[PHARMACEUTICALS AND PERSONAL CARE PRODUCTS (PPCPs)]

[PESTICIDES]

[CARBAMATES]

[TECHNOLOGY BRIEF]

Minimizing Carryover During Dioxin Analysis Using the Xevo TQ-S with APGC

Adam Ladak, Waters Corporation, Beverly, MA, USA
Kari Lynn Organtini and Frank L Dorman, Pennsylvania State University, University Park, PA, USA

GOAL

To eliminate carryover from sample to sample to ensure accurate quantification of unknown dioxin and furan containing samples.

BACKGROUND

Dioxins and furans are produced when organic compounds are incinerated in the presence of chlorine for example during PVC production, paper bleaching, and from natural sources such as volcanoes. Dioxins are extremely toxic and readily bioaccumulate in many animal species due to their lipophilic properties. They are also suspected mutagens and carcinogens. They are also suspected mutagens and carcinogens.

The Xevo TQ-S with Atmospheric Pressure GC (APGC) has provided a very sensitive detection system for the accurate determination of dioxins and furans at regulatory levels. During the analysis of samples of an unknown concentration, extremely high levels of these compounds may be observed. Therefore there is the potential for carryover of target compounds into the following sample injection. The consequence of this would be a falsely elevated quantitative result.

The carryover was investigated on an APGC fitted with a split/splitless injector coupled with a Waters® Xevo TQ-S. A single goose-neck splitless liner was installed into the injector. Five nonane washes were performed pre and post injection. A 1 in 10 dilution of the CS 5 standard from Wellington Laboratories (Guelph, ON) was injected followed by several nonane blanks.

Carryover was significantly reduced to 0.007% which is a 20-fold decrease compared to the original values. This virtually eliminated the chance of a false positive result.

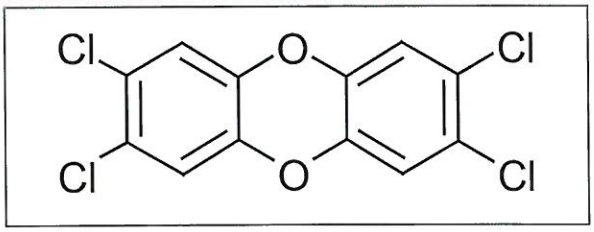

Figure 1. 2,3,7,8-Tetrachlorodibenzodioxin (TCDD).

The initial carryover, calculated using peak height, was 0.15% (Figure 2). This level of carryover could cause inaccurate quantification in samples analyzed immediately following this in a batch analysis. Experiments were performed in order to reduce the carryover observed to an acceptable level.

THE SOLUTION

A number of possible approaches to reduce carryover were investigated:

- Reducing the number draw/purge cycles during wash
- Placing glass wool in the liner
- Changing the type of autosampler syringe
- Changing solvent washes
- Using different liners

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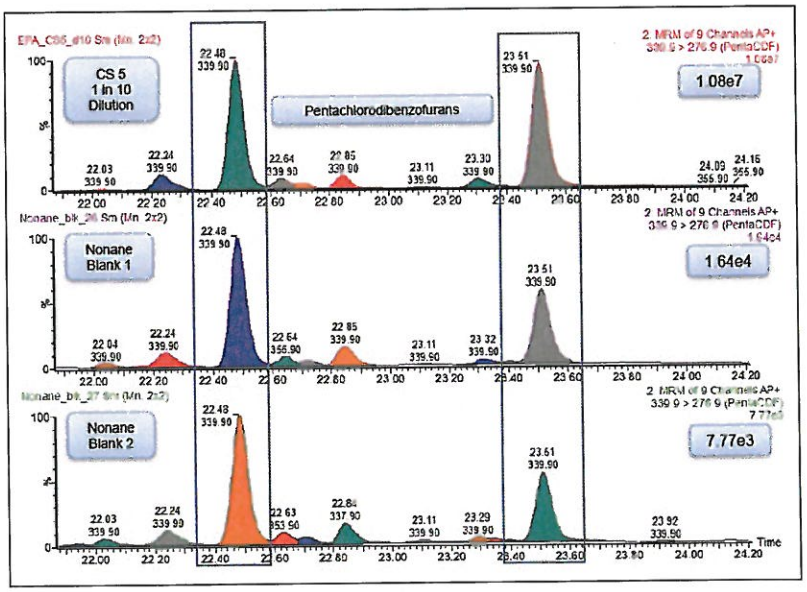

Figure 2. Extracted ion chromatograms for pentachlorodibenzofurans displaying ~0.15% carryover prior to the implementation of optimized injection cycle parameters.

Each of these approaches were tested to see how they affected the carryover from the 1 in 10 dilution of the CS 5 Standard to the response seen from the nonane blank injected immediately afterwards. The largest reduction in carryover was obtained by changing the wash solvents to toluene and nonane combined with the use of a Restek Uniliner (Table 1). By combining both of these changes, the carryover was significantly reduced to 0.007% which was a 20-fold decrease compared to the original values (Figure 3). This virtually eliminated the chance of a false positive result.

Parameter	Standard CS 5; 1:10 dilution (peak height)	Nonane blank (peak height)
No sample draw/purge cycles	31,500,000	23,900
No glass wool in inlet	8,250,000	2170
Vendor 1 syringe	9,040,000	920
Vendor 1 gas-tight syringe	8,190,000	1160
Vendor 2 gas-tight syringe	7,800,000	1320
Toluene/Nonane wash 1	2,760,000	528
Toluene/Nonane wash 2	8,580,000	838
Use of Uniliner 1.0 µl	4,170,000	126
Use of Uniliner 0.5 µl	2,420,000	166

Table 1. The effects of different injection cycle parameters (applied in sequence) upon the observed carryover for pentachlorodibenzofurans.

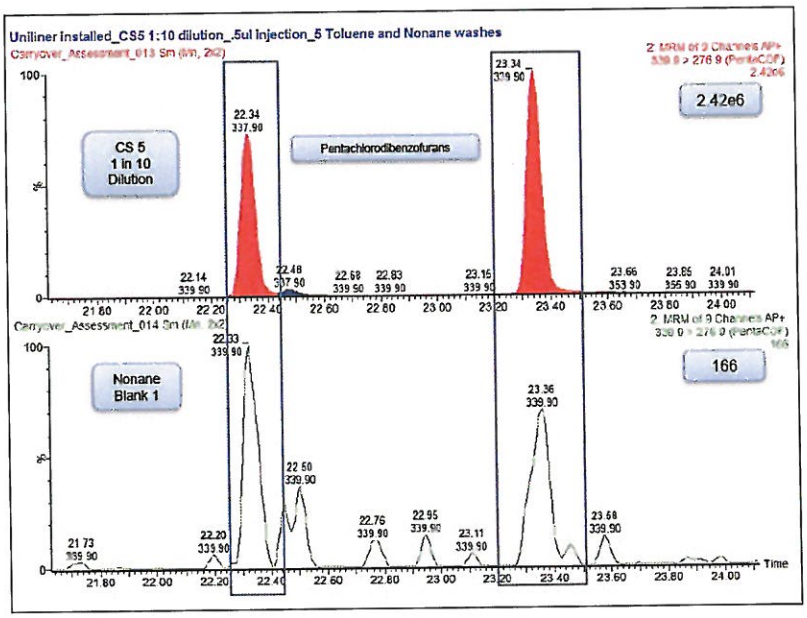

Figure 3. Extracted ion chromatograms for pentachlorodibenzofurans displaying greatly reduced carryover (0.007%) after the implementation of optimized injection cycle parameters.

SUMMARY

In order to ensure accurate quantification during dioxins and furans analysis on the Xevo TQ-S with APGC, the correct solvent washes and inlet liner should be used. Five washes of toluene followed by five washes of the sample diluent pre- and post-injection should be performed. Also a Uniliner should be installed into the inlet. The Sky 4.0 mm ID Drilled Uniliner Inlet Liner with Hole near Top from RESTEK (Part number 23311.1) was used successfully in the tests described here. The Uniliner design minimizes active sites in the sample pathway and reduces injection port discrimination. The analytical column connects directly to the bottom of the Uniliner via a press-fit seal, eliminating sample contact with any part of the injector below the column inlet and thus minimizing carryover.

By performing the analysis with this recommended configuration, confident and accurate analysis of dioxins and furans can be performed at low detection limits.

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[APPLICATION NOTE]

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Determination and Characterization of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS's) in Environmental Samples Using UPLC Ion Mobility MS

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APPLICATION BENEFITS

- Individual PFOS isomers are resolved from chromatographically co-eluting isobaric biological matrix interferences with ion mobility.
- Efficiency of structrural elucidation is improved through mobility spectral clean up.
- Ion mobility drift times can be used as identification information in a routine screening workflow to identify PFOS isomers.
- Identification based on retention time, precursor ion accurate mass measurements, fragmentation data with accurate mass measurements, and ion mobility drift times can be generated in one analysis.

WATERS SOLUTIONS

Oasis® WAX Solid Phase Extraction Cartridge

ACQUITY UPLC® I-Class System

ACQUITY UPLC BEH C_{18} Column

SYNAPT® G2-S High Definition Mass Spectrometry® (HDMS®)

MassLynx® Software with the UNIFI® Scientific Data Management System

KEY WORDS

PFOS isomers, drift times, ion mobility, spectral clean up, PFAS, PFOS, collision cross section, CCS

INTRODUCTION

Perfluoroalkyl and polyfluoroalkyl substances (PFAS's) are a class of man-made compounds that are frequently detected in biological and environmental samples. PFAS's are used in a multitude of commercial/industrial processes and products, ranging from fire-fighting foams, insecticide formulations, water-resistant coatings, and floor polishes, to oil-resistant coatings for paper products approved for food contact. As with many anthropogenic compounds, the incidence of cancers resulting from exposure has become a cause for concern.

Perfluorooctane sulfonate (PFOS) is frequently detected in biological and environmental samples and occurs due to abiotic or biotic environmental processes. MRM transition based LC-MS/MS analyses have been used previously to investigate PFOS in marine animals and human serum. Benskin *et al.* reported that common matrix interferents (taurodeoxycholate [TDCA]) can complicate PFOS quantification because they undergo the same transition (m/z 499 ⇒ m/z 80) and tend to co-elute with PFOS, leading to a positive bias.[1,2]

In this application note we explore the use of the Waters® ACQUITY UPLC I-Class System with ion mobility as an important tool for the unequivocal identification of PFOS isomers in environmental samples.[3,4,5] This technique has been utilized to analyze a series of environmental extracts, including mink and fish muscle, to determine the presence of PFOS. There are some unique advantages to profiling complex matrices using this technique which employs a combination of high resolution mass spectrometry, with high efficiency ion mobility-based measurements and separations. Ion mobility spectrometry (IMS) is a rapid, orthogonal, gas phase separation technique which allows another dimension of separation to be obtained within an LC timeframe. Compounds can be differentiated based on size, shape, and charge. In addition, both precursor ion and fragment ion information can be acquired in a single injection for all components analyzed.

EXPERIMENTAL

UPLC conditions

UPLC system:	ACQUITY UPLC I-Class (equipped with PFC Kit)
Column:	ACQUITY UPLC BEH C_{18} 100 mm x 2.1 mm, 1.7 µm
Column temp.:	50 °C
Flow rate:	0.3 mL/min
Mobile phase:	70% 2 mM NH_4Ac in water / 30% 2 mM NH_4Ac in methanol/ACN 80/20 (A) mM NH_4Ac in methanol/ ACN 80/20 (B)

Gradient:

Time (min)	%A	%B
Initial	100.0	0.0
0.5	100.0	0.0
16.00	65.0	35.0
22.00	65.0	35.0
27.00	10.0	90.0
27.10	0.0	100.0
28.00	0.0	100.0
28.10	100.0	0.0
34.00	100.0	0.0

MS conditions

MS system:	SYNAPT G2-S
Ionization mode:	ES –
Desolvation temp.:	550 °C
Acquisition mode:	Ion mobility
Mass range:	50 to 600 Da
Acquisition rate:	10 spectra/s
Capillary voltage:	2.3 kV
Cone voltage:	15V
Ion mobility gas:	CO_2 and N_2
Collision energy ramp:	35 to 75 eV
IMS wave velocity range:	400 m/s and 550 m/s
IMS wave height:	40 V
IMS duty cycle:	10.8 ms

Sample preparation

Whole mink carcasses (juvenile and adult males) were provided by licensed hunters and kept frozen (-20 °C) before being autopsied at the Swedish University of Agricultural Sciences.

The procedure used was in accordance with the method reported by Kärrman *et al.*,[7] with minor modifications. Liver samples were homogenized using Ultra-Turrax (IKA). A sub-sample of liver (1 g) was taken and 10-mL acetonitrile was added. The mixture was repeatedly vortex mixed and sonicated for 30 min. The supernatant was removed after centrifugation (10,000 x g, 30 min), and the extraction procedure was repeated upon the resulting pellet. The acetonitrile fractions were combined and reduced in volume to 10-mL after which 25-mL water was added. After mixing and centrifugation, the extract was passed through an Oasis WAX Solid Phase Extraction (SPE) Cartridge previously conditioned using 4-mL methanol followed by 4-mL water. After sample loading, the Oasis SPE Cartridge was washed with 4-mL 25 mM sodium acetate (pH 4) and 4-mL 40% methanol in water, followed by drying under vacuum. A final wash with 8-mL methanol was employed before the perfluorinated compounds were eluted using 2-mL 2% ammonium hydroxide in methanol into a tube with 50-mg ENVI-Carb (Supelclean, 120/400 mesh) and 100-µL acetic acid. The carbon solution was mixed by vortexing for 30 s, then filtered through a 0.2-µm GHP membrane, and reduced to 200 µL using N_2, after which 300-µL 2 mM ammonium acetate in water and the performance standard 7HPFHpA were added.

The study undertaken investigates the use of the Waters SYNAPT G2-S Platform to determine if UPLC® in combination with ion mobility can provide a route to specific and unambiguous identification, enabling the unequivocal distinction of PFOS isomers. A schematic representation and illustration of the mechanism of ion mobility are shown in Figure 1. For additional research purposes only, the separation power of ion mobility was enhanced by substituting N_2 with CO_2 for the mobility drift gas.[5] Use of CO_2 enabled characteristic drift time separation for the PFOS isomers analyzed. It is important that PFOS isomers are identified correctly because their physical, chemical, and biological properties may be affected by perfluoromethyl branching. As a result there has been increased scientific interest in relating toxicity, environmental transport, degradation, and bioaccumulation to perfluoromethyl branching patterns.

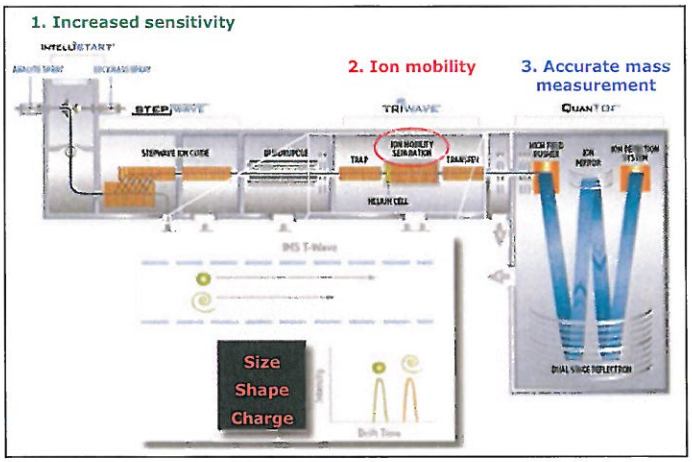

Figure 1. Schematic of the SYNAPT G2-S Mass Spectrometer and illustration of the mechanism of ion mobility.

RESULTS AND DISCUSSION

The UNIFI Scientific Data Management System is designed to enable the day-to-day use of ion mobility in screening assays. Data were acquired using MassLynx Software, and processed using UNIFI. Using mass spectral information generated from a standard mixture of PFOS isomers, a scientific library in UNIFI was created incorporating the expected retention times and drift times of PFOS isomers. This allowed non-targeted acquisition and a targeted screen of the environmental extracts analyzed with the combination of orthogonal ion mobility separation and UPLC chromatographic separation.

The results obtained in determining the presence of PFOS in mink clearly show the benefits of using ion mobility. It is possible to separate co-eluting isobaric interferences from PFOS isomers. In Figure 2, accurate mass extracted ion chromatograms are presented. The interferences (peaks A and B) overlap with the different major PFOS isomers (peaks C-F). Since TCDCA (taurochenodeoxycholate)/TDCA interferences and PFOS isomers also produce isobaric fragments, it is difficult to characterize and accurately quantify these components using conventional MS techniques. PFOS and TDCA, as well as other cholic acids, have similar isomeric profiles, retention times, and transitions (*m/z* 499 ⇒ *m/z* 80). Using quadrupole technology's selectivity to target PFOS 498.9, typical mass resolution would result in a 1 Da span across the mass selected when performing MS/MS. With this information, it is easy to understand how the interferences can be mistaken for PFOS.

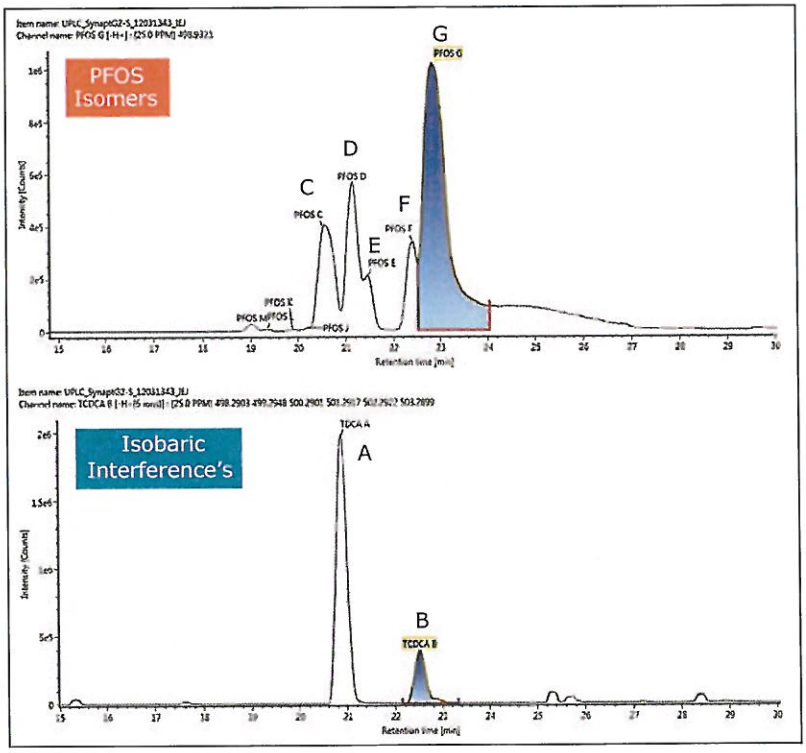

Figure 2. Accurate mass extracted ion chromatograms for the isobaric biological matrix interferences (peaks A and B) and PFOS isomers (peaks C-G).

The approach undertaken here negates the need to use complex chromatography, sample clean up and highly specific MS experimental design. Using ion mobility, it is possible to acquire mobility resolved mass spectral information from the sample, including precursor and fragmentation information, as well as drift times to enable further characteristic profiling. PFOS isomers can be resolved from interfering components as they have vastly different mobility drift times, as shown in the component drift plot in Figure 3. The orthogonal separation of TDCA and TCDCA produces a drift time differentiation of 2 ms from PFOS isomers.

Drift times of PFOS isomers provide more definitive information regarding their identity. Ordinarily, retention time information and subtle differences in observed product ions, as well as their intensity are used to characterize individual isomers. This can be very challenging at low concentrations. Using drift times that directly relate to collison cross section (CCS), provide an additional identification point related to the physical properties of the molecules, (over *m/z* and chromatographic retention time).

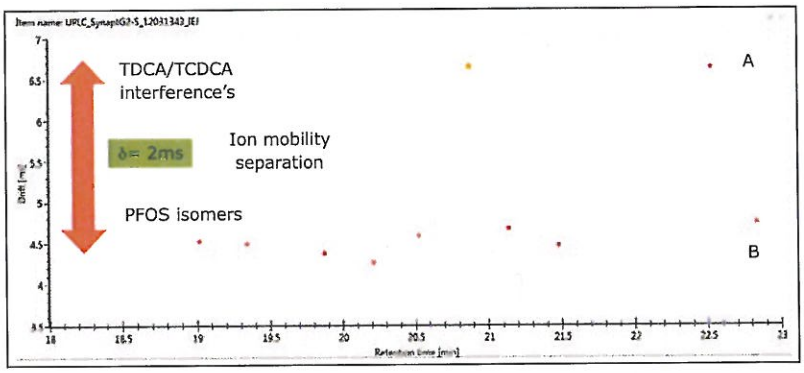

Figure 3. Component drift plot of drift time versus retention time for the nominally isobaric interferences (A) and the PFOS isomers (B).

Through the combination of orthogonal ion mobility separation and UPLC chromatographic separation, peak capacity is increased, hence, single component accurate mass spectra can be obtained. It is now possible to create a characteristic assignment profile of PFOS isomers using drift time, retention time, and accurate mass measurements (Table 1). The highly specific mobility aligned precursor and fragment ions, which are resolved from matrix interferences are also used to produce elemental composition information and proposed fragmentation pathways.

Table 1. A summary of drift times, retention time, and isomer assigment for major PFOS isomers and co-eluting biological matrix interferences.

	PFOS isomer identification					
PFOS isomers	J 3mPFOS	C 5mPFOS	D IsoPFOS	E 2,2 perfluoro methyl PFOS (tentative)	F 1mPFOS	G nPFOS
Drift time (ms) mass measurement error	4.27 -0.23 ppm	4.59 3.4 ppm	4.68 3.66 ppm	4.47 3.12 ppm	4.43 3.72 ppm	4.75 -14.91 (2.68 ppm HE)
Retention time (min)	20.21	20.55	21.14	21.48	22.40	22.80
TDCA interferences		A TDCA	B TCDCA			
Drift time (ms) mass measurement error		6.65 3.59 ppm	6.64 1.64 ppm			
Retention time (min)		20.88	22.52			

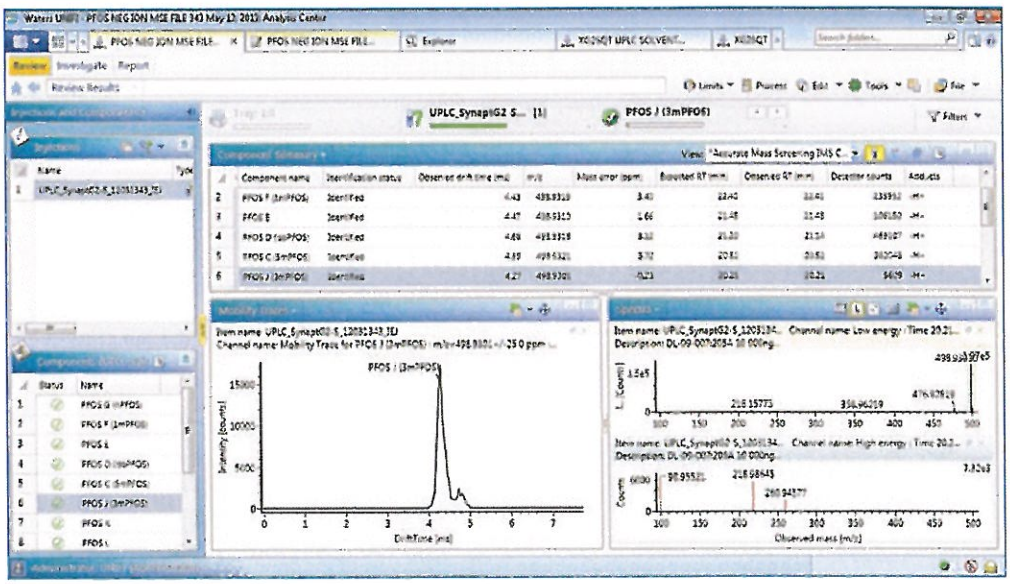

Figure 4. Minor PFOS (J) (3mPFOS) isomer fragmentation spectra, ion mobility resolved from co-eluting PFOS isomer C at retention time 20.21 mins.

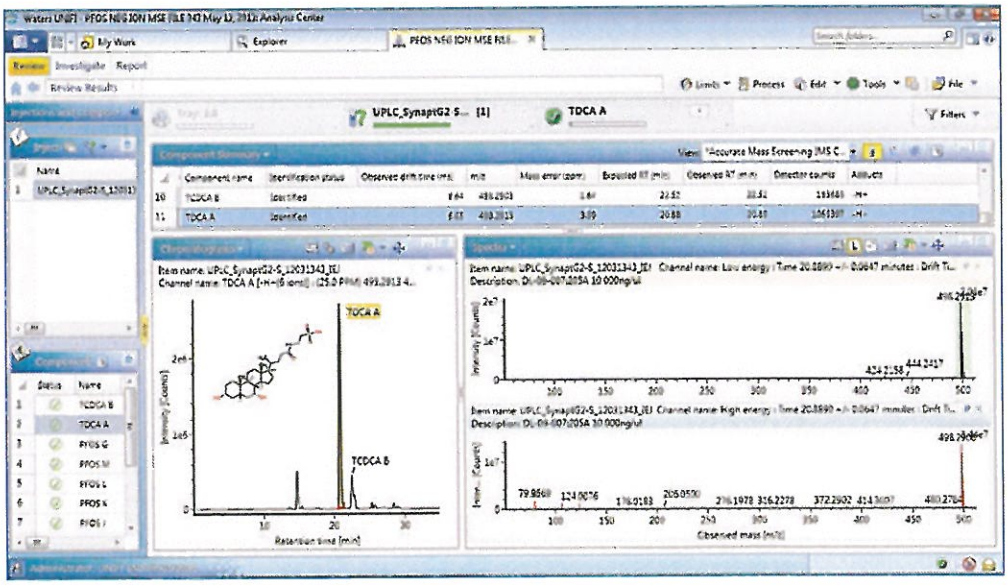

Figure 5. Ion mobility resolved characteristic fragmentation spectra of isobaric interference TDCA (A) at retention time 20.88 mins were generated using the combination of orthogonal ion mobility separation and UPLC chromatographic separation.

Examples of individual ion mobility resolved fragmentation spectra that were obtained for isomers of co-eluting PFOS and co-eluting isobaric biological matrix interferences, are shown in Figures 4, 5, 6, and 7. In Figure 4, the fragmentation spectrum and mobility trace for 3mPFOS is presented; it is mobility separated from 5mPFOS (C) and TDCA (A), which chromatographically co-elute. The enhanced peak capacity obtained with ion mobility enabled the comparison of fragment ion spectra from the different PFOS isomers without interference from the co-eluting TDCA/TCDCA. TDCA co-elutes with PFOS isomers C, and D at retention times 20.55 and 21.14 mins (see Figure 2). The characteristic fragmentation spectrum of isobaric interference TDCA is shown in Figure 5. A commonality of fragments to those obtained for PFOS isomers can be seen in Figures 6 and 7. During the targeted screen, retention time, drift time, and precursor ion/fragmentation spectra were produced for nine PFOS isomers. Spectra associated with matrix interferences were also generated. It can be seen that PFOS isomers C and D have different fragmentation profiles as well as drift times of 4.59 and 4.68 ms respectively (Figures 6 and 7). This data demonstrates that drift time information can be used as specific identification criteria for PFOS isomers and would greatly increase confidence in isomer identification. The use of drift time information greatly reduces reliance upon chromatographic retention time for correct identification of isomers. The complexity of matrices used to study PFOS in environmental samples has been shown to cause shifts in retention times.

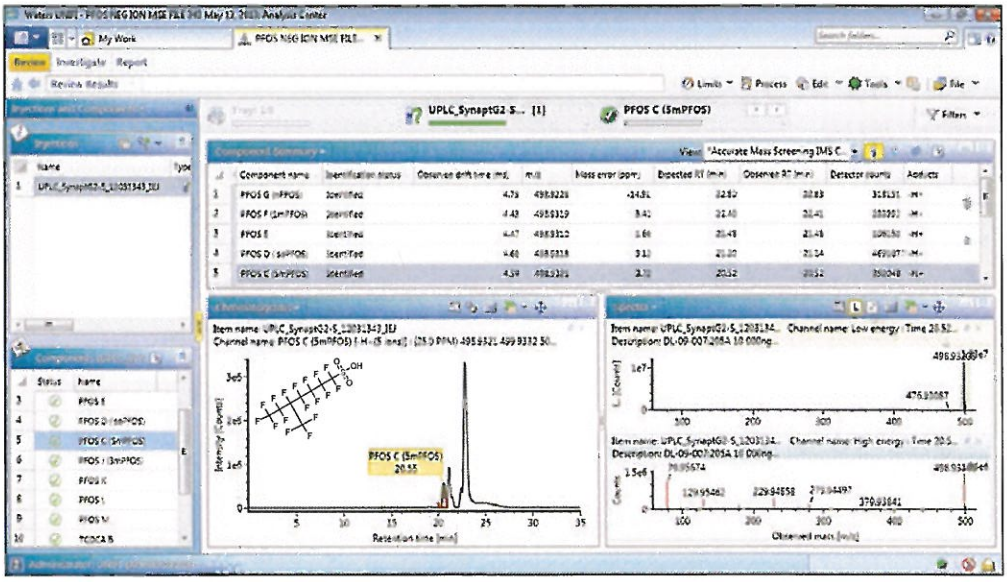

Figure 6. PFOS (C) (5mPFOS) isomer ion mobility precursor ion and characteristic fragmetation spectra, ion mobility resolved from isobaric interference TDCA (A) at retention time 20.55 mins.

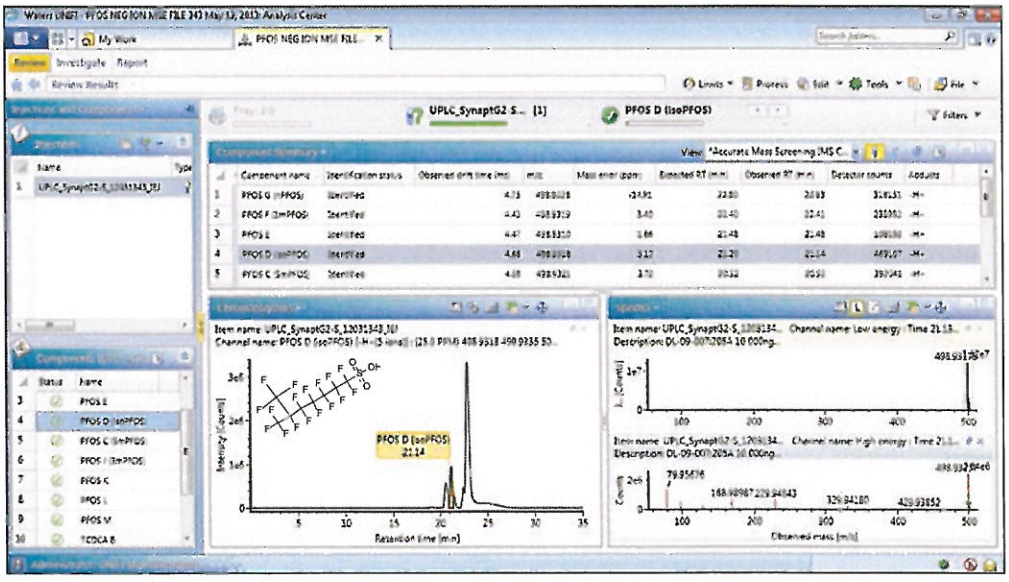

Figure 7. PFOS (D) (isoPFOS) isomer ion mobility precursor ion and characteristic fragmetation spectra, ion mobility resolved from isobaric interference TDCA (A), at retention time 21.14 mins.

Beskin *et al.* have previously shown the elution order of PFOS isomers.[1] Where performed, the PFOS isomer assignments are presented in Table 2. Structural elucidation was performed according to the methodology introduced by Langlois and Oehme.[8] Unbranched nPFOS is known to be retained strongest at 22.80 mins under reversed phase conditions. This was confirmed with the data presented which showed a combination of the presence of "O" series and "9" series ions in the fragmentation data occurs. From the elucidation of fragments it is concluded that there is no branching in the isomer fragmented. Elucidation based on formation of product ions is indeed a challenging task where a reliance on low intensity ions is required. Optimum sensitivity and collision energies are required. Also the challenge of lower intensity product ions as chain length increases needs to be overcome. A profile of nine PFOS isomer drift times has been generated and warrants further studies to expand the applicability of ion mobility to specific PFOS isomer identification. Our initial investigation indicates that PFOS isomers with a more linear structure have longer drift times, compared to those that have branching further away from the PFOS end groups.

In total, the drift times of nine PFOS isomers have been determined and where sufficient response was obtained, identities were confirmed by examination of their fragmentation spectra. Drift times of PFOS isomers have been shown to increase with linear chain length, and this is a trend that might be used in structural elucidation exercises in future studies. The data presented shows that ion mobility has utility in isomer-specific analysis of PFOS in environmental samples and that further investigation of its application in this field is warranted. Software enhancements will enable further studies to be performed with direct determination of collision cross sections of PFOS isomers.

CONCLUSIONS

- Co-eluting isobaric biological interferences TDCA and TCDCA have been resolved from PFOS isomers using ion mobility N_2 and CO_2 as a drift gas.
- Increased confidence can be obtained from distinct drift times for the PFOS isomers and used as an additional identification point to reduce the dependence upon chromatographic retention times.
- Using UPLC IMS-MS, single component precursor ion and fragmentation spectra have been generated for PFOS isomers and TDCA/TCDCA isomers.
- UPLC IMS-MS offers an uncompromised unique approach for the determination and characterization of PFOS within the environment by enabling isomer-specific analysis.
- UPLC IMS-MS in combination with targeted screening can provide an efficient route to specific identification of PFOS isomers.

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[APPLICATION NOTE]

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Rapid Sample Preparation for Determination of PAHs in Wild-Caught Avian Eggs Utilizing QuEChERS Extraction and Ostro 96-Well Plate Cleanup Followed by UPLC-UV Analysis

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APPLICATION BENEFITS

- Rapid and efficient extraction of PAHs from a complex avian egg matrix with established QuEChERS methodology.
- Novel Ostro™ sample preparation approach eliminates the use of conventional GPC followed by SPE cleanup and successfully reduces sample preparation time to hours, instead of several days.
- Minimal sample mass is required.
- Ensures effective removal of proteins and phospholipids and generates excellent sensitivity with PDA detection, even without a pre-concentration step.
- Simplicity of the method ensures robustness and reproducibility of results.
- Eliminates the use of large amounts of potentially harmful and costly chemical solvents.

WATERS SOLUTIONS

Ostro Well Plates

ACQUITY UPLC® System

ACQUITY UPLC PDA Detector

MassLynx® Software v.4.1

KEY WORDS

PAHs, eggs, QuEChERS extraction, protein, phospholipid, removal, SPE, UPLC-UV

INTRODUCTION

The British Petroleum offshore rig explosion on April 20, 2010 released an estimated 4.9 billion barrels of crude oil into the Gulf of Mexico, raising immediate environmental concerns regarding potential threats to the inhabiting wildlife and surrounding ecosystem.[1] Polycyclic Aromatic Hydrocarbons (PAHs) are a large group of organic compounds present in crude oil, consisting of two or more aromatic rings fused together.[2] PAHs are highly toxic, and while metabolizable they have been shown to bio-accumulate, especially heavier molecular weight PAHs. PAHs are highly carcinogenic and mutagenic compounds that have been shown to generate reactive oxygen species.[3] Owing to their lipophilic nature, PAHs readily accumulate in eggs where residues may be orders of magnitude higher than in other organs, including the liver.[4] While sufficient data are available regarding the carcinogenicity of the PAHs, other long-term toxicological effects, including neurotoxicity, are not as well documented.[5] Therefore, the development of new, rapid, and sensitive techniques for analysis of PAHs in various tissues would therefore be beneficial.

Commonly used sample preparation techniques for the isolation of PAHs from various matrices are liquid-liquid extraction, basic digestion in KOH followed by gel permeation chromatography and solid-phase extraction (SPE).[3] Recently, a more modern high-throughput QuEChERS method was used by our research group for the determination of PAHs in avian eggs and blood.[1] A similar approach was used to screen for PAHs in seafood.[6] The simplicity of the approach, its effectiveness, and its speed provided an excellent alternative to traditional, lengthy extraction methods. However, the complexity of the biological matrix with high protein and phospholipid content as well as low concentrations of PAHs, meant further extensive cleanup and enrichment was required prior to analysis. This was performed using gel permeation chromatography (GPC) followed by additional SPE to minimize matrix effects which extended the total sample preparation time to several days.[7]

A novel, one-step protein and phospholipid clean-up using Waters® Ostro 96-well plates served as an alternative to a GPC and SPE approaches. It has been shown that sample preparation using Ostro 96-well plates can provide an effective means for the removal of phospholipids in plasma and serum allowing for more

EXPERIMENTAL

UPLC conditions

LC system:	ACQUITY UPLC
Column:	ACQUITY UPLC CSH C_{18} 2.1 X 100 mm, 1.7 µm
Column temp.:	50 °C
Sample temp.:	20 °C
Mobile phase A:	80:20
Water:	Methanol
Mobile phase B:	90:10
Acetonitrile:	Methanol

Gradient:

Time (min)	Flow (mL/min)	%A	%B
0.0	0.6	85.0	15.0
0.25	0.6	66.0	34.0
4.0	0.65	61.0	39.0
13.0	0.65	35.0	65.0
13.5	0.65	3.0	97.0
15.0	0.6	85.0	15.0

Total runtime:	16 min
Injection volume:	8.5 µL

UV conditions

UV detector:	ACQUITY UPLC PDA
Mode:	Scan/3D mode
Sampling rate:	20 pts/s
Resolution:	1.2 nm
Range:	200 to 450 nm

sensitive analyses, increased sample throughput, and reduced instrument downtime.[8] Our research group utilized a similar approach with Ostro 96-well plate technology, coupled with QuEChERS dispersive extraction, to develop and validate a rapid, high-throughput method for the preparation of eggs for the analysis of PAHs.

The most widely used analytical techniques for the quantification of PAHs are HPLC with fluorescence detection and GC-MS. Other analytical approaches have been employed including APPI-LC-MS/MS and GC-MS/MS.[6] The work described here shows that the desired chromatographic resolution and detection limits were achieved using a Waters® ACQUITY UPLC System equipped with PDA detection.

Compound	Retention time (min)	λ_{max} (nm)	R^2 (5 to 500 ng/mL)
Naphthalene-d8 (SUR.)	3.03	219	0.9995
Naphthalene*	3.19	229	0.9986
Acenaphthylene	4.11	227	0.9984
Acenaphthene*	5.34	264	0.9998
Fluorene	5.56	227	0.9996
Anthracene	6.24	251	0.9997
Phenanthrene	6.66	252	0.9991
Fluoranthene*	7.81	236	0.9990
Pyrene	7.99	240	0.9991
Chrysene-d12 (IS)	9.10	267	-
Chrysene	9.31	268	0.9997
Benz(a)anthracene	9.47	288	0.9997
Perylene-d12 (SUR.)	10.27	250	0.9997
Benzo(b)fluoranthene	10.63	256	0.9995
Benzo(a)pyrene	10.90	296	0.9997
Dibenz(a,h)anthracene	11.93	297	0.9994
Benzo(g,h,i)perylene	12.10	299	0.9972
Indeno(1,2,3-cd)pyrene	12.10	299	0.9999

Table 1. The retention times, λmax and R2 value for EPA's 16 priority pollutant PAHs, surrogate (SUR.) and internal standard (IS) compounds.

**2-bromonaphthalene and benzo(k)fluoranthene are part of the QTM PAH mixture, but were not a part of the analytical procedure, so consequently were omitted from the table. QTM PAH mix includes all PAHs; EPA 525 mix A is missing compounds marked with an asterisk.*

In this application note, a QuEChERS extraction method in conjunction with the novel Ostro 96-well plate clean-up was developed for rapid analysis of PAHs in avian egg samples. The use of this methodology greatly reduced sample preparation time from a three-day process to just three hours by avoiding the need to use GPC and SPE.

Certified PAH standards – QTM PAH mix (total of 16 PAHs – cat. # 47930-U) with concentrations of 2.0 mg/mL and EPA 525 mix A (total of 12 PAHs – cat. # 48953-U) with concentration of 500 µg/mL – were both obtained from Supelco and served as the initial stock solutions. The surrogates (perylene-d12 and naphthalene-d8), as well as the internal standard (chrysene-d12), were purchased as neat materials and initial stock solutions of 1.0 mg/mL each were prepared in acetonitrile. All working standards were prepared from stock solutions by serial dilution in acetonitrile and stored in amber vials at 4 °C.

Due to unavailability of a commercially certified source, chicken eggs were obtained from a local farm and these served as the matrix for the preparation of the standard reference material (SRM). The avian egg samples for analysis were collected by our collaborators; the U.S. Geological Survey, U.S. Fish and Wildlife Service, and Minnesota Department of Natural Resources.

SAMPLE PREPARATION

Step 1: QuEChERS extraction

Weigh approximately 1.0 g of homogenized egg sample into an 8-mL disposable glass vial. Spike the samples with surrogate compounds and QC standards as needed. Add 5 mL of 1% formic acid in acetonitrile to all samples. In order to ensure an effective interaction between the sample and the solvent, vortex the vials to disrupt the formed egg mass. Add 1.5 g of QuEChERS powder (0.3 g sodium acetate + 1.2 g magnesium sulfate) to all samples and shake vigorously for 1 to 2 min. Centrifuge the vials at 3000 RPMs for 3 minutes.

Step 2: Ostro cleanup

Take 0.5 mL of the top organic layer and transfer it into an Ostro Plate Well for cleanup. Spike the sample with the internal standard solution and apply 10 to 15 psi pressure to draw the sample through the plate. Collect the eluate. To ensure complete transfer of PAHs through the Ostro material, pass an additional 0.25 mL of 100% acetonitrile through the well and collect eluate. Combine both eluates and transfer into LC vials or inject directly from the collection plate.

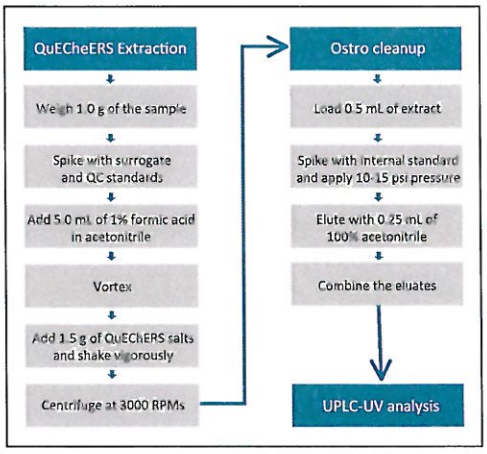

Figure 1. QuEChERS extraction followed by Ostro 96-well plate cleanup protocol.

Data was acquired using an ACQUITY PDA Detector operating (scanning 200 to 450 nm) under MassLynx Software v.4.1 control, followed by processing with QuanLynx™. The λ_{max} for each of the compounds are listed in Table 1. The correlation coefficient, R^2, ranged from 0.9972 to 0.9999 for all the analytes over three orders of magnitude. The method detection limit (MDL), accuracy and precision were calculated using results from the analysis of fortified chicken egg extracts injected in replicate. Standard Environmental Protection Agency protocols were followed and the results are shown in Table 2.

	1. Naphthalene	2. Acenaphthylene	3. Acenaphthene	4. Fluorene	5. Anthracene	6. Phenanthrene	7. Fluoranthene	8. Pyrene	9. Chrysene	10. Benzo(a)anthracene	11. Benzo(b)fluoranthene	12. Benzo(a)pyrene	13. Dibenz(a,h)anthracene	14+15. Benzo(g,h,i)perylene	14+15. Indeno(1,2,3-cd)pyrene
Method detection limit (n=7), spike concentration – 25 ng/mL															
Average %recovery	108.8	104.3	103.3	112.2	102.9	105.2	97.4	95.4	106.3	105.5	87.2	103.9	117.1	94.3	94.8
St. dev.	1.1	2.3	1.8	2.3	2.2	2.8	1.4	1.1	0.8	0.9	1.9	2.1	2.3	0.6	1.2
MDL (ng/mL)	3.5	7.1	5.6	7.2	7.1	8.7	4.5	3.6	2.7	2.7	6.1	6.6	7.1	1.7	3.7
Accuracy and precision (n=4), spike concentration – 400 ng/mL															
Average %recovery	97.0	97.5	96.4	97.2	98.3	96.7	94.0	93.2	97.2	92.1	89.3	87.1	89.0	89.6	105.5
%RSD	3.5	1.7	1.3	1.5	1.8	1.3	1.4	1.7	1.5	1.5	1.6	1.1	1.5	1.6	1.1

Table 2. MDL, accuracy, and precision results for 15 PAHs analyzed in chicken egg samples.

RESULTS AND DISCUSSION

As part of the initial evaluation step, a more generic technique was tested with the egg sample and acetonitrile being directly mixed inside the Ostro 96-well plate. This approach was unsuccessful since the viscous mixture did not allow the extraction solvent to pass through the plate. Additionally, aspiration and dispensing of such a viscous matrix was troublesome and a more effective method had to be employed. It was apparent that a completely new approach was required to utilize Ostro 96-well plates for this application. The combination of a quick and reliable QuEChERS extraction as the first step, followed by the Ostro cleanup, provided the desirable results. Acidified acetonitrile solution was initially added to the sample in order to "crash" out the proteins and served as a preliminary clean-up step. QuEChERS powder (magnesium sulfate and sodium acetate mix) was added to absorb the water present in the sample. To ensure the accuracy of results, quality control standards were added to samples prior to the addition of QuEChERS salts. Any analyte losses could therefore be accounted for from the earliest point in the sample preparation process.

The extraction efficiency of this new method is presented in the Table 2. It needs to be emphasized that a PDA detector was utilized for the quantification of PAHs which provided not only acceptable low detection limits associated with this analytical technique, but also high accuracy and precision. The recoveries for the MDL study were in the range of 87.2 to 117.1%, providing detection limits between 1.7 to 8.7 ng/mL. These low limits were achieved without incorporating a pre-concentration step prior to analysis as commonly used in most traditional techniques. In fact, samples are effectively diluted during this sample preparation protocol and this is only possible because of the extensive clean-up offered by the Ostro material. Figure 2 demonstrates the efficacy of this sample preparation protocol by comparing chromatograms resulting from chicken egg extracts with and without cleanup using Ostro material.

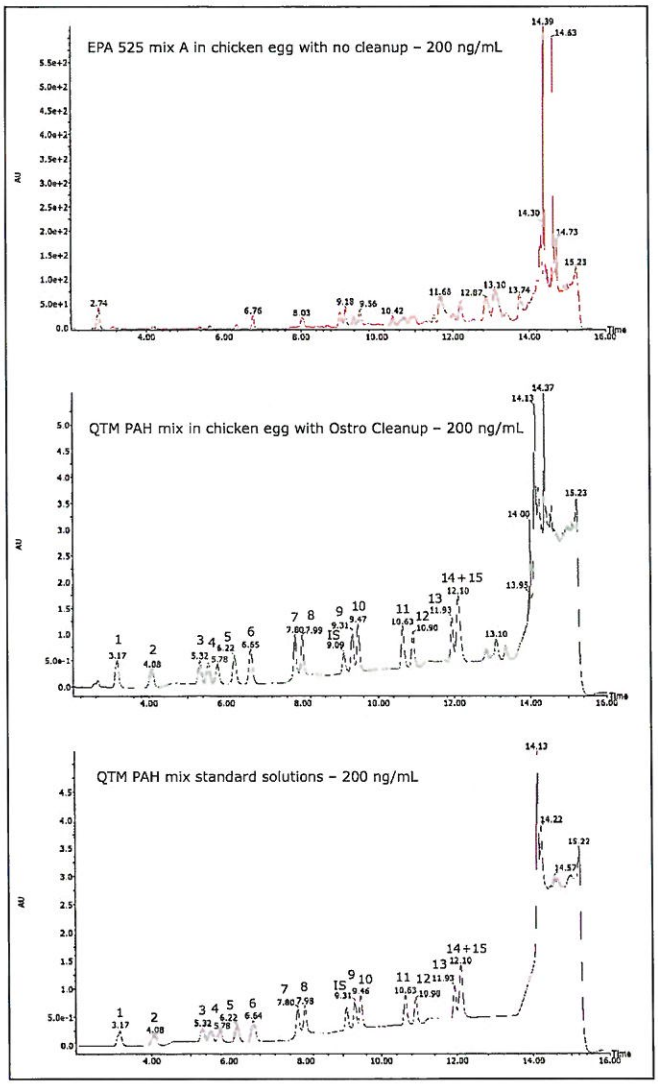

Figure 2. The results for chicken egg samples spiked with 200 ng/mL QTM PAH mix that were subject to Ostro cleanup and a chicken egg sample spiked with 200 ng/mL EPA 525 mix A with no cleanup. For peak anotation refer to Tables 2 and 3.

A set of 20 wild-caught eggs were analyzed as part of this development study and the results are shown in Table 3. For the matrix spike samples (MS1 and MS2) spiked with 200 ng/mL concentration of EPA 525 mix A, the method resulted in recoveries for all analytes ranging between 84.3 to 113.4%. Calibration verification standards CV1 (QTM PAH mix) and CV2 (EPA 525 mix A), at a concentration of 200 ng/mL, confirmed the linearity of the calibration curve and provided a check for any analyte degradation during sample preparation. With the recoveries ranging between 91.9% and 117.2%, no adjustment was necessary to account for degradation in these analyses. The analyte recoveries in the set of wild-caught egg samples were reported as total PAHs in ng/g (by wet weight). Individual compounds quantified at greater than the MDL are shown in Table 3.

Sample ID	Naphthalene-d8 (SUR.)	Perylene-d12 (SUR.)	Total PAH (ng/g)	1. Naphthalene	2. Acenaphthylene	3. Acenaphthene	4. Fluorene	5. Anthracene	6. Phenanthrene	7. Fluoranthene	8. Pyrene	9. Chrysene	10. Benzo(e)anthracene	11. Benzo(b)fluoranthene	12. Benzo(e)pyrene	13. Dibenz(a,h)anthracene	14+15. Benzo(g,h,i)perylene	14+15. Indeno(1,2,3-cd)pyrene
Wild-caught eggs																		
A-001	95.0	95.0	279.1	–	–	–	–	–	–	–	–	–	279.1	–	–	–	–	–
A-002	98.7	101.8	191.3	–	–	–	–	–	–	–	–	–	191.3	–	–	–	–	–
A-003	104.1	108.7	1354.6	–	–	933.2	–	421.4	–	–	–	–	–	–	–	–	–	–
A-004	113.2	102.5	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-005	86.1	86.9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-006	102.8	104.3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-007	112.8	103.9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-008	104.8	108.1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-009	76.2	85.2	1667.7	–	591.6	705.4	370.7	–	–	–	–	–	–	–	–	–	–	–
A-010	112.6	100.2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-011	100.2	103.2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-012	108.8	97.0	1470.6	–	1470.6	–	–	–	–	–	–	–	–	–	–	–	–	–
A-013	99.5	112.4	1455.0	–	–	–	–	–	–	1275.7	–	–	179.3	–	–	–	–	–
A-014	110.7	100.5	2610.2	–	1775.1	335.7	499.4	–	–	–	–	–	–	–	–	–	–	–
A-015	97.4	96.1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-016	97.7	95.4	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-017	99.7	98.6	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-018	96.6	101.8	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
A-019	93.8	102.9	4412.3	–	–	3093.0	–	888.0	–	431.3	–	–	–	–	–	–	–	–
A-020	98.2	95.0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Quality control standard recoveries																		
IB	N/A	N/A	N/A	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
MB	N/A	N/A	N/A	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
CV1	N/A	N/A	N/A	N/A	99.8	N/A	117.2	103.5	104.3	N/A	99.7	106.4	105.6	91.9	109.9	114.5	109.3	118.1
CV2	N/A	N/A	N/A	106.1	104.0	107.0	111.8	108.6	109.7	96.4	103.9	107.4	108.2	104.2	106.2	106.1	110.8	104.5
MS1	N/A	N/A	N/A	N/A	96.2	N/A	113.2	98.5	94.6	N/A	98.5	97.9	99.0	84.3	98.1	84.5	96.5	110.9
MS2	N/A	N/A	N/A	N/A	113.4	N/A	111.9	90.1	105.6	N/A	98.5	97.4	100.5	77.6	93.9	103.4	99.4	114.2
SRM	N/A	N/A	N/A	N/A	79.0	N/A	88.0	74.7	72.2	N/A	74.2	67.8	68.5	61.4	66.5	71.5	71.3	83.9

Table 3. Analytical results for 16 turtle and 4 avian egg samples reported in ng/g, and corresponding surrogates (naphthalene-d8 and perylene-d12) percent recoveries. IB – instrumental blank (acetonitrile), MB – chicken egg, CV1 – QTM PAH mix calibration verification (200 ng/mL), CV2 – EPA 525 mix A (200 ng/mL), MS1 and MS2 – wild caught egg matrix spike, SRM – standard reference material (chicken egg). MS1, MS2, and SRM all spiked with EPA 525 mix A at 200 ng/mL; (-) no detection, N/A – not applicable.

CONCLUSIONS

The combination of QuEChERS extraction and Ostro clean-up technologies proved to be an effective, efficient, and sensitive technique for analysis of 16 priority PAHs in an extremely complex biological matrix. This method provided excellent recoveries from the fortified wild-caught egg samples while minimizing matrix effects. In comparison to traditional extraction methods which use GPC followed by SPE cleanup and take several days to complete, this validated method reduced sample preparation time to just three hours for a batch of 20 samples. The reduced preparation time and high-throughput of the method resulted in increased laboratory productivity and a significant reduction in sample preparation costs. This method also required significantly less solvent volume which resulted in a more environmentally-friendly process. The simplicity of our developed and validated method, its robustness, and reproducibility, make it a viable alternative to more traditional approaches such as GPC and other normal phase cleanup strategies.

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[APPLICATION NOTE]

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Multi-Residue Analysis of Pharmaceuticals and Personal Care Products (PPCPs) in Water Using the ACQUITY UPLC H-Class System and the Xevo TQD Tandem Mass Spectrometer

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Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

- Extraction and concentration of low levels of compounds with a wide range of chemical diversity
- Use of a single LC-MS/MS method for separation and detection of PPCPs
- Quantification of PPCPs in the sub part-per-trillion range

WATERS SOLUTIONS

ACQUITY UPLC® H-Class System

Xevo® TQD

ACQUITY UPLC HSS Column

Oasis® Sample Extraction Products

TargetLynx™ Application Manager

KEY WORDS

environmental, personal care products, water, endocrine disruptors, PPCPs, PCPs

INTRODUCTION

In recent years, there has been increasing concern about the presence of pharmaceutical and personal care products (PPCPs)[1] in water bodies throughout the world. The effect of these emerging contaminants on human health and their potential impact on the environment is not yet fully understood. As concern continues to grow, many government agencies around the world are funding studies to assess if PPCPs can cause harmful ecological effects.

Many publications have shown that PPCPs are present at parts-per-trillion (PPT) levels in rivers and streams.[2-7] Methods therefore need to be able to detect compounds at these trace levels. In addition to the low level detection of PCPPs, a major analytical challenge for analysis lies in the wide chemical diversity of compound classes and structures, examples of which are shown in Figure 1. Furthermore, the complexity of the water samples requiring analysis can be very diverse. This application note demonstrates the extraction, separation, and detection of 78 PPCPs including acidic, basic, and neutral compounds in well and surface water samples.

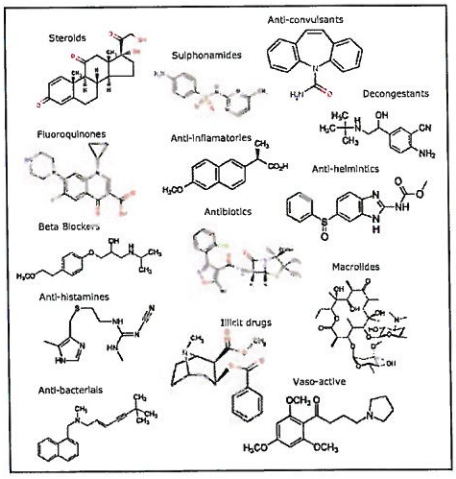

Figure 1. Example compounds from the range of pharmaceuticals and personal care products used in this work.

UPLC conditions

System:	ACQUITY UPLC H-Class
Runtime:	8.0 min
Column:	ACQUITY UPLC HSS T3 C_{18} 1.7 µm, 2.1 x 100 mm
Column temp.:	60 °C
Mobile phase A:	10 mM NH_4formate pH 3.2 in water
Mobile phase B:	10 mM NH_4formate pH 3.2 in methanol
Elution:	5 min linear gradient from 5% (B) to 95% (B)
Flow rate:	0.450 mL/min
Injection volume:	100 µL

MS conditions

MS system:	Xevo TQD
Ionization mode:	ESI+/-
Capillary voltage:	3.0 kV
Cone voltage:	30.0 V
Source temp.:	150 °C
Desolvation temp.:	550 °C
Desolvation gas:	1100 L/hr
Cone gas:	50 L/hr

Samples

Two different water sample types were collected for analysis and stored at 4 °C prior to analysis. In addition, a reagent grade water sample with low levels of the PPCPs of interest was purchased for comparative analyses and to serve as a blank.

Reagent grade water: LC-MS grade water (Fisher Chemical, Optima brand)

Well-water sample: Sample collected from a local, private well-water source

Surface water sample: Sample collected from a local water reservoir

Sample preparation

The extraction process was performed using a tandem cartridge configuration with a Waters® 6-cc Oasis MAX and a 6-cc Oasis MCX SPE cartridge. This configuration allows for a three-tiered extraction mechanism that uses reversed-phase, anion exchange, and cation exchange. The extraction protocol was designed to ensure retention of acidic, basic, and neutral PPCPs. The Oasis MCX Cartridge was connected below the Oasis MAX Cartridge, and both were conditioned by passing through 5 mL of methanol followed by 5 mL of water. The water samples (1 L) were loaded at 10 mL/min onto the dual stack by vacuum using a bottle-to-SPE adapter. Once the loading step was completed, the cartridge stack was disassembled and each cartridge followed specific wash and elution steps, as shown schematically in Figure 2. The Oasis MAX Cartridge was washed with 5 mL of 5% ammonium hydroxide in water. The elution was performed in two steps, first with 5 mL of methanol (neutral PPCPs), and second with 5 mL of methanol containing 5% formic acid (acidic PPCPs). Both elution fractions were collected in a 20-mL glass tube. The Oasis MCX Cartridge was washed with 5% formic acid and eluted with 5 mL methanol containing 5% ammonium hydroxide (basic PPCPs). The MCX and MAX elution fractions were pooled and evaporated to dryness at 60 °C under a gentle stream of nitrogen. The dried eluate was reconstituted with 900 µL (2x 450 µL) 10 mM ammonium formate. The internal standard mix (100 µL) was then added to give a final concentration of 1.0 ppb. Matrix-matched calibration standards were prepared with the same protocol with the exception of the final eluate, which was reconstituted in 800 µL (2x 400 µL) 10 mM ammonium formate, and 100 µL of the internal standard mix was added. The final 100 µL was utilized to post spike 100 µL of the PPCP mix at various concentrations in 10 mM ammonium formate. The standards for the majority of compounds were spiked at concentrations ranging from 0.1 to 5.0 ppb (0.1, 0.2, 0.25, 0.5, 1.0, 2.0, 2.5, and 5.0 ppb final concentration). This range equates to 0.1 to 5.0 ppt in the original sample.13 compounds demonstrated higher limits of detection and were therefore analyzed from 1.0 to 50.0 ppb (equivalent to 1.0 to 50.0 ppt in the water samples). These compounds were cefalexin, cinoxacin, codeine, corticosterone, dicloxacillin, erythromycin, gemfibrozil, ibuprofen, ketoprofen, naproxen, tolfenamic acid, triamcinolone, and warfarin. The internal standard mix consisted of three isotopically labeled standards: Cimetidine-d3-N-methyl-d3, Chlorpheniramine-d6-maleate-N,N dimethyl-d6, and Gemfibrozil-d6-2,2 dimethyl-d6 (purchased from C/D/N Isotopes Inc.).

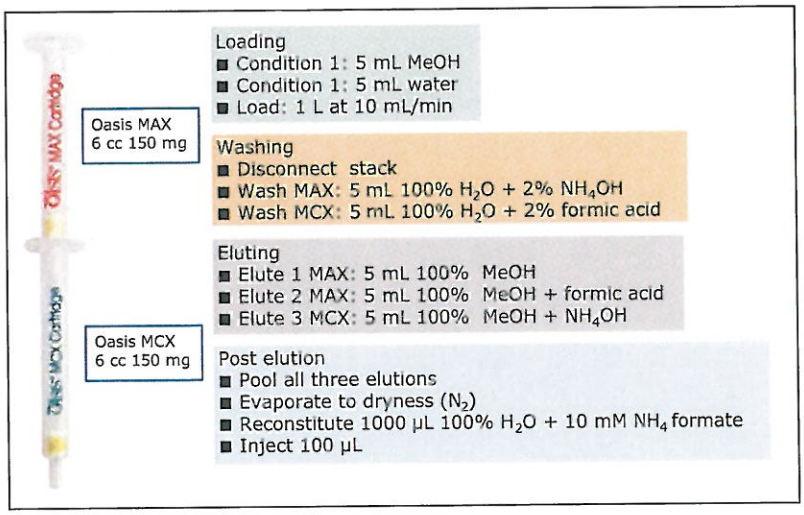

Figure 2. Schematic of solid phase extraction protocol for PPCPs in water.

LC-MS/MS

Two MRM transitions (quantification and confirmation) for the PPCPs were selected and optimized (Table 1). These results were added to the Quanpedia™ database for future use in our own and other laboratories. For this application, finding the optimum chromatographic conditions for the multi-residue analysis posed a difficult challenge due to the chemical diversity of PPCPs. The best chromatographic separation was achieved with a 2.1 x 100 mm ACQUITY UPLC HSS T3 analytical column (1.7 µm). The mobile phase that showed the best chromatography for the majority of compounds consisted of methanol/water with 10 mM ammonium formate (pH 3.2). Optima LC-MS grade methanol and water were purchased from Fisher Scientific.

Compound	Ion mode	Precursor ion	Cone	Product ion	CE	RT (min)
6a-Methylprednisolone	ESI +	375.4	30	357.3	10	6.00
				339.3	10	
Acetaminophen	ESI +	152.1	35	110.0	15	2.58
				93.0	20	
Atenolol	ESI +	267.2	40	145.1	25	3.40
				190.1	20	
Azithromycin	ESI +	749.5	30	158.2	40	5.13
				591.5	30	
Beclomethasone dipropionate	ESI +	521.3	25	503.3	10	7.03
				319.2	15	
Benzocaine	ESI +	166.1	25	138.1	15	5.06
				77.0	25	
Brimhexine	ESI +	377.1	30	114.1	15	6.05
				263.9	30	
Bufornedil HCl	ESI +	308.3	30	140.1	15	4.46
				237.1	15	
Carazolol	ESI +	299.2	30	116.1	15	4.76
				221.1	25	
Cefalexin	ESI +	348.2	40	158.0	20	5.76
				139.9	35	
Chlorphenamine	ESI +	275.2	25	230.1	15	5.14
				167.0	35	
Cimbuterol	ESI +	234.2	30	160.1	15	3.57
				143.1	25	
Cimetidine	ESI +	253.1	30	159.1	15	3.36
				117.1	15	
Cinoxacin	ESI +	263.2	35	245.1	15	4.79
				189.1	30	
Cocaine	ESI +	304.3	25	182.1	15	4.51
				82.0	25	
Codeine	ESI +	301.1	25	166.1	35	3.57
				216.1	25	
Corticosterone	ESI +	347.4	35	329.3	15	6.05
				311.2	15	
Cortisone	ESI +	361.3	40	163.1	25	5.61
				342.2	20	
Cotinine	ESI +	177.1	40	80.0	20	3.31
				98.0	20	
Dapsone	ESI +	249.2	40	156.0	15	3.89
				108.1	20	
Dexamethasone	ESI +	393.3	20	373.2	10	5.96
				355.2	10	
Dicloxacillin	ESI +	470.0	40	211.9	40	6.02
				254.0	25	
Diethylcarbamazine	ESI +	200.2	25	100.1	15	3.15
				72.0	25	
Difloxacin	ESI +	400.3	30	382.2	20	4.43
				356.2	20	
Digoxigenin	ESI +	391.5	30	355.3	15	5.00
				373.3	10	
Diltiazem	ESI +	415.2	30	178.1	20	5.51
				310.1	20	
Diphenhydramine	ESI +	256.1	20	167.1	5	5.20
				152.0	30	
Enrofloxacin	ESI +	360.3	25	342.3	20	4.28
				316.3	20	
Erythromycin	ESI +	734.50	30	158.1	30	5.89
				576.5	20	
Fleroxacin	ESI +	370.4	30	326.3	20	3.98
				269.3	25	
Flumequine	ESI +	262.1	35	244.0	15	5.60
				202.0	35	
Flumethasone	ESI +	411.4	25	391.2	5	5.85
				253.2	15	
Gemfibrozil	ESI -	249.1	30	121.0	10	7.06
				127.0	10	
Hydrocortisone	ESI +	363.4	35	121.1	25	5.73
				327.3	15	
Ibuprofen	ESI -	205.1	20	161.1	5	6.91
				NA		
Josamycin	ESI +	828.5	40	109	40	6.23
				174.2	35	
Ketoprofen	ESI -	253.1	20	209.1	5	6.02
				NA		
Levamisole (tetramisole)	ESI +	205.2	25	178.1	20	3.68
				91.1	30	
Lincomycin	ESI +	407.2	40	126.1	25	4.00
				359.3	20	
Metoprolol	ESI +	268.2	40	116.1	15	4.58
				74.1	20	
Miconazole	ESI +	417.1	40	161.1	30	7.12
				69.0	25	

Compound	Ion mode	Precursor ion	Cone	Product ion	CE	RT (min)
Nalidixic acid	ESI +	233.1	30	215.0	15	5.45
				187.0	25	
Naproxen	ESI -	229.0	20	170.1	15	6.12
				185.0	10	
Ofloxacin	ESI +	362.3	25	318.3	20	4.06
				261.3	30	
Ordendazole	ESI +	316.1	40	159.0	30	5.29
				284.1	20	
Oxprenolol	ESI +	266.2	35	72.1	20	4.83
				116.1	15	
Penicillin G	ESI +	335.1	40	217.0	20	5.38
				317.0	20	
Praziquantel	ESI +	313.2	40	203.1	15	6.23
				83.1	25	
Procaine	ESI +	237.2	25	100.1	15	3.45
				120.0	25	
Promethazine	ESI +	285.2	25	86.1	15	5.59
				198.1	25	
Pyrimethamine	ESI +	249.2	40	177.1	30	4.95
				233.1	30	
Ranitidine	ESI +	315.2	25	176.1	15	3.38
				130.1	25	
Rifaximin	ESI +	786.5	40	151.1	45	6.61
				754.5	30	
Roxithromycin	ESI +	837.6	40	158.1	35	6.30
				679.5	20	
Salbutamol (albuterol)	ESI +	240.1	30	148.0	15	3.36
				222.1	10	
Sparfloxacin	ESI +	393.3	30	349.3	20	4.64
				292.3	25	
Sulfabenzamide	ESI +	277.1	30	156.0	15	4.45
				92.0	25	
Sulfadiazine	ESI +	251.1	30	156.0	15	3.41
				92.0	25	
Sulfadimethoxine	ESI +	311.1	40	156.0	15	4.78
				92.0	25	
Sulfadoxine	ESI +	311.3	40	156	15	4.40
				108.0	25	
Sulfamerazine	ESI +	265.1	35	92.0	25	3.72
				156.0	15	
Sulfamidine	ESI +	281.1	35	92.0	25	3.90
				156.0	15	
Sulfamethazine	ESI +	279.1	35	186.0	15	4.13
				124.1	25	
Sulfamethizole	ESI +	271.1	30	156.0	15	3.93
				92.0	25	
Sulfamethoxazole	ESI +	254.1	30	92.0	25	4.18
				156.0	15	
Sulfamethoxypyridazine	ESI +	281.1	35	92.0	25	4.09
				156.0	15	
Sulfapyridine	ESI +	250.1	35	92.0	25	3.68
				156.0	15	
Terbinafine	ESI +	292.3	35	141	10	6.37
				93.0	15	
Ternidazole	ESI +	186.2	30	128.1	15	3.80
				82.0	25	
Tiamulin	ESI +	494.4	30	192.0	15	5.72
				119.0	30	
Ticlopidine	ESI +	264.1	30	125.0	25	5.32
				154.0	15	
Tilmicosin	ESI +	869.5	25	174.2	45	5.44
				696.5	40	
Tolbutamide	ESI +	271.1	30	91.0	30	5.77
				74.0	10	
Tolfenamic acid	ESI -	260.1	35	216.0	15	7.09
				180.0	15	
Triamcinolone	ESI +	395.4	30	375.0	10	4.80
				357.0	30	
Triamcinolone acetonide	ESI +	435.4	25	397.3	15	6.06
				415.3	5	
Triclocarban	ESI +	315.1	40	162.0	20	6.98
				128.0	30	
Trimethoprim	ESI +	291.3	40	123.0	30	3.95
				230.2	30	
Tripelidine	ESI +	279.1	25	208.2	15	5.26
				193.2	35	
Tulobuterol	ESI +	228.2	30	154.1	15	4.69
				118.0	25	
Warfarin	ESI -	307.1	40	161.0	20	6.22
				250.0	25	
Xylazine	ESI +	221.1	40	90.0	20	4.43
				164.0	25	

Table 1. MRM tuning parameters and retention times for the PPCPs.

RESULTS AND DISCUSSION

Despite the chemical diversity of the compounds analyzed, excellent chromatographic profiles were obtained for all 82 compounds. Example chromatograms for the different classes of compounds are shown in Figure 3. Of the 82 PPCPs included in this work, 78 were found to be effectively extracted using the dual-cartridge SPE methodology. Five compounds (digoxigenin, fleroxacin, erythromycin, 6a-methylprednisolone, and tolbutamide) gave poor recoveries in the well water and surface water samples using this extraction protocol, although they were acceptable for the reagent water sample. Those compounds were therefore excluded from the quantitative analysis.

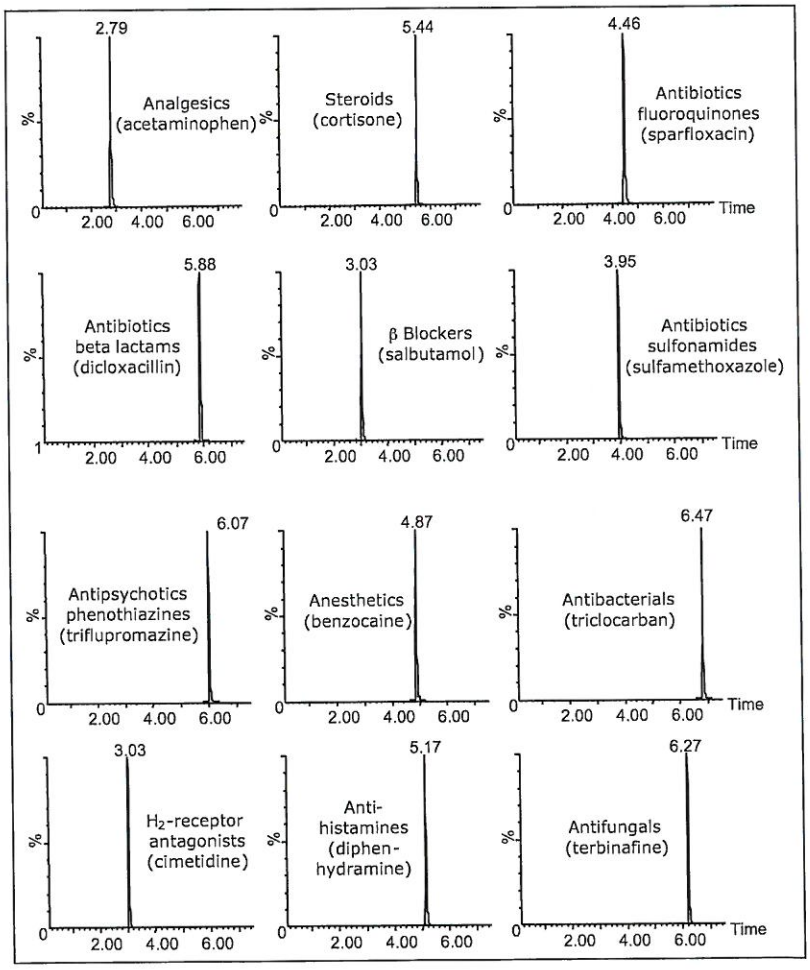

Figure 3. Example MRM chromatograms for compounds from the different classes of PPCPs represented in this work.

To ensure that the method did not result in carryover or false detections of PPCPs, blank reagent water samples were tested to find a clean water source that could be used as a blank sample and in order to create calibration standards. After screening several sources, Optima LC-MS grade water (Fisher Scientific) gave the best results. A blank sample of this reagent water was enriched using the SPE protocol. This extracted sample was analyzed and compared to post-spike samples of the same extract. From this work an estimation of the background level of the PPCPs in the reagent water could be made to determine whether it was sufficiently devoid of the target PPCPs. The results demonstrated that only four PPCPs were detected above the 100 ppq level in the reagent water sample (Table 2). Those compounds were enrofloxacin, fleroxacin, rifaximin, and diltiazem. These compounds were deemed to be present at levels between 100 ppq and 1 ppt in the reagent water. None of the compounds were found to have a response in the reagent water above 1 ppt. 46 compounds were detected below the lowest calibration point and 28 PPCPs were not detected at all in the reagent water blank.

Compound	Level detected	Compound	Level detected	Compound	Level detected
6a-Methylprednisolone	ND	**Enrofloxacin**	<1.0 ppt	Salbutamol (albuterol)	<0.1 ppt
Acetaminophen	<0.1 ppt	Erythromycin	ND	Sparfloxacin	<0.1 ppt
Atenolol	<0.1 ppt	**Fleroxacin**	<1.0 ppt	Sulfabenzamide	ND
Azithromycin	<0.1 ppt	Flumequine	<0.1 ppt	Sulfadiazine	ND
Beclomethasone dipropionate	ND	Flumethasone	ND	Sulfadimethoxine	<0.1 ppt
Benzocaine	<0.1 ppt	gemfibrozil	ND	Sulfadoxine	ND
Bromhexine	<0.1 ppt	Hydrocortisone	ND	Sulfamerazine	<0.1 ppt
Buflomedil HCl	<0.1 ppt	Ibuprofen	ND	Sulfameter	ND
Carazolol	<0.1 ppt	Josamycin	<0.1 ppt	Sulfamethazine	ND
Cefalexin	ND	ketoprofen	ND	Sulfamethoxazole	<0.1 ppt
Chlorpheniramine	<0.1 ppt	Levamisole (tetramisole)	<0.1 ppt	Sulfamethoxypyridazine	ND
Cimbuterol	<0.1 ppt	Lincomycin	<0.1 ppt	Sulfapyridine	ND
Cimetidine	<0.1 ppt	Metoprolol	<0.1 ppt	Terbinafine	<0.1 ppt
Cinoxacin	<0.1 ppt	Miconazole	<0.1 ppt	Ternidazole	<0.1 ppt
Cocaine	<0.1 ppt	Nalidixic acid	<0.1 ppt	Tiamulin	<0.1 ppt
Codeine	ND	naproxen	ND	Ticlopidine	<0.1 ppt
Corticosterone	<0.1 ppt	Ofloxacin	<0.1 ppt	Tilmicosin	<0.1 ppt
Cortisone	ND	Oxfendazole	<0.1 ppt	Tolbutamide	ND
Cotinine	<0.1 ppt	Oxprenolol	<0.1 ppt	tolfenamic acid	ND
Dapsone	<0.1 ppt	Praziquantel	ND	Triamcinolone	ND
Dexamethasone	ND	Procaine	<0.1 ppt	Triamcinolone acetonide	ND
Dicloxacillin	ND	Promethazine	<0.1 ppt	Trimethoprim	<0.1 ppt
Difloxacin	<0.1 ppt	Pyrimethamine	<0.1 ppt	Tripolidine	<0.1 ppt
Digoxigenin	ND	Ranitidine	<0.1 ppt	Tulobuterol	<0.1 ppt
Diltiazem	<1.0 ppt	**Rifaximin**	<1.0 ppt	warfarin	ND
Diphenhydramine	<0.1 ppt	Roxithromycin	<0.1 ppt	Xylazine	<0.1 ppt

Table 2. Results from the analysis of blank reagent water extract to determine levels of detected compounds. Any compounds that showed a response are indicated. Compounds that showed a response lower than the response of the post-spiked 0.1 ppt are labeled <0.1 ppt. Four compounds were detected above 0.1 ppt but below the 1.0 ppt level and are shown in ***bold*** *text. Compounds that did not show any response in the blank reagent water extract are labeled ND (not detected).*

Figure 4 shows the MRM chromatograms (quantification transition) of four selected PPCPs that were not detected at all in the reagent water standard. The blank extracted reagent water and spiked extracted reagent water are shown together to demonstrate the response that would equate to 0.1 ppt (100 ppq) in the non-extracted sample.

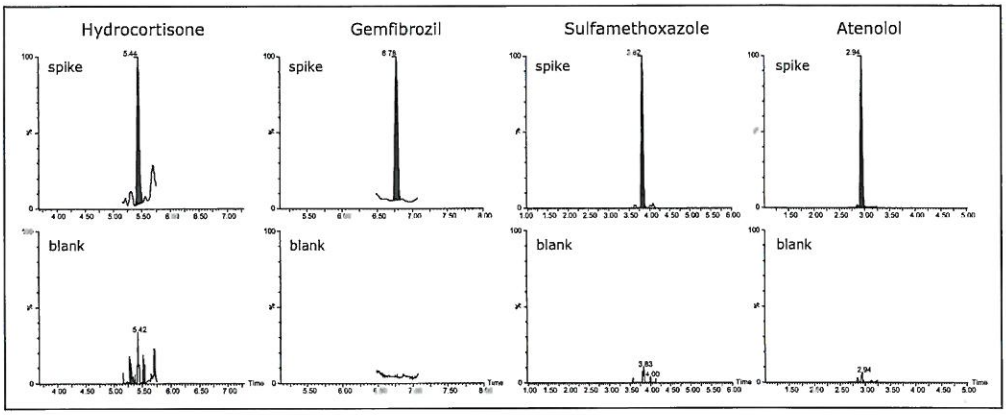

Figure 4. MRM chromatograms for example compounds that demonstrate blank responses in the extracted reagent water. The chromatograms in the top row demonstrate the expected response for the example compounds at the 0.1 ppt level (post-spiked into extracted reagent water). The bottom row shows the response in the blank extract of the reagent water.

In order to assess the quantitative capabilities of the method, three selected deuterated compounds were used as internal standards. Along with the reagent water, a well water sample, and surface water sample were used to demonstrate the method performance in different water matrices. From the 78 PPCPs applicable to this extraction protocol, excellent quantification results were obtained for 58 of the compounds with this initial work employing three of the selected deuterated compounds as internal standards. Further work with additional internal standards is required for the remaining compounds. Recoveries of those 58 compounds at the 1-ppt spike level are shown in Figure 5. For the PPCPs with appropriate internal standards, the R^2 value ranged from 0.991 to 0.997 (linear fit, 1/x weighting). The internal standard used and linear regression R^2 value for each of the compound are described in Table 3.

Compound	Internal standard used	R^2	Compound	Internal standard used	R^2
Nalidixic acid	Cimetidine-d3	0.994	Tulobuterol	Cimetidine-d3	0.996
Rifaximin	Chlorpheniramine-d6	0.994	Cimbuterol	Cimetidine-d3	0.997
Trimethoprim	Cimetidine-d3	0.991	Chlorpheniramine	Chlorpheniramine-d6	0.993
Erythromycin	Chlorpheniramine-d6	0.995	Cimetidine	Cimetidine-d3	0.997
Josamycin	Cimetidine-d3	0.993	Promethazine	Chlorpheniramine-d6	0.993
Lincomycin	Cimetidine-d3	0.993	Tripolidine	Chlorpheniramine-d6	0.993
Roxithromycin	Chlorpheniramine-d6	0.994	Diphenhydramine	Chlorpheniramine-d6	0.995
Tilmicosin	Chlorpheniramine-d6	0.994	Ranitidine	Cimetidine-d3	0.994
Azithromycin	Chlorpheniramine-d6	0.994	Acetaminophen	Cimetidine-d3	0.995
Tiamulin	Cimetidine-d3	0.991	Cocaine	Cimetidine-d3	0.996
Sulfadiazine	Cimetidine-d3	0.996	Codeine	Cimetidine-d3	0.992
Sulfadoxine	Cimetidine-d3	0.995	Dapsone	Cimetidine-d3	0.993
Sulfamerazine	Cimetidine-d3	0.995	Pyrimethamine	Chlorpheniramine-d6	0.996
Sulfameter	Cimetidine-d3	0.995	Terbinafine	Chlorpheniramine-d6	0.993
Xylazine	Cimetidine-d3	0.993	Ternidazole	Cimetidine-d3	0.995
Bromhexine	Chlorpheniramine-d6	0.996	Miconazole	Chlorpheniramine-d6	0.991
Buflomedil HCl	Chlorpheniramine-d6	0.994	Levamisole (tetramisole)	Cimetidine-d3	0.993
Ticlopidine	Chlorpheniramine-d6	0.994	Oxfendazole	Cimetidine-d3	0.995
Gemfibrozil	Gemfibrozil-d6	0.994	Praziquantel	Cimetidine-d3	0.994
Warfarin	Gemfibrozil-d6	0.992	Benzocaine	Cimetidine-d3	0.995
Procaine	Cimetidine-d3	0.993			

Table 3. Assignment of the most appropriate internal standard for compound quantification. The resulting R^2 value for the calibration curve is also reported.

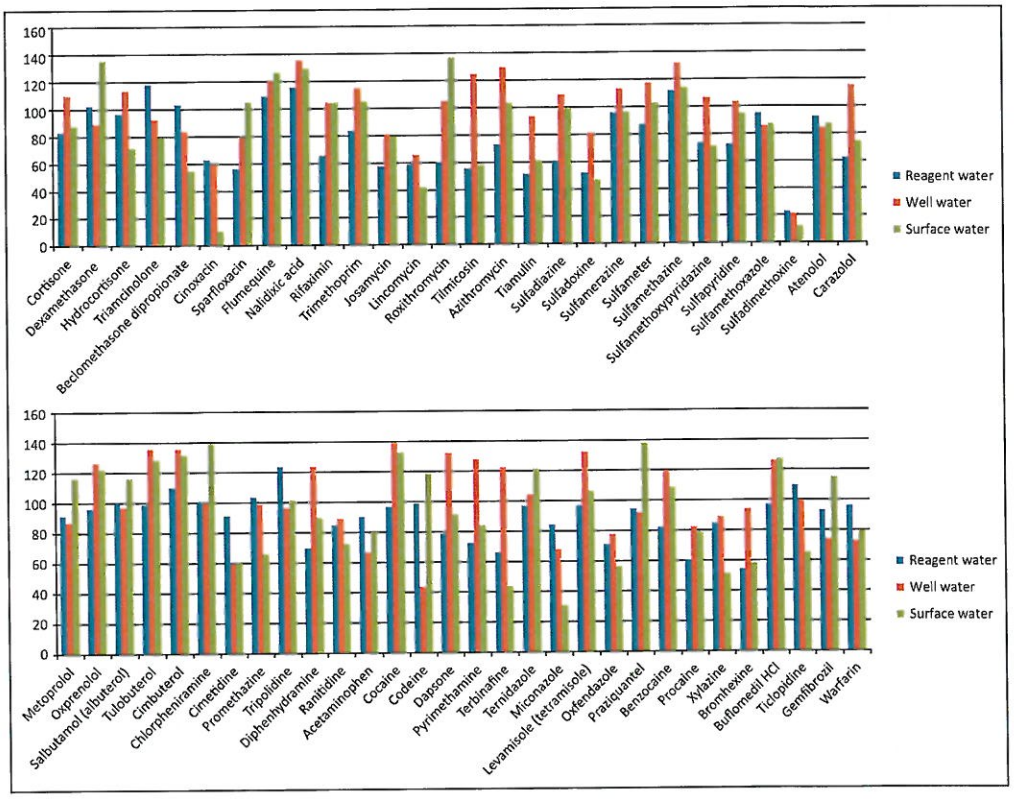

Figure 5. Column chart showing calculated recovery in different water matrices for a 1 ppt spike.

To assess the matrix effects in the three water samples, the response of a standard in non-extracted reagent water was compared to the post-spike extracted samples of the reagent water, the well water sample, and the surface water sample at the 1 ppt level, which are shown in Figure 6. The majority of PPCPs in the reagent water showed a matrix effect of <20%. This clearly indicates the cleanliness of this water sample. For the well and surface water samples, more than half of the PPCPs showed matrix effects of >20%. The surface water samples showed significantly higher complexity, with approximately one-third of the compounds showing a >50% matrix effect, shown in the orange pie sections of Figure 6. Since the extraction protocol was optimized for maximum trapping efficiency of a wide range of compound types, both extraction cartridges were subjected only to a mild wash protocol to ensure no compound breakthrough before final elution. With this mild wash, it is expected that complex water samples will still potentially show matrix effects compared to a clean sample, such as the reagent water. In order to contend with the high complexities, additional wash steps within the SPE protocol could be employed. Further investigation into the most appropriate internal standards could also help to account for heavy matrix loads. Other work,[2] has showed similar effects for two distinct surface water samples.

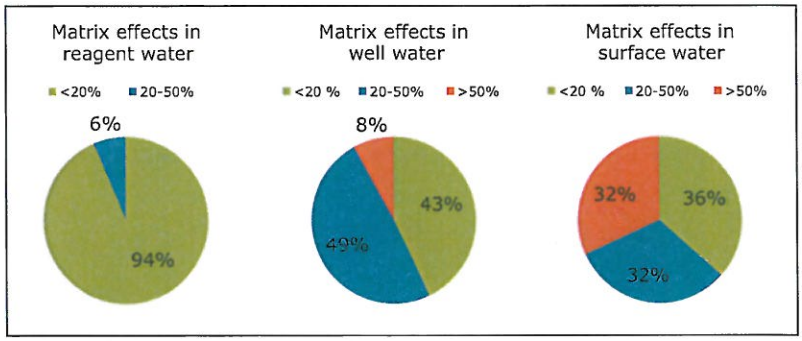

Figure 6. Pie charts showing the level of the matrix effects on the different PPCPs in three different water sample types. Low matrix effect (<20%) is shown in green; medium matrix effect (20% to 50%) is shaded blue; high matrix effect (>50%) is colored orange. The percentage of compounds showing the specified matrix effect are labeled on the pie segments.

The extraction method was used to evaluate the current PPCP level in the well and surface water samples. In well water, two PPCPs tested positive above the 100 ppq level: sulfamethoxazole at 0.97 ppt and atenolol at 0.32 ppt, and 14 PPCPs were detected below this level. For the surface water sample, 17 PPCPs were detected below 100 ppq. An example of a detected compound in each of the samples is shown in Figure 7. To demonstrate a blank sample, the equivalent compound trace for the other sample is also shown with the baseline magnified to show the noise level.

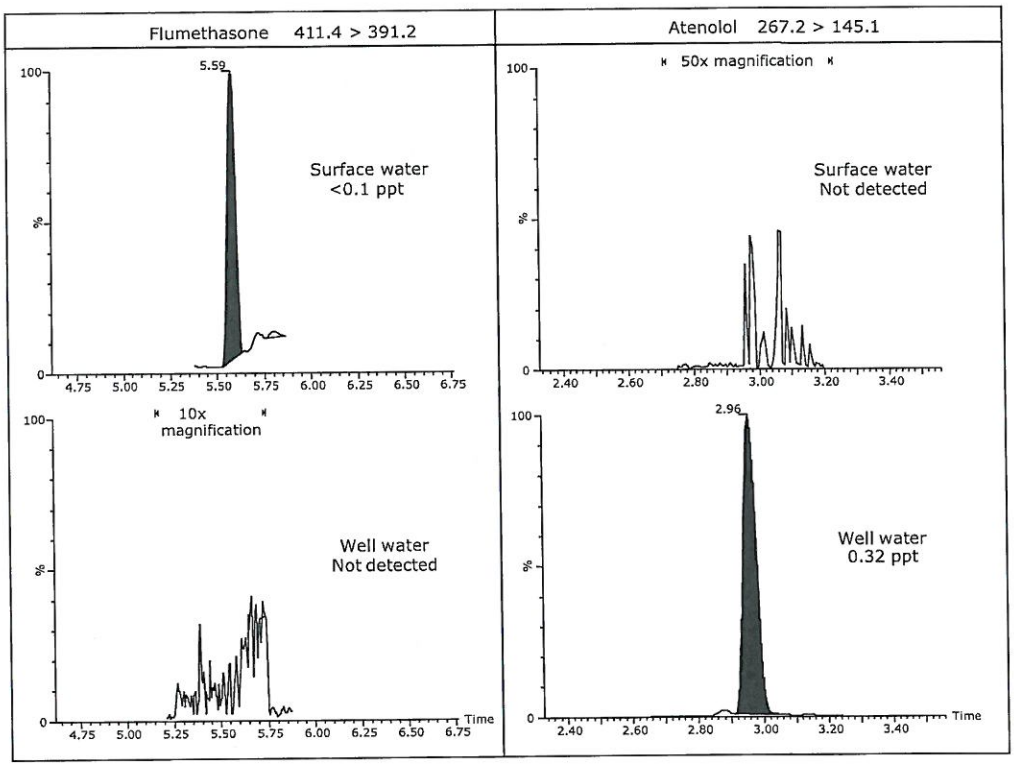

Figure 7. Example compounds that were detected as incurred residues in surface water (flumethasone) and well water (atenolol). To demonstrate a blank sample, the baseline of the sample that did not show the compound detection is shown with the noise level magnified.

CONCLUSIONS

- A method for the extraction, concentration, and quantification of diverse PPCPs including acidic, basic, and neutral compounds was developed.
- Using the ACQUITY UPLC H-Class System with the small, benchtop Xevo TQD, it was possible to analyze all compounds in a single injection.
- Sensitive detection was achieved with limits of detection in the sub parts per trillion range, and incurred residues were detected in both a surface water and a well water sample.

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[APPLICATION NOTE]

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Identification of Potential Metabolites of Pharmaceutical Residues Detected in an Environmental Water Sample

Gareth Cleland, Mark Wrona, Lauren Mullin, and Jennifer Burgess
Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

- HRMS Screening of a large target list, with adducts
- Fast UPLC® analysis with the ACQUITY UPLC® HSS C_{18} Column
- Incurred residue metabolite identification

WATERS SOLUTIONS

Screening Platform Solution with UNIFI®

ACQUITY UPLC I-Class System

Xevo® G2-S QTof Mass Spectrometer

ACQUITY UPLC HSS 1.7 µm, C_{18} Column

KEY WORDS

Pharmaceuticals, personal care products, PPCPs, pesticide, environmental water sample, UNIFI, screening, HRMS, metabolite identification, pesticide screening

INTRODUCTION

In recent years, there has been increasing concern regarding the presence of pesticides, pharmaceuticals, and personal care products (PPCPs) in water bodies throughout the world.[1] A greater demand is being placed on techniques not only used to screen for these compounds, but to screen for the presence of their metabolites.

Data obtained from a non-targeted acquisition on a high resolution mass spectrometer can be used to target a theoretical unlimited number of compounds. Moreover, information rich datasets collected using UPLC-MS^E can be used to reduce the large number of false detects that arise when targeting a large number of compounds verses accurate mass as a sole point of contaminant identification. MS^E provides accurate mass measurements for both precursor and fragment ion information in a single experiment by alternating scans between low and high collision energies. In combination with UNIFI, an integrated scientific information system, it is now possible to screen for the presence of PPCPs, their adducts, and potential metabolites in a routine laboratory environment.

Previous work presented described the use of the Waters Screening Platform Solution in combination with Waters' toxicology library to initially screen a local well water sample for the presence of a large number (>1000) of PPCPs, pesticides and drugs of abuse.[2] In this application note, we have processed the same dataset with the metabolite identification aspect of the integrated software system to isolate known and potential metabolites of the confident screening matches in the dataset. Once discovered, metabolites were made available for future screening experiments by adding the detection results (retention time and identified fragment ions) into a scientific library.

EXPERIMENTAL

A locally obtained well water sample was enriched one thousand times as previously described.[2,3] A comprehensive dataset, collected using UPLC-MS^E was obtained within UNIFI. The toxicology screening solution within UNIFI contains pre-defined LC-MS conditions and processing parameters. The toxicology library in UNIFI is comprised of over 1000 compounds including many PPCPs, such as drugs of abuse, veterinary medicines, and pharmaceuticals. Library entries also contain retention times and accurate theoretical fragment masses. Experimental conditions, sample preparation protocols, and data processing parameters are available in a previous application note by the same authors.[2]

RESULTS AND DISCUSSION

From a previous application note,[2] the screening of a local well water sample against the full toxicology library in UNIFI, with up to three adducts (H^+, Na^+, K^+), indicated the presence of the four compounds shown in Table 1.

Component na...	Formula	m/z	Retention Time Error (min)	Mass error (ppm)	Identified High Energy Fragments	Response	Adducts
Carbamazepine	C15H12N2O	237.1021	0.01	0.62	3	10282	+H
Mexazolam	C16H13N4	141.1136	0.38	0.82	3	40806	+H
Imidacloprid	C9H10ClN5O2	256.0597	0.38	0.66	1	7967	+H
Tramadol	C16H25NO2	264.1956	0.42	-0.68	1	16459	+H

Table 1. Component summary table in UNIFI showing details of confident matches made during a screening of the extracted well water sample against a library of over 1000 compounds.

The inclusion of retention times and accurate mass fragment ions in the toxicology screening library allowed for confident matches to be made since they were based on more information other than accurate mass of the precursor ions alone. As indicated, this is critical for reducing false detection rates, enabling rapid data review for screening experiments.

Further investigation of the comprehensive dataset was possible using the metabolite identification functionality of UNIFI's screening solution software.

This functionality requires a target molecule with mol file and a list of possible transformations, that are shown in Figure 1.

Selected transformations

	Name	Delta Mass (Da)	Formula	Classifier
1	Ketone to alcohol	2.0157	+H2	Phase I
2	Oxidation	15.9949	+O	Phase I
3	Glucosylation	162.0528	+C6H10O5	Phase II
4	Methylation of alcohol	14.0157	+CH2	Phase II
5	Glucuronide conjugation of anything	176.0321	+C6H8O6	Phase II
6	Sulfate conjugation	79.9568	+SO3	Phase II

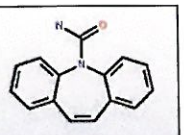

Figure 1. Transformations and an example mol file used to identify potential metabolites of compounds found in a screening experiment.

Primarily, using chemical intelligence,[4] the target mol file is systematically cleaved. This essentially increases the target list to include parent compounds and potential breakdown products in the metabolite search. Interrogation of the low energy function of the MS^E comprehensive dataset was performed, which automatically extracted the masses corresponding to the parent as well as the permutations of provided transformations, with and without systematic cleavages of the parent molecule. The list of possible metabolites for carbamazepine is shown in Table 2 and Figure 2.

No metabolites were observed for the other three compounds found in the screening experiment.

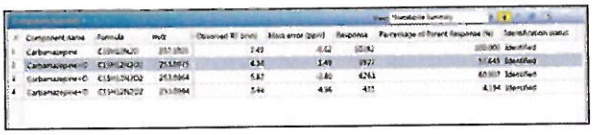

Table 2. Component summary of potential metabolites found for carbamazepine using the transformations and mol file shown in Figure 1.

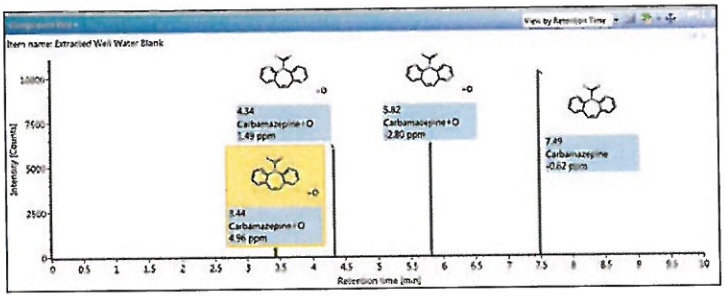

Figure 2. Component plot showing potential metabolites found for carbamazepine using the transformations and mol file shown in Figure 1.

Figures 3 and 4 show the full UI information details for the identification of carbamazepine and a carbamazepine oxidation respectively. Fragment match functionality within UNIFI uses similar intelligence as the cleavage algorithm above. It systematically dissects the mol file of the parent or proposed metabolite and assigns potential accurate mass fragment ions from the high energy function of the MS^E data. Identified fragment ions are annotated, as shown in Figure 3 for the mass 194.06691 Da, and in Figure 4 for the masses 210.09098 Da and 236.07105 Da.

Figure 3. Full user interface (UI) information within UNIFI showing identification details of the carbamazepine parent. Component summary shows identification details while the chromatogram shows extracted ion chromatograms of all identified components with the component highlighted in the component summary. The spectra section shows precursor and fragmentation spectra for the highlighted component.

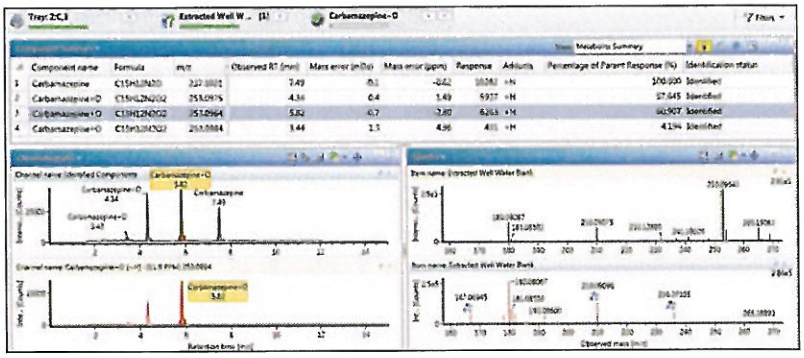

Figure 4. Full user interface (UI) information within UNIFI showing identification details of a proposed carbamazepine metabolite. Component summary shows identification details while the chromatogram shows extracted ion chromatograms of all identified components with the component highlighted in the component summary. The spectra section shows precursor and fragmentation spectra for the highlighted component.

Just as in screening experiments, the high energy fragment ions provided increased confidence that identified metabolites were correct. Common fragment and neutral loss discovery tools, readily available in UNIFI, can also be used to enhance the confidence in metabolite identification. Figure 5 shows the results of running a common fragment search. The two +O metabolites of carbamazepine at 4.3 and 5.8 minutes are shown to be related to each other by the fragment 210.0910 Da, which is the loss of 43.005 Da from the parent 253.0964 Da. This is the same neutral loss from the carbamazepine parent (237.1021 Da) to the primary fragment (194.0969 Da) thus giving further confidence in the metabolites identified.

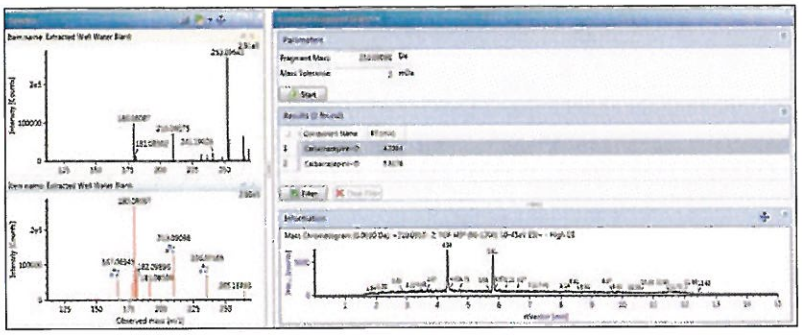

Figure 5. Results from a common fragment search of 210.09098 Da, performed within the elucidation toolset in UNIFI.

Once the presence of a metabolite has been confirmed, the entry can be easily exported to an existing or new scientific library within UNIFI with the right click of the mouse, as shown in Figure 6. Details such as formula, retention time, theoretical accurate mass fragment ions, and spectra are made available for future users and analyses.

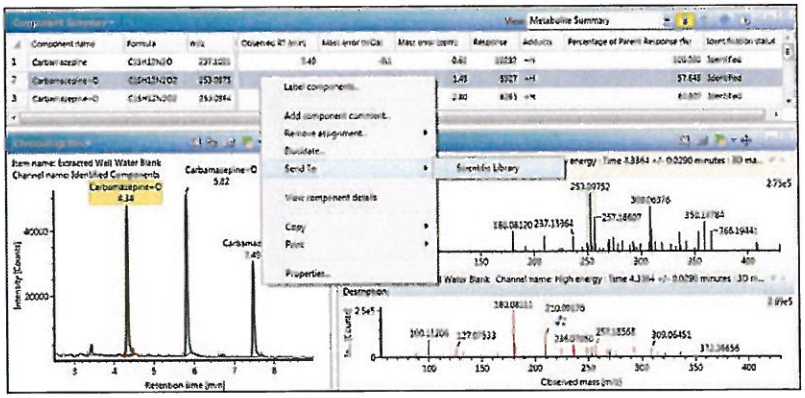

Figure 6. Sending reviewed metabolites to UNIFI's scientific library.

CONCLUSIONS

- Information rich MS^E acquisition and an integrated scientific information system make it possible to screen for the presence of compounds of interest, their adducts, and potential metabolites in a routine laboratory environment.
- The presence of retention times and accurate mass fragment ions in scientific libraries within UNIFI allowed identifications to be made on more information than accurate mass of the precursor ions alone. This proves critical for reducing false detection rates and enabling rapid data review for screening experiments.
- Using the metabolite identification functionality of UNIFI, three metabolites of carbamazepine were identified with confidence in an enriched local well water sample.
- Identified metabolites can easily be added to UNIFI's scientific library to expand the list of compounds targeted in future screening analyses.

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[APPLICATION NOTE]

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Screening Environmental Samples for a Diverse Range of Compounds With Accurate Mass LC-MS and an Integrated Scientific Information System

Gareth Cleland, Claude Mallet, and Jennifer Burgess
Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

- High resolution mass spectrometry (HRMS) screening of a large target list of diverse compound classes and structures.
- Faster UPLC® analysis with the ACQUITY UPLC® HSS C_{18} Column.
- Accurate mass precursor and fragment ion information integrated into the identification and review process.

WATERS SOLUTIONS

Waters® Screening Platform Solution with UNIFI®

ACQUITY UPLC I-Class System

Xevo® G2-S QTof Mass Spectrometer

ACQUITY UPLC HSS Column

KEY WORDS

Pharmaceuticals, personal care products, PPCPs, environmental water sample, UNIFI, screening, HRMS

INTRODUCTION

The presence of an increasingly complex array of pharmaceuticals and personal care products (PPCPs)[1] in water bodies throughout the world is placing a greater demand on techniques used to screen for these compounds. Figure 1 illustrates an example of the range of PPCP compounds and classes.

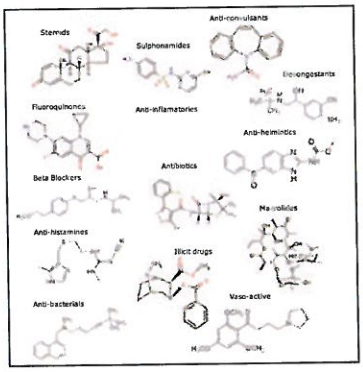

Figure 1. Examples of the range of compounds and classes describing PPCPs.

Conventional MS/MS screening methods, utilizing a tandem mass spectrometer, have target list limitations as the maximum duty cycle of the instrument is achieved. Data obtained from a non-targeted acquisition on a high resolution mass spectrometer can be used to target a theoretical unlimited number of compounds. Moreover, information rich datasets collected using UPLC/MS^E can be used to reduce the large number of false detects that arise when targeting a large number of compounds with accurate mass as the sole point of contaminant identification. MS^E provides accurate mass measurements for both precursor and fragment ion information in a single experiment.

In combination with UNIFI, an integrated scientific information system, it is now possible to screen for the presence of PPCPs, their fragments, adducts, and potential metabolites in a routine laboratory environment. This application note describes the use of Waters Screening Platform Solution in combination with the UNIFI Toxicology library to screen a local well water sample for the presence of a large number (>1000) of PPCPs, pesticides, and drugs of abuse.

EXPERIMENTAL

Sample preparation

The following samples were prepared.

PPCP standards: High level standards (10 µg/L) in UHPLC-grade water

Extracted blank: Treated as a reference. A UHPLC-grade water sample (Fisher Optima), enriched using the protocol in Figure 2.

Extracted well water sample: Treated as the unknown. A well water sample enriched as above.

Extracted well water sample, post spike: Enriched as above and post spiked with the 35 PPCPs in Table 1 at a level of 1 µg/L.

Extracted well water sample, pre spike: Well water sample pre-spiked with the 35 PPCPs described in Table 1 (at 1 ng/L) then enriched as above. Pre-spike samples were prepared in duplicate.

Non-extracted well water: Well water sample neither enriched nor spiked.

Extracted calibration standards: Eight levels (1.0, 2.0, 2.5, 5.0, 10.0, 25.0, and 50.0 ng/L) of the 35 PPCPs in Table 1 spiked into the UHPLC-grade water and enriched as above.

LC-MS conditions

Comprehensive datasets were collected using UPLC/MS^E data acquisition. MS^E uses parallel low and elevated collision energy MS acquisition to provide accurate mass precursor and product ion information in a single injection.

UPLC conditions

LC system:	ACQUITY UPLC I-Class
Runtime:	15.00 min
Flow rate:	0.40 mL/min
Injection:	100.0 µL
Column:	ACQUITY UPLC HSS C_{18} 1.8 µm, 2.1 x 150 mm
Column temp.:	50 °C
Mobile phase A:	Water with 5 mM NH_4HCO_2 adjusted to pH 3.0 with formic acid
Mobile phase B:	Acetonitrile with 0.1% (v/v) formic acid

Time	Flow rate mL/min	Composition A	Composition B	Curve
0.00	0.400	87.0	13.0	Initial
0.50	0.400	87.0	13.0	6
10.00	0.400	50.0	50.0	6
10.75	0.400	5.0	95.0	6
12.25	0.400	5.0	95.0	6
12.50	0.400	87.0	13.0	6
15.00	0.400	87.0	13.0	6

MS conditions

MS system:	Xevo G2-S QTof
Ionization mode:	ESI+
Scan time:	0.2 seconds
Capillary voltage:	1.0 kV
Sampling cone:	20.0 V
Source temp.:	120 °C
Desolvation temp./gas:	550 °C/1000 L/H
Mass range:	*m/z* 50 to 1200
MS^E low energy:	4.0 V
MS^E high energy:	10.0 to 45.0 V
LockSpray™ solution:	Leucine enkephalin
LockSpray mass:	*m/z* 556.2766

Due to the wide chemical diversity of compounds described as PPCPs, the extraction and separation of the many classes and structures poses a major analytical challenge. A method employing mixed mode solid phase extraction was used to prepare samples, as shown in Figure 2 and described in a previous work.[2]

The concentration level of the post spiked compounds was chosen to account for the 1000-fold enrichment achieved in the sample preparation. A concentration of 1 ppt (1 ng/L) in the sample equated to an in-vial concentration at the same level as the post spike sample, 1 ppb (1 µg/L).

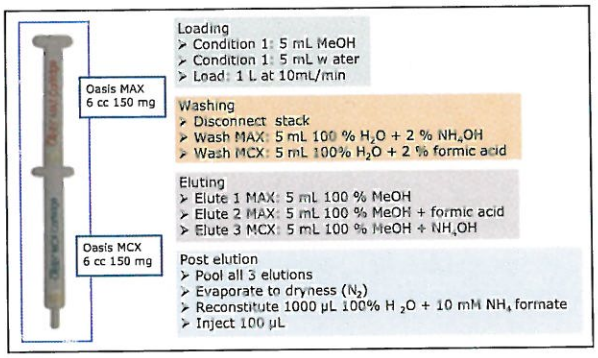

Figure 2. Sample preparation protocol used to extract water samples. Sample preparation resulted in a 1000:1 enrichment.

Acetaminophen	Codine	Naproxen	Sulfamethoxazole
Atenolol	Corticosterone	Ofloxacin	Ticlopidine
Azithromycin	Cortisone	Oxprenolol	Tolbutamide
Benzocaine	Cotinine	Procaine	Triamcinolone acetonide
Bromhexine	Digoxigenin	Promethazine	Trimethoprim
Buflomedil HCl	Ketoprofen	Pyrimethamine	Tripolidine
Chlorpheniramine	Levamisole	Ranitidine	Warfarin
Cimetidine	Metoprolol	Roxithromycin	Xylazine
Cocaine	Miconazole	Salbutamol (albuterol)	

Table 1. 35 PPCPs for the analyses performed.

Data processing

All MS^E data were collected and processed within the UNIFI, Scientific Information System. Data within UNIFI is passed through the apex peak detection and alignment processing algorithms.[3] This enables related ion components to be grouped together and analyzed as a single entity. Charged species, salt adducts, and fragments are all automatically aligned and grouped, so that all this information can be used to automatically interpret the data.

The Forensic Toxicology Screening Application Solution with UNIFI comes with pre-defined LC-MS conditions and processing parameters encompassed within an analysis method.[4] The Toxicology Library in UNIFI is comprised of over 1000 compounds including many PPCPs, such as drugs of abuse, veterinary medicines, and pharmaceuticals. Library entries contain names, formula, mol files, retention times, and theoretical accurate mass fragment ions.

RESULTS AND DISCUSSION

The analysis of compounds spiked into the well water sample demonstrates the applicability of the method for targeted analysis. An example of a calibration curve for one of the standards is shown in Figure 3. Of the 35 standards included, none were detected as incurred residues in the well water sample.

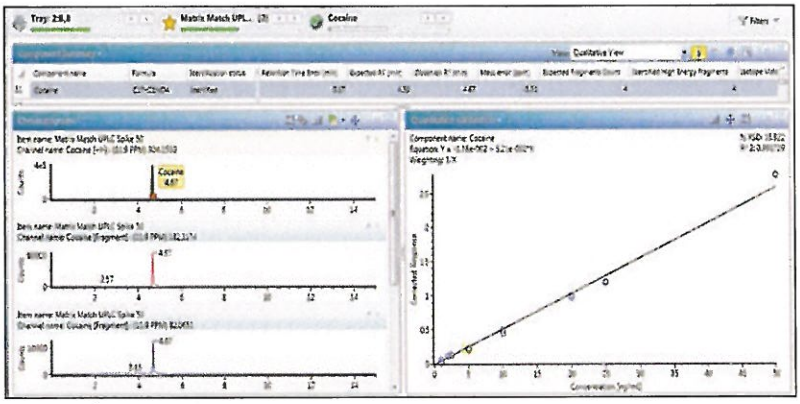

Figure 3. An example of the quantification aspects of UNIFI for a matrix-matched cocaine standard. Identification details are provided in the component summary section. Extracted ion chromatograms for precursor and fragments are shown in the chromatograms section, and the calibration curve with replicate injections is shown in the quantitation calibration section.

In order to determine whether other compounds were present, the Toxicology Library with up to three adducts (H^+, Na^+, K^+) for each entry was employed. It has previously been demonstrated that screening against a large library using the accurate mass of only one diagnostic ion can result in an unreasonable number of false detects.[5] The importance of well resolved, reproducible chromatography in order to reduce the false detect rate has also been highlighted in previous work.[6] In the approach used here, full advantage was taken of both retention times and accurate mass fragment ions that are stored in UNIFI's scientific library. With a mass accuracy tolerance of 5 ppm, a retention time tolerance of 0.5 minutes, and the requirement of at least one fragment ion detection, four incurred residues were found to be present in the well water sample. These are shown in Table 2 and Figure 4.

Component na...	Formula	m/z	Retention time Error (min)	Mass error (ppm)	Identified High Energy Fragments	Response	Adducts
Carbamazepine	C15H12N2O	237.1021	0.21	-0.67	3	10282	+H
Hexamine	C6H12N4	141.1136	0.38	0.92	3	40806	+H
Imidacloprid	C9H10ClN5O2	256.0597	0.18	0.66	1	7907	+H
Tramadol	C16H25NO2	264.1956	0.42	-0.68	1	16859	+H

Table 2. Component summary table in UNIFI showing details of each compound identified by screening the extracted well water sample against a library of over 1000 compounds.

Readily available standards and an existing MS/MS tandem quadrupole method enabled the confirmation and quantification of carbamazepine and imidacloprid. This was achieved using standard addition in a non-extracted well water sample, which was then injected directly for analysis using the ACQUITY UPLC I-Class System with the Xevo TQ-S tandem mass spectrometer (data not shown). Concentrations were found to be 0.31 ng/L and 0.58 ng/L respectively. Tramadol and hexamine were neither confirmed nor quantified.

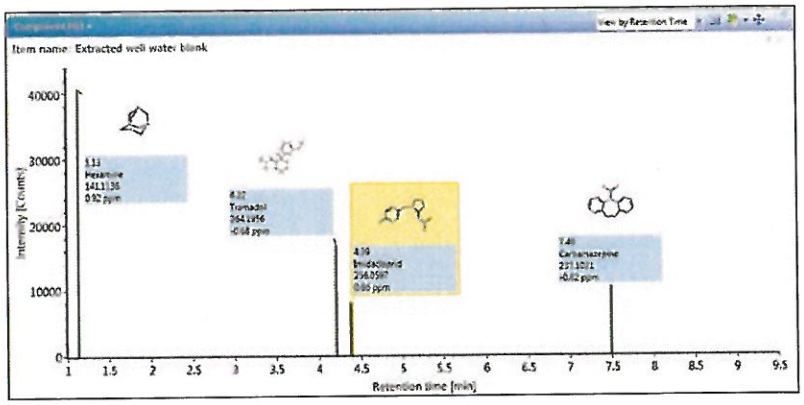

Figure 4. Component plot in UNIFI showing all identifications with respect to retention time. Each identification can be annotated as defined by the user. In this example, structure, retention time, compound name, expected m/z, and mass error (ppm) were labeled.

In UNIFI, the criteria set for identification is completely customizable, giving maximum flexibility to users. The bar chart in Figure 5 shows the effect of changing the retention time tolerances for identification with the sample containing the 35 spiked compounds shown in Table 1. With a mass accuracy tolerances of 5 ppm (SANCO 12495 guidelines) and no retention time or fragment ion criteria, 735 detections were returned (red bars at the far right of Figure 5). A reduction in false detects was observed when incorporating and decreasing a retention time tolerance, (red bars in Figure 5). Even with a retention time tolerance of 1 minute, the number of detects are reduced by over 65%. However, if this tolerance is set too low, false negatives may arise, as shown for the 35 spiked compounds as shown for the 35 compounds at a tolerance of 0.25 minutes or below (purple bars in Figure 5). A considerable decrease in false detects is observed when fragment ion presence is used to enhance the identification (green bars in Figure 5).

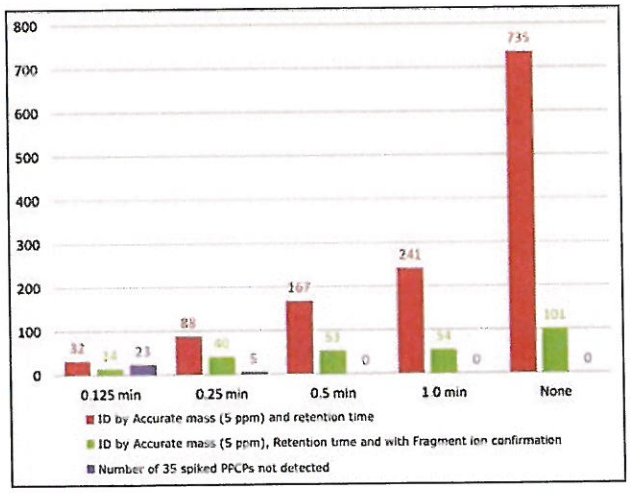

Figure 5. Chart showing the reduced number of false detects observed when using retention time and fragment ions in the identification criteria.

The key to success with HRMS screening is to use wider tolerances for multiple identification criteria. This results in a considerable reduction of false detects while minimizing false negatives. UNIFI provides the flexibility for users to combine criteria in a simplified workflow, enabling rapid data review and improved analyst efficiency.

CONCLUSIONS

- Four compounds of interest were detected during an HRMS screening of a locally sourced well water sample enriched using an SPE protocol.
- Mixed-mode SPE allowed for the analysis of acidic, basic, and neutral compounds of interest in a single sample.
- The inclusion of both the retention times and accurate mass fragment ions in the Toxicology Library reduced the false detection rates, which is critical for rapid data review in screening experiments.
- Using multiple criteria with wider tolerances controls the number of false detects and minimizes the number of false negatives in HRMS screening.

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[APPLICATION NOTE]

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Direct Quantification of Diquat and Paraquat in Drinking Water Samples Using Ultra-Sensitive UPLC-MS/MS Analysis

Claude R Mallet
Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

- Direct injection of clean water samples removes the need for sample extraction or concentration, saving valuable analyst time.
- Fast UPLC® analysis on an ACQUITY UPLC® BEH C_{18} Column decreases sample turn around time and improves lab productivity.
- The high sensitivity of Xevo TQ-S enables excellent trace-level quantification using a 100-µL direct injection, with no deterioration in performance apparent even after 250 sample injections.

WATERS SOLUTIONS

ACQUITY UPLC

Xevo® TQ-S
ACQUITY UPLC BEH C_{18} Column

TrendPlot™ MS Software

KEY WORDS

diquat, paraquat, drinking water, Xevo TQ-S, herbicide, bipyridyls

INTRODUCTION

Crop protection in countries around the globe is usually associated with the use of a wide range of pesticides, insecticides, or herbicides. These agricultural products can potentially have harmful effects on the environment and impact the health of both humans and animals. Despite the risk, they are a crucial part of the global economy[1] For example, the use of herbicides is important to control the growth of weeds, for if not suppressed weeds can reduce crop yields up to 80%.[2] In the herbicides family the bipyridyls are used extensively in agriculture to control broadleaf and aquatic weeds. The most common bipyridyls are diquat and paraquat. They constituted the largest share of the global market until recently overtaken by glyphosate.[3] Due to their high efficiency as pre-harvest desiccants and defoliants, diquat and paraquat are also classified as highly toxic.[4] The World Health Organization (WHO) has classified these compounds as moderately hazardous.[5] Even with a half-life in water of 48 hours, accidental or intentional ingestion can have serious health effects. For drinking water, the U.S. Environmental Protection Agency (U.S. EPA) has established a maximum contaminant level of 20 ppb for diquat and a desired goal of 3 ppb for paraquat[6] (not EPA regulated). The European Union (EU) has not regulated the levels of these compounds specifically in drinking water and continues to apply the value of 0.1 ppb.[7]

The analysis of bipyridylium herbicides can be difficult mainly because they are cationic molecules. Their inherent high polarity and positive charge, require the use of ion pairing additives when analyzing quaternary amines by reversed-phase chromatography. The U.S. EPA method 549.2 utilizes reversed-phase chromatography with ion pairing for the separation of diquat and paraquat using UV detection.[8] Ion pairing agents are typically avoided with ESI-MS applications owing to suppression of the ionization in the MS source. For MS applications, HILIC has provided suitable chromatography without the requirement of ion pairing agents.[9] However, recent advances in MS sensitivity have made the direct analysis of trace-level contaminants in water attainable and very attractive. The possibility of removing laborious and time-consuming solid phase extraction and sample concentration is highly desirable. Direct injection of an aqueous sample for RP chromatography is ideal as the sample matrix is similar to the initial mobile phase conditions. For HILIC, a water sample would first require dilution with the organic solvent.

EXPERIMENTAL

Diquat and paraquat standards were purchased from Sigma Alrich (St-Louis, MO, USA). HFBA (HPLC grade) was purchased from Thermo Scientific (Rockford, IL). MilliQ water was used to produce calibration standards. The water samples were collected from bottled and in-house tap water. The chemical structure and MRM conditions used for the quaternary herbicides are listed in Figure 1 and Table 1, respectively. MRM transitions stored in the Quanpedia™ database were selected for analysis. Chromatographic separation was performed on Waters® ACQUITY UPLC System equipped with an ACQUITY UPLC BEH C_{18} 2.1 x 30 mm Column. A one -minute linear water/methanol gradient with 10 mM HFBA was used. The detection was performed using a Xevo TQ-S.

UPLC conditions

System:	ACQUITY UPLC
Runtime:	3.0 min
Column:	ACQUITY UPLC BEH C_{18} 2.1 x 30 mm, 1.7 µm
Column temp.:	25 °C
Mobile phase A:	10 mM HFBA in water
Mobile phase B:	10 mM HFBA in methanol
Elution:	1 minute linear gradient from 2% (B) to 95% (B)
Flow rate:	0.6 mL/min
Injection volume:	100 µL

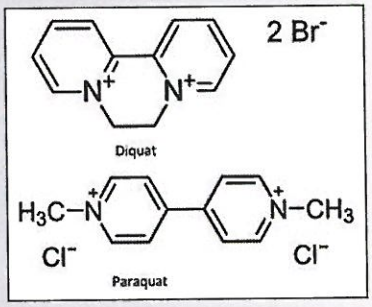

Figure 1. Chemical structure of diquat and paraquat.

MS conditions

MS system:	Xevo TQ-S
Ionization mode:	ESI positive
Capillary voltage:	3.0 kV
Cone voltage:	50.0 V
Source temp.:	140 °C
Desolvation temp.:	550 °C
Desolvation gas:	1100 L/hr
Cone gas:	50 L/hr

Herbicides	Precursor	Product	Cone	Collision
Diquat	183.0	157.0	50	20
	183.0	78.0	50	35
Paraquat	185.0	170.0	50	20
	185.0	107.0	50	30

Table 1. Diquat and paraquat MRM conditions.

This application note presents the analysis of diquat and paraquat herbicides in drinking water by direct injection using a volatile ion pairing reagent (heptafluorobutyric acid-HFBA), RP-UPLC, and the highly sensitive Xevo TQ-S.

RESULTS AND DISCUSSION

With the StepWave™ ion optics, Waters® Xevo TQ-S offers unsurpassed performance for trace-level analysis. The high sensitivity allows for the option to bypass the tedious sample concentration requirement associated with trace-level detection of contaminants in drinking water. With this high level of sensitivity, a clean water sample can be pre-concentrated directly on column by using a direct injection technique with the ACQUITY UPLC System. As shown in Figure 2, diquat and paraquat gave well-defined Gaussian peak shapes on the RP column. The vertical axes are linked in Figure 2 and show the difference in response of the two analytes. Even with the lower response seen for paraquat compared to diquat, the required levels of quantification for both compounds were achieved.

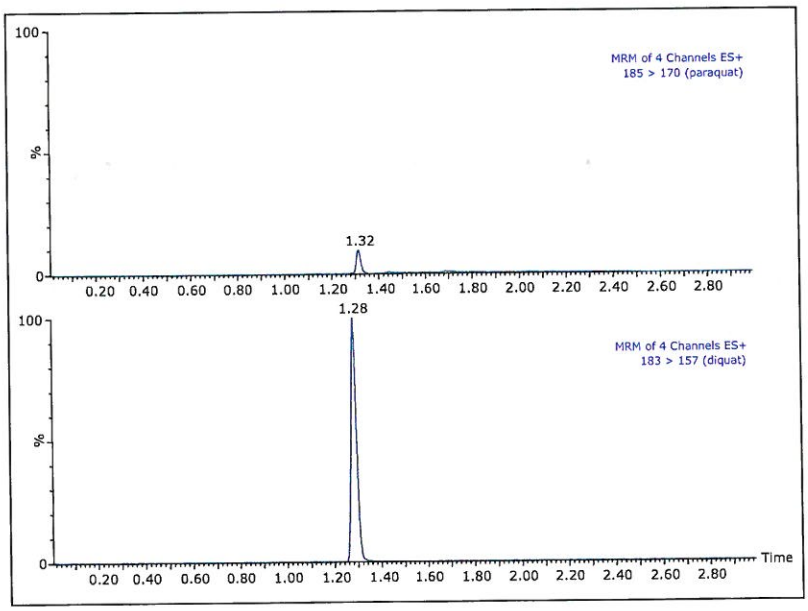

Figure 2. Reversed chromatograms of diquat and paraquat (1 ppb spike).

Quantification

Using the direct injection protocol, the quantification of bottled and tap water was measured against a calibration curve generated using standards made in MilliQ water. In this case, external calibration showed excellent results and an internal standard was not deemed necessary. As shown in Figure 3, the calibration curves for diquat and paraquat for tap water showed excellent linearity from 50 ppt to 100 ppb, with r^2 of 0.997 and 0.995 for diquat and paraquat, respectively. The recoveries for a 1 ppb spike are shown in Table 2, with recoveries in the range of 75% to 107%. The relative standard variation (RSD's) for diquat and paraquat was below 8% in both water samples.

Herbicides	Bottled water	Tap water
Diquat	107.0 (2.6)	75.1 (4.4)
Paraquat	99.0 (3.9)	76.5 (6.1)

Table 2. Recoveries and coefficient of variations at 1 ppb in bottle and tap water (n=3).

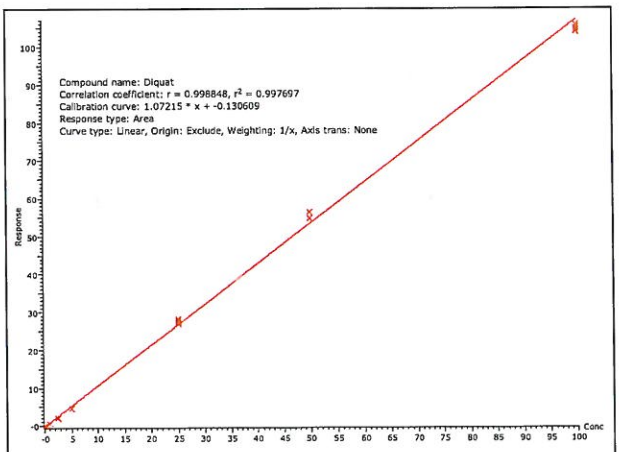

Figure 3A. Calibration curve for diquat from 50 ppt to 100 ppb.

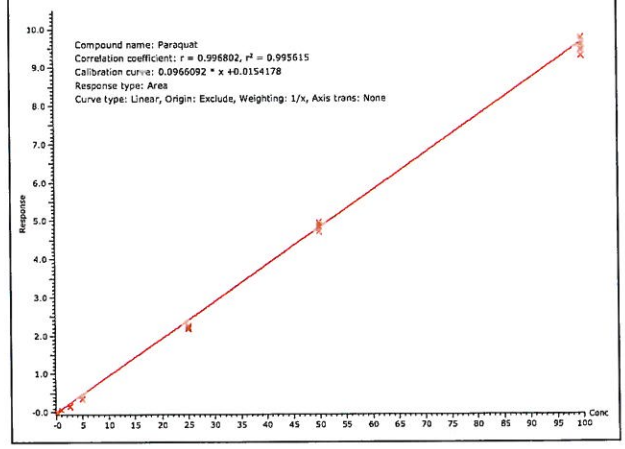

Figure 3B. Calibration curve for paraquat from 50 ppt to 100 ppb.

In this application, since the ion pairing agent was added to both the mobile phases (aqueous and organic) and the sample, the purity of HFBA was crucial. During the development phase, the 185 → 170 *m/z* MRM transition for paraquat showed an interferent near the expected retention time of paraquat. It also showed high background levels which made it difficult to quantify paraquat below 500 ppt. This issue was attributed to the ion pair additive, most likely due to a lower purity grade that was employed. With a higher purity grade, the interferent was eliminated and the background noise was reduced to a satisfactory level. As a consequence, the limit of detection (LOD) of 50 ppt was achieved and the MRM chromatograms are presented in Figure 4 for bottled water. The ion ratios for both diquat and paraquat, calculated from the quantification and the confirmation MRM transitions (Figure 5) showed good correlation between the standard and spiked samples, further supporting the applicability of the direct injection method.

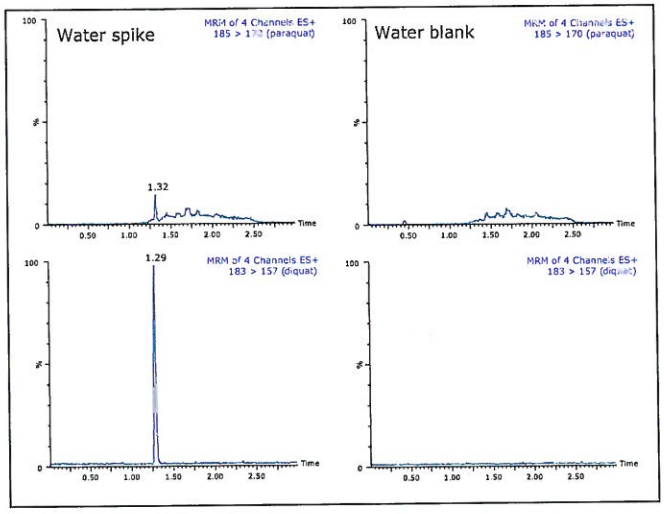

Figure 4. Chromatograms for paraquat and diquat at 50 ppt spike and blank (bottled water).

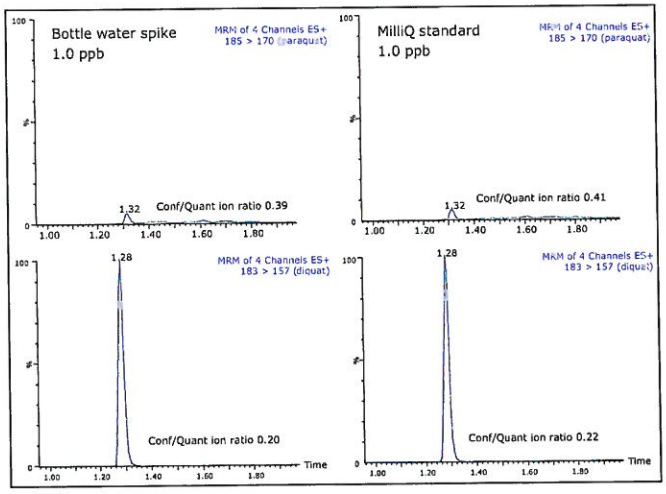

Figure 5. Ion ratio for diquat and paraquat using quantification and confirmation MRM transitions.

Lifetime and robustness

The direct injection approach is very efficient in term of speed and ease of use. However, the technique is not immune to potential situations which could affect the analytical performance over extended periods of time. The repeated injection and high injection volume of unfiltered and un-extracted samples could lead to peak distortion. During lifetime and robustness studies, the peak shape and column backpressure are excellent indicators of the column's overall performance. In this application, as seen in Figure 6, the peak shape of diquat and paraquat showed no noticeable distortion between the first and 250th injection. The initial column backpressure readout before injection of the first sample was recorded at 3500 psi. After 250 injections of tap water samples, the initial column backpressure shows a reading of 3900 psi, an increase of 400 psi. The key feature for quantification remains for the target analyte to elute with a Gaussian peak shape throughout the analysis.

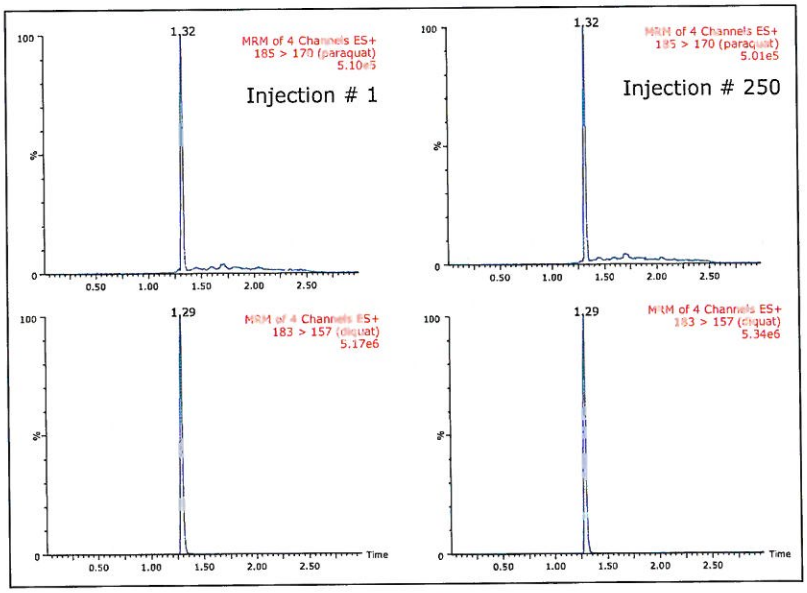

Figure 6. Example MRM chromatograms over the column lifetime study. Injections 1 and 250 are shown for diquat and paraquat in tap water.

In this application, the lifetime chromatograms for diquat and paraquat showed no signs of peak distortion and the RSDs on the quantification results were below 5%. Therefore, the small backpressure increase recorded for the tap water samples did not influence the overall analytical performance during this study. The TrendPlot™ profile report for diquat and paraquat are shown in Figure 7. As it can be seen in Figure 7, the TrendPlot shows excellent linearity for both compounds with RSDs at 4.7% and 7.5% for 100 injections, respectively.

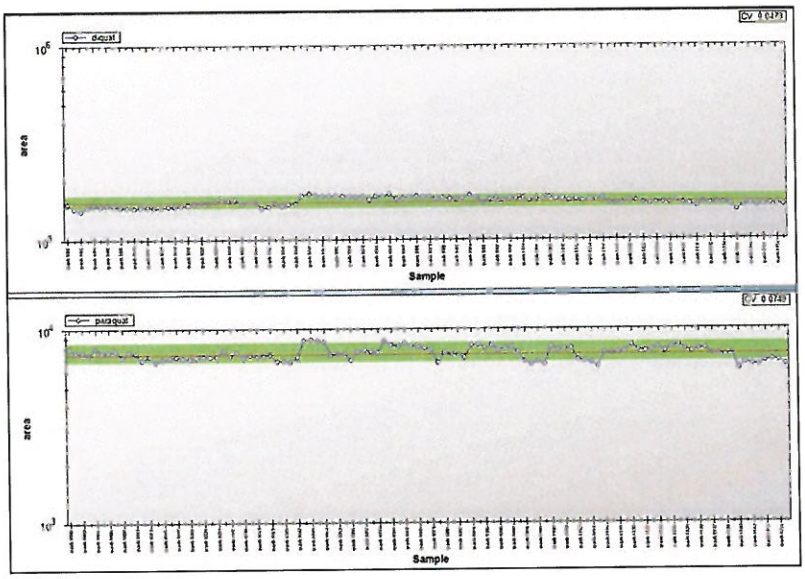

Figure 7. TrendPlot profiles of diquat and paraquat in tap water.

CONCLUSIONS

This application note has demonstrated the versatility of direct injection using the ACQUITY I-Class UPLC System with the Xevo TQ-S Mass Spectrometer for the analysis of diquat and paraquat in tap water and bottled water. The limit of detection in this study was 50 ppt, which is below the European Union Directive LOD of 100 ppt. The high sensitivity of Xevo TQ-S enabled excellent quantitation using a 100-µL injection without sample extraction or concentration prior injection. The recovery data showed good results with excellent RSD's below 8% for both water samples.

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Direct Quantification of Acidic Herbicides in Drinking Water Samples Using Ultra-Sensitive UPLC/MS/MS Analysis

Claude R. Mallet, Dimple Shah, Jennifer Burgess
Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

- Fast UPLC® analysis with ACQUITY UPLC® BEH C_{18} Column
- Sensitive and selective UPLC/MS/MS analysis with 5 ppt LOQ
- Requires no sample handling or sample preparation

WATERS SOLUTIONS

ACQUITY UPLC I-Class System

Xevo® TQ-S Mass Spectrometer

ACQUITY UPLC BEH C_{18} Column

RADAR™ Technology

Quanpedia™ Database

KEY WORDS

Phenoxyacetic acids, drinking water, direct injection

INTRODUCTION

Phenoxyacetic acids are classified as herbicides. They were first introduced in the 1940's and were in widespread use in agriculture by the middle of the 1950's. Phenoxyacetic acids are widely used in forestry applications, and to some extent in home gardening, and they account for approximately 70% of the weed killers used in agriculture.[1] Consequently, these herbicides are of interest for environmental monitoring in surface and ground waters and are also monitored in drinking water supplies.

When using chemicals for crop protection, toxicity is a crucial factor and these chemicals will often be subject to health evaluations and risk assessments. For example, 2,4-D is used for a variety of crop protection (fruit and vegetable), as well as for turf and lawn care. This herbicide is registered in the United States because it has a favorable environmental profile, and exposures are expected to be minimal in both terrestrial and aquatic environments. 2,4-D is also rapidly broken down by microbial action in soil and it does not persist, accumulate, or leach into groundwater under proper use.[2] In 2005, the U.S. EPA approved the continued use of 2,4-D,[3] with a maximum contaminant level goal (MCLG) of 70 ug/L. The European Union has also evaluated 2,4-D and included it on the list of approved pesticides, since residue levels do not produce any measurable harmful health issues in humans or animals.[4]

Not all phenoxyacetic acid herbicides exhibit low toxicity levels. For example, the toxicity of 2,4,5-T came to light during the Vietnam War. Because phenoxyacetic acids exhibit a rapid activity against broad-leaf plants, they were extensively used as a fast-acting defoliant under the code name "Agent Orange".[5] The formulation was equal parts of 2,4,5-T and 2,4-D. Its toxicity was linked to the contamination of 2,4,5-T with an extremely toxic dioxin.[6] In 1985, the U.S. EPA banned all remaining uses of 2,4,5-T within the United States.

For those phenoxyacetic acids currently registered for commercial use, the EU council directive[7] states that water intended for human consumption should not contain more than 100 ng/L for individual pesticides, and must not exceed 500 ng/L for the sum of all pesticides. In the U.S., they are monitored with EPA methods 515.4 (GC/ECD) with minimum detection limits (MDL's) at 50 ng/L, and method 555 (LC/UV) with MDL's at 100 ng/L.

EXPERIMENTAL

UPLC conditions

UPLC system:	ACQUITY UPLC I-Class
Runtime:	8.0 min
Column:	ACQUITY UPLC BEH C_{18}, 2.1 x 100 mm, 1.7 µm
Column temp.:	60 °C
Mobile phase A:	0.5 % Formic acid in water
Mobile phase B:	0.5 % Formic acid in acetonitrile
Elution:	5-min linear gradient from 5% (B) to 95% (B)
Flow rate:	0.5 mL/min
Injection volume:	100 µL

MS conditions

MS system:	Xevo TQ-S
Ionization mode:	ESI negative
Capillary voltage:	2.0 kV
Cone voltage:	20.0 V
Source temp.:	140 °C
Desolvation temp.:	550 °C
Desolvation gas:	1100 L/hr
Cone gas:	50 L/hr

This application note presents a novel analytical approach for the analysis of phenoxyacetic herbicides in drinking water by direct injection using Waters® highly sensitive Xevo TQ-S tandem quadrupole Mass Spectrometer with the ACQUITY UPLC System. The option of direct injection on the ACQUITY UPLC I-Class System permitted trace level analysis as low as 2.5 ng/L; without the traditional requirement of high volume enrichment during sample preparation. This resulted in faster analysis times and the ability to rapidly report results.

The chemical structures and MRM conditions used for the phenoxyacetic acid herbicides are listed in Figure 1 and Table 1, respectively.

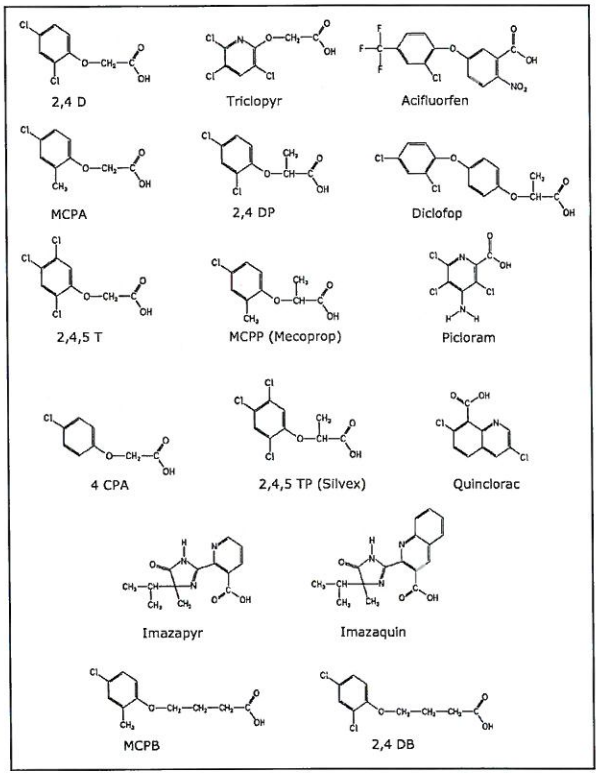

Figure 1. Chemical structure of phenoxyacetic acids used in this study.

The application began by selecting MRM transitions stored in the Quanpedia database and using IntelliStart™ Technology to optimize conditions for one additional compound. Quanpedia is an extensible and searchable database for quantitative LC/MS and LC/MS/MS method information that simplifies and accelerates quantitative analytical method creation. IntelliStart's intuitive software is used to start up, tune, and calibrate Waters' mass spectrometers and, more importantly, to automate analyte tuning and MS method building. Chromatographic separation was performed on an ACQUITY UPLC I-Class System, equipped with an ACQUITY UPLC BEH C_{18} 2.1 x 100 mm Column. A 5-minute linear water/acetonitrile gradient with 0.5 % formic acid was used. The detection was performed using the Xevo TQ-S Mass Spectrometer. The phenoxyacetic acids standards were purchased from Sigma Aldrich (St-Louis, MO, U.S.A.). MilliQ water was used to produce calibration standards. The deuterated 2,4 D was selected as the internal standard. Water samples were collected from natural spring water sources.

Herbicides	Precursor	Product	Cone	Collision
4CPA	185.0	90.9	20	40
	185.0	127.0	20	15
MCPA	199.0	105.0	20	40
	199.0	141.0	20	15
MCPP	213.0	105.0	20	40
	213.0	141.0	20	15
2,4 D	218.9	125.0	20	40
	218.9	160.9	20	15
MCPB	227.0	105.0	20	40
	227.0	141.0	20	15
2,4,5 T	254.9	160.9	20	40
	254.9	196.9	20	15
2,4DP	233.0	125.0	20	40
	233.0	160.9	20	15
2,4,5 T	254.9	160.9	20	40
	254.9	196.9	20	15
Triclopyr	255.9	175.7	20	30
	255.9	197.8	20	10
Imazapyr	260.0	173.0	20	20
	260.0	216.0	20	10
2,4,5 TP	268.9	160.9	20	40
	268.9	196.9	20	15
Imazathapyr	288.0	201.1	20	25
	288.0	244.1	20	15
Diclofop	324.9	145.0	20	25
	324.9	253.0	20	15
Haloxyfop	359.0	252.0	20	25
	359.0	288.0	20	15
Acifluorfen	359.9	194.9	20	20
	359.9	315.9	20	10

Table 1. Phenoxyacetic acids MRM conditions.

RESULTS AND DISCUSSION

When dealing with trace level analysis in the ng/L range, the extraction protocol incorporates an enrichment factor to reach the targeted level of sensitivity. This sensitivity requirement means processing a large sample volume (up to 1000 mL), which translates into long and laborious sample handling. With the introduction of the novel StepWave™ ion optics, the Xevo TQ-S Mass Spectrometer offers unsurpassed performance for trace-level analysis. Its high sensitivity allows for the option to bypass the tedious sample concentration requirement associated with trace-level detection of contaminants in drinking water. A clean water sample can be pre-concentrated directly on-column by simply increasing the injection volume (up to 100 µL) using the ACQUITY UPLC I-Class System with Xevo TQ-S.

Quantification

In this application, MilliQ water was used to prepare calibration standards for quantification of natural spring water. As shown in Figure 2, the calibration curve for 2,4-D and 2,4,5-T for natural spring water showed excellent linearity from 5 ng/L to 1000 ng/L (r^2 at 0.995). The other phenoxyacetic acids in the mix showed similar linear regression with r^2 ranging from 0.995 to 0.999 for the same dynamic range, with the exception of Triclopyr, which showed good linearity from 25 ng/L to 1000 ng/L with an r^2 value of 0.995.

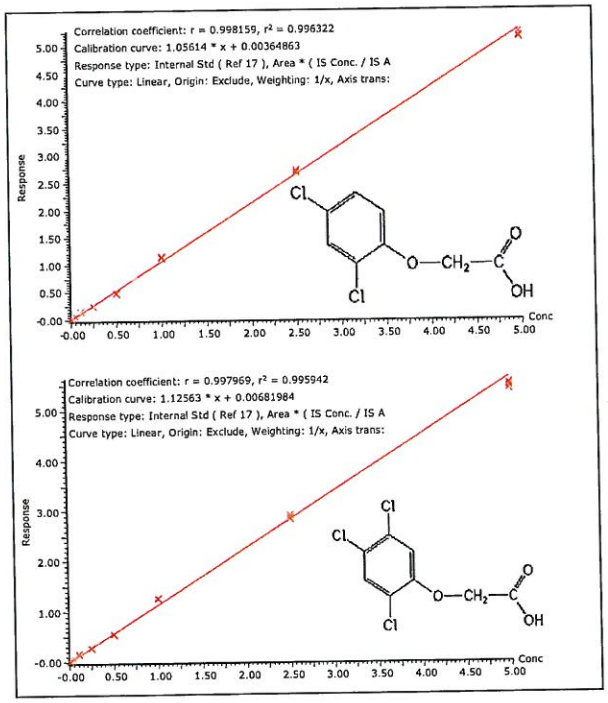

Figure 2. Calibration curve for 2,4 D and 2,4,5 T in natural spring water from 5 to 1000 ppt.

The limit of detection (LOD) was 2.5 ng/L for all phenoxyacetic acids, except for Triclopyr, which had an LOD value of 5 ng/L. The MRM chromatograms at the LOD for a selection of the analytes are shown in Figure 3. The recoveries for a 100 ng/L spike for the phenoxyacetic acids are shown in Table 2. The fortified natural spring water samples were measured against a MilliQ water standard curve and showed recoveries in the range of 107% to 117%. For the majority of the herbicides, the average coefficient of variation (CV's) was well below 5% in natural spring water samples.

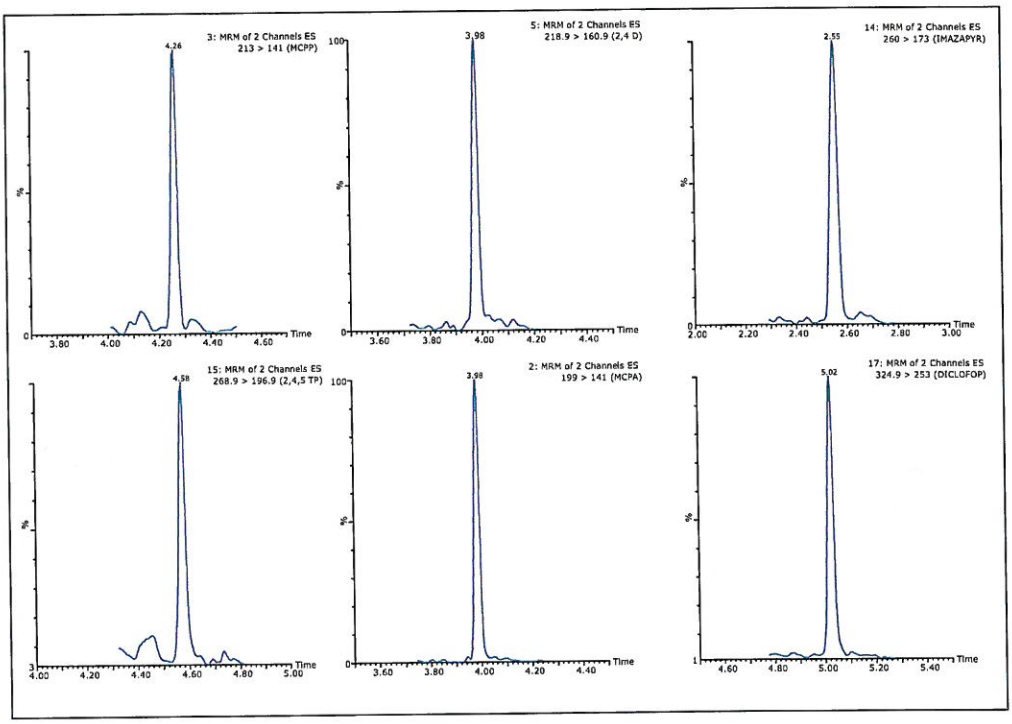

Figure 3. MRM chromatograms at 2.5 ppt for seletected phenoxyacetic acids.

Herbicides	MilliQ	Natural spring
4 CPA	0.14 (3.3)	0.15 (1.5)
MCPA	0.14 (0.9)	0.16 (1.3)
MCPP	0.15 (1.3)	0.16 (1.2)
2,4 D	0.14 (1.4)	0.16 (1.5)
MCPB	0.12 (3.6)	0.14 (2.1)
2,4 DP	0.14 (2.2)	0.16 (1.3)
2,4,5 T	0.14 (2.1)	0.15 (2.1)
Triclopyr	0.12 (1.5)	0.14 (5.2)
IMAZAPYR	0.12 (1.0)	0.14 (0.7)
2,4,5 TP	0.14 (0.9)	0.16 (0.6)
Diclofop	0.14 (0.9)	0.17 (2.4)
ACIFLUORFEN	0.12 (1.9)	0.14 (1.6)
QUINCLORAC	0.13 (4.7)	0.14 (2.3)
PICLORAM	0.13 (1.1)	0.14 (3.8)
2,4 DB	0.13 (1.8)	0.14 (4.6)
IMAZAQUIN	0.12 (0.7)	0.14 (1.0)

Table 2. Recoveries and (coefficient of variations) at 100 ppt in natural spring water samples (n=3).

RADAR TECHNOLOGY

RADAR Technology, is a unique capability of Waters' Xevo tandem quadrupole Mass Spectrometers that enables the simultaneous acquisition of full scan MS data and MRM transitions. This functionality leads to the ability to make informed decisions during the method development process. Using RADAR mode, crucial information can be collected, such as an overview of the water sample's complexity, which will ultimately impact the lifetime of the analytical column and the robustness of the method. Figure 4 shows the MRM chromatograms for a standard of the herbicides at 100 ng/L.

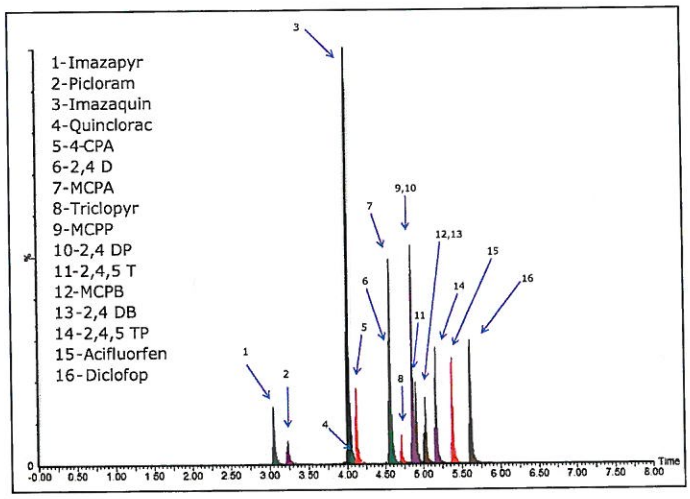

Figure 4. MRM chromatogram of phenoxyacetic acids standards in MilliQ water at 100 ppt.

Overall, the chromatogram showed well-resolved peaks with a Gaussian distribution for all analytes, which is a key parameter for peak integration during quantitation. The chromatography also showed three co-elution zones. With mass spectrometry detection, analytes co-eluting during chromatography are resolved according to their mass-to-charge ratio. The RADAR data – which is acquired simultaneously – can be used to identify whether the herbicides are eluting in regions of potential matrix interferences. The TIC chromatogram of the RADAR data for MilliQ, and natural spring water samples are shown in Figure 5. The MilliQ and natural spring water, shown in Figure 5, detail a potential matrix effect zone during the last minute of the gradient, with a retention time range from 4.2 to 5.2 minutes.

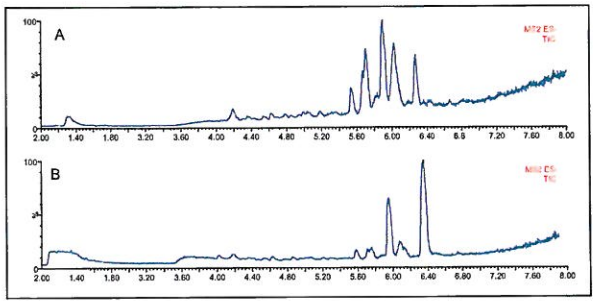

Figure 5. RADAR Full scan total ion chromatograms for A) MilliQ water, B) natural spring water.

By overlaying the MRM chromatograms of the earliest and latest eluting herbicides with the RADAR data, shown in Figure 6, it can be seen that the herbicides eluted at least 30 seconds ahead of the matrix zone. With the information gleaned from the use of RADAR Technology, confidence in the robustness of the method is gained, and changes in the matrix over time can be monitored for any new potential interference.

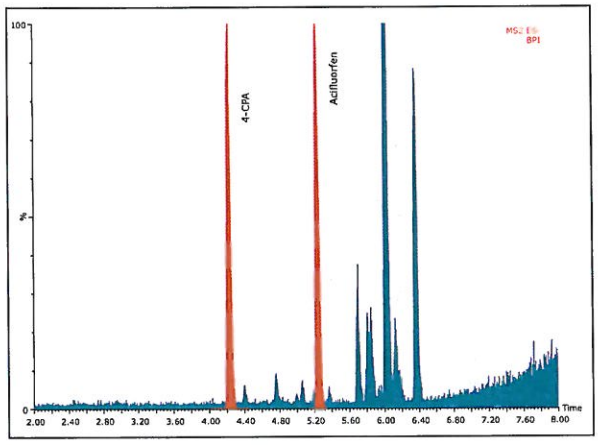

Figure 6. RADAR Full scan BPI chromatogram versus MRM's chromatograms for the earliest and latest eluting analytes.

Lifetime and robustness

The results for a column lifetime study using natural spring water are shown in Figure 7. Samples were injected onto the same analytical column, and demonstrated that even after 500 injections, the analytical performance was not compromised. As shown in Figure 7, the peak shape from the first and the 500th injections for both water samples show no indication of distortion or tailing.

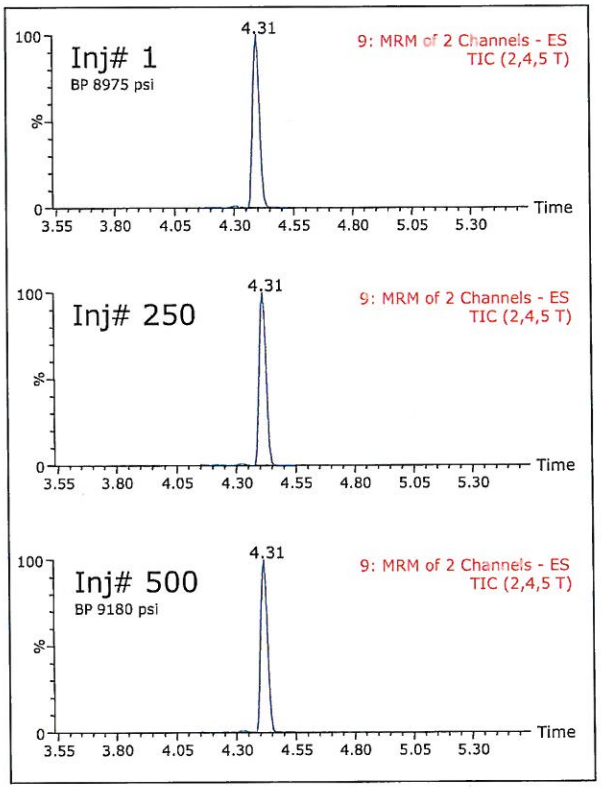

Figure 7. Example MRM chromatograms over the column lifetime study. Injections 1, 250, and 500 are shown for 2,4,5-T for natural spring water samples.

An example of TrendPlot™ Software, shown in Figure 8, gives an overall perspective of the excellent reproducibility for 150 injections of 2,4,5-T in natural spring water.

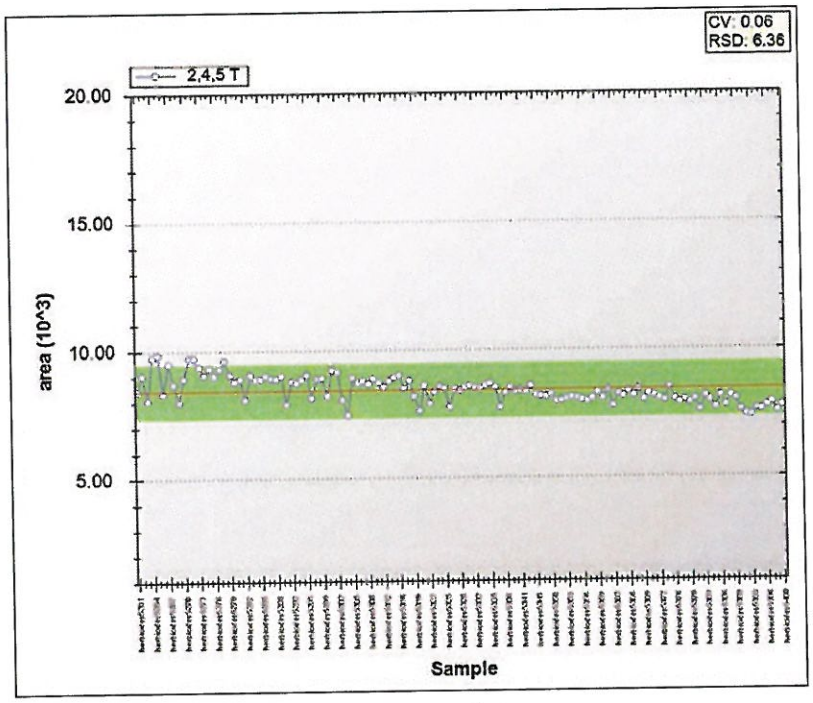

Figure 8. TrendPlot showing peak area of 2,4,5-T for 150 injections in natrual spring water.

Monitoring the analytical column's backpressure throughout its use provides a good indicator of the analytical performance of the column. With UltraPerformance Liquid Chromatography (UPLC) using sub-2 µm particles in an analytical column that is pressure rated at 18,000 psi, the direct injection technique showed reliable results for these drinking water samples.

For example, in this application, the backpressure for natural spring water showed an increase of less than 200 psi after 500 injections. Overall, for this application, the peak shape for phenoxyacetic acids in natural spring water samples showed excellent peak shape with no distortion after 500 injections. The chromatography indicates that the system is still operating at peak performance.

CONCLUSIONS

Trace level analysis using legacy analytical instrumentation (*e.g.* HPLC) will always be associated with tedious and laborious standard operating procedures (SOPs). This application note has demonstrated the versatility of direct injection using the ACQUITY I-Class UPLC System combined with the Xevo TQ-S Mass Spectrometer for the analysis of phenoxyacetic herbicides in natural spring water. The limit of detection (LOD) for the majority of the phenoxyacetic acids in this study was 2.5 ng/L, which exceeded the detection requirements of the U.S. EPA and European Union Directives. The high sensitivity of the Xevo TQ-S enabled excellent quantitation for acidic herbicides using a 100-µL injection without any pre-treatment prior to injection. The recovery data showed good results with excellent CV's below 5% for natural spring water samples. RADAR Technology proved its value during the chromatography optimization process by identifying potential interferences or matrix effect zones.

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Additional Information

Please contact the application note authors for additional information required for this application.

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[TECHNOLOGY BRIEF]

Maintaining Mass Accuracy for High Concentration Residue Violations During an HRMS Screening Experiment Using the Waters Pesticide Screening Application Solution with UNIFI

Gareth Cleland, Lauren Mullin, and Jennifer Burgess

GOAL

To demonstrate the ability to maintain mass accuracy on high-level violations for compounds of interest when using the Waters® Pesticide Screening Application Solution (PSAS) with UNIFI.®

BACKGROUND

Multi-residue pesticide analysis is challenging due to the low limits of detection required in a diverse range of food commodities. As there are currently well over 1000 pesticides in use, laboratories are under increasing pressure to broaden the range of pesticides determined. The use of high resolution, accurate mass Time-of-flight (Tof) MS shows great potential for this type of analysis for several reasons. In full spectrum mode, Tof instruments are not limited by the number of compounds that can be analyzed in a single run in the way that tandem quadrupoles are. With Tof MS the number of compounds that can be screened is not dependent on the duty cycle of the instrument, but on the chemical compatibility with the extraction and analysis methods. Using a non-targeted, non-data dependant approach to data acquisition (MS^E) allows the user to collect a comprehensive dataset that can be used to screen for a large target list of compounds as well as unexpected compounds. The data can be fully interrogated at a later date for emerging compounds of interest that were not included in the initial screen. In addition to reaching low level MRLs, an HRMS screening must be able to identify residues present at high concentrations since a considerable number of violations in fruits and vegetables are likely to be in the mg/kg range. These high level violations may cause detector saturation which in some cases, can cause a shift in mass accuracy beyond the threshold set for identification.

The Waters Pesticide Screening Application Solution with UNIFI ensures that mass accuracy is maintained across all peaks, even at high concentrations. This removes the risk of false negatives associated with the presence of high concentration pesticide violations in food and environmental samples.

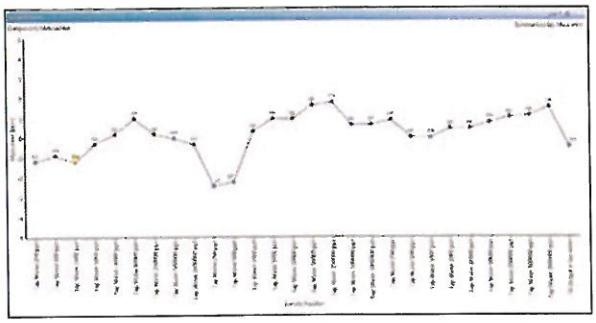

Figure 1. Screen shot of the summary plot available in UNIFI which allows the user to track any result component across all injections via a line or bar plot. The plot above summarizes the mass accuracy of an individual compound (metolachlor) across all levels of spiked tap water injections from 250 ng/L to 1 mg/L.

Data presented in this technology brief demonstrates the ability to maintain mass accuracy on high concentration violations for compounds of interest in a screening experiment.

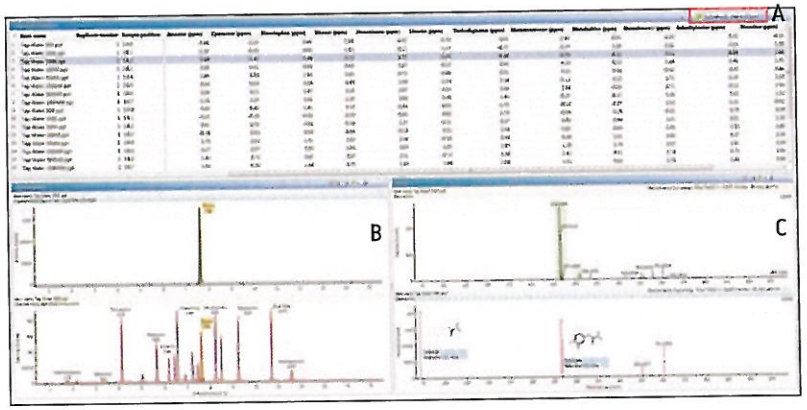

Figure 2. Screen shot showing the results from injection of increasing concentrations of the Waters pesticide screening mix (PSM) spiked in locally filtered tap water. The component summary section (2A) shows a table displaying the mass accuracy (in ppm) of 15 compounds over replicate injections of nine calibration levels. The parameter displayed can easily be changed to another parameter (for example the observed retention time) by clicking in the area highlighted in the red box. The chromatogram section (2B) shows an XIC for all compounds identified from the PSM as well as an XIC for the highlighted compound diuron. Low energy and high energy spectra for the selected component are displayed in the spectra window (2C).

THE SOLUTION

A dilution series of the Waters Pesticide Screening Mix (PSM), that contains 20 pesticides of varying polarities and ionizing ability, was prepared in locally filtered tap water. An extension loop on the ACQUITY UPLC® I-Class System enabled large volume (100 µL) injections of 9 points ranging from 250 ng/L to 1 mg/L. This resulted in an on-column amount ranging from 0.025 ng to 100 ng.

Tracking mass accuracy across all injections is greatly simplified in the UNIFI Scientific Information System. Customizable views allow the user to display identification details for a specific component across all injections. Figure 1 shows the summary plot available in UNIFI with a line graph depicting the mass accuracy of the compound metolachlor across all injections from 250 ng/L (250 ppt) to 1 mg/L (1,000,000 ppt). Even with an on-column concentration amount of 100 ng, excellent mass accuracy is maintained allowing the software to make a target match within the 5 ppm tolerance set in the analysis method. This level on column would equate to a 10 µL-injection of a 10 mg/L (or 10 ppm) solution, far above the linear dynamic range expected in LC-MS analyses.

With a single click, analysts can invoke a pivot table within UNIFI's component summary in order to display the data obtained for all compounds in all injections. Figure 2A shows the display of mass errors across all identified components in all injections. The criteria that can be viewed across all identified components in all injections are easily changed with a click in the highlighted area of Figure 2A. Other criteria that are useful to compare across all injections include the response and observed retention time. Also shown in Figure 2 is the extracted ion chromatogram of the highlighted level for diuron (upper chromatogram in Figure 2B) and an overlay of the extracted ion chromatograms for all identified components (lower chromatogram in Figure 2B). Figure 2C shows the corresponding low energy and high energy spectra for diuron.

Maintaining mass accuracy for high-level pesticide violations in food and environmental samples avoids false negatives and gives the user confidence in the identifications returned from a routine screening experiment.

SUMMARY

The example presented demonstrates the preservation of mass accuracy, even for compounds present at concentrations well beyond the linear dynamic range of MS systems. This is critical to ensure that high concentration level violations of compounds are not missed in a screening experiment.

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[APPLICATION NOTE]

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Comparing the Performance and Reliability of Waters Alliance HPLC Systems for Carbamate Analysis

Mark E. Benvenuti
Waters Corporation, Milford, MA, USA

APPLICATION BENEFITS

Waters® Alliance® System for Carbamate Analysis provides a complete system solution for the analysis of N-methylcarbamate and N-methylcarbamoyloxime pesticides in drinking water and a variety of environmental and food matrices.

- Carbamate analysis at sub-ppb levels
- Compatible with US EPA Method 531.2
- Baseline separation of analytes

WATERS SOLUTIONS

Alliance System for Carbamate Analysis

Empower® Software

2475 Fluorescence (FLR) Detector

Waters Carbamate Column

KEY WORDS

Carbamates, fluorescence detection, HPLC, ternary gradient

INTRODUCTION

The Waters Alliance System for Carbamate Analysis has been offered as a system solution since 1998. With the release of the 2013 Alliance HPLC System, we wish to show equivalency of the two platforms relative to linearity, precision, reproducibility, and limit of detection (LOD).

RESULTS AND DISCUSSION

Figures 2 and 3 show overlaid chromatograms of the standards on the legacy and 2013 Alliance platforms, respectively. The linearity on both platforms is compared in Table 1. R^2 is greater than 0.999 for all compounds regardless of which platform was used. The reproducibility for both retention time and concentration was investigated for both platforms using seven injections of three different standard concentrations (10-, 25-, and 75-ppb) with the results shown in Tables 2 through 5. The relative standard deviation for the retention time for the 21 injections was less than 0.25% on both platforms, as shown in Table 2. Tables 3 through 5 show comparisons for the amount for seven injections each of the 75-, 25-, and 10-ppb carbamate mixes run as unknowns. The %RSD was less than 0.8% for the 75-ppb and 0.9% for the 25-ppb mixes using both the legacy and 2013 Alliance platforms. One exception to this is 1-Naphthol, which is a hydrolysis product of carbaryl[4] and is, therefore, expected to show more variability. The %RSD was shown to be less than 1.5% for the 10-ppb mix on both platforms.

Figure 1. Alliance HPLC System.

EXPERIMENTAL

LC conditions

System:	Alliance HPLC for Carbamate Analysis (both legacy and 2013 systems)
Run time:	25.0 min
Column:	Waters Carbamate 3.9 x 150 mm, 4.0 µm at 30 °C
Mobile phase A:	Water
Mobile phase B:	Methanol
Mobile phase C:	Acetonitrile
Flow rate:	1.5 mL/min
Injection volume:	400 µL (1000 µL for 0.2- and 0.1-ppb levels)
Detection:	Fluorescence (Ex-339 nm, Em-445 nm)
Data management:	Empower 2 Software

Time (min)	Flow rate (mL/min)	%A	%B	%C	Curve
Initial	1.5	88	12	0	*
5.3	1.5	88	12	0	1
5.4	1.5	68	16	16	5
14.0	1.5	68	16	16	3
16.1	1.5	50	25	25	7
20.0	1.5	50	25	25	6
22.0	1.5	88	12	0	5

The basic system, components, and experimental procedure are described in the Waters Alliance System for Carbamate Analysis Method Manual.[1]

Standard and sample preparation

Two reference materials, M531M and M531-IS, were purchased from AccuStandard. These were diluted with preservation solution[2] to prepare the following levels: 100-, 75-, 50-, 25-, 10-, 5-, and 1-ppb. 0.2- and 0.1-ppb mixes were also prepared. These levels were also run as unknowns for the tests described in this study.

Linearity

The seven levels described above were injected in triplicate to construct a linear calibration curve.

Precision and reproducibility

The 75-, 25-, and 10-ppb levels were injected seven times as unknowns to determine precision and reproducibility for amount. The 21 injections (seven of each of the three levels) were used to determine precision and reproducibility for retention time.

Limit of detection

A 0.2-ppb carbamate mix was run three times as a standard, then seven times as an unknown to determine a limit of detection per 40 CFR pt 136 App, B[3]. A 0.1-ppb mix was also run for comparative purposes.

Performance evaluation

A Performance Evaluation Carbamate mix was purchased from ERA. The mix was prepared as directed, and quantified using both systems.

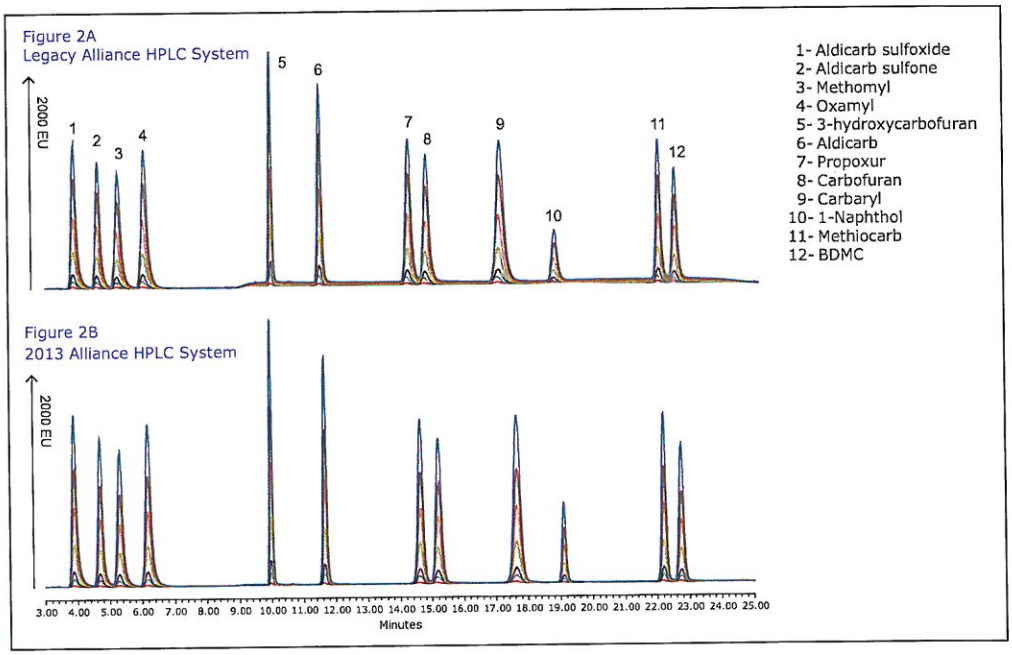

Figure 2. Chromatograms of 100-, 75-, 50-, 25-, 5-, and 1-ppb carbamate mixes using the legacy and 2013 Alliance HPLC systems.

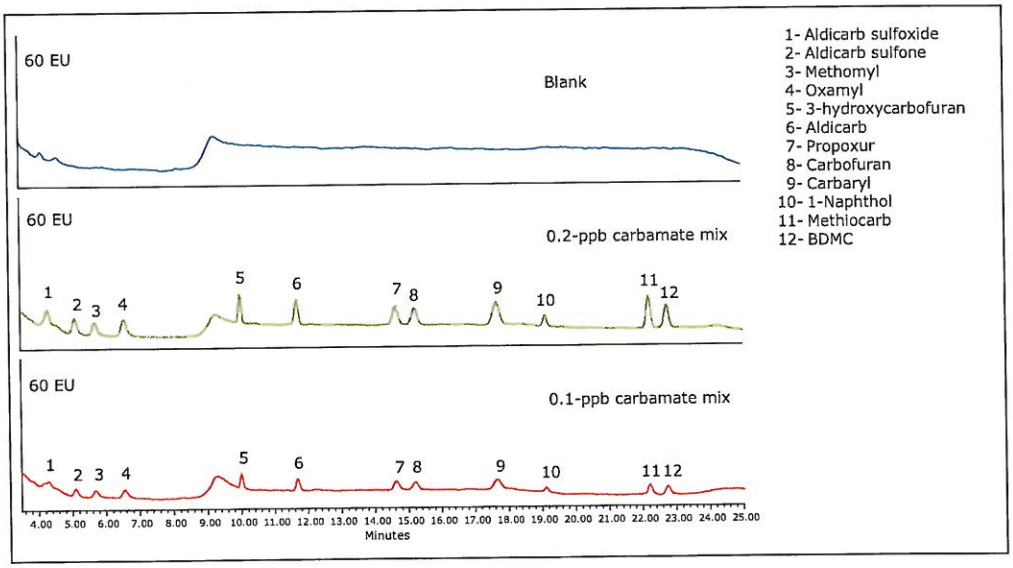

Figure 3. Chromatograms of low-level carbamate mixes on the legacy Alliance HPLC System, 1000-µL injection.

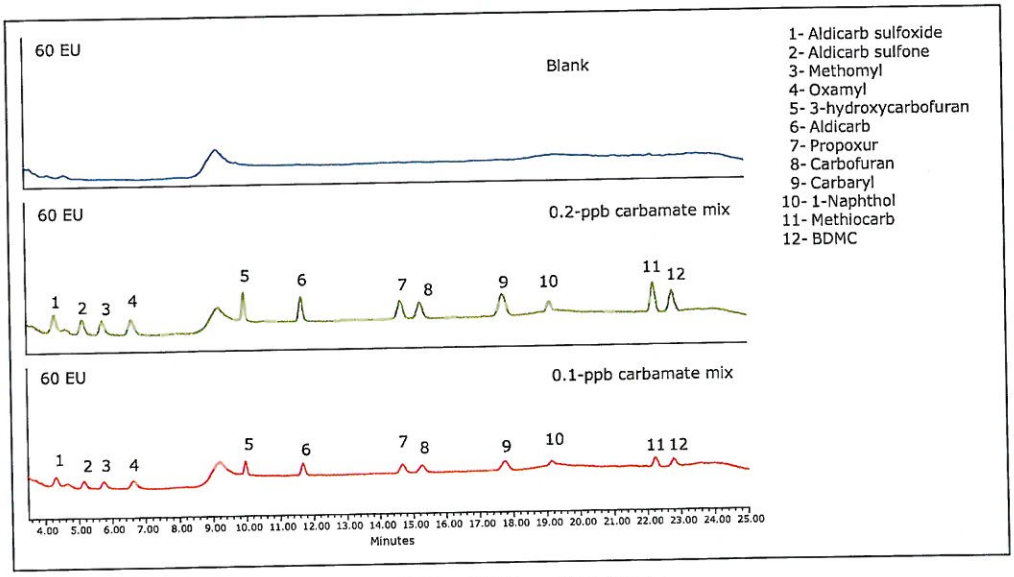

Figure 4. Chromatograms of low-level carbamate mixes on the 2013 Alliance HPLC System, 1000-µL injection.

Linearity (R^2)	Legacy Alliance HPLC	2013 Alliance HPLC
Aldicarb sulfoxide	0.9998	0.9998
Aldicarb sulfone	0.9998	0.9997
Oxamyl	0.9997	0.9998
Methomyl	0.9997	0.9997
3-Hydroxycarbofuran	0.9998	0.9997
Aldicarb	0.9998	0.9998
Propoxur	0.9997	0.9998
Carbofuran	0.9997	0.9996
Carbaryl	0.9998	0.9996
1-Naphthol	0.9998	0.9995
Methiocarb	0.9998	0.9996
BDMC	0.9999	0.9996

Table 1. Linearity for carbamate analytes.

Reproducibility (RT) 21 injections	Legacy Alliance HPLC			2013 Alliance HPLC		
Analyte	Mean RT	Std Dev	%RSD	Mean RT	Std Dev	%RSD
Aldicarb sulfoxide	3.86	0.003	0.086	3.94	0.005	0.132
Aldicarb sulfone	4.59	0.008	0.174	4.65	0.008	0.170
Oxamyl	5.18	0.010	0.193	5.27	0.011	0.209
Methomyl	5.99	0.012	0.197	6.08	0.011	0.186
3-Hydroxycarbofuran	9.94	0.009	0.089	9.93	0.007	0.072
Aldicarb	11.44	0.012	0.104	11.44	0.011	0.100
Propoxur	14.12	0.017	0.119	14.13	0.020	0.144
Carbofuran	14.65	0.018	0.125	14.67	0.021	0.146
Carbaryl	16.89	0.025	0.146	16.93	0.027	0.158
1-Naphthol	18.63	0.021	0.114	18.62	0.018	0.097
Methiocarb	21.87	0.013	0.059	21.85	0.013	0.062
BDMC	22.36	0.013	0.059	22.33	0.015	0.065

Table 2. Reproducibility data for retention time for 21 injections, seven injections each, of 75-, 25-, and 10-ppb carbamate mixes using the legacy and 2013 Alliance HPLC systems.

Amount 7 injections (75-ppb)	Legacy Alliance HPLC			2013 Alliance HPLC		
Analyte	Mean RT	Std Dev	%RSD	Mean RT	Std Dev	%RSD
Aldicarb sulfoxide	75.0	0.41	0.552	74.9	0.419	0.559
Aldicarb sulfone	75.3	0.46	0.610	75.2	0.367	0.488
Oxamyl	75.3	0.59	0.779	75.5	0.246	0.327
Methomyl	74.3	0.69	0.415	77.1	0.254	0.330
3-Hydroxycarbofuran	75.9	0.32	0.415	74.7	0.318	0.427
Aldicarb	74.0	0.46	0.621	77.2	0.331	0.429
Propoxur	75.4	0.37	0.493	73.5	0.309	0.421
Carbofuran	77.0	0.25	0.329	76.3	0.303	0.398
Carbaryl	75.2	0.31	0.416	77.3	0.251	0.324
1-Naphthol	70.0	0.92	1.321	88.3	0.289	0.327
Methiocarb	76.0	0.36	0.479	74.9	0.314	0.419
BDMC	76.6	0.44	0.572	76.2	0.353	0.464

Table 3. Reproducibility data for the amount of seven injections of the 75-ppb carbamate mix using the legacy and 2013 Alliance HPLC systems.

Amount 7 injections (25-ppb)	Legacy Alliance HPLC			2013 Alliance HPLC		
Analyte	Mean RT	Std Dev	%RSD	Mean RT	Std Dev	%RSD
Aldicarb sulfoxide	25.4	0.099	0.391	24.8	0.133	0.539
Aldicarb sulfone	25.4	0.083	0.328	24.9	0.148	0.594
Oxamyl	25.6	0.108	0.422	25.1	0.076	0.303
Methomyl	25.3	0.106	0.420	25.6	0.122	0.477
3-Hydroxycarbofuran	25.7	0.095	0.369	24.8	0.115	0.465
Aldicarb	24.9	0.124	0.499	25.6	0.158	0.619
Propoxur	25.2	0.130	0.515	24.4	0.104	0.425
Carbofuran	25.8	0.108	0.418	25.4	0.154	0.607
Carbaryl	25.1	0.100	0.399	25.7	0.108	0.420
1-Naphthol	24.3	0.319	1.313	29.4	0.226	0.771
Methiocarb	25.4	0.113	0.445	24.7	0.220	0.889
BDMC	25.1	0.154	0.614	25.6	0.216	0.843

Table 4. Reproducibility data for amount for seven injections of the 25-ppb carbamate mix using the legacy and 2013 Alliance HPLC systems.

Amount 7 injections (10-ppb)	Legacy Alliance HPLC			2013 Alliance HPLC		
Analyte	Mean RT	Std Dev	%RSD	Mean RT	Std Dev	%RSD
Aldicarb sulfoxide	10.1	0.034	0.338	9.7	0.062	0.638
Aldicarb sulfone	10.0	0.041	0.415	9.7	0.070	0.724
Oxamyl	10.2	0.051	0.501	9.8	0.067	0.678
Methomyl	10.0	0.049	0.490	9.9	0.094	0.939
3-Hydroxycarbofuran	10.2	0.041	0.405	9.7	0.077	0.794
Aldicarb	9.8	0.059	0.602	10.0	0.106	1.055
Propoxur	10.0	0.057	0.578	9.6	0.076	0.793
Carbofuran	10.2	0.067	0.655	10.0	0.100	1.005
Carbaryl	10.0	0.042	0.419	10.0	0.041	0.410
1-Naphthol	10.2	0.099	0.967	11.6	0.146	1.262
Methiocarb	10.1	0.071	0.698	9.5	0.088	0.924
BDMC	10.3	0.142	1.368	9.5	0.098	1.032

Table 5. Reproducibility data for amount for seven injections of the 10-ppb carbamate mix on the legacy and 2013 Alliance HPLC systems.

To investigate the detection of low levels of the pesticides, a blank, 0.2-ppb, and 0.1-ppb carbamate mix was injected with the resulting chromatograms shown in Figures 3 and 4. The calculated limits of detection, shown in Table 6, were 0.1-ppb or less for both systems with the exception of 1-Naphthol which, as previously mentioned, is a degradation product.

To test the two systems using a blind sample, the ERA performance evaluation sample was used. For both the previous and current systems, the calculated amounts were found to be within the acceptable QC performance limits and within 1-ppb of each other, as shown in Table 7.

Limit of detection	Legacy Alliance HPLC	2013 Alliance HPLC
Aldicarb sulfoxide	0.05	0.03
Aldicarb sulfone	0.06	0.03
Oxamyl	0.10	0.04
Methomyl	0.06	0.07
3-Hydroxycarbofuran	0.09	0.02
Aldicarb	0.02	0.03
Propoxur	0.04	0.03
Carbofuran	0.07	0.10
Carbaryl	0.09	0.05
1-Naphthol	0.19	0.36
Methiocarb	0.04	0.04
BDMC	0.07	0.10

Table 6. MDL data for seven injections of a 0.2-ppb mix calculated per 40 CFR pt 136 App B (ppb).

ERA Certified Mix Lot #5180-707	Cert value	QC acceptable range	Legacy Alliance HPLC	2013 Alliance HPLC
Aldicarb sulfoxide	16.2	11.9-21.6	13.7	13.3
Aldicarb sulfone	19.0	14.2-23.4	17.9	18.0
Oxamyl (Vydate)	70.9	52.5-85.8	59.8	58.9
Methomyl	53.7	41.1-67.1	46.9	46.2
3-Hydroxycarbofuran	45.6	34.8-57.0	39.6	38.9
Aldicarb	30.1	21.9-37.9	26.4	26.0
Propoxur (Baygon)	42.1	32.5-51.8	36.7	36.2
Carbofuran	39.5	27.2-50.2	35.1	34.3
Carbaryl	24.4	16.9-29.8	20.3	20.0
Methiocarb	82.8	61.4-97.7	69.8	69.1

Table 7. Analysis of ERA QC carbamate mix units are ppb.

CONCLUSIONS

The data show that similar results are obtained on the legacy and 2013 Alliance HPLC systems for Carbamate Analysis, yielding the following benefits:

- Conformance to EPA Method 531.2
- Baseline separation of analytes
- Run time of 25 minutes
- Provides a complete Waters solution for carbamate analysis

References

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Company information

The term "Waters" shall mean Waters Corporation and/or a Related Company of Waters Corporation. A Related Company of Waters Corporation means any corporation or other business entity that is directly controlled by Waters Corporation. Control means direct or indirect ownership of or other beneficial interest in fifty percent (50%) or more of the voting stock, other voting interest, or income of a corporation or other business entity.

Copyright notice

The information in this document is subject to change without notice. Waters Corporation assumes no responsibility for any typographic errors that may appear in this document. This document is believed to be complete and accurate at the time of publication.

Trademarks

Contacting Waters

Contact Waters® with technical questions regarding the use, transportation, removal, or disposal of any Waters product. You can reach us via the Internet, telephone, or conventional mail.

Waters contact information:

Contacting medium	Information
Internet	The Waters Web site includes contact information for Waters locations worldwide. Visit www.waters.com.
Telephone and fax	From the USA or Canada, phone 800 252-HPLC, or fax 508 872 1990. For other locations worldwide, phone and fax numbers appear in the Waters Web site.
Conventional mail	Waters Corporation 34 Maple Street Milford, MA 01757 USA

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License, Warranty, Support, Shipment, Damage, Claim, and Return Information

Software license and warranty

All use of the Waters Software shall be governed by the terms and conditions of the Waters Software License Agreement, attached hereto as Appendix A.

The term "Software" includes the object code version of the MassLynx software, Breeze software, Empower software, Waters NuGenesis Scientific Data Management System (SDMS) software, Waters SDMS Vision Publisher software, Waters Analytical Workflow Manager (AWM) software, Waters UNIFI software and/or such other software licensed to you by Waters. The Software is comprised of the computer programs, media containing the computer programs (including Oracle® Network Embedded Software, where applicable), user documentation, and any upgrades that Waters may provide to you.

Instrumentation and service warranty

Limited warranty: instrumentation

Waters warrants from the date of shipment for the applicable warranty period that its instrumentation identified and/or marketed as Waters products shall be free from defects in design, material, and workmanship and shall conform to and perform materially in accordance with the specifications set forth in the applicable operator or user manual when used in the proper operating environment under normal use and service. This warranty covers all new instrumentation products manufactured by Waters. Any warranty that may be applicable to third-party instrumentation products and accessories shall be provided by the respective manufacturers or suppliers of such third-party components.

Waters instruments are for use only by properly qualified personnel. Waters instruments labeled and identified as *in vitro* diagnostic ("IVD") devices may

be used for IVD purposes. Such IVD uses must be in accordance with the instrument's intended use statement provided in the product literature. Any patient diagnosis or treatment determination made as a result of data generated using a Waters IVD instrument must be made by a qualified health care professional. Waters instruments that are not labeled and identified as IVDs are general laboratory instruments intended for research use only and are not for use in IVD procedures. Customer shall not use any such general laboratory instruments for IVD purposes.

This instrumentation limited warranty is subject to the conditions set forth below.

Exclusions

The foregoing limited warranty does not apply to any material deviation from the specifications by any instrumentation product that results from (a) use of the instrumentation for any purpose other than general purpose use unless specifically expressed otherwise in the product literature; (b) use of the instrumentation products for investigational use with or without confirmation of diagnosis by another, medically established diagnostic product or procedure; (c) errors or defects in any third-party component; (d) modification of the instrumentation products by anyone other than Waters; (e) failure by customer to install any standard enhancement or update in accordance with an update procedure or release of firmware or any operating system release; (f) any willful or negligent action or omission of customer; (g) any misuse, or incorrect use, of the instrumentation product; (h) any malfunction of any information system or instrument with which the instrumentation product may be connected; or (i) failure to establish or maintain the operating environment for the instrumentation product in accordance with the applicable operator or user manual.

Exclusive remedy

In the event of any failure of a Waters' instrumentation product to perform in accordance with the foregoing limited warranty, Waters' sole liability and customer's sole and exclusive remedy, shall at Waters' sole discretion be the repair or replacement of the instrumentation product or refund of amounts paid by customer for the instrumentation product that does not meet the limited warranty.

Warranty service

Warranty service is performed at no charge and at Waters' option and in Waters' sole discretion in one of four ways:

- With your authorization, a service representative will access your system remotely.
- A service representative is dispatched to the customer facility.
- The instrumentation product is returned for repair at a Waters facility.
- Replacement parts with appropriate installation instructions are sent to the customer.

Warranty service is performed only if the customer notifies Waters during the applicable warranty period.

Unless otherwise agreed in writing at the time of sale, if the instrumentation product for which warranty service is sought has been removed from the initial installation geographic site, no warranty service will be provided.

Warranty service is provided during normal business hours (8:00 A.M. to 5:00 P.M., Monday through Friday). Service is not available when Waters offices are closed in observance of legal holidays.

Warranty service exceptions for instrumentation

Warranty service is not performed on

- any instrumentation product or part that has been repaired by others, improperly installed, altered, or damaged in any way.
- any instrumentation product or parts not manufactured by Waters.
- any instrumentation product that malfunctions because the customer has failed to perform maintenance, calibration checks, or observe good operating procedures.
- any instrumentation product that malfunctions due to the use of unapproved maintenance, or repair parts, or operating supplies and computers not meeting minimum hardware requirements, or as a result of network-related problems.

Repair or replacement is not made

- for expendable items such as filament devices, panel lights, fuses, batteries, filters, seals, and other items contained in a Performance Maintenance Kit, when such items were operable at the time of initial use.

- because of decomposition due to chemical action.
- because of poor facilities, operating conditions, or inadequate utilities.

Limited warranty: repair and maintenance service

Waters warrants repairs and maintenance services for a period of ninety (90) days from the date of delivery of such services. Waters also warrants the parts used shall be free from defects in design, material and workmanship and shall conform to and perform materially in accordance with the specifications set forth in the applicable operator or user manual when used in the proper operating environment under normal use and service.

Repair and maintenance warranty service is not provided for

- any instrument, maintenance or repair part that has been repaired by others, improperly installed, altered, or damaged in any way.
- any instrumentation product that malfunctions because the customer has failed to perform maintenance, calibration checks, or observe good operating procedures.
- any instrumentation product that malfunctions due to the use of unapproved maintenance or repair parts or operating supplies and computers not meeting minimum hardware requirements or as a result of network related problems.
- any system component or assembly that falls outside the scope of the repair or maintenance service that fails either during or within ninety (90) days of the service event.

Repair or replacement is not made

- because of decomposition due to chemical action.
- because of poor facilities, operating conditions, or inadequate utilities.

Warranty disclaimers

TO THE EXTENT PERMITTED BY APPLICABLE LAW, THE LIMITED WARRANTIES SET FORTH HEREIN ARE EXCLUSIVE AND IN LIEU OF ALL OTHER REPRESENTATIONS, WARRANTIES AND GUARANTEES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS OF THE PRODUCTS FOR A PARTICULAR PURPOSE, INCLUDING FITNESS FOR USE IN CLINICAL DIAGNOSTIC PROCEDURES OR FOR INVESTIGATIONAL USE WITH OR WITHOUT CONFIRMATION OF DIAGNOSIS BY ANOTHER MEDICALLY ESTABLISHED DIAGNOSTIC PRODUCT OR PROCEDURE, OR NONINFRINGEMENT, AND ANY WARRANTIES ARISING OUT OF COURSE OF DEALING OR COURSE OF PERFORMANCE. CUSTOMER EXPRESSLY ACKNOWLEDGES THAT BECAUSE OF THE COMPLEX NATURE OF THE PRODUCTS AND THEIR MANUFACTURE, WATERS CANNOT AND DOES NOT WARRANT THAT THE OPERATION OF THE PRODUCTS WILL BE WITHOUT INTERRUPTION OR ERROR-FREE OR WITHOUT DEFECT. CUSTOMER EXPRESSLY ACKNOWLEDGES THAT CUSTOMER IS SOLELY RESPONSIBLE FOR USE OF THE PRODUCTS IN CLINCIAL DIAGNOSTIC PROCEDURES OR FOR INVESTIGATIONAL USE WITH OR WITHOUT CONFIRMATION OF DIAGNOSIS BY ANOTHER MEDICALLY ESTABLISHED DIAGNOSTIC PRODUCT OR PROCEDURE.

TO THE EXTENT PERMITTED BY APPLICABLE LAW, IN NO EVENT SHALL WATERS OR ITS SUPPLIERS BE LIABLE FOR ANY INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR CONSEQUENTIAL DAMAGES INCLUDING, WITHOUT LIMITATION, DAMAGES FOR LOSS OF BUSINESS INFORMATION OR PECUNIARY LOSS ARISING OUT OF THE USE OR INABILITY TO USE THE PRODUCTS, EVEN IF WATERS HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. WATERS' TOTAL LIABILITY IN ANY EVENT SHALL NOT EXCEED THE PURCHASE PRICE OF THE GOODS AND SERVICES TO WHICH THE DAMAGES RELATE AND, THE PARTIES AGREE THAT SUCH LIMITED LIABILITY IS A REASONABLE ALLOCATION OF THE RISKS INVOLVING THE PRODUCT.

Transfer of warranty

The warranty is not transferable from the original owner or original installation site to another geographic location without the written consent of Waters. In the event that the instrument(s) must be relocated within the same company and country during the warranty period, Waters offers relocation services to ensure proper care is taken when de-installing, packing and re-installing in order to maintain the warranty coverage.

Warranty periods

Note that warranty periods begin when products are shipped.

Instrumentation:

Warranted item	Component or components	Warranty period
Electronic and mechanical assemblies	Entire instrument, except for maintenance parts, operating supplies, and expendable components.	One year (12 months) from the date of shipment, unless otherwise stated in the instrument's accompanying user documentation as in the case of the Waters 2695 Separations Module, whose documentation specifies that a two-year warranty applies to the instrument's sample manager and solvent manager drive mechanism. For instruments that have served as demonstration models, the warranty period is 90 days.
Normal wear and maintenance parts	As defined in the instrument Performance Maintenance Kit, if available.	Ninety (90) days from date of shipment.
Operating supplies and expendables	Autosampler vials, solvent and sample filters, and fuses.	Warranted to function properly when delivered.

Service:

Warranted item	Component or components	Warranty period
Parts installed during a demand service repair	Mechanical and electronic assemblies	Ninety (90) days from date of shipment.
Service labor	Service workmanship	Ninety (90) days from date of service delivery.

Warranty returns

No returns may be made without prior notification of, and authorization from, Waters. If it is necessary to return products to Waters, contact Waters Customer Service, the Waters subsidiary nearest you, or your Waters representative for a return merchandise authorization (RMA) number and forwarding address.

Extended and enhanced warranty coverage is available for instrumentation and software products under the applicable service and support plan. Contact your local Waters office for more information.

Warranty: non-Waters hardware

Waters does not assemble, configure, or install software on any computer or computer peripheral that has not been purchased from Waters.

The warranty for hardware not manufactured by Waters follows the warranty, if any, of the original equipment manufacturer.

Support and extended coverage

Waters' USA and Canadian customers seeking service and support may contact Waters Technical Service (800 252-4752). Others may phone their local Waters subsidiary or Waters corporate headquarters in Milford, Massachusetts (USA), or they may visit the Waters Web site (http://www.waters.com) and click Support.

Extended support and coverage are available through a Total Assurance Warranty (TAW), or a Total Assurance Plan (TAP).

Total Assurance Warranty is available during the first 90 days of system ownership and receives system discount. It provides full support coverage for two years and guarantees a scheduled Performance Maintenance (PM) Visit in year two.

Total Assurance Plan is available at the end of the Warranty and is renewable annually, it also provides annual scheduled PM visit.

Both TAW, and TAP provide technical telephone support ,priority service, repair visits and replacement parts as needed to ensure your system is running at peak performance.

Installation and extended training

Instrument startup

As part of the purchased installation charge, Waters offers familiarization traning for a single, designated primary operator.

Instrument startup consists of these procedures:

- Assembling computer hardware and connecting the printer.
- Connecting computer hardware to the system instruments.
- Configuring and testing a system for proper instrument function and data collection.

Optional installation services are available to purchasers of workstation add-on kit software products. The services consist of software installation, system configuration, and primary operator familiarization training. During this day of system installation service, a certified Waters field service technician will configure the customer's computer, load software, and interface the computer with the system.

Extended training

Waters Educational Services provides instrument and software training beyond that which is provided at startup. Courses are available at the customer site, our worldwide campus in Milford, Mass., U.S.A., in our Regional Training Centers in Europe and Asia, and at most Waters subsidiaries. Programs can be generic or customized to address specific challenges.

For details about the training and extended support programs, Waters' USA, and Canadian customers may contact Waters Technical Service (800 252-4752). Others may phone their local Waters subsidiary or Waters corporate headquarters in Milford, Massachusetts (USA), or they may visit the Waters Web site (http://www.waters.com), and click Education, or Services & Support.

Shipments, damages, claims, and returns

All shipments are made free on board (FOB) shipping point. Waters suggests that you authorize insurance for all shipments. Instruments and major components are packed and shipped via ground transportation unless otherwise required. Supplies and/or replacement parts are packed and shipped via a ground courier, air parcel post, or parcel post, unless otherwise requested.

Damages

The U.S. Interstate Commerce Commission (ICC) has determined that carriers are as responsible for concealed damages that occur during transit as they are for obvious damages. Concealed damage is damage that occurs to the contents of a shipping package where the package exterior remains apparently undamaged. Therefore, unpack the instrument or component promptly after receiving it, aware that it may have sustained concealed damage while in transit.

Claims

If you discover the item shipped has sustained concealed damage, do not continue to unpack it. Instead, request the local agent or carrier to immediately inspect the unit, and secure a written (inspection) report of his or her findings to support the claim. You must make this request within 15 days

of receiving the damaged unit, otherwise, the carrier will not honor the claim. Do not return damaged goods to Waters without first securing the inspection report and contacting Waters for a return merchandise authorization (RMA) number.

Ensure the shipment is protected and secure after you receive it. Components removed from the shipment, or damaged while awaiting installation, are the responsibility of the customer.

After a damage inspection report is secured, Waters cooperates fully in supplying replacements and handling a claim, which either party may initiate.

Returns

No returns may be made without prior notification and authorization, If for any reason it is necessary to return material to Waters, contact Waters Customer Service, the Waters subsidiary nearest you, or your local Waters representative for a return merchandise authorization (RMA) number and forwarding address.

A Waters Software License Agreement

This is a legal agreement ("Agreement") between you (the "Customer") and Waters Corporation and/or a Related Company of Waters Corporation (collectively, "Waters"). A Related Company of Waters Corporation means any corporation or other business entity that is directly controlled by Waters Corporation. Control means direct or indirect ownership of or other beneficial interest in fifty percent (50%) or more of the voting stock, other voting interest, or income of a corporation or other business entity.

By using Waters' Software including any Upgrades (as defined below), you represent that you have the power and authority to enter into this Agreement on behalf of your company. In such event, "you" refers to your company. YOU MUST READ AND AGREE TO THE TERMS OF THIS AGREEMENT BEFORE ANY WATERS' SOFTWARE CAN BE INSTALLED OR USED. BY CLICKING ON THE "ACCEPT" BUTTON OF THIS AGREEMENT, OR BY INSTALLING OR USING WATERS' SOFTWARE, YOU ARE AGREEING TO BE BOUND BY THE TERMS AND CONDITIONS OF THIS AGREEMENT.

IF YOU DO NOT AGREE WITH THE TERMS AND CONDITIONS OF THIS AGREEMENT, THEN YOU SHOULD EXIT THIS PAGE AND NOT INSTALL OR USE ANY WATERS' SOFTWARE. BY DOING SO YOU FOREGO ANY IMPLIED OR STATED RIGHTS TO INSTALL OR USE WATERS' SOFTWARE, AND YOU SHALL RETURN IT TO US FOR A FULL REFUND (IF APPLICABLE).

All use of Waters' Software shall be governed by the following terms and conditions.

1. **Definitions.**

    a. The term "Software" includes the object code version of the MassLynx software, Breeze software, Empower software, Waters NuGenesis Scientific Data Management System (SDMS) software, Waters SDMS Vision Publisher software, Waters Analytical Workflow Manager (AWM) software, Waters UNIFI software and/or such other software indicated on the Waters' Quotation and accepted by you on your Purchase Order ("PO") and licensed to you by Waters. The Software is comprised of the computer programs, media containing the computer programs (including Oracle®

Network Embedded Software, where applicable), user documentation, and any Upgrades that Waters may provide to you. You acknowledge and agree that the Software constitutes Waters' confidential information.

b. "Upgrades" shall mean and include any changes, additions, or corrections made by Waters to the Software.

c. "Quotation" shall mean a document provided by an authorized representative of Waters which describes the Software, Waters' products, and/or those certain Waters Partners' product(s), if any, that you, the Customer, may purchase, including pricing. All such Quotations shall include and be subject to the terms and conditions contained in this Agreement unless otherwise agreed in writing.

d. "Purchase Order" shall mean a written authorization from you, the Customer, to Waters for the purchase of Software and products. All such Purchase Orders shall reference a Quotation and be subject to the terms and conditions contained in this Agreement.

2. License and Usage of Software

Subject to the terms and conditions of this Agreement and upon payment of the applicable license fees, Waters hereby grants to you a non-exclusive, non-transferable, non-sublicenseable right and license during the Term (as defined below) to use the Software in connection with Waters' products and/or those certain Waters' Partner product(s) authorized by Waters, if any. In this regard, you may install, copy, operate and transmit the Software in whole or in part: (i) for single-seat licenses, only as necessary to use the Software either on a single personal computer or workstation, and (ii) for client/server licenses, in a reasonable manner to ensure that the number of users does not exceed the number of users for which you have paid license fees. The Software is protected by the copyright laws of the United States and international treaties. A "Waters' Partner" is an entity with which Waters has a business alliance.

3. **Ownership of the Software.**

The Software is licensed to you, not sold. Subject to the rights granted above, Waters and the manufacturers of any third-party software included within the Software retain all right, title and interest in and to the Software. You acknowledge that the Software is licensed in object code for use solely in conjunction with Waters' products. Use of the Software in conjunction with non-Waters products, other than those certain Waters' Partner product(s) authorized by Waters, if any, is not licensed hereunder and is prohibited.

4. **General Usage Restrictions.**

a. You may not use the Software for any purpose beyond the scope of the license granted in this Agreement.

b. Without limiting the generality of the foregoing, you will not: (i) authorize or permit use of the Software by persons not authorized to do so; (ii) market or distribute the Software; (iii) assign, sublicense, sell, lease or otherwise transfer, convey or pledge as security or otherwise encumber, your rights under the license granted in Section 2 above; (iv) use the Software in any time-sharing,

subscription, rental or service bureau arrangement, including, without limitation, any use to provide services or process data for the benefit of, or on behalf of, any third party; (v) modify the Software; (vi) combine or integrate the Software with hardware, software or technology not provided to you by Waters; (vii) decompile, disassemble, reverse engineer (unless required by law for interoperability) or otherwise attempt to obtain or perceive the source code from which any component of the Software is compiled or interpreted, and you hereby acknowledge that nothing in this Agreement shall be construed to grant you any right to obtain or use such source code; (viii) disclose the results of any benchmark tests run on the Software (whether or not the results were obtained with assistance from Waters) to any party; or (ix) make copies of the Software other than a reasonable number of copies solely for archival purposes, provided that you reproduce and include Waters' and any third party manufacturer's copyright notices on any backup, disaster recovery or archival copies of the Software and on copies of any user documentation. It is understood and agreed that you may temporarily move, install and operate the Software at a

different computer or workstation in the event of computer or workstation malfunction.

c. The Software is not for use by individuals other than properly qualified personnel. Generally, the Software is not intended for use in *in vitro* diagnostic ("IVD") procedures, but is general laboratory software intended for research use only. Customer shall not use any such general laboratory software for IVD purposes. Notwithstanding the foregoing, certain Software may be labeled and identified as an IVD device ("IVD Software") and as such may be used for IVD purposes. Customer shall not use such IVD Software except in accordance with the IVD Software's intended use statement provided in the product literature. Any patient diagnosis or treatment determination made as a result of data generated using the IVD Software must be made by a qualified health care professional.

5. Oracle Software.

a. Waters has provided, as part of the Software, access to certain Oracle embedded software as a convenience. To the extent that the Software contains Oracle software, you acknowledge that Oracle has no express or implied obligation to provide any technical or other support to you for such software. Please contact Waters directly for technical support and customer service related to the Oracle software.

b. Oracle may provide to its own customers, who may include you, as part of an Oracle software package source code identical to the Oracle source code embedded in the Software. Regardless of whether Oracle does do so, the Oracle source code embedded in the Software shall be governed solely by the terms of this Agreement. If you have obtained an Oracle software license, you must not attempt to use the Oracle software to access, use, reproduce, modify reverse, engineer or otherwise tamper with the Software.

c. Third party technology that is appropriate or necessary for use with some Oracle software, if any, is specified in the Software

documentation or otherwise by Waters and such third party technology is licensed to you only for use with the Software under the terms of the third party license agreement specified in the Software documentation or otherwise by Waters and not under the terms of this Agreement.

d. Oracle is a third party beneficiary of the rights and obligations of this Agreement.

6. Exclusion of the Uniform Computer Information Transactions Act ("UCITA").

It is understood and agreed that the provisions of the UCITA do not apply to this Agreement and the license contained herein.

7. Warranties; Disclaimers.

a. **Representations and Warranties.** Each party to this Agreement hereby represents and warrants (i) that it is duly organized, validly existing and in good standing under the laws of its jurisdiction of incorporation; and (ii) that the first installation or use of the Software in the designated operating environment constitutes a valid and binding obligation between you and Waters and will be

enforceable against you in accordance with the terms of this Agreement.

b. <u>Waters Limited Warranty</u>.

i.Waters warrants for a period of ninety (90) days from the date of shipment (the "Warranty Period") that the Software will, when used in the designated operating environment, perform substantially in accordance with the operating specifications set forth in the user manual as amended by any release notes issued during the Warranty Period and that the Software will be free of defects in materials and workmanship (the "Limited Warranty"). The Limited Warranty shall apply only to the most current version of the Software that was supplied to you by Waters.

ii.The Limited Warranty is subject to the conditions set forth below:

(a.) You must give written notice to Waters during the Warranty Period with an explanation of the circumstances of any claim that the Software fails to conform to this Limited Warranty.

(b.) Your sole and exclusive remedy in the event of any such failure is expressly limited to the correction or replacement of the defective Software or the refund of the fees paid for the defective Software.

(c.) The Limited Warranty shall not apply to any Software delivered to you that has been improperly installed or modified or that has been the subject of neglect, misuse, abuse, misapplication or alteration.

(d.) No representative of Waters is authorized to commit Waters to any warranty other than the Limited Warranty contained herein.

c. **Disclaimer.** SUBJECT TO THE LIMITED WARRANTY SET FORTH ABOVE, TO THE MAXIMUM EXTENT PERMITTED BY APPLICABLE LAW, WATERS AND ORACLE DISCLAIM ANY AND ALL PROMISES, REPRESENTATIONS AND WARRANTIES, WHETHER EXPRESS, IMPLIED OR STATUTORY, INCLUDING, BUT NOT LIMITED TO, ANY WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, DATA ACCURACY, SYSTEM INTEGRATION, TITLE, NON-INFRINGEMENT AND/OR QUIET ENJOYMENT, AND THE SOFTWARE, DOCUMENTATION AND ANY OTHER INFORMATION OR MATERIALS OTHERWISE PROVIDED ARE PROVIDED "AS IS" AND ARE SUBJECT TO NO OTHER WARRANTY. NO WARRANTY IS MADE BY WATERS AND/OR ORACLE ON THE BASIS OF TRADE USAGE, COURSE OF DEALING OR COURSE OF TRADE. NEITHER WATERS NOR ORACLE WARRANTS THAT THE SOFTWARE WILL MEET YOUR REQUIREMENTS OR THAT THE OPERATION OF THE SOFTWARE WILL BE UNINTERRUPTED OR ERROR-FREE,

OR THAT ALL ERRORS WILL BE CORRECTED. YOU ACKNOWLEDGE THAT WATERS' AND/OR ORACLE'S OBLIGATIONS UNDER THIS AGREEMENT ARE FOR YOUR BENEFIT ONLY.

d. **Exclusions of Remedies; Limitation of Liability.** OTHER THAN AS SET OUT IN SECTION 7.b ABOVE AND TO THE EXTENT PERMITTED BY APPLICABLE LAW, IN NO EVENT SHALL WATERS AND/OR ORACLE BE LIABLE TO YOU FOR ANY INCIDENTAL, INDIRECT, SPECIAL, CONSEQUENTIAL OR PUNITIVE DAMAGES, REGARDLESS OF THE NATURE OF THE CLAIM, INCLUDING, WITHOUT LIMITATION, LOST PROFITS, COSTS OF DELAY, ANY FAILURE OF DELIVERY, BUSINESS INTERRUPTION, COSTS OF LOST OR DAMAGED DATA OR DOCUMENTATION OR LIABILITIES TO THIRD PARTIES ARISING FROM ANY SOURCE, EVEN IF WATERS AND/OR ORACLE HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. THIS LIMITATION UPON DAMAGES AND CLAIMS IS INTENDED TO APPLY WITHOUT REGARD TO WHETHER OTHER PROVISIONS OF THIS AGREEMENT HAVE

BEEN BREACHED OR HAVE PROVEN INEFFECTIVE. TO THE EXTENT PERMITTED BY APPLICABLE LAW, ORACLE SHALL NOT BE LIABLE TO YOU FOR ANY OTHER DAMAGES, INCLUDING DIRECT DAMAGES. THE CUMULATIVE LIABILITY OF WATERS TO YOU FOR ALL CLAIMS ARISING FROM OR RELATING TO THIS AGREEMENT, INCLUDING, WITHOUT LIMITATION, ANY CAUSE OF ACTION ARISING IN CONTRACT, TORT, OR STRICT LIABILITY, SHALL NOT EXCEED THE TOTAL AMOUNT OF ALL FEES, IF ANY, THEN PAID TO WATERS BY YOU DURING THE TWELVE (12) MONTH PERIOD IMMEDIATELY PRIOR TO THE EVENT, ACT OR OMISSION GIVING RISE TO SUCH LIABILITY. THIS LIMITATION OF LIABILITY IS INTENDED TO APPLY WITHOUT REGARD TO WHETHER OTHER PROVISIONS OF THIS AGREEMENT HAVE BEEN BREACHED OR HAVE PROVED INEFFECTIVE.

e. **Essential Basis.** The parties acknowledge and agree that the disclaimers, exclusions and limitations of liability set forth in this Section 7 form an essential basis of this Agreement, and that, absent any such disclaimers, exclusions or limitation of liability, the terms of this Agreement, including, without limitation, the economic terms, would be substantially different.

8. **Term and Termination.**

a. **Term.** This Agreement shall remain in effect for as long as you are not in violation of any material provision contained in this Agreement (the "Term"). A substantial deviation of Waters' hardware from the specifications in the corresponding documentation will not be considered a breach that allows you to terminate this Agreement.

b. **Rights to Terminate.**

i. Each party has the right to terminate this Agreement, by giving written notice of termination to the other party, if: (a) the other party breaches this Agreement and (b) either the breach cannot be cured or, if the breach can be cured, it is not cured by the breaching

party within fifteen (15) days after receiving written notice of the breach from the non-breaching party; provided, however, in the event of a breach by you, at the discretion of Waters, this Agreement may be immediately revoked and terminated. In such event, Waters' shall have the following rights: (x) the right of termination as set forth above; (y) the right to obtain an injunction to enjoin your continued or repeated breaches; and (z) the right to all costs incurred by Waters as a result of the breach, including reasonable attorney's fees and costs.

ii. You may terminate this Agreement at any time by giving written notice of termination to Waters.

c. **Consequences of Termination**. When this Agreement expires or is terminated:

i.You must (a) immediately cease all use of the Software, (b) promptly return to Waters or destroy all copies of the Software in your possession or control and (c) certify in writing to Waters that you have complied with Sections (a) and (b).

ii. You will l remain obligated to pay any amounts you owe to Waters at that time.

9. Export Control.

a. The Software is subject to export controls under the U.S. Export Administration Regulations. Therefore, the Software may not be exported or re-exported to entities within, or residents or citizens of, embargoed countries or countries subject to applicable trade sanctions, nor to prohibited or denied persons or entities without proper government licenses. Information about such restrictions can be found at the following websites: http://www.treas.gov/ofac/ and www.bis.doc.gov/complianceandenforcement/Liststocheck.htm. Countries embargoed by the U.S. include Cuba, Iran, North Korea, Sudan and Syria. You are responsible for any violation of the U.S. export control laws related to the Software. By accepting this Agreement, you confirm that you are not a resident or citizen of any country currently embargoed by the U.S. and that you are not otherwise prohibited from receiving the Software.

b. If you are a branch of the United States government, you shall have "restricted rights" to use, duplicate, or disclose the Software as set forth in subdivision (c)(1)(ii) of Rights in Technical Data and Computer Software Federal Acquisition Regulations in Technical Data and Computer Software Federal Acquisition Regulations Supplement (DFARS) 252.227-7013 or subparagraphs (c)(1) and (2) of the Commercial Computer Software-Restricted Rights at 48 CFR 52.227_19.

10. Audit Rights.

You shall maintain accurate records as to your use of the Software as authorized by this Agreement. During the Term hereof, Waters, or persons designated by Waters, will, at any time, be entitled to inspect such records and your computers, in order to verify that the Software is being used by you in accordance with the terms of this Agreement, provided that Waters may conduct no more than one (1) audit in any twelve (12) month period. Any such audit will be performed at Waters' expense during normal business hours, provided that you shall promptly

reimburse Waters for the cost of such audit if such audit reveals that your use of the Software is not as authorized by this Agreement.

11. Transfer.

This Agreement shall be assignable by Waters. It shall not be assignable by you without the prior written consent of Waters.

12. Dispute Resolution.

a. All disputes arising in connection with this Agreement shall be finally settled under the Rules of Conciliation and Arbitration of the International Chamber of Commerce (the "Rules") by one or more arbitrators appointed in accordance with the Rules.

b. Notwithstanding the provisions of Section 12.a above, either party hereto shall be entitled to seek equitable relief against the other party in any competent court having jurisdiction over the parties without first submitting the matter to arbitration with respect to alleged breaches or threatened breaches of any material term or provision of this Agreement. The parties hereby irrevocably submit to the jurisdiction of any of said courts in any such claims and waive any claim or defense of inconvenient forum or lack of personal jurisdiction under any applicable law, decision, treaty or otherwise. In making the foregoing submission to jurisdiction, each party

expressly waives the benefit of any contrary provision of the laws of the jurisdiction of its incorporation or where it is doing business. Both parties represent and warrant that they are not immune from judicial proceeding and will not claim immunity for themselves or their property in any claims that may arise hereunder. The parties further agree that service of process or notice in any such action, suit or proceeding shall be effective if delivered in the same manner as the Quotation and PO. You acknowledge that the breach of the terms or conditions of this Agreement by you, including any unauthorized use, reproduction or transfer of the Software, may substantially diminish the value of the Software and irrevocably harm Waters.

13. Entire Agreement.

This Agreement sets forth the entire understanding and agreement between you and Waters and may be amended only in writing signed by both parties. NO LICENSOR, DISTRIBUTOR, DEALER, RETAILER, RESELLER, SALES PERSON, OR EMPLOYEE IS AUTHORIZED TO MODIFY THIS AGREEMENT OR TO MAKE ANY REPRESENTATION OR PROMISE

THAT IS DIFFERENT FROM, OR IN ADDITION TO, THE TERMS OF THIS AGREEMENT.

14. Waiver.

No waiver of any right under this Agreement will be effective unless in writing, signed by a duly authorized representative of the party to be bound. No waiver of any past or present right arising from any breach or failure to perform will be deemed to be a waiver of any future right arising under this Agreement.

15. Severability.

If any provision of this Agreement is invalid or unenforceable, that provision will be construed, limited, modified or, if necessary, severed, to the extent necessary, to eliminate its invalidity or unenforceability, and the other provisions of this Agreement will remain unaffected.

16. Relationship of the Parties; No Agency.

Nothing contained herein shall be construed to place Waters and you in a relationship of partners, joint ventures, principal agent or employer employee, and neither party shall have any authority to obligate or bind the other

whatsoever, except as specifically provided by the terms of this Agreement. In no event shall either party hold itself out to be an agent of the other with the authority to bind such other party to any agreement, contract or obligation.

17. Force Majeure.

Waters shall have no liability for failure to perform, or delay in performance, in the delivery of any and all Software caused by circumstances beyond Waters' reasonable control, including, but not limited to, acts of God, acts of nature, floods, fire, explosions, war or military mobilization, United States governmental action or inaction, request of governmental authority, delays of any kind in transportation or inability to obtain material or equipment, acts of other governments, strikes, or labor disturbances.

[XEVO TQ-S MICRO]

REDEFINING COMPACT PERFORMANCE

ROBUST SENSITIVITY BEYOND EXPECTATION

TQ-S micro

Waters

THE SCIENCE OF WHAT'S POSSIBLE.®

Xevo TQ-S micro

CLASS-LEADING PERFORMANCE THAT **CAN FIT INTO**

From the most powerful family of tandem quadrupole instruments, the Xevo® TQ-S micro from Waters® epitomizes our key elements of design. Reliable instrument operation is essential to maximize laboratory efficiency. The Xevo TQ-S micro is able to reproduce high quality analytical performance injection after injection, even with the most complex sample matrices.

Designed to acquire sensitive, robust and dependable data at accelerated rates of acquisition:

- Robust performance enabled by proven ZSpray™ and StepWave!™
  - Detect analytes at low concentrations in complex matrices.
  - Inject less sample with precision, accuracy and consistency.
- Xtended Dynamic Range™ (XDR) provides accessible sensitivity and method transfer.
- Confidently quantify more analytes using reproducible high acquisition rates with Xcelerated Ion Transfer™ (XIT) electronics.

ACQUITY UPLC I-Class with Xevo TQ-S micro

ANY LAB

UPLC/MRM comparison of Xevo TQ-S micro relative to Xevo TQD

Compound	Ionisation Mode	Relative S/N	Relative Peak Area
Bentazon	ESI-	3	4
Hexaflumuron	ESI-	3	7
Ioxynil	ESI-	12	10
Teflubenzuron	ESI-	5	10
Amphetamine	ESI+	2	10
Atrazine	ESI+	5	5
Buprofezin	ESI+	5	6
Chlortoluron	ESI+	4	6
Dicrotophos	ESI+	10	11
Hexazinone	ESI+	3	8
Methomyl	ESI+	5	5
Metolachlor	ESI+	4	6
Metoxuron	ESI+	3	6
Monolinuron	ESI+	3	5
Sebuthylazine	ESI+	5	5
Terbuthylazine	ESI+	5	4
Vitamin D	ESI+	4	16
Mean Value		**5**	**7**

GET AHEAD WITH FAST, SENSITIVE DATA

Reduced Laboratory Footprint

Innovative technological design has resulted in a mass spectrometer with a very small footprint (42% smaller than the Xevo TQ MS) that delivers unmatched performance in its class.

ENGINEERED SIMPLICITY

The design philosophy of Engineered Simplicity™ ensures maximum system performance with minimum effort.

- Uncomplicated IntelliStart™ software simplifies instrument set-up and operation.
- New features in TargetLynx XS™ provide quick and easy results review and reporting.
- Universal source architecture gives access to the widest range of ionization techniques in minutes.

T-Wave™

The next generation of collision cell technology further improving rapid, high quality, UPLC®-compatible MS/MS data acquisition.

Enabled by StepWave Technology

Revolutionary off-axis ion source technology that removes neutral molecules, reducing noise and providing robust performance.

XIT Electronics

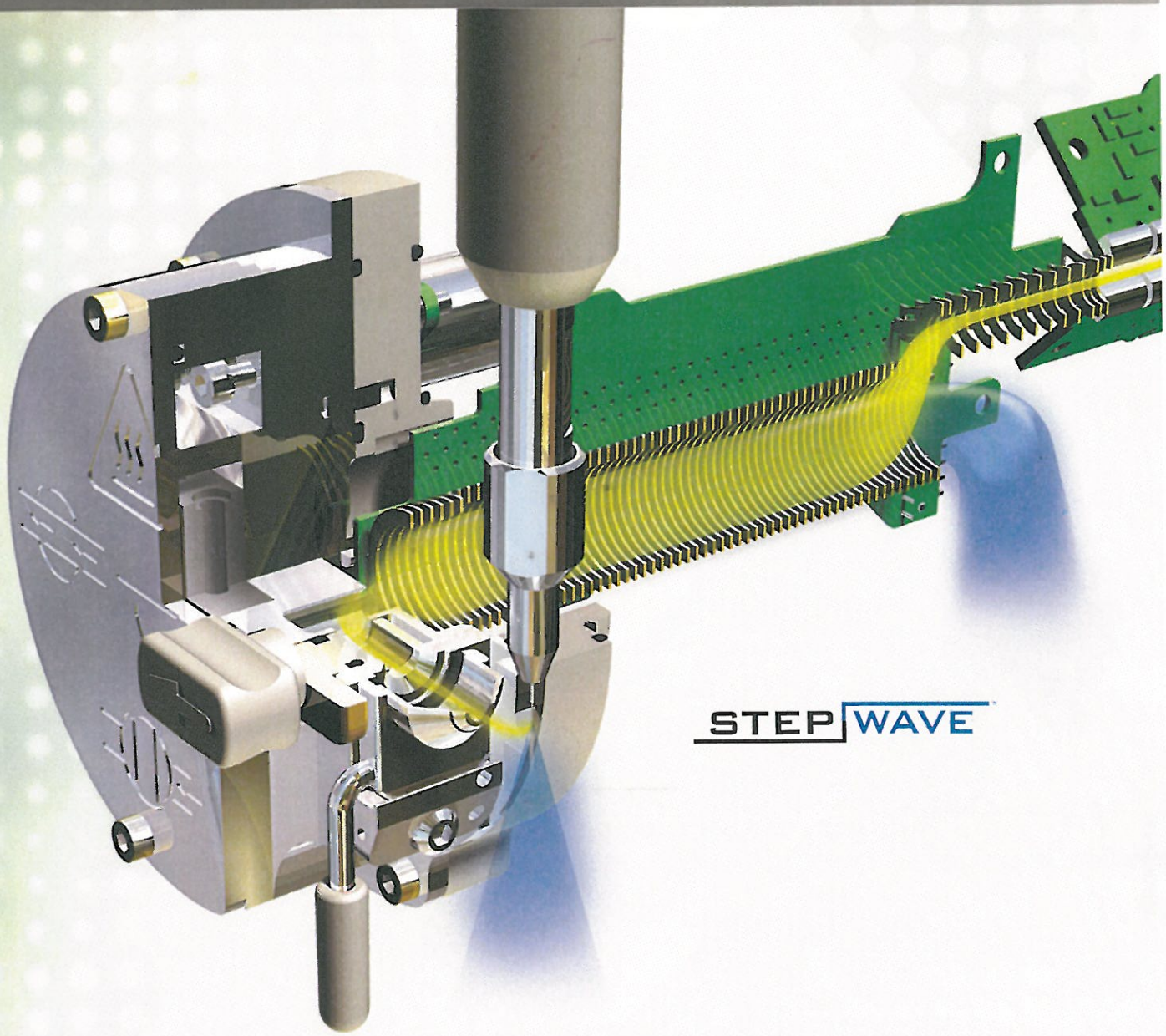
The new Xcelerated Ion Transfer electronics, featuring SpaceWire technology, enables rapid data acquisition so that narrow chromatographic peak widths are no barrier to reproducibility. Improved dynamic range is made possible by the XDR detector.

RADAR™

Using simultaneous quantitative and qualitative data acquisition it is possible to understand sample complexity, enabling intelligent method development while accurately quantifying target compounds with no compromise on performance.

PICs™

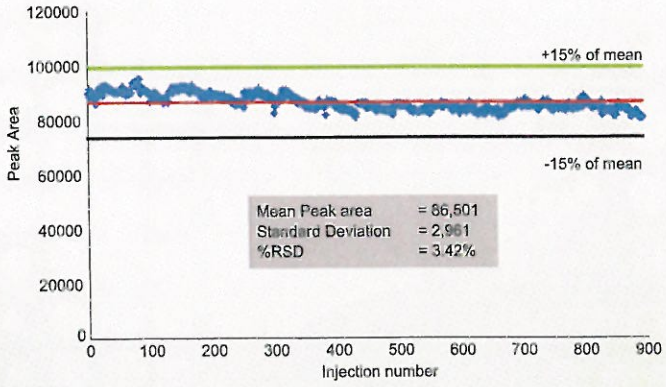
Product Ion Confirmation scanning is a data-directed product ion scanning acquisition capability, activated by a single check box, for additional confidence in analyte identification.



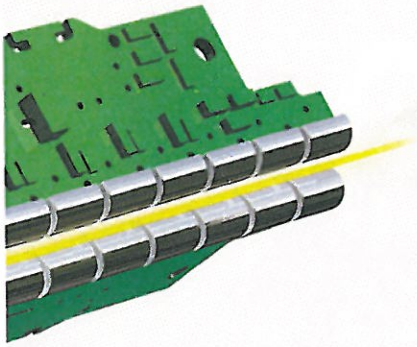
ROBUST **PERFORMANCE**

Robust performance begins in the source with proven ZSpray geometry, efficiently removing neutral molecules while drawing ions through the sample cone into the analyzer.

StepWave in the Xevo TQ-S micro is designed to cope with the challenges in the modern laboratory that are produced by high sample throughput and difficult matrices. Neutral molecules and gas load are passively removed for enhanced transmission, with the ion beam actively transferred into the mass analyzer, improving sensitivity and robustness.



Robust sensitivity for 900 injections of verapamil in protein-precipitated plasma (2.5 pg on column) with reproducibility of 3.4% RSD.



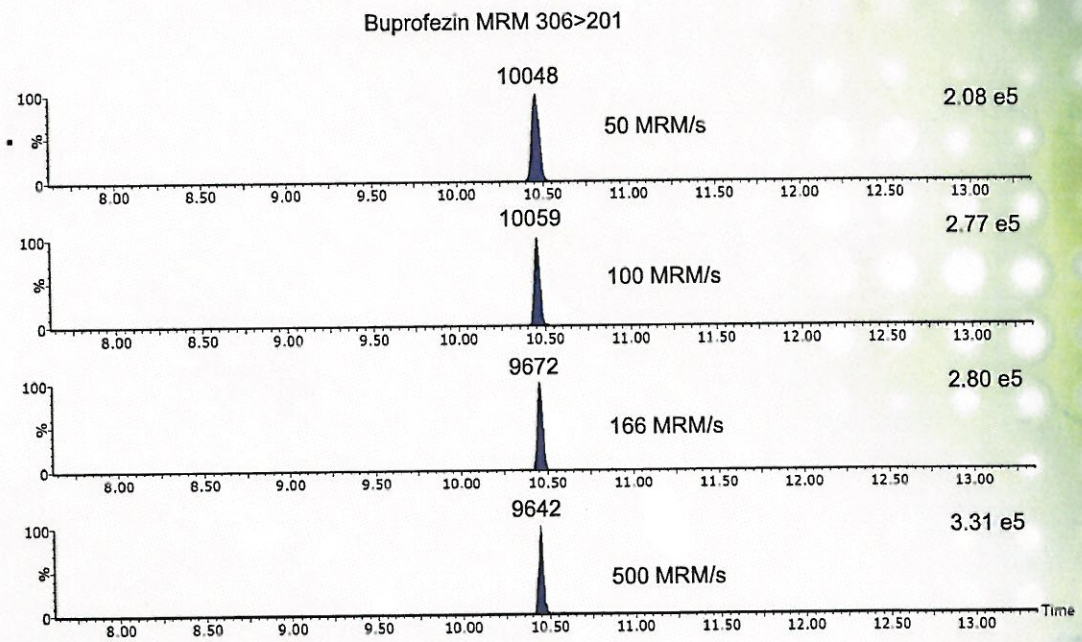
IMPROVED MRM ACQUISITION **PEAK CAPACITY**

Making Sensitivity Accessible with a Larger Dynamic Range

XIT electronics, using SpaceWire technology and the next generation of T-Wave collision cell, enable acquisition rates of 500 MRM/s with no compromise in data quality. The advanced XDR detector further increases the working range, allowing for easy method transfer.

As standard with the entire Xevo tandem quadrupole range, rapid polarity switching gives coverage of both positive and negative ionizing compounds in a single injection.

Repeatable Performance at High Speed



Injections of buprofezin pesticide showing only 4% loss in peak area (annotated above peaks) and no loss in peak height when increasing the rate of MRM transition acquisition from 50 MRM/s to 500 MRM/s. Ten injections were made at each rate of acquisition and reproducibility of peak area was excellent (<5.5% at each speed).

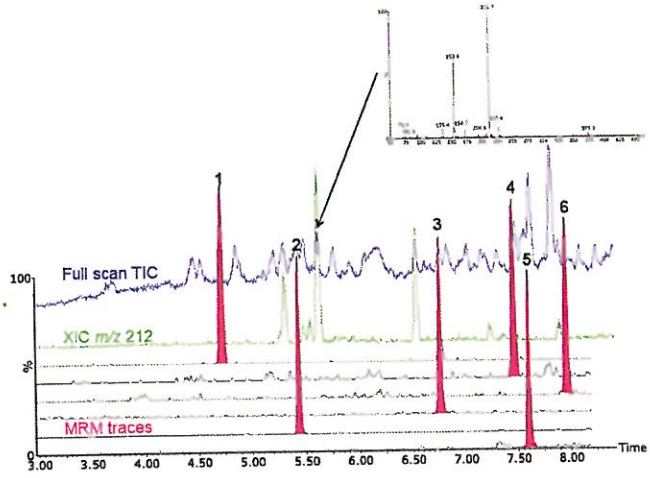
UNDERSTANDING **SAMPLE COMPLEXITY**

Use RADAR to Acquire Information – Rich Quantitative Data:

- Detect unexpected contaminants while performing routine quantitation.
- Characterize the background matrix for every sample, increasing data quality.
- Detect analytes that are not in a targeted MRM screening method.
- Improve method development by discovering more matrix components.
- Intelligent troubleshooting during routine analysis.

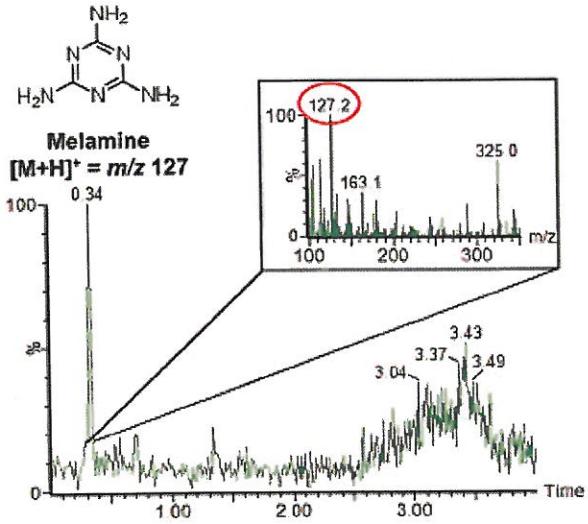
With RADAR it is possible to rapidly alternate between MS, MS/MS, positive and negative ion modes without compromising performance in any mode.

Characterization of the Background Matrix



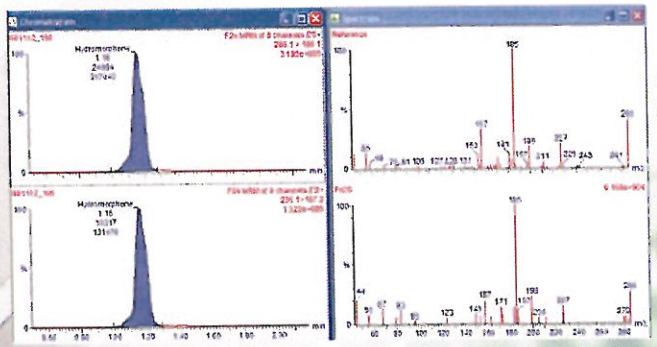
Extracted MRM chromatograms for 6 pesticides (methomyl (1), dicrotophos (2), metoxuron (3), simazine (4), hexazinone (5) and monolinuron (6) in ginger matrix at 10 ppb) acquired using simultaneous MRM and full scan MS m/z 50-450. Inset is the full scan spectrum of a peak acquired at 5.63 min and the green trace shows the XIC for m/z 212.

Unexpected Contaminant Detection



XIC for melamine from the full scan RADAR data Inset shows the background subtracted spectrum acquired at 0.34 minutes

Quantitate with Confidence



Hydromorphone reference spectrum

Hydromorphone acquired PICs spectrum

Product Ion Confirmation scanning (PICs) provides full confidence in results. Activated by a single check box in the method editor, PICs automatically triggers a product ion scan when a peak is detected by MRM.

Xevo® TQ-S micro

INFORMATICS **EXPANDING CAPABILITIES**

Easy to Use, Even with Minimal Experience

Intellistart simplifies system setup with a user-friendly interface that automates routine tasks and reduces the burden of complicated operation.

Simple, Integrated Method Databases

The extensive and searchable QUANPEDIA™ database allows for efficient management and optimization of quantitative LC/MS/MS method information, including automatic scheduling of MRMs and automated generation of acquisition and processing methods.

Instant Critical QC Information Delivery

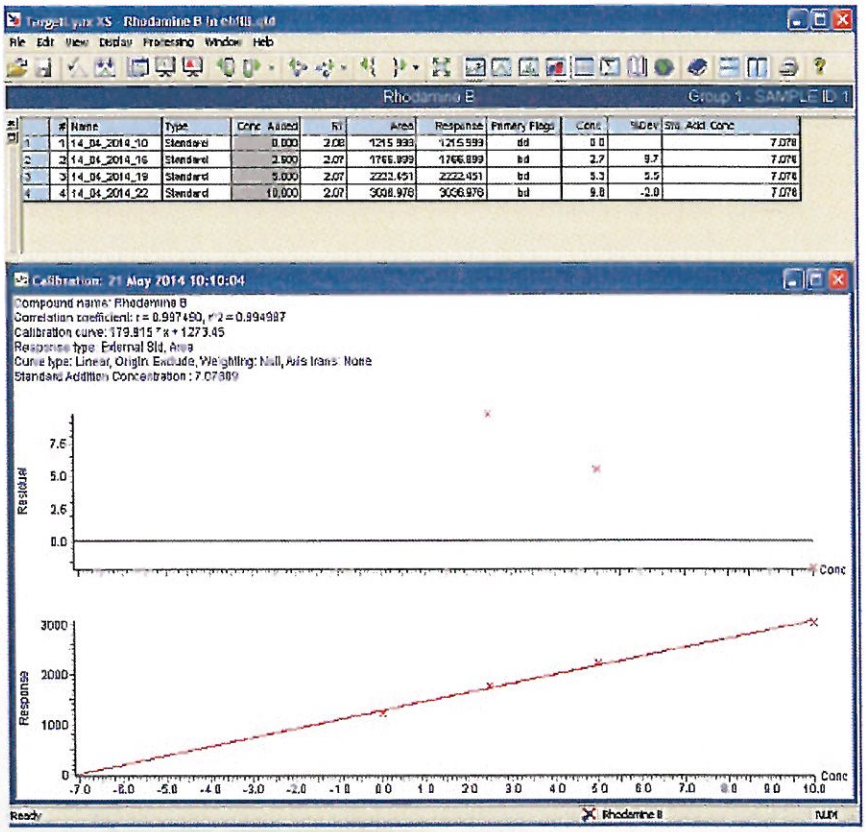
Automated real-time QC checking ensures that valuable samples are not wasted; if pre-defined tolerances are not met, QCMonitor will automatically send an email to notify the analyst.

Comprehensive Data Processing with Uncomplicated Results Review

TargetLynx XS now provides the ability to perform standard addition to accurately calculate analyte concentrations in complex samples despite extreme matrix variability. This software streamlines automated quantitative data review and reporting, minimizing the possibility of errors by providing a clear overview of QC checks and results.

Confidence in Your System Performance

Monitoring QC and sample results over time is easy with TrendPlot, which has simple graphical displays to enable quick decision making, allowing faster results delivery to the customer.



The TargetLynx XS browser showing the use of standard addition to calculate the concentration of Rhodamine B.

FLEXIBLE SEPARATION TO **COVER EVERY APPLICATION**

High resolution chromatographic peaks require the increased rates of high quality data acquisition provided by the Xevo TQ-S micro. Waters market-leading separation technologies include the ACQUITY UPLC® family of LC systems, UPC²® and APGC. Application flexibility is further enhanced by the range of quickly interchangeable ion source options made possible by universal ion source architecture.

ACQUITY UPC²

ACQUITY UPLC H-Class

ACQUITY UPLC I-Class

ACQUITY UPLC M-Class

APGC – Atmospheric Pressure Gas Chromatography

APPI – Atmospheric Pressure Photo Ionization
APCI – Atmospheric Pressure Chemical Ionization

ionKey/MS™

CHANGE YOUR ION SOURCES
NOT YOUR INSTRUMENTS

Universal Ion Source Architecture Covers Every Application, with Unlimited Potential.

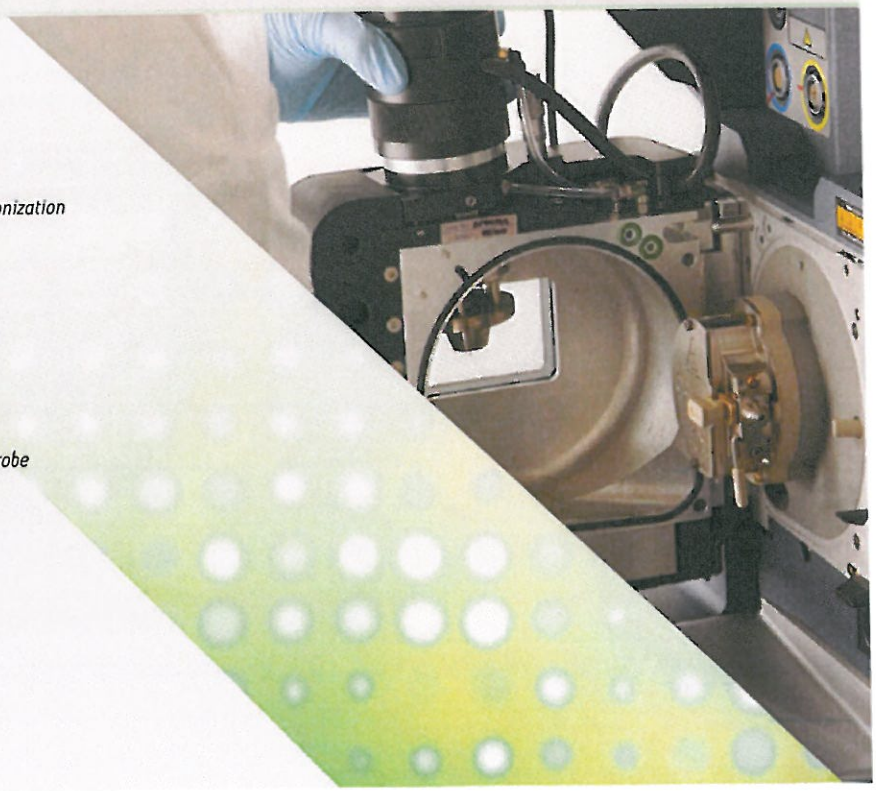
The Xevo range of mass spectrometers all have multiple ion source options which are interchangeable in minutes and provide optimal ionization for each function required in the laboratory.

The Xevo TQ-S micro is compatible with ESI, ESCi,® APCI, APPI, APGC, ASAP and ionKey/MS™ and is also simply changed with DESI (Prosolia), DART (IonSense) and LDTD (Phytronix) ion sources.

nanoFlow™ ESI

ESI – Electrospray Ionization
APCI – Atmospheric Pressure Chemical Ionization
ESCi – Dual ESI and APCi

ASAP – Atmospheric Solids Analysis Probe



The

Xevo TQ-S

A STEP UP TO THE
ULTIMATE SENSITIVITY

Xevo TQ-S micro

THE NEXT STEP IN
ROBUST SENSITIVITY

Xevo TQD

RUGGED, ROBUST
AND PROVEN

Power of Xevo

Whatever your quantitative application, the Xevo tandem quadrupole family is up to the challenge.

Unparalleled reliability, sensitivity, and accessibility completes the Xevo tandem quadrupole family. Bringing results when you need them, helping you to overcome your complex scientific challenges.

Xevo TQD, Xevo TQ-S micro and Xevo TQ-S are designed for quantitative UPLC/MS/MS applications; you can quantify and confirm trace components at even lower levels in the most complex of samples.

Best of all, every Xevo system allows you to achieve your goals with unparalleled speed and ease.

Xevo®

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Finland 358 9 5659 6288

France 33 1 30 48 72 00

Germany 49 6196 400 600

Hong Kong 852 2964 1800

Hungary 36 1 350 5086

India 91 080 49292200 03

Ireland 353 1 448 1500

Israel 9723 3731391

Italy 39 02 265 0983

Japan 81 3 3471 7191

Korea 82 2 6300 9200

Mexico 52 55 52 00 1860

The Netherlands 31 76 508 7200

Norway 47 6 384 6050

Poland 48 22 101 5900

Portugal 351 21 893 61 77

Puerto Rico 1 787 747 8445

Russia/CIS 7 495 727 4490 / 290 9737

Singapore 65 6593 7100

Spain 34 93 600 9300

Sweden 46 8 555 115 00

Switzerland 41 56 676 7000

Taiwan 886 2 2501 9928

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US 1 800 252 4752

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June 2014 720005046EN VW-KP

Waters® Xevo® TQ-S micro

Site Preparation Guide

Notice

Table of Contents

Introduction

This document describes the environmental conditions, power supplies and gas supplies that are required for the operation of the Xevo TQ-S micro. Operating the instrument in conformance with these conditions will enable the instrument to achieve its optimum performance.

Responsibilities

Warning: Observe Good Laboratory Practice (GLP) at all times, particularly when working with hazardous materials, and consult the safety representative for your organization regarding its protocols for handling such materials.

Warning: Safety glasses must be worn at all times when working with hazardous materials and pressured fluidics.

A Waters engineer will be responsible for installing and commissioning the system to ensure that the instrument is properly installed and operational. The laboratory must be prepared in advance to allow the engineer to carry out the installation efficiently. A site preparation checklist is included at the end of this document for you to fill in and return to Waters when the laboratory is ready.

Important: The installation of the system cannot begin until the checklist has been completed and returned to the mass spectrometer sales support representative at your local Waters office.

The installation time may vary, depending on the instrument options being installed. The site preparation checklist must be completed as accurately as possible to help minimize installation time.

A major aspect of the system installation is the implementation of tests designed to evaluate the instrument functionality under specific operating conditions. At the completion of each test, the actual test result obtained is entered in the Installation Checklist or Instrument Qualification Workbook, whichever is appropriate.

Important: A user who has been designated to be responsible for the normal use and upkeep of the instrument must be present during the installation.

The user must be present during the functionality tests at installation; this allows the user to be trained in the basic system operation. If there are foreseen periods when the intended user cannot be present, please notify us in advance; this will enable us to schedule the installation for a more convenient time.

If you have questions regarding the information in this document or any specific site problems, contact your local Waters sales representative. If necessary, we will arrange a site survey.

Storage

The following storage conditions are required prior to installation:

- Unopened shipping crates
- Crates stored away from heavy machinery such as compressors or generators, which generate excessive floor vibration
- Storage area temperature 0 to 40 °C (32 to 104 °F) and humidity <80%, non-condensing

Contact your local Waters representative if you need further advice regarding storage conditions.

Unpacking and moving

The instrument is delivered in several palletized cartons and crates. Their sizes may vary dependent on instrument specification and optional accessories, typical sizes for the instrument crate are:

- Width 560 mm (22 inch)
- Length 1100 mm (43.5 inch)
- Height 1040 mm (41 inch)
- Weight 130 kg (287 lbs)

It is a warranty condition that the shipping crates are unpacked only when the Waters engineer is present. At the end of the installation, it is the customer's responsibility to dispose of the crates and packaging.

It is essential that the instrument is not bumped or jolted during unpacking or any subsequent transport. If the instrument needs to be transported across an uneven surface, the instrument must be carried on a forklift truck or trolley.

Doorways must be at least 600 mm (24 inch) wide. Elevators and corridors (including corners) must be sufficiently wide for maneuvering of the instrument. Special handling arrangements may be necessary if access to the laboratory is via a staircase.

Lifting equipment

Once unpacked, the instrument weights are approximately as shown in Table 1:

Table 1: Instrument weights

Xevo TQ-S micro	100 kg (220 lbs)
Data system (computer, monitor, and optional printer)	<50 kg (110 lbs)
Rotary pump*	40 kg (88 lbs)
Scroll pump*	42 kg (93 lbs)

***System includes either a rotary or scroll pump option.

Warning: The instrument must only be lifted using lifting equipment capable of raising the instrument's weight safely. The instrument must not be lifted manually.

Important: It is essential that you provide suitable equipment for lifting the instrument. The installation cannot be implemented unless this equipment is made available. The engineer will require assistance lifting and positioning the instrument.

A forklift truck or A-frame hoist is recommended for lifting and transporting the instrument. The instrument is fitted with a lifting harness, which must be used to lift the instrument from the shipping crate onto the bench.

Bench loading

The bench must be able to support the combined weight of the mass spectrometer, data system and LC system. Nominal weights for the instrument and data system are shown in Table 1. Refer to the UPLC, HPLC, or GC system site preparation guide for specific weight information.

Space requirements

Instrument

The instrument has the following dimensions:

- Width 352 mm (13.85 inch)
- Length 913 mm (36.0 inch)
- Height 593 mm (23.25 inch)

Note: A moveable workbench of suitable load rating is the preferred arrangement for the system setup, to provide ease of access for servicing.

For service access, a minimum clearance of 600 mm (23.6 inch) is required for the front, back, and right side of the instrument; a temporary clearance of 1000 mm (39.5 inch) is required for the left side of the instrument. If the instrument is placed on a bench that can be moved out during service visits, the minimum clearance at the back is 150 mm (6 inch) with the rotary/scroll pump positioned beneath the instrument. The mass spectrometer must be installed on a surface that is level to within ±1° in any direction.

The instrument is fitted with a 2.5-m (8-ft) power cable.

A possible layout for the Xevo TQ-S micro, rotary/scroll pump, data system, and ancillary equipment is shown in Figure 1 and Figure 2.

Note: An additional 150 mm (6 inch) is recommended behind the workbench to accommodate vacuum tubing.

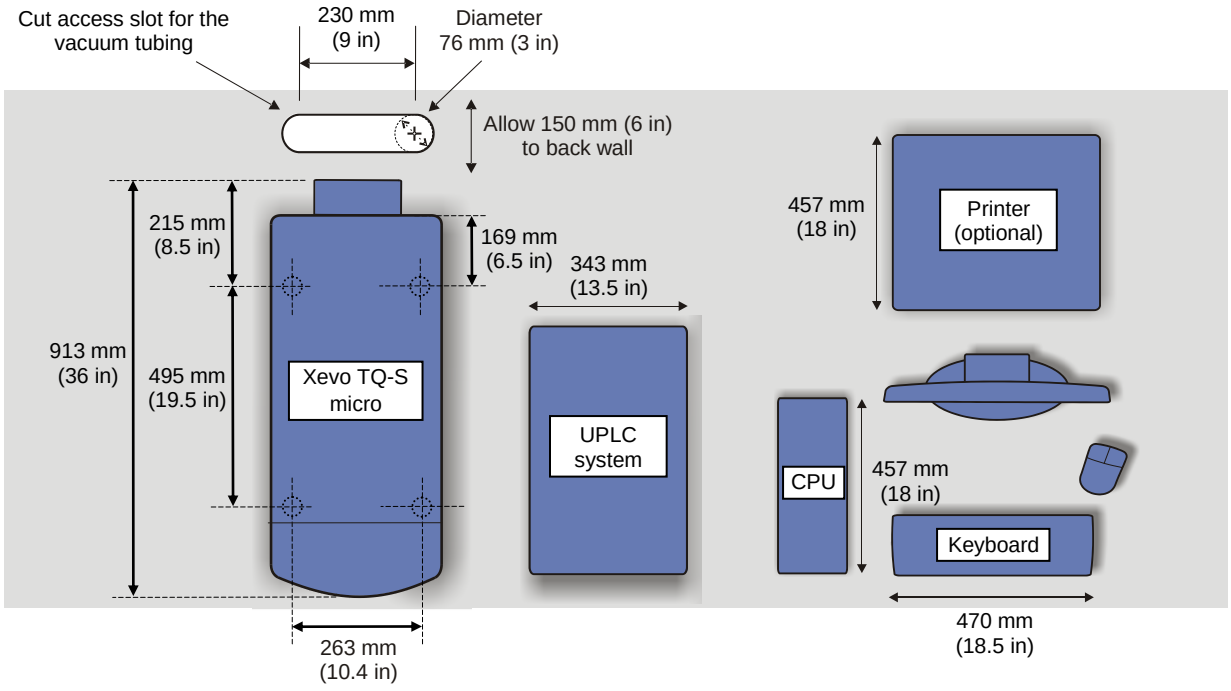

Figure 1 - Plan view, showing space requirements

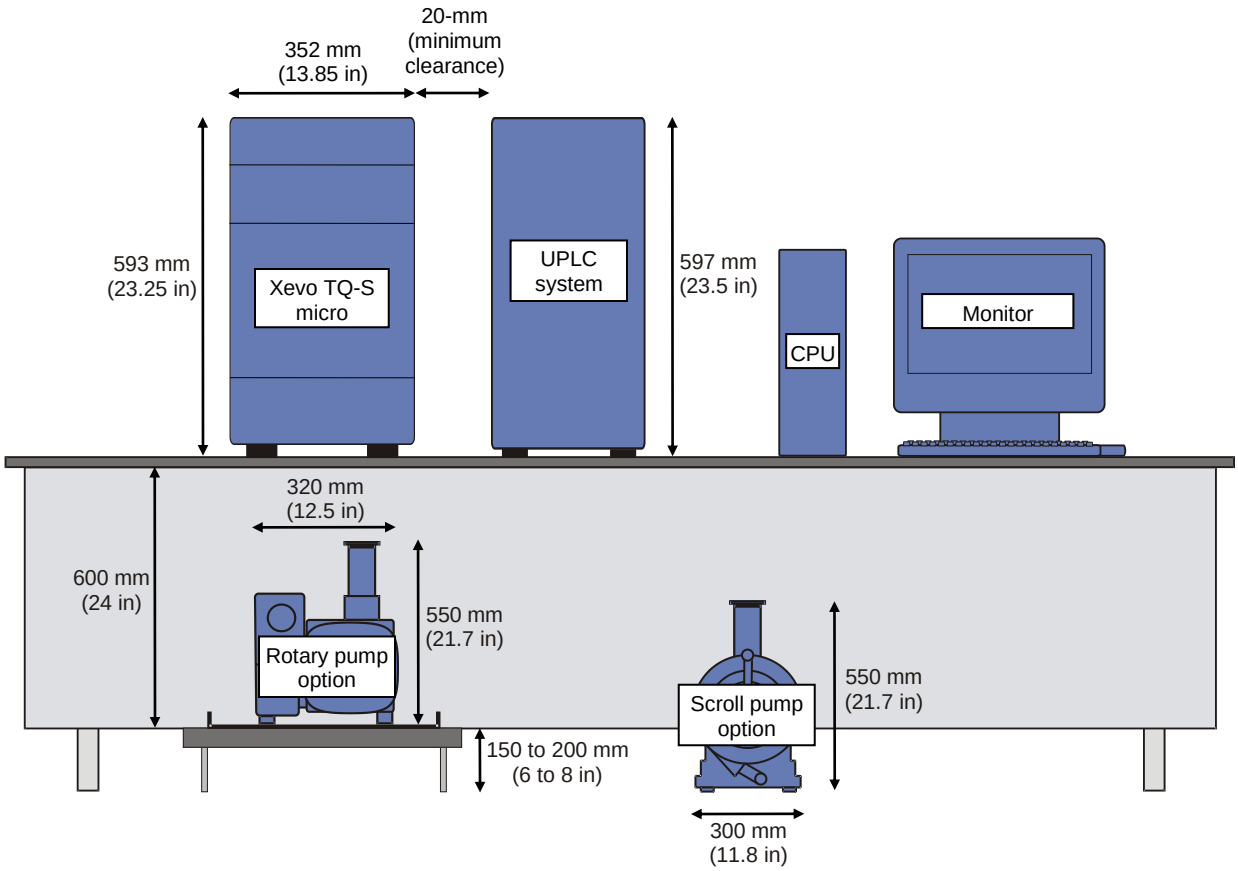

Figure 2 - Front view, showing space requirements

Rotary/scroll pump

The rotary pump or optional scroll pump must be positioned on the floor, either behind or underneath the instrument and within 1 m (3.3 ft) of the rear of the chassis. The pump is supplied with a 2-m (6.5-ft) power cable.

Make sure there is adequate ventilation around the rotary/scroll pump so that the ambient temperature around the pump does not exceed 40 °C.

Allow at least 150-mm clearance for the pump cooling fans.

LC system

Ensure that there is sufficient space to the left of the mass spectrometer for the LC system. Refer to the UPLC or HPLC system site preparation guide for the relevant space requirements.

Data system

The data system can be positioned on the same bench as the mass spectrometer or on a separate desk (available as an option). A 3-m (10-ft) X-wire network cable connects the computer to the mass spectrometer. The two data system power cables for the PC and monitor are approximately 2 m (6.5 ft) in length.

Warning: To avoid damage to and/or risk of electric shock and fire, the data system and any ancillary equipment must not be exposed to dripping or splashing liquids; nor should objects filled with liquid, such as solvent bottles, be placed on them.

Connections INSIGHT® Installation Requirements

Installation of the Waters Connections INSIGHT software (Intelligent Services that provide real-time system monitoring and notification), requires the following:

- An active Internet connection (direct, or through a firewall or proxy server)
- SSL (secure sockets layer) port 443 to be activated

Note: Connections INSIGHT software directly communicates with the Waters Enterprise Server using 128-bit data encryption. For further information see *Connections INSIGHT Frequently Asked Questions* (p/n 720001131EN).

Electrical safety

The Xevo TQ-S micro detector complies with the International Safety Standard IEC 61010-1:2001 and meets the European Low Voltage Directive 2006/95/EC by means of European Harmonized Standard EN 61010-1:2001.

For installations in Australia and New Zealand, the building installation must comply with AS3000: electrical installations for Australia and New Zealand.

The instrument is suitable for use in environments categorized as Pollution Degree 2 and Over-voltage Category II.

Power requirements

The Xevo TQ-S micro detector and rotary/scroll pump require one power socket each. The power supply sockets must be located within 2 m (6.5 ft.) of the instrument. Do not position the equipment so that it is difficult to disconnect the mains cable.

The data system typically requires two power sockets located adjacent to the Xevo TQ-S micro for the instrument PC and monitor. Further outlets may be required for optional equipment, such as a printer. Do not position the equipment so that it is difficult to disconnect the mains cable.

A typical LC system may require three or more additional sockets – refer to the relevant LC documentation for information.

Important: Mains voltage fluctuations must not exceed ±10%.

The power requirements for the equipment are summarized in Table 2.

Table 2: Summary of power requirements

	Nominal rated voltage	**Supply fuse / circuit breaker rating**	**Typical power consumption**	**Power connection**	**Power sockets**	**Power sockets** (with optional UPS)
Xevo TQ-S micro	200 to 240 V, 50/60 Hz	13 to 16 A	900 W	IEC 60320 C20 receptacle	1	1
Data system	100 to 127 V /200 to 240 V, 50/60 Hz	5 to 15 A 2.5 to 16 A	200 W	IEC 60320 C14 receptacles	2	
Scroll pump option						
XDS46i	200 to 230 V, 50/60 Hz	13 to 16 A	350 W	IEC 60320 C20 receptacles	1	
Rotary pump option						
SV40BI	200 to 240 V, 50 Hz	13 to 16 A	1.3 kW	CO16 3	1	
	200 to 240 V, 60 Hz	13 to 16 A	1.6 kW	CO16 3	1	
SV40BIFC	200 to 240 V, 50/60 Hz	13 to 16 A	1.5 kW	CO16 3	1	

Important: Voltage supply stability is critical for instrument operation. The nominal power supply voltage must fall within the ranges specified in Table 2 at all times to allow for the occasional 10% surge.

The supplies must be wired with a protective earth and fused or fitted with circuit-breakers of the specified ratings, in accordance with local regulations.

The mains supply must not have brown-outs/surges greater than ±10%, and must not exceed the specified maximum operating range for more than 0.3 sec. Transient voltage drops to half nominal voltage or less must have a duration of less than 20 ms. There must be less than 1.0 V RMS of ripple on the mains supply.

On pump start-up, currents of up to 36 A (200 to 240 V) or 50 A (115 to 120 V) may be drawn for several seconds, because of the initial pump loading. It is recommended that time delay fuses and circuit-breakers are used to prevent nuisance tripping.

The rotary/scroll pump is normally in continuous operation; it is recommended that the system is installed such that the supply cannot be inadvertently switched off.

It is also recommended that additional protection is provided for the instrument by means of:

- Residual Current Devices (RCD's) for UK and Europe
- Ground Fault Circuit Interrupters (GFCI's) for Rest of the World

In the case of instruments fitted with a transformer, the RCD/GFCI must be fitted on the primary (supply) side of the transformer.

Electrical transformers

If there is a possibility that the supply voltages will not meet the specified operating range under all conditions, a transformer must be used to change the primary supply voltage to the specified range. Mains conditioners/stabilizers are also available as an optional accessory. Contact Waters with advance notification if power supply problems are likely to be experienced and for additional advice.

In the case of instruments fitted with a transformer, the RCD/GFCI must be fitted on the primary (supply) side of the transformer.

If your order includes a nitrogen generator and the mains supply is known to run continuously at voltages less than 220 V, Waters and Peak Scientific recommend fitting one of the following transformers between the generator and mains supply.

Caution: Running nitrogen generators continuously at voltages less than 220 V is not recommended and extended periods at these extremes can affect the operation and life of the generator.

Table 3: Nitrogen generator transformer options

Model type	**06-3100**	**06-3110**
View		
Description	208 volt AC to 230 volt AC boost transformer	115 volt AC to 230 volt AC boost transformer

System plug options

The system plug options are shown in Table 4. The instrument is shipped with the plugs that were requested at the point of order. The user must provide appropriate sockets for the relevant type of plug used. If the available sockets are incompatible with the plugs supplied, the customer must supply appropriate cord sets for the instrument and pumps. The cord sets must comply with local regulations.

Computer equipment is typically rated at 100 to 120 V / 220 to 240 V, 50/60 Hz. In some cases, it may be necessary to set the appropriate voltage using a voltage selector switch before connecting the equipment to the power supply. For full details, refer to the instructions provided with the equipment.

Note: If ancillary equipment is to be installed (for example, compressors) additional power outlets, possibly requiring 3-phase supplies, may be needed. Such supplemental needs must be confirmed with the local Waters agent prior to the start of the installation.

Table 4: Power cords supplied by Waters

Plug option	Plug type	System components
US/Canada (125 V) 	5-15P (UL817 and CSA C.22.2)	Data System
US/Canada (250 V) 	L6-15P (UL817 and CSA C.22.2)	Mass Spectrometer Rotary/Scroll Pump Nitrogen Generator
UK 	3-pin (BS1363)	Data System Mass Spectrometer Rotary/Scroll Pump Nitrogen Generator
Europe 	2-pin (CEE7)	
Denmark 	3-pin (Afsnit 107-2-D1)	
Australia 	3-pin (AS/NZS 3112)	
China 	GB2099 (10 A version)	Data System
China 	GB2099 (16 A version)	Mass Spectrometer Rotary/Scroll Pump Nitrogen Generator

Uninterruptible power supply

To prevent instabilities in local mains power impacting system reliability and performance, Waters recommends the use of an uninterruptible power supply (UPS). In support of this recommendation, Waters supplies UPS units that have been specifically configured and evaluated for use with Waters MS systems. Your local Waters field sales representative can provide further details.

These UPS units step up single-phase line voltage to 230 V AC, provide power conditioning and protection for the MS system.

For North America, the UPS system requires one L6-30 (30 amp) wall socket. In other areas, the UPS system will typically connect to your laboratory mains power using the standard MS instrument power cord and wall socket required for your system. See Table 2 and Table 4.

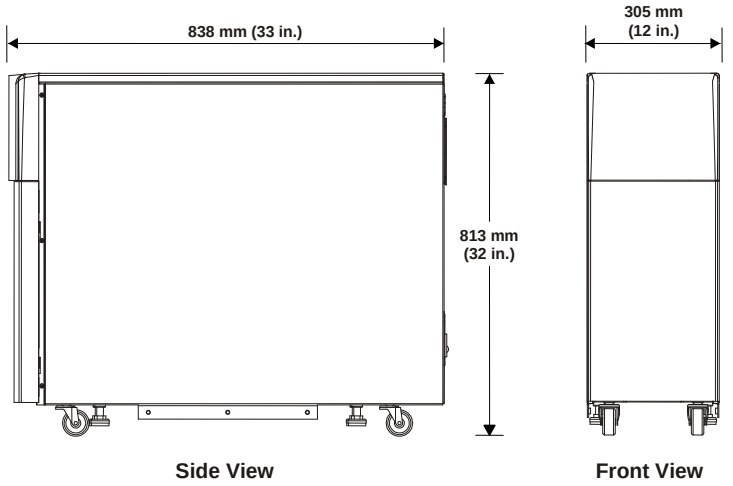

Figure 3 - Approximate maximum dimensions of the UPS

Environment requirements

Safety recommendations

Because of the operation of atmospheric pressure sources, the user must be aware of potential chemical hazards. In particular, the user must assess the risks associated with nitrogen gas (oxygen deficiency) and solvents vented into the laboratory. Note that because of the fluidic nature of the sample inlet, ionization and exhaust system, there is a potential for gas/liquid leaks to occur. The user must give due consideration to the laboratory environment (including volume and air changes) before installation and during operation of the system.

Warning: The active exhaust vent must provide a minimum vacuum of 2 millibar below atmospheric pressure (negative pressure). It must be capable of supporting a maximum instrument exhaust gas load of 2500 L/hour.

Warning: Exhaust venting must comply with all local safety and environmental regulations. The ANSI/AIHA Z9.2-2001 standard for "Fundamentals governing the design and operation of local exhaust ventilation systems" provides guidance on compliant exhaust systems.

Positioning

It is recommended that the instrument is installed in an air conditioned laboratory, in a draft-free position, away from excessive amounts of dust. Air conditioning units must not be positioned directly above the mass spectrometer. To avoid adverse operation, do not locate the instrument in direct sunlight.

Ventilation

The maximum overall heat dissipation into the room from the instrument and pumps is approximately 2.7 kW. This figure does not take into account the data system or other ancillary equipment such as LC systems. Air conditioning systems may have to be installed or upgraded to accommodate additional heat load into the room when these systems are installed.

Temperature

The ambient temperature range required for normal operation is 15 to 28 °C (59 to 82 °F).

Short-term (1.5 h) variations must be no more than 2 °C (3.5 °F).

Humidity

The relative humidity in which the instrument and pumps are to operate must be in the range of 20% to 80%, non-condensing.

Altitude

The instrument is designed and tested to operate below 2000 m (6500 ft).

Vibration

The instrument must not be placed close to heavy machinery such as compressors and generators, which may generate excessive floor vibration.

Magnetic fields

The instrument must be positioned away from magnetic fields of greater than 10 Gauss, such as those generated by NMR spectrometers and magnetic sector mass spectrometers.

Radio emissions

The instrument must not be placed within a Radio Frequency (RF) field of greater than 1.0 V/m.

Possible sources of RF emission include RF-linked alarm systems, Local Area Networks (LANs), mobile telephones, and hand-held transmitters.

Gases and regulators

Nitrogen gas

Caution: Where the APGC source is ordered, nitrogen purity must be >99.999%.

Refer to the *APGC Site Preparation Guide* (p/n 715002164) for specific external nitrogen gas supply and connection requirements.

The Xevo TQ-S micro requires a supply of dry, oil-free nitrogen with a purity of at least 95%. The nitrogen must be regulated at 6.75 ±0.25 bar (98 ±4 psi) outlet pressure, using a two-stage gas regulator with an appropriate outlet range, for example, 0 to 8 bar (0 to 116 psi).

Important: It is the customer's responsibility to provide a two-stage regulator fitted with an adapter to connect to a 6-mm push-in fitting, see Table 5.

Caution: The nitrogen must be connected using the 5-m (16 ft.) of 6-mm OD Teflon tubing supplied. Do not cut the tubing to size. The nitrogen line must be checked for leaks under pressure.

If copper tubing is used for the nitrogen line, the copper must be chemically cleaned; if stainless steel tubing is used, the stainless steel must be medical grade. Ensure that there are no soldered or brazed joints in the line, as these may result in contamination of the instrument with tin or lead oxide. Any joints in the nitrogen line must be compression fittings.

During API operation, typical nitrogen usage varies from 600 to 1200 L/h (at atmospheric pressure). This equates approximately to the consumption of a large cylinder of compressed nitrogen each day. You may prefer to use a liquid nitrogen Dewar, which will last for several weeks, consult your local gas supplier for an ideal gas supply configuration.

Note: The use of nitrogen cylinders is not recommended. Because of high consumption, a cylinder is likely to empty during long sample runs. The supply must be constant in case venting occurs.

Collision gas

Argon is required for the collision cell. The argon must be dry, high purity (99.997%), and regulated at a pressure of 0.5 ±0.1 bar (7 ±2 psi), using a two-stage high purity gas regulator with an appropriate outlet range, for example, 0 to 2 bar (0 to 29 psi).

Important: It is the customer's responsibility to provide a two-stage regulator fitted with an adapter to connect to a $^{1}/_{8}$-inch Swagelok type fitting, see Table 5.

Caution: Ensure that there are no soldered or brazed joints in the argon line, as these may result in contamination of the instrument with tin or lead oxide. Any joints in the collision gas line must be compression fittings.

The gas supply must be connected using the clean, $^{1}/_{8}$-inch OD, medical-grade stainless steel tubing supplied and checked for leaks under pressure.

Exhaust outlets

Rotary/scroll pump exhaust

The rotary/scroll pump exhaust gases must be vented to the atmosphere outside the laboratory via a user-supplied fume hood or industrial vent. The exhaust may be connected to an existing laboratory vent carrying gases from other sources.

Five meters (16 ft) of 12-mm ID PVC tubing is supplied. If this length is insufficient, the user must supply an adapter and tubing with an internal diameter of at least 51 mm (2 inch) for the extra distance to the vent point.

Note: The fume hood/industrial vent must be equipped with an extraction fan system to enable adequate displacement of the exhaust gases.

Source exhaust (nitrogen)

The source exhaust line must be connected to either a laboratory fume hood or to an active exhaust system.

Refer to the exhaust warnings in the Environment requirements section on page 15 for additional source exhaust information.

Caution: Severe contamination of the instrument may result if the source exhaust line is connected to the rotary pump exhaust line. The damage will occur when the nitrogen supply is turned off, or when the nitrogen runs out, as any rotary pump oil vapor will migrate via the source exhaust to the ion source and then through the sample cone into the analyzer.

Five meters (16 ft) of 12-mm OD Teflon tubing is supplied for the source exhaust. If this length is insufficient, the user must supply an adapter and tubing with an ID of at least 16 mm (⅝ inch) for the extra distance to the vent point.

The instrument software can be configured to switch the LC system off if it detects that the nitrogen gas supply has failed. In the event that the nitrogen gas is switched off (or runs out) and the LC system continues to operate, excess solvent is drained from the source via the source exhaust line.

Solvent delivery system

The instrument includes an ACQUITY ever-flow valve and syringe drive for infusion. A gas-tight, 250-µL syringe, with a flow rate range of 5 to 200 µL/min is included.

For ESI / ESCI / APCI, a UPLC / HPLC pump giving a stable, pulse-free flow of 50 to 2000 µL/min is required.

Before returning the checklist at the end of this document, please ensure that any locally supplied solvent delivery system has either already been commissioned or that a commissioning date has been scheduled.

Note: If a solvent delivery system suitable for running performance specifications will not be available at the time of installation (for example, in the case of instruments supplied with an ACQUITY M-Class) inform the local Waters service agent so that special arrangements can be made.

Test samples

Warning: Hazardous samples must be handled with care and in a manner that conforms to the manufacturers' guidelines.

Test samples are required for verifying the performance of instruments at the time of installation; they are also used for routine operations such as tuning and mass calibration.

Note: A Test Sample Kit is supplied with the instrument for the installation setup. It is the customer's responsibility, in conjunction with the local Waters sales representative, to ensure that any additional samples required for customer-specific tests and post-installation testing are available.

Note: The Waters engineer will not carry test samples to the installation. If the Waters engineer is unable to complete the installation because of a lack of facilities, costs incurred will be charged. The installation will be rescheduled when the chemicals are available.

Important: Storage instructions provided with the test samples must be adhered to; the use of inferior quality test chemicals caused by adverse storage conditions could impair the instrument installation.

Note: If your laboratory practices require full sample certification documentation, Waters Analytical Standards and Reagents provide ready-to-use reference materials and reagents that are fully traceable and certified (www.waters.com).

Solvents and reagents

Caution: Clean, high-purity solvents and reagents and clean glassware must be used to ensure the optimum performance of the LC-MS system. Significant delays to the installation may occur if clean solvents and glassware are not provided by the customer prior to commencing the installation.

High-purity solvents (i.e. LC-MS grade) are required, as shown in the following list; these are used for making up standard solutions for performance tests and for cleaning instrument components. For detail on controlling contamination, and information on solvent brands, refer to *Controlling Contamination in Ultra Performance LC™/MS and HPLC/MS Systems* (p/n 715001307), located in the Support area of the Waters website (www.waters.com).

- Water
- Acetonitrile
- Methanol
- Formic acid

Caution: If using a water purification system, maintain it regularly in accordance with the manufacturer's guidelines.

Sample preparation equipment

Facilities for making up test samples must be available at site. Typical equipment required for sample preparation includes (but is not limited to):

- Calibrated syringes - Eppendorf (or equivalent), spanning range 1 µL to 1 mL
- Measuring cylinders, spanning range 100 mL to 1 L
- Volumetric flasks - 10-mL flasks (up to 11 required); 50-mL flasks (up to 7 required)
- Calibrated analytical balance
- Nitrile gloves
- Lint-free tissue

Cleaning test sample glassware

For detailed information on properly cleaning glassware or other components, refer to *Controlling Contamination in Ultra Performance LC®/MS and HPLC/MS Systems* (p/n 715001307), located in the Support area of the Waters website (www.waters.com).

Cleaning equipment

An ultrasonic bath is required for the routine cleaning of instrument parts. The bath must be at least 300 mm x 150 mm x 100 mm deep (12 inch x 6 inch x 4 inch).

Caution: Surfactants must not be used for cleaning glassware or other components. Refer to the document *Controlling Contamination in Ultra Performance LC®/MS and HPLC/MS Systems* (p/n 715001307), located in the Support area of the Waters website (www.waters.com).

Surfactant-free glass vessels are required in which to place instrument components for cleaning. These vessels must be made available for use at the time of installation. The vessels must have a diameter of at least 120 mm (5 inch) and be approximately 120 mm (5 inch) high.

Summary of fittings

Table 5 shows a summary of the waste and gas connections for the installation of the Xevo TQ-S micro.

Table 5: Summary of instrument fittings required

	Fittings on the system	Items supplied with the instrument	Items to be supplied by the customer
Rotary/scroll pump exhaust	12-mm OD tail pipe	5-m (16-ft) PVC tube, 12-mm ID	Industrial vent or fume hood
Source exhaust (nitrogen)	12-mm push-in fitting	6-m (19.6-ft) Teflon tube, 12-mm OD	Industrial vent or fume hood
Liquid waste	0.375 x 0.25 ID one-touch fitting	2-m (6.5-ft), Tygon tubing	Waste bottle, 1 L (minimum)
Nitrogen supply (API)	6-mm push-in fitting	5-m (16-ft) Teflon tube, 6-mm OD	Nitrogen supply, regulated to 6.75 ±0.25 bar (98 ±4 psi) via a 6-mm adapter
Collision gas supply	$^1/_8$-inch fitting (Swagelok type)	3-m (10-ft) of $^1/_8$-inch OD stainless steel tubing	Argon supply, regulated to 0.5 ±0.1 bar (7 ±2 psi), via a $^1/_8$-inch adapter (Swagelok recommended)
ACQUITY Ever-Flow valve	Rheodyne nuts and ferrules	Tubing and Rheodyne nuts and ferrules	Tubing and Rheodyne nuts and ferrules

Xevo TQ-S micro site preparation checklist

This checklist must be completed and returned to Waters when all the amenities are available.

Note: If any items are on order, please indicate this on the checklist and include the anticipated arrival date.

Note: It is the customer's responsibility to ensure that all the correct laboratory supplies are present. If you need any additional information or have difficulties acquiring parts or samples, please contact your local Waters Sales representative.

Access (see page 5)
The instrument is located on the ground floor/basement/___ floor (delete as appropriate) ..... ❑

All elevators, staircases, corridors and doorways through which the instrument must pass are adequate to allow easy access to the laboratory ..... ❑

Lifting equipment (see page 6)
Suitable equipment is available to lift the instrument onto the laboratory bench ..... ❑

Bench/floor space (see page 7)
Adequate bench or floor space is available for the system ..... ❑

Connections INSIGHT® installation requirements (see page 9)
If you are planning to install Waters Connections INSIGHT software, an Internet connection is available ..... ❑

Power supply (see page 10)
An appropriate number of sockets with earth connections are available and they meet the stipulated power requirements ..... ❑

Positioning/ventilation (see page 15)
There is no direct air conditioning flow onto the instrument ..... ❑

Temperature (see page 15)
The room temperature is as specified in this document ..... ❑

Humidity (see page 15)
The humidity is as specified in this document ..... ❑

Altitude (see page 15)
The instrument will be operated below 2000 m (6500 ft) ..... ❑

Floor vibration (see page 16)
The site is free from known vibration ..... ❑

Magnetic fields (see page 16)
The site is free from magnetic fields of greater than 10 Gauss ..... ❑

Radio emissions (see page 16)
The RF field strength is less than 1 V/m ..... ❑

Gases and regulators (see page 16)

Dry, oil-free, ≥95% purity nitrogen gas is available, regulated at 6.75 ±0.25 bar (98 ±4 psi) with a 6-mm adapter ..... ❑

High purity ≥99.999% nitrogen gas is available when APGC source is supplied ..... ❑

High purity ≥99.997% argon gas is available, regulated at 0.5 ±0.1 bar (7 ±2 psi) with a $^{1}/_{8}$-inch adapter ..... ❑

Rotary/scroll pump exhaust (see page 17)

A suitable outlet is available for the rotary/scroll pump exhaust ..... ❑

Source exhaust (see page 17)

A separate exhaust, 2 mbar below atmospheric pressure is available ..... ❑

Solvent delivery system (see page 18)

Make and model of system to be used:

Make _____

Model _____

Flow rate capability of the system _____

Delivery system is already on site and commissioned ..... ❑

or

Delivery system is scheduled to be commissioned on: _____

A second (customer-supplied) syringe pump is available ..... ❑

Ancillary equipment

If you plan to use any other equipment with the system (e.g. Gilson Autosampler; UV Detector), please give details below.

Make / type	Model	Already commissioned	To be commissioned on

Test samples (see page 18)
All samples required for the installation are available ..... ❑

Solvents/reagents (see page 19)
Solvents are available ..... ❑

Sample preparation equipment (see page 19)
Sample preparation equipment, as specified in this document, is available ..... ❑

Cleaning (see page 20)
An ultrasonic bath is available ..... ❑

Vessels for cleaning components are available ..... ❑

I confirm all supplies are now available and all specified environmental conditions have been met*.

During the installation, the user intends to be available for demonstration and training by the Waters engineer:

At all times ..... ❑

Approximately _____% of the time ..... ❑

Not at all ..... ❑

During the likely period of installation, the following dates are NOT convenient:

_____

Signed: _____

***Important:** If an authorized Waters service engineer arrives on site to begin installation work and can not complete the installation because of lack of facilities (i.e. lifting equipment, power, water, test samples, laboratory readiness), costs incurred will be charged to the customer.

Please complete the following sections in block letters:

Name _____

Position _____

Organization _____

Street _____

City _____

ZIP/postcode _____

Country _____

Telephone _____

Fax _____

E Mail _____

Important: The installation of your system cannot begin until pages 21 through 26 of this document have been fully completed and returned to the Mass Spectrometer Sales Support Representative at your local Waters office.

Applications survey

As part of our commitment to provide greater customer service, we have found it necessary to obtain a little more information concerning our user base.

We would be grateful if you could take the time to complete the following questions to provide us with some information about how the instrument will be used.

This information will enable us to inform you of relevant current application notes and seminars and allows us to identify common interest groups so that we can promote cross transfer of information between customers.

What is your scientific field?
(e.g. pharmaceutical, environmental, general, etc.)

_____

_____

Which classes of compounds will be analyzed?
(e.g. carbohydrate, peptides, pesticides, etc.)

_____

_____

What is your application area?
(e.g. quantitation, purity analysis, structural determination, etc.)

_____

_____

Our sales team often requires reference sites for specific applications.
Would you be willing to be used as a contact reference site for prospective customers?

_____

_____

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Xevo TQ-S micro

Xevo® TQ-S micro is a sensitive but compact tandem quadrupole mass spectrometer featuring reliable performance with a wide dynamic range and high rates of data acquisition. Robust sensitivity is enabled by proven ZSpray™ and StepWave™ which facilitate the detection of analytes at low concentrations in complex matrices and enable low volume injections with accurate, precise, and consistent results. Xtended Dynamic Range™ (XDR) technology provides accessible sensitivity and method transfer. The Xevo TQ-S micro makes it easier to confidently quantify more analytes using reproducible high acquisition rates with Xcelerated Ion Transfer™ (XIT). Using RADAR,™ which enables rapid switching between MS full scan and MS/MS acquisition modes, analysts can understand sample complexity and improve method development.

SYSTEM HARDWARE SPECIFICATIONS

API sources and ionization modes	High performance ZSpray dual-orthogonal API sources: 1) Multi mode source – ESI/APCI/ESCi®(standard) NB – Dedicated APCI requires an additional probe (optional) 2) APCI IonSABRE II probe (optional) 3) Dual mode APPI/APCI source (optional) 4) nanoFlow™ ESI source (optional) 5) ASAP (optional) 6) APGC ion source (optional) 7) ionKey/MS™ source (optional) Optimized gas flow dynamics for efficient ESI desolvation (supporting LC flow rates up to 2 mL/min) Tool-free source exchange Vacuum isolation valve Tool free access to customer serviceable elements Plug and play probes De-clustering cone gas Software control of gas flows and heating elements
Ion source transfer optics	StepWave ion transfer optics (Waters patent pending) delivering class leading UPLC®/MS/MS sensitivity. The unique off-axis design dramatically increases the efficiency of ion transfer from the ion source to the quadrupole MS analyzer at the same time as actively eliminating undesirable neutral contaminants.

Mass analyzer	Two high resolution, high stability quadrupole analyzers (MS1/MS2), plus pre-filters to maximize resolution and transmission while preventing contamination of the main analyzers
Collision cell	T-Wave™ enabled for optimal MS/MS performance at high data acquisition rates
Detector	Low noise, off axis, long life photomultiplier detector
Vacuum system	One split-flow air-cooled vacuum turbomolecular pump evacuating the source and analyzer; One vacuum backing pump
Dimensions	Width: 35.6 cm (14.0 in) Height: 60.0 cm (23.6 in) Depth: 93 cm (36.6 in)
Regulatory approvals	CE and NRTL

SYSTEM SOFTWARE SPECIFICATIONS

Software	Systems supported on MassLynx™ version 4.1; OpenLynx™ and TargetLynx™ XS Application Managers are included as standard
IntelliStart™ Technology	System parameter checking and alerts Integrated sample/calibrant delivery system + programmable divert valve Automated mass calibration Automated sample tuning Automated SIR and MRM method development LC/MS System Check – automated on-column performance test
Quantification methods database	Quanpedia™ – a database for storing and sharing user defined LC/MRM acquisition methods and associated processing methods for the targeted quantification of named compounds is provided as standard; database entries for a number of applications are also provided as a standard
Automated MRM scheduling (acquisition rate assignment)	Dwell time, inter-channel delay time, and inter-scan delay time for individual channels in a multiple MRM experiment can be automatically assigned (using the Auto-Dwell feature) to ensure that the optimal number of MRM data points per chromatographic peak is acquired. The Auto-Dwell feature can dynamically optimize MRM cycle times to accommodate retention time windows that either partially or completely overlap. This greatly simplifies MRM method creation, irrespective of the number of compounds in a single assay, while at the same time ensuring the very best quantitative performance for every experiment.
Automated MRM scheduling (acquisition window assignment)	Multiple MRM experiments can be scheduled (manually or automatically using the Quanpedia database) using retention time windows to optimize the cycle time for each MRM channel monitored. If required, MRM retention time windows can overlap partially or completely. This ensures that MRM data acquisition rates will be optimal for the quantification of all analytes in a given assay.

PERFORMANCE SPECIFICATIONS

Acquisition modes	Full scan MS Product ion scan Precursor ion scan Constant neutral loss Selected ion recording (SIR) Multiple reaction monitoring (MRM) Simultaneous full scan and MRM (RADAR)
Survey scan modes	Full scan MS triggered product ion scan Precursor ion scan triggered product ion scan Constant neutral loss triggered product ion scan
Product ion confirmation (PIC) mode	MRM acquisition acts as an automatic trigger for the acquisition of product ion spectra
RADAR	An information rich acquisition approach that allows you to collect highly specific quantitative data for target compounds while providing the ability to visualize all other components
Mass range	2 to 2048 *m/z*
Scan speed	Up to 20,000 Da/s Examples of achievable acquisition rates: 20 scans per second (*m/z* 50 to 1000) 40 scans per second (*m/z* 50 to 500)
Mass stability	Mass drift is <0.1 Da over a 24 hour period
Linearity of response	The linearity of response relative to sample concentration, for a specified compound, is six orders of magnitude from the limit of detection
Polarity switching time	15 ms to switch between positive and negative ion modes
MS to MS/MS switching time	3 ms
ESCi mode switching time	20 ms to switch between ESI and APCI
MRM acquisition rate	Maximum acquisition rate of 500 MRM data points per second; Minimum dwell time of 1 ms per MRM channel; Minimum inter-channel delay of 1 ms; At an MRM acquisition rate of 500 MRM data points per second there is no more than 20% loss in signal compared to 50 MRM data points per second
Inter-Channel cross talk	The inter-Channel cross talk between two MRM transitions will be less than 0.001% (less than 10 ppm)
Number of MRM channels	Up to 32,768 MRM channels (1024 functions, 32 channels per function) can be monitored in a single acquisition; up to 1,024 MRM channels when operating in GLP/secure mode (32 functions, 32 channels per function)
Mass resolution	Automatically adjusted (IntelliStart) to desired resolution; (0.50 Da, 0.75 Da or 1.00 Da FWHM)

[INSTRUMENT SPECIFICATIONS]

MRM sensitivity (ESI+)	A 1 pg on-column injection of reserpine will give a chromatographic signal-to-noise greater than 200,000:1, using raw unsmoothed data (LC mobile phase flow rate of 0.4 mL/min, MRM transition 609 > 195 *m/z*).
MRM sensitivity (ESI-)	A 1 pg on-column injection of Chloramphenicol will give a chromatographic signal-to-noise greater than 100,000:1, using raw unsmoothed data (LC mobile phase flow rate of 0.8 mL/min, MRM transition 321 > 152 *m/z*)
MRM sensitivity (APCI+)	A 1 pg on-column injection of 17-α-hydroxyprogesterone will give a chromatographic signal-to-noise greater than 30:1, using raw unsmoothed data (LC mobile phase flow rate of 0.8 mL/min, MRM transition 331 > 109 *m/z*)

It should be noted that the above are not standard installation specifications. All Xevo TQ-S micro instruments will be installed and tested in accordance with standard performance tests as detailed in Waters document (Xevo TQ-S micro Installation Checklist). Test criteria are routinely reviewed to ensure quality is maintained and are therefore subject to change without notice. See Site Preparation Guide and Product Release Notes for additional productand specification information.

Related Patents:

1. ZSpray (US Patent 5,756,994).
2. StepWave (US Patent 8,581,181 and US Patent 8,581,182).

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