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Patricia McConville
Manager
Product Positioning Laboratory

Acquity™
Ultra Performance LC

Next Generation Instrument Design

For Complete Confidence

Patricia McConville – Manager
Product Positioning Laboratory

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Next Generation Instrument Design

ACQUITY UPLC™ is a fully integrated modular system which delivers unprecedented uptime, throughput and productivity. The application of advanced system diagnostics, eCord™ technology and Connections® INSIGHT™ remote monitoring capabilities will be discussed.

UPLC™ Technology Review

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- A new class of separation science
  - Based on chromatography columns with very small particles
  - Based on instruments designed to take advantage of the small particles
- Provides improved resolution, speed, and sensitivity
- Suitable for chromatographic applications in general
  - Appropriate for improving existing methods
  - Appropriate for developing new methods

HPLC: 7 Analgesics in 25 minutes

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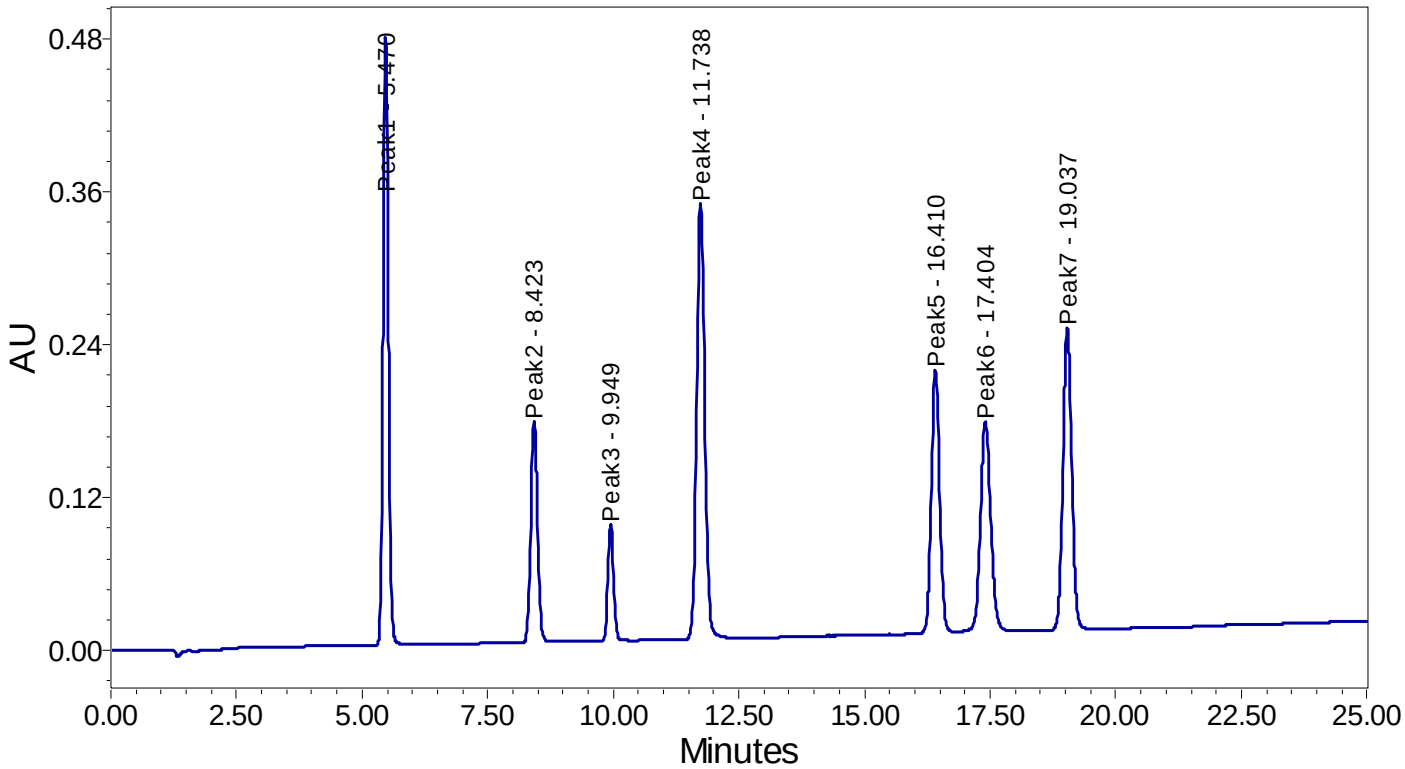
Gradient Table

Time	Flow	%A	%B	%C	%D	Curve
	1.00	98.0	2.0	0.0	0.0	
25.00	1.00	75.0	25.0	0.0	0.0	6
25.01	1.00	98.0	2.0	0.0	0.0	6
60.00	0.05	98.0	2.0	0.0	0.0	6

Components

Peak #1 – Acetaminophen
Peak #2 - 2-Acetomidophenol
Peak #3 - Caffeine
Peak #4 - Acetanilide
Peak #5 - Acetylsalicylic Acid
Peak #6 - Salicylic Acid
Peak #7 – Phenacetin



UPLC™:7 analgesics in 25 seconds

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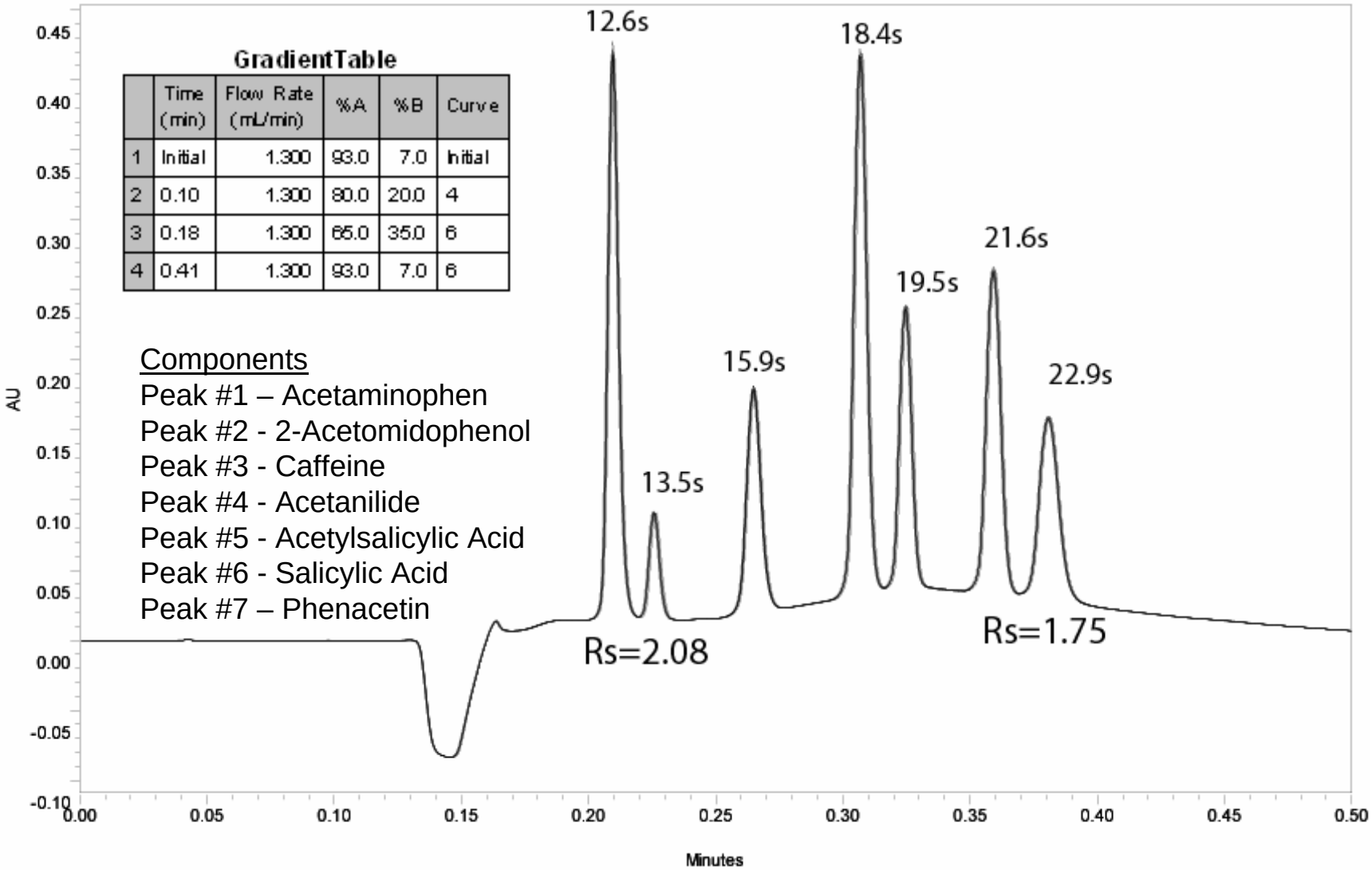
GradientTable

	Time (min)	Flow Rate (mL/min)	%A	%B	Curve
1	Initial	1.300	93.0	7.0	Initial
2	0.10	1.300	80.0	20.0	4
3	0.18	1.300	65.0	35.0	6
4	0.41	1.300	93.0	7.0	6



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Moving from HPLC to UPLC™
Increased Productivity and Solvent Savings

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		Column Volume (X5)	System Volume (x3)	Re-equilibration time (min.)	Total cycle time (min.)	# of injections in 24hours	Solvent consumed per injection
HPLC 4.6 x 100 5µ 25 min. run time	1.0 mL/min.	1.66mL (8.3mL)	620uL (1.86mL)	10.2.	35.2	41	35.2mL
UPLC™ 2.1 x 50 1.7µ 0.41 min run time	1.3 mL/min	0.20mL (1.0mL)	120uL (0.360mL)	1.04	1.45	993	1.9mL

Total Liters of solvent for 1000 injections:
HPLC: 35.2L Vs. UPLC™: 1.9L

Moving from HPLC to UPLC™
Improved Resolution

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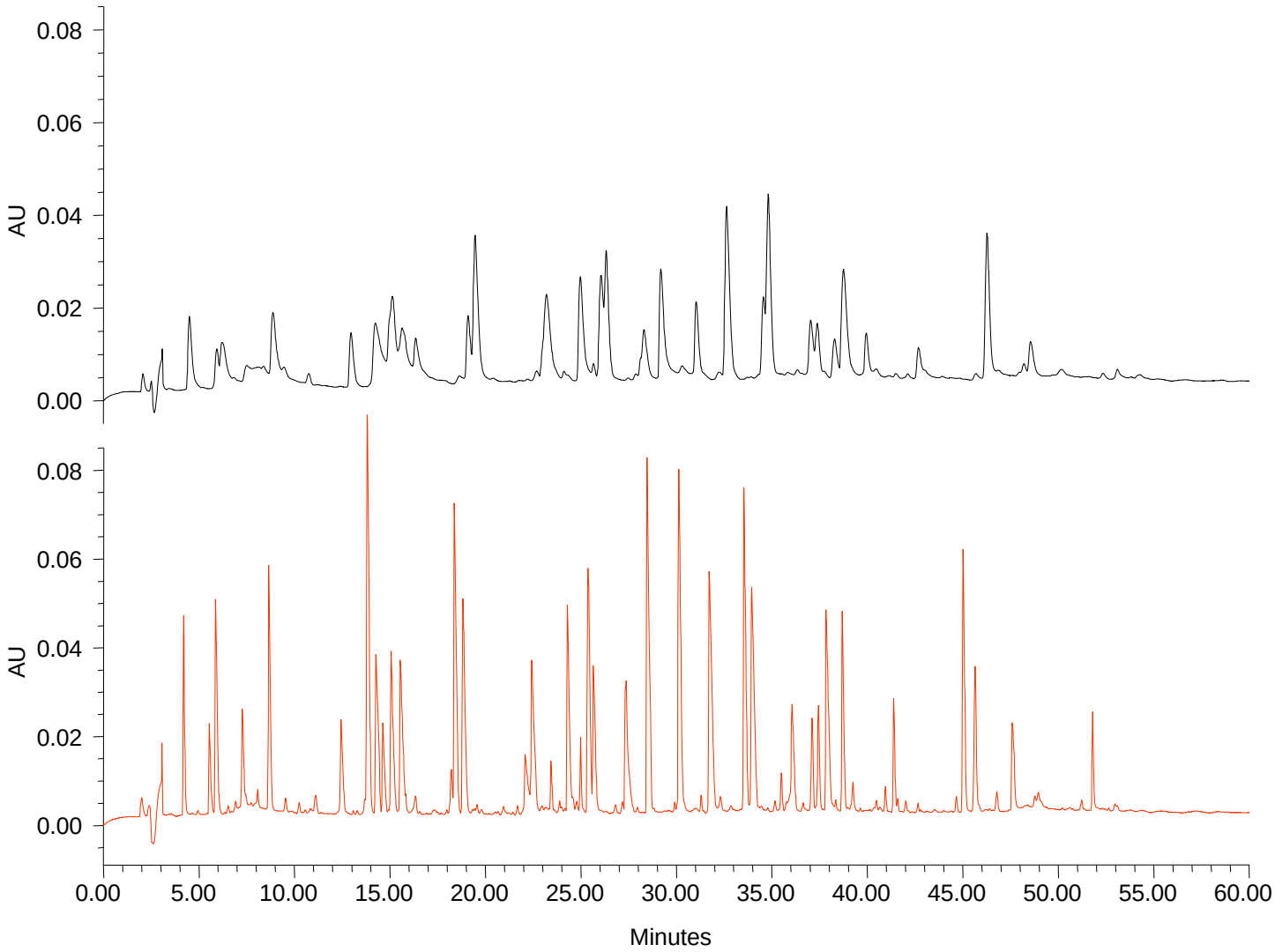

HPLC
4.8 µm
Peaks = 70
P_c = 143

UPLC™
1.7 µm
Peaks = 168
P_c = 360

2.5X increase

Why Change from HPLC to UPLC™?
Improved sensitivity

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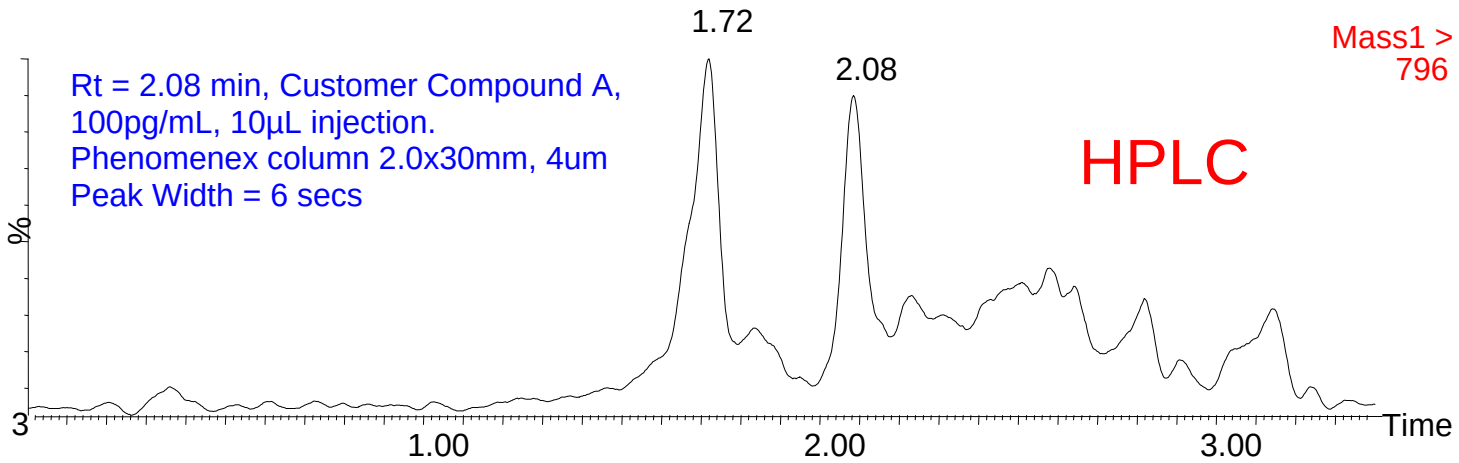
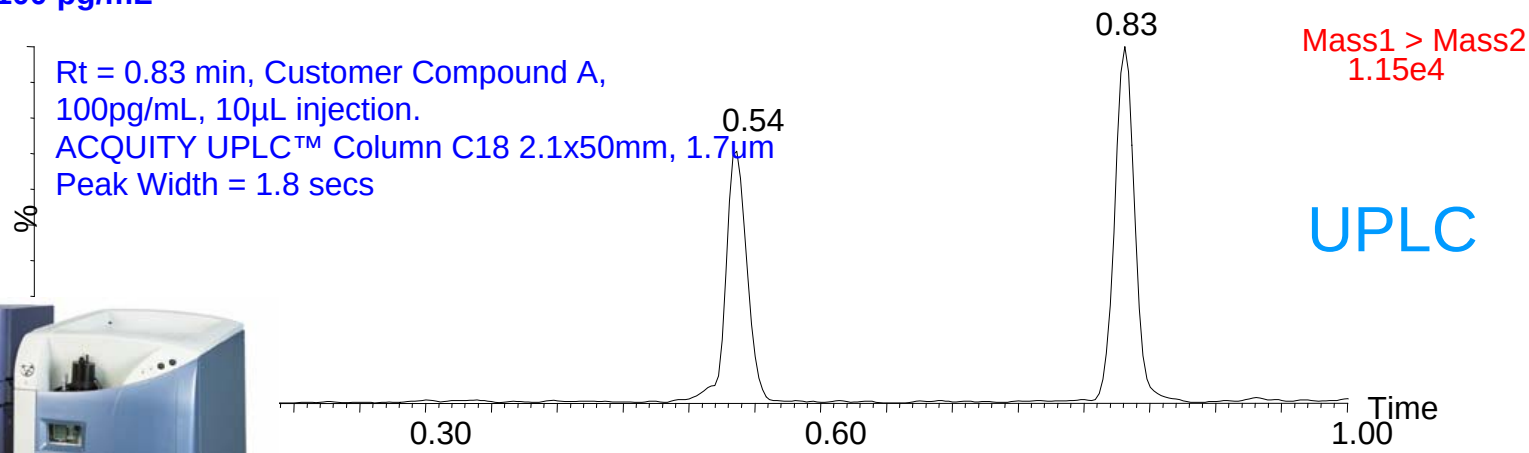
100 pg/mL



100 pg/mL



Method Comparison 100pg/mL, 10µL injection

2nd Generation Hybrid:
Bridged EthylSiloxane/Silica Hybrid Particles

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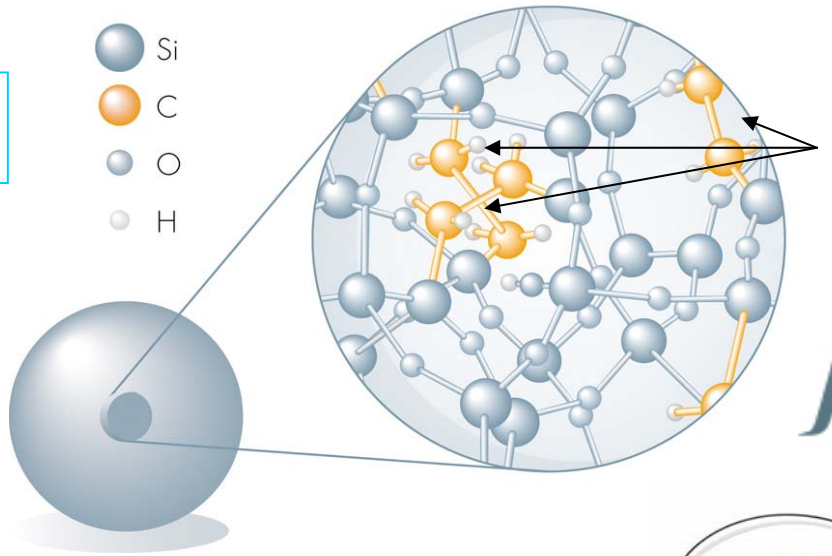
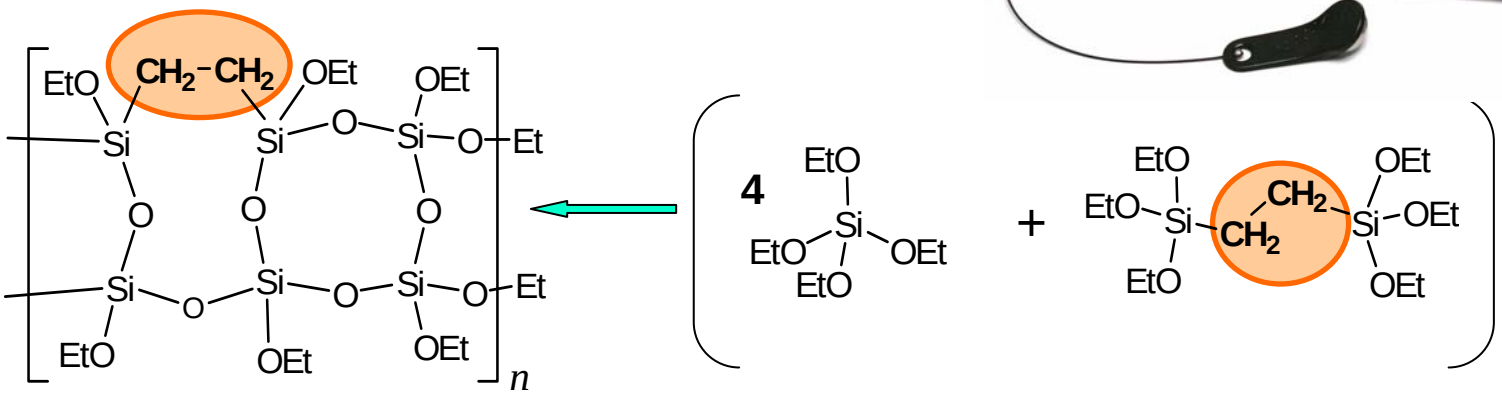
Waters Patented Technology
No. 6,686,035 B2



Acquity™
Ultra Performance LC



Polyethoxysilane (BPEOS)

Tetraethoxysilane (TEOS)

Bis(triethoxysilyl)ethane (BTEE)

Anal. Chem. **2003**, *75*, 6781-6788

ACQUITY UPLC™ Technology
Ultra performance by design

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Acquity™ Ultra Performance LC

Detectors:
Optical and/or Mass Spec
Tunable UV or Photodiode Array
Optimized flow cell for UPLC™
High speed data sampling for

System Considerations:
Small Footprint
Redesigned tubing and fittings
Consolidated waste management
Integrated system diagnostics
Connections Insight™ remote diagnostics

Sample Organizer: (option)
Expands capacity (22/15/8)
Shuttles plate feed
Heated/chilled

Column Manager:
Innovative pivot design
Positions column to detector
E-Cord™ connection

Sample Manager:
Low dispersion XYZZ' Format
Fast cycle times
Low carryover
Plates and/or vials
Optional Sample Organizer

Binary Solvent Manager:
High pressure blending
Binary gradients
Four solvent choices
On-line degassing
Low dispersion design
UPLC pressure capabilities

Next Generation Instrument Design:
Synergistic Design: Hardware and Software

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- Integrated hardware and software
  - Visual system status indicators on hardware
  - Instrument Control Panel
- Instrument Console
  - A customizable *Instrument Console* enables operators to easily stay in control of all system functionality including instrument control, interactive system monitoring, status monitoring, and user diagnostic capabilities.
- eCord™ Technology
  - Accurate permanent record of column history
- Connections® INSIGHT™ remote monitoring capabilities

ACQUITY UPLC™ Modules: *Visual Indicators of Hardware Status*

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- Front Panel LEDs
- Power LED (left)
  - ON GREEN
    - Instrument is on, has power
- Flow LED (right)
  - OFF
    - Currently idle, not flowing, appears in good health
  - ON GREEN
    - Pump is currently flowing, in good health
  - FLASHING RED
    - Pump has stopped on error, no longer flowing
  - ON RED
    - Serious system failure prevents further operation

ACQUITY UPLC™
Instrument Control Panel from Run Samples View

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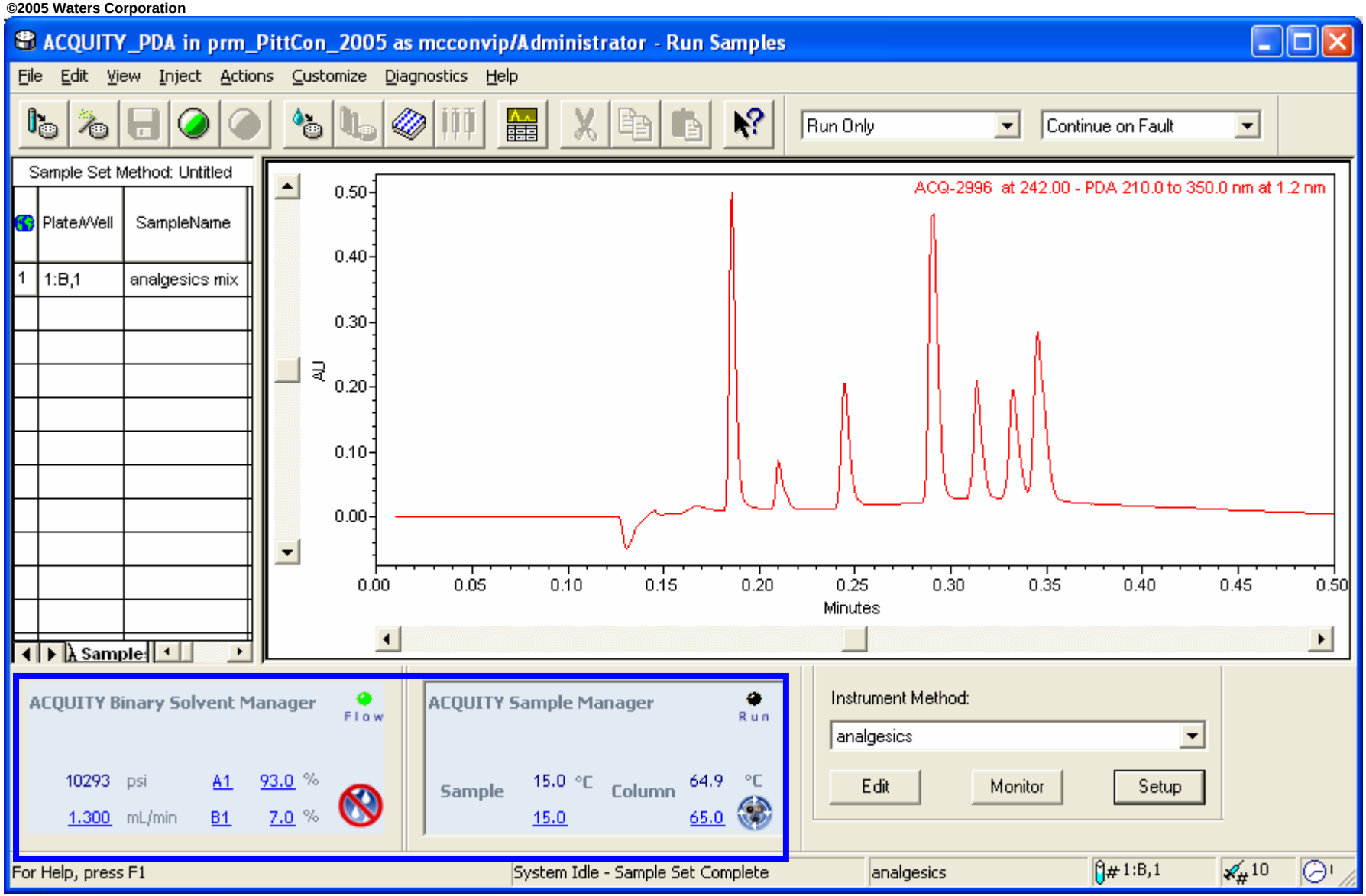

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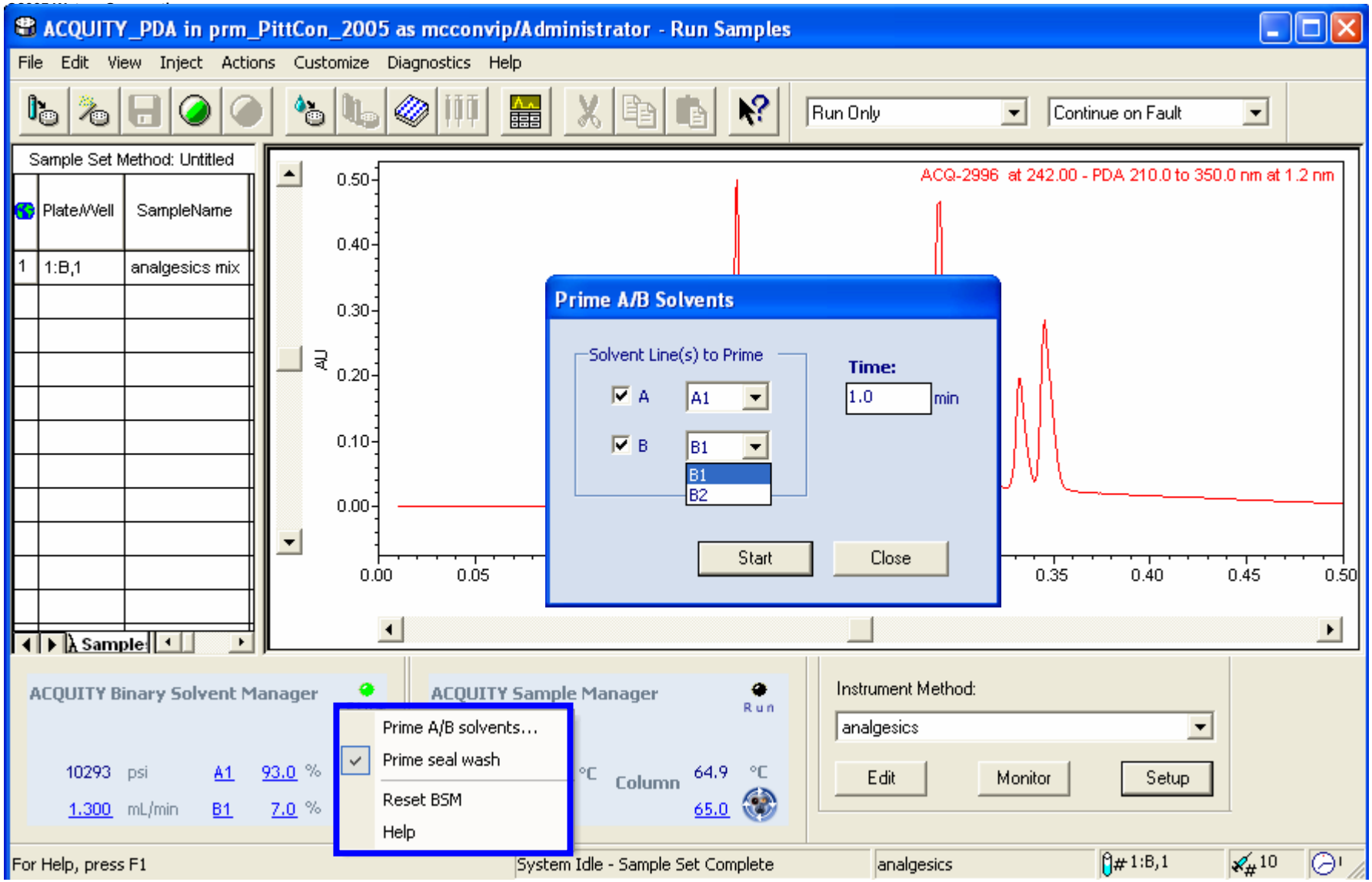
Instrument Control Panel from Run Samples View



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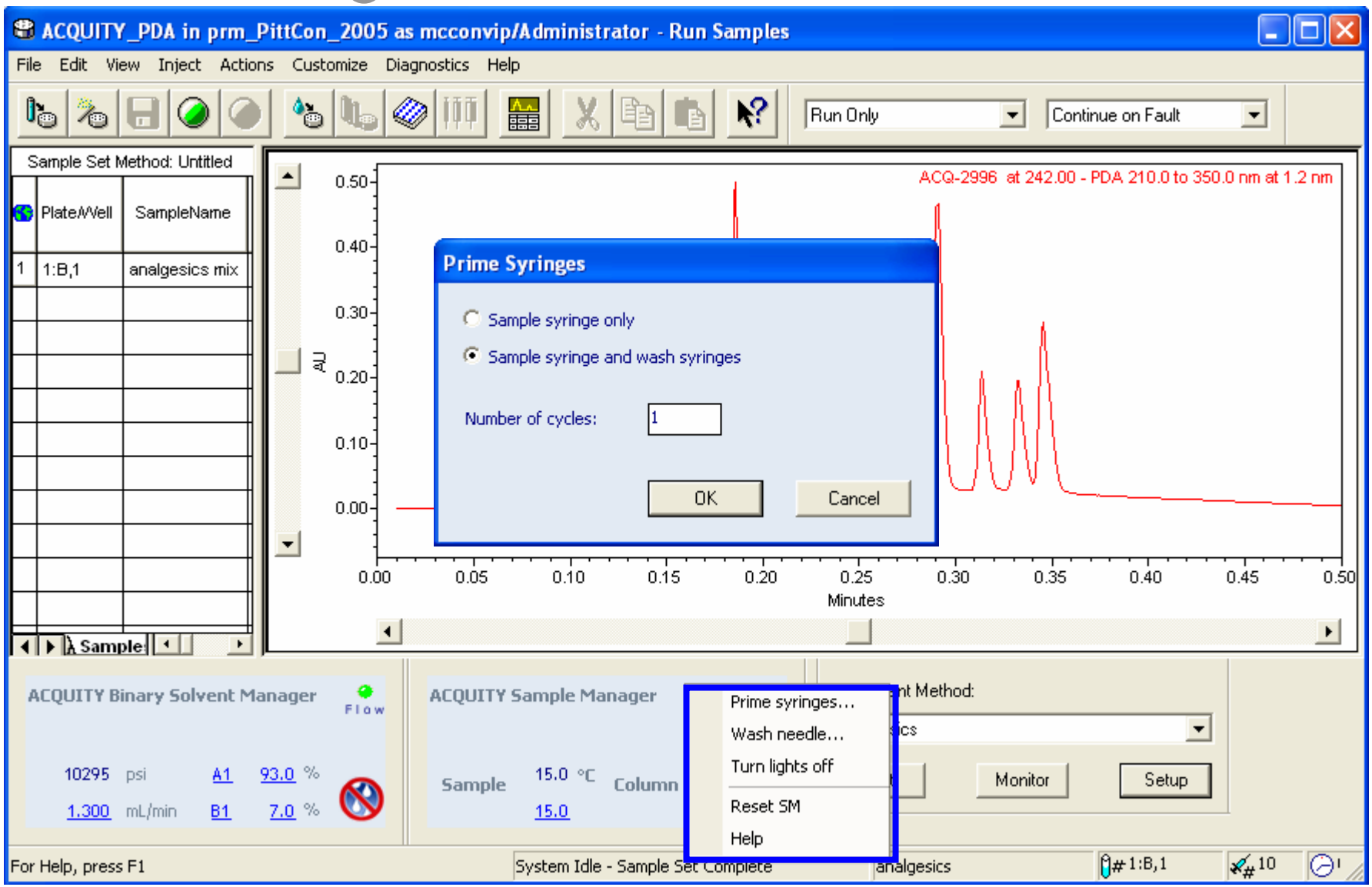
ACQUITY UPLC™

Instrument Control Panel from Run Samples View



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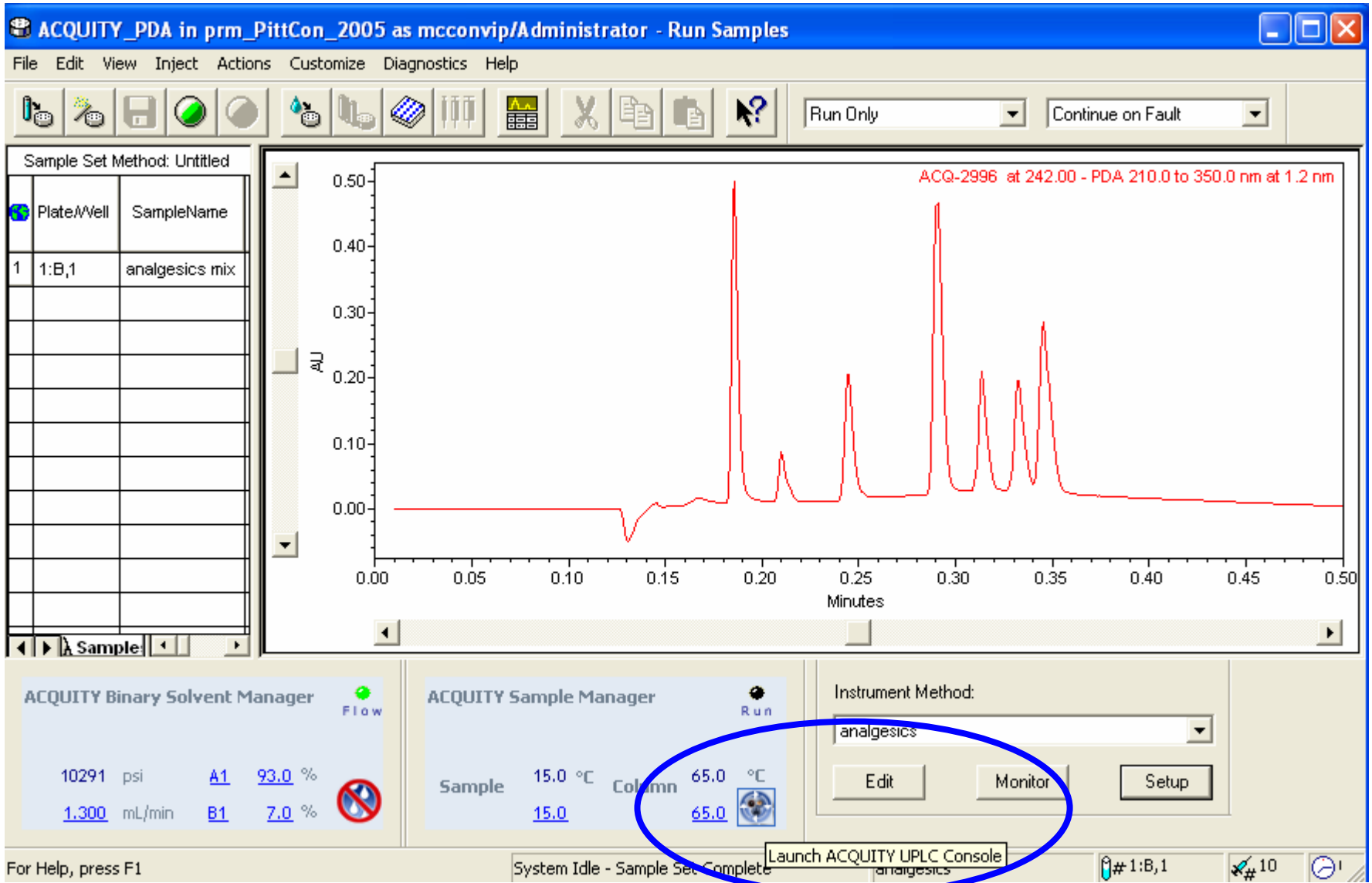
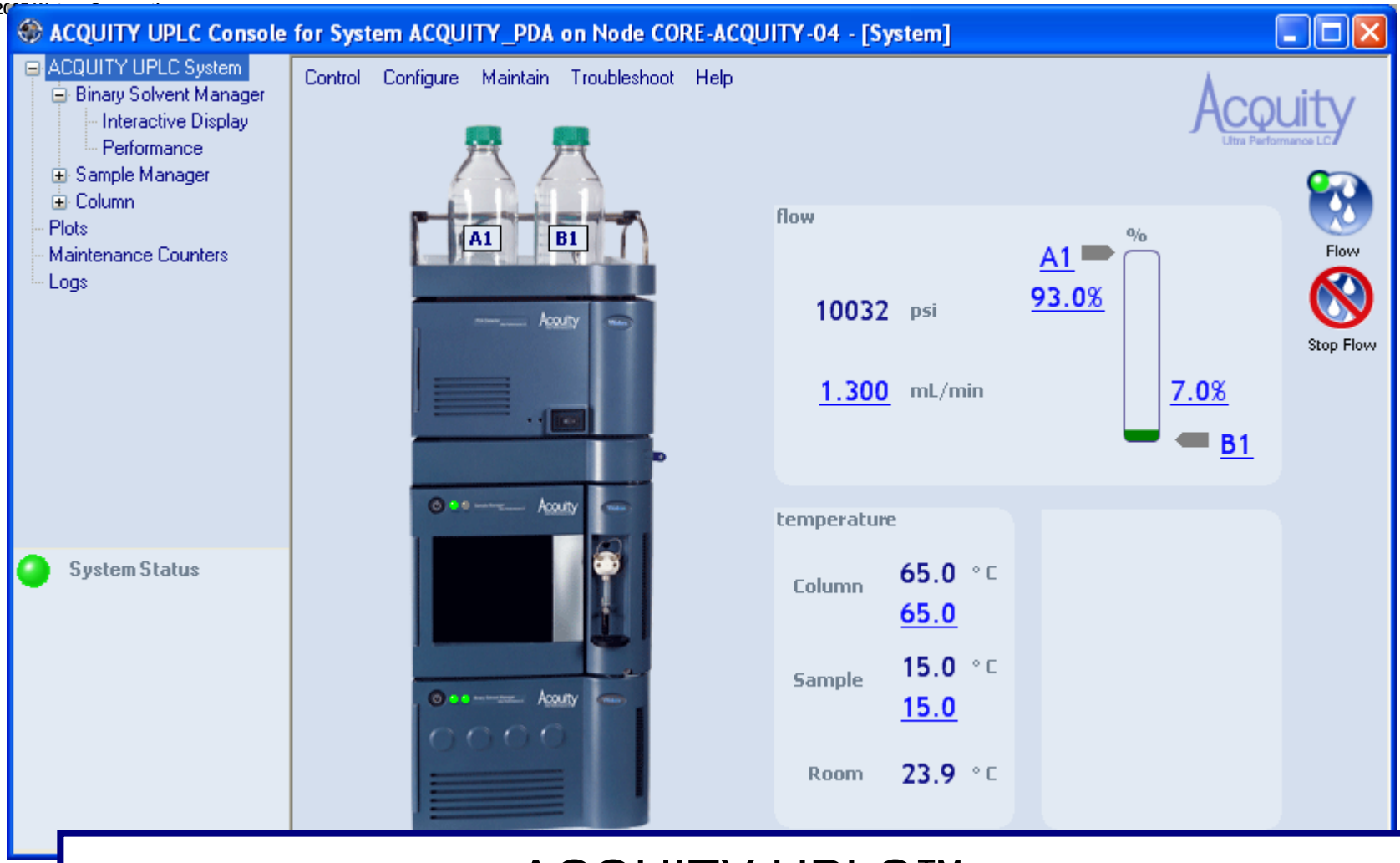
ACQUITY UPLC™
Instrument Console



ACQUITY UPLC™
Console Main View



ACQUITY UPLC™
Console same in Empower™ and Mass Lynx™

ACQUITY UPLC™
Console Main View: Help!

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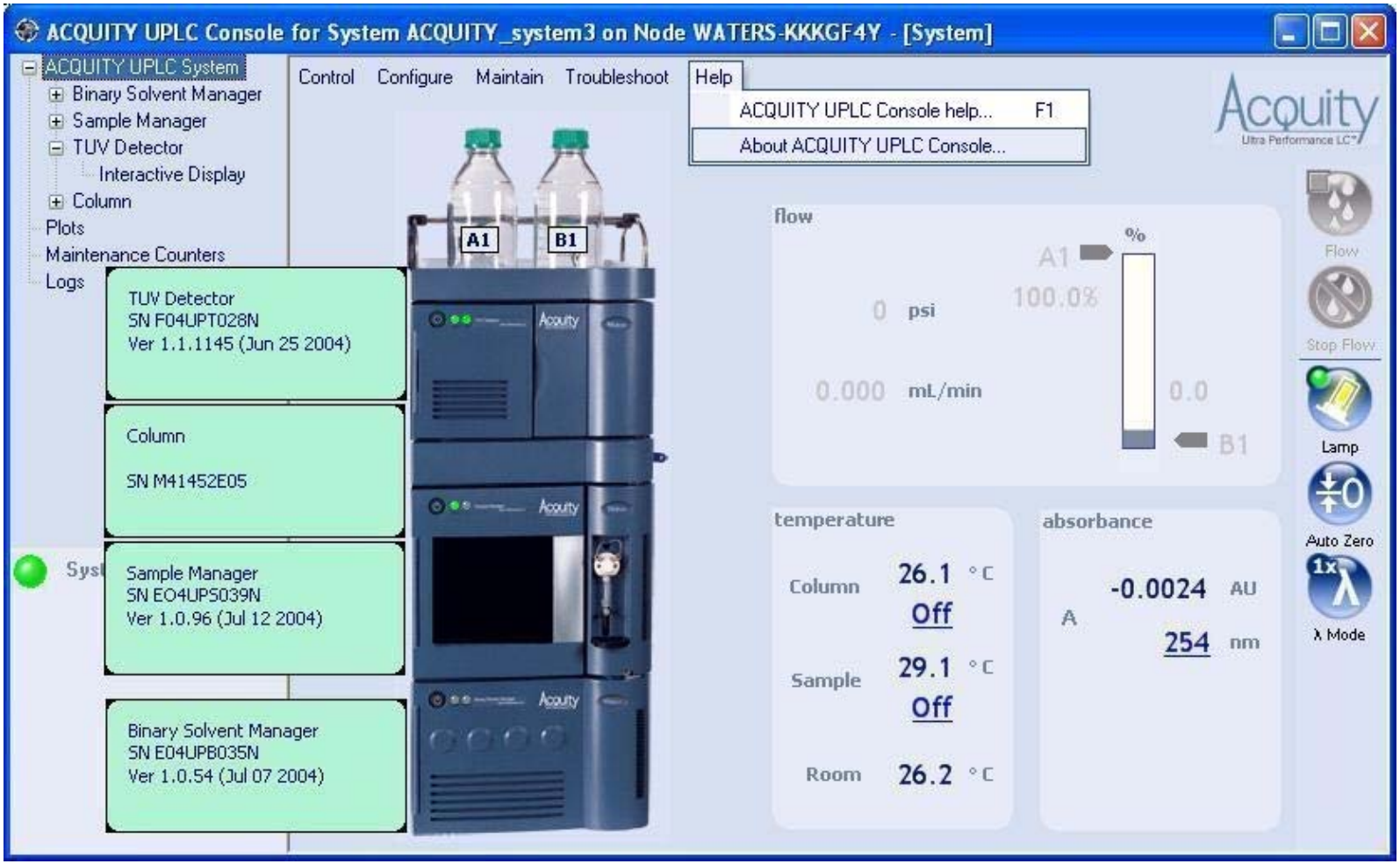

ACQUITY UPLC™
Console Main View: System Set-Up

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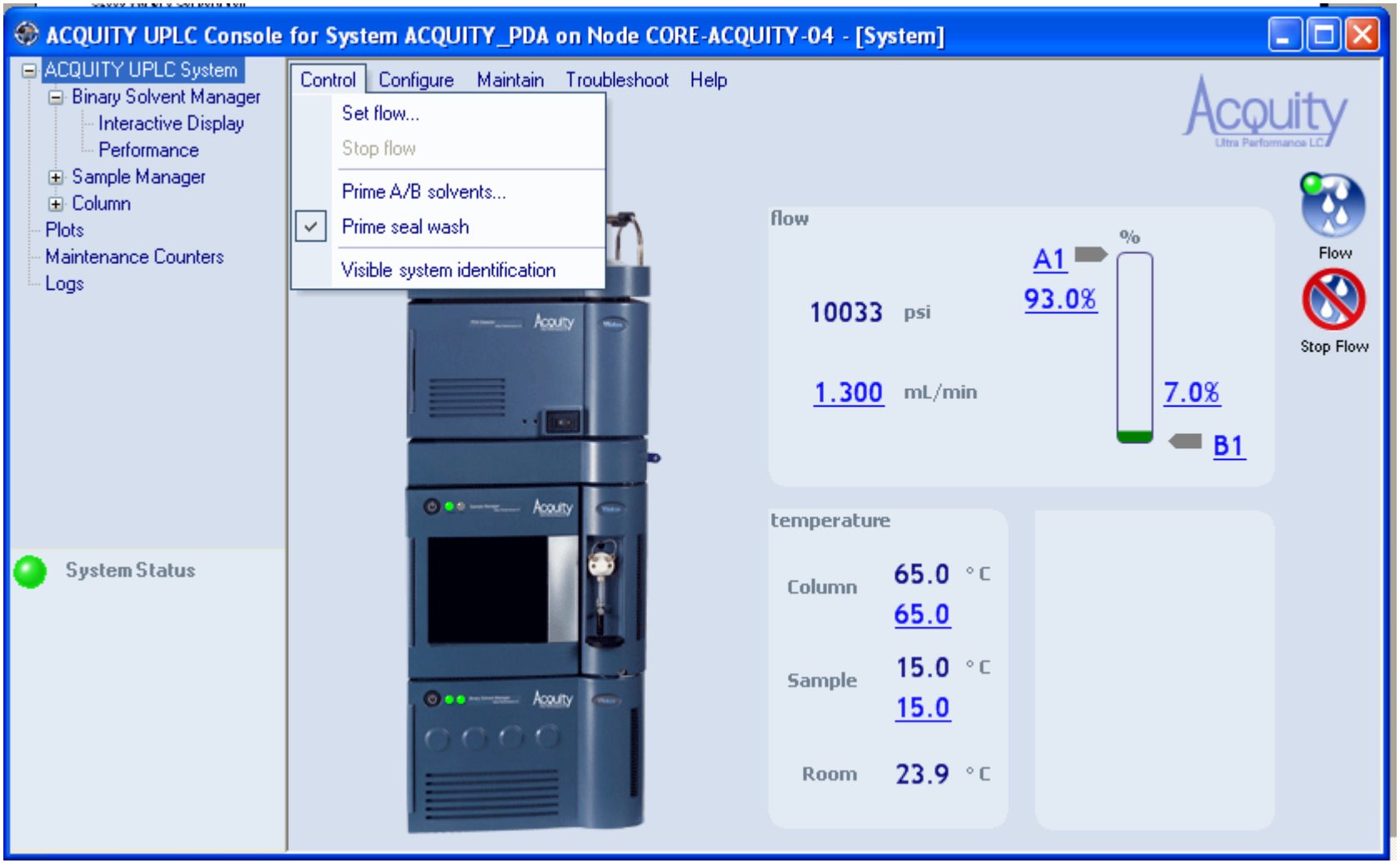

ACQUITY UPLC™
Console Main View : System Preferences

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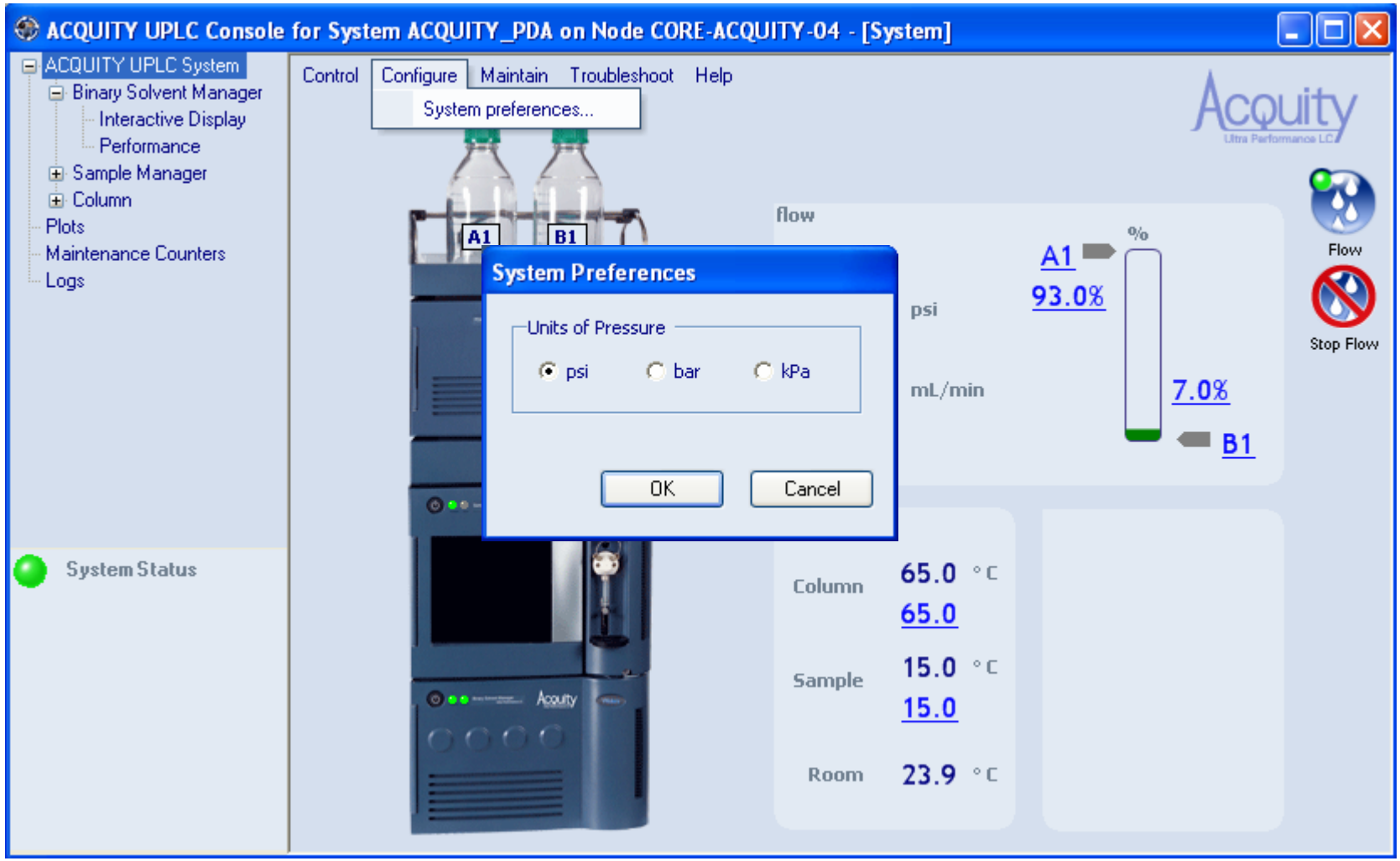

ACQUITY UPLC™
Console Main View: Log Entries

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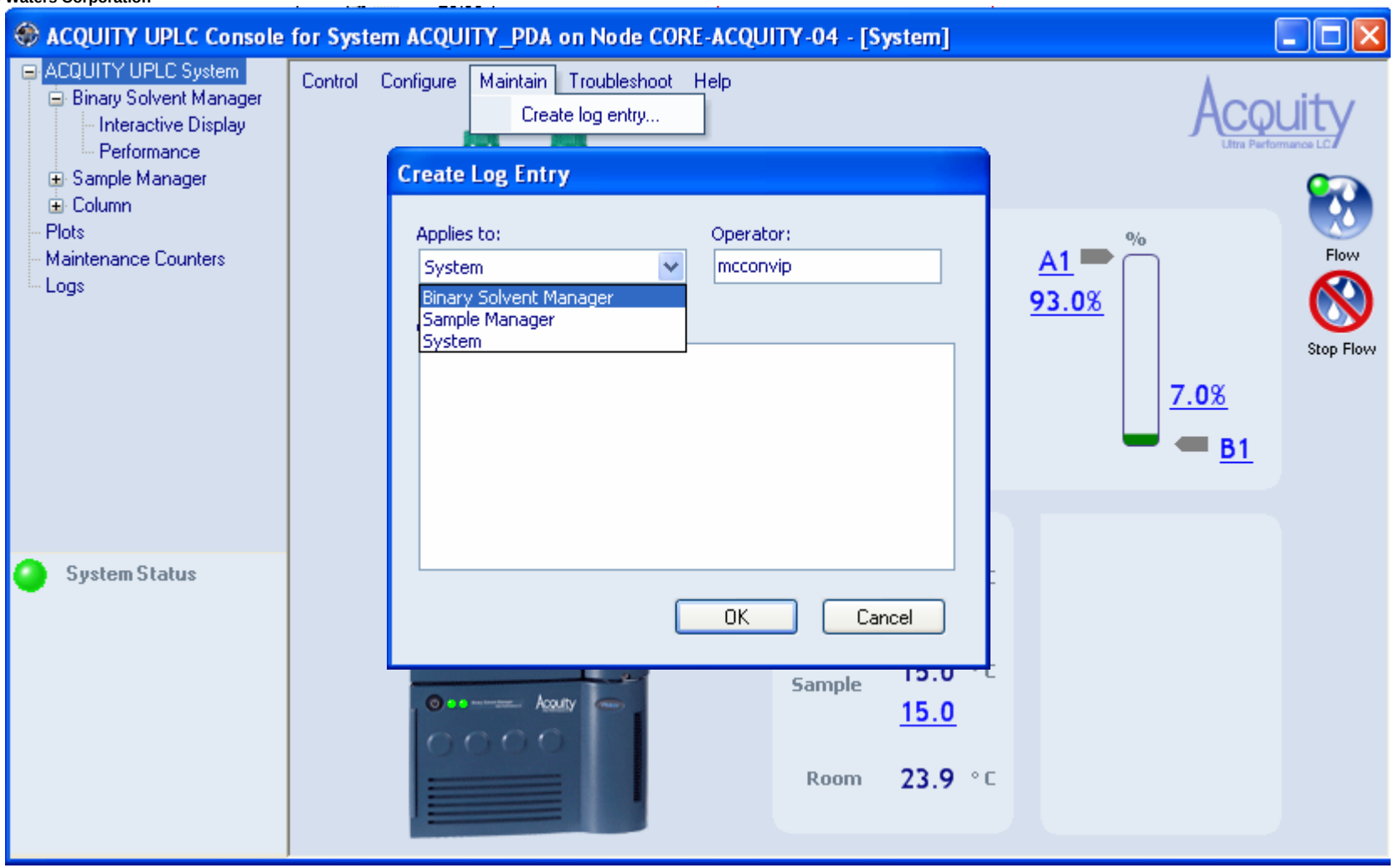

ACQUITY UPLC™ : *Console Main View: Service Mode*

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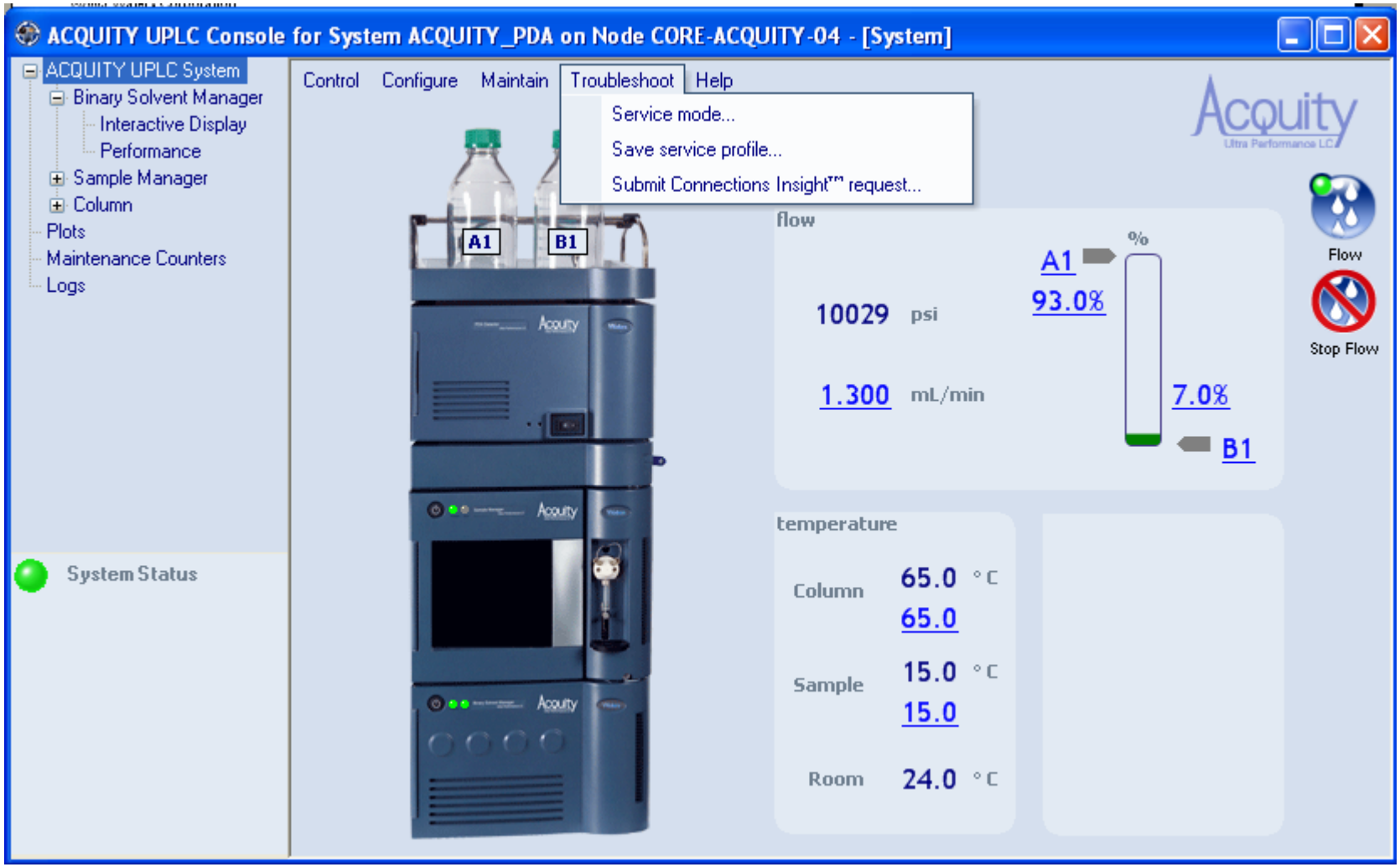

ACQUITY UPLC™ Binary Solvent Manager : *Main Interface*

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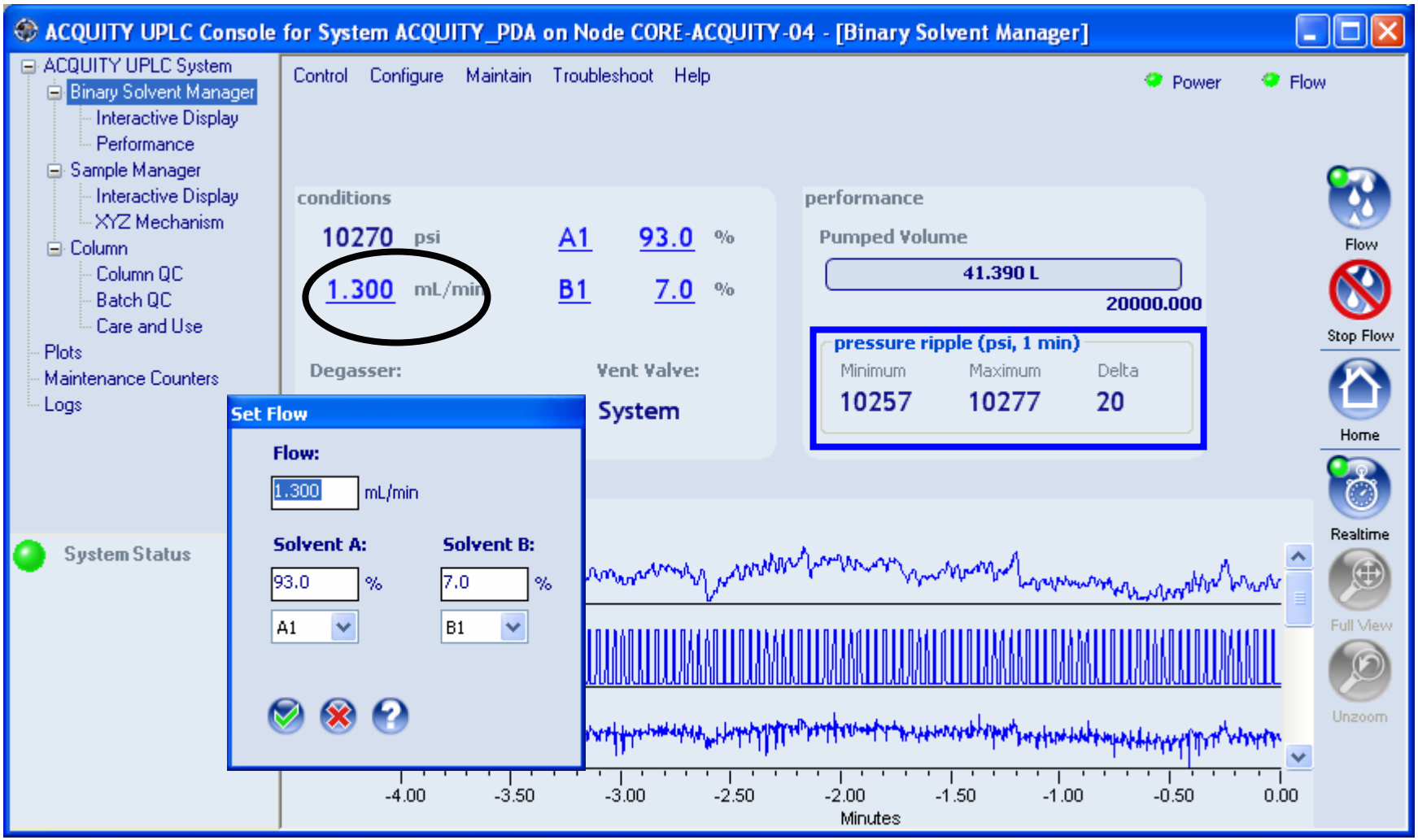

ACQUITY UPLC™ Binary Solvent Manager :
Automated Maintenance & Performance Testing

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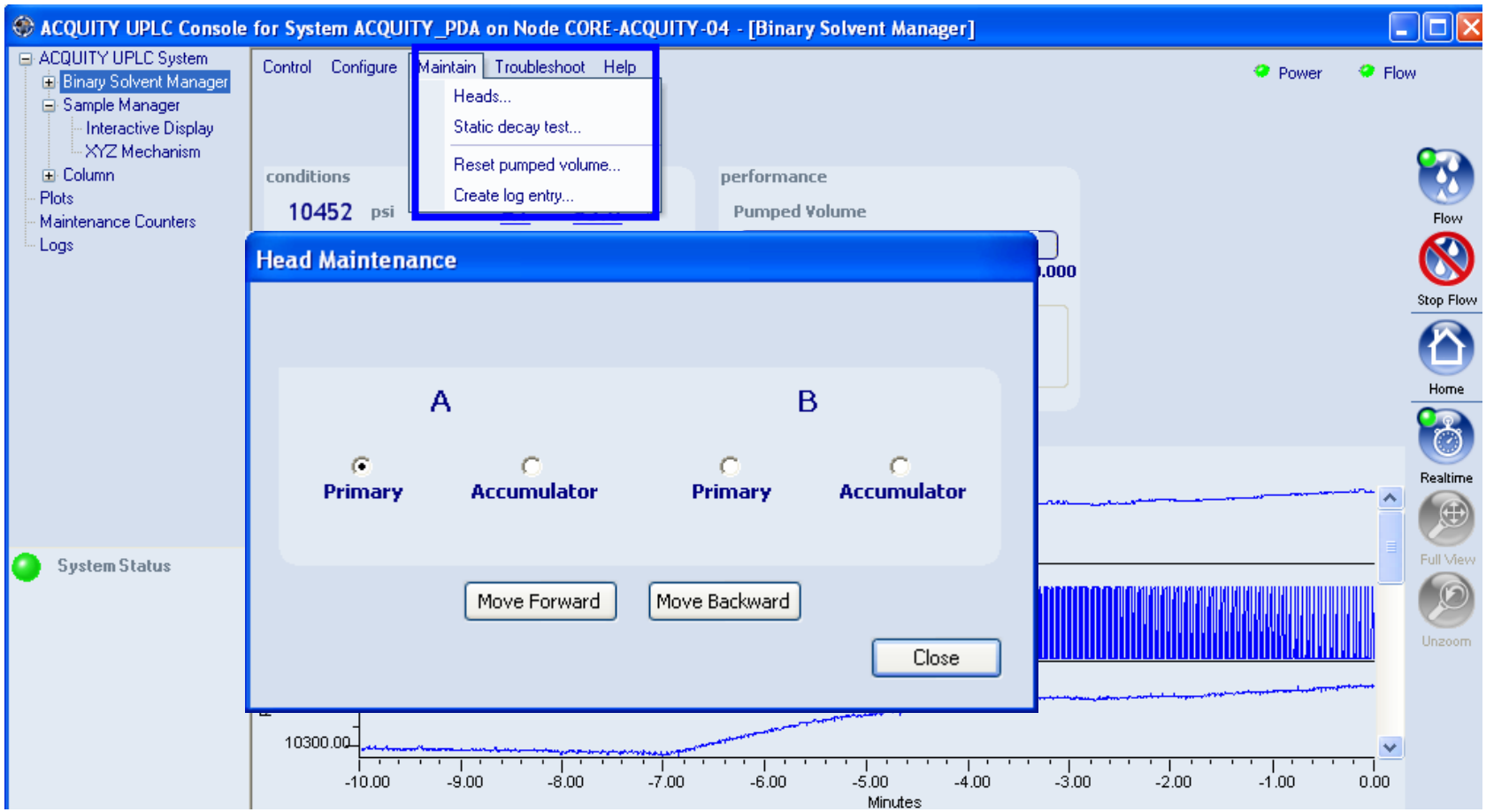

ACQUITY UPLC™ Binary Solvent Manager :
Automated Maintenance & Performance Testing

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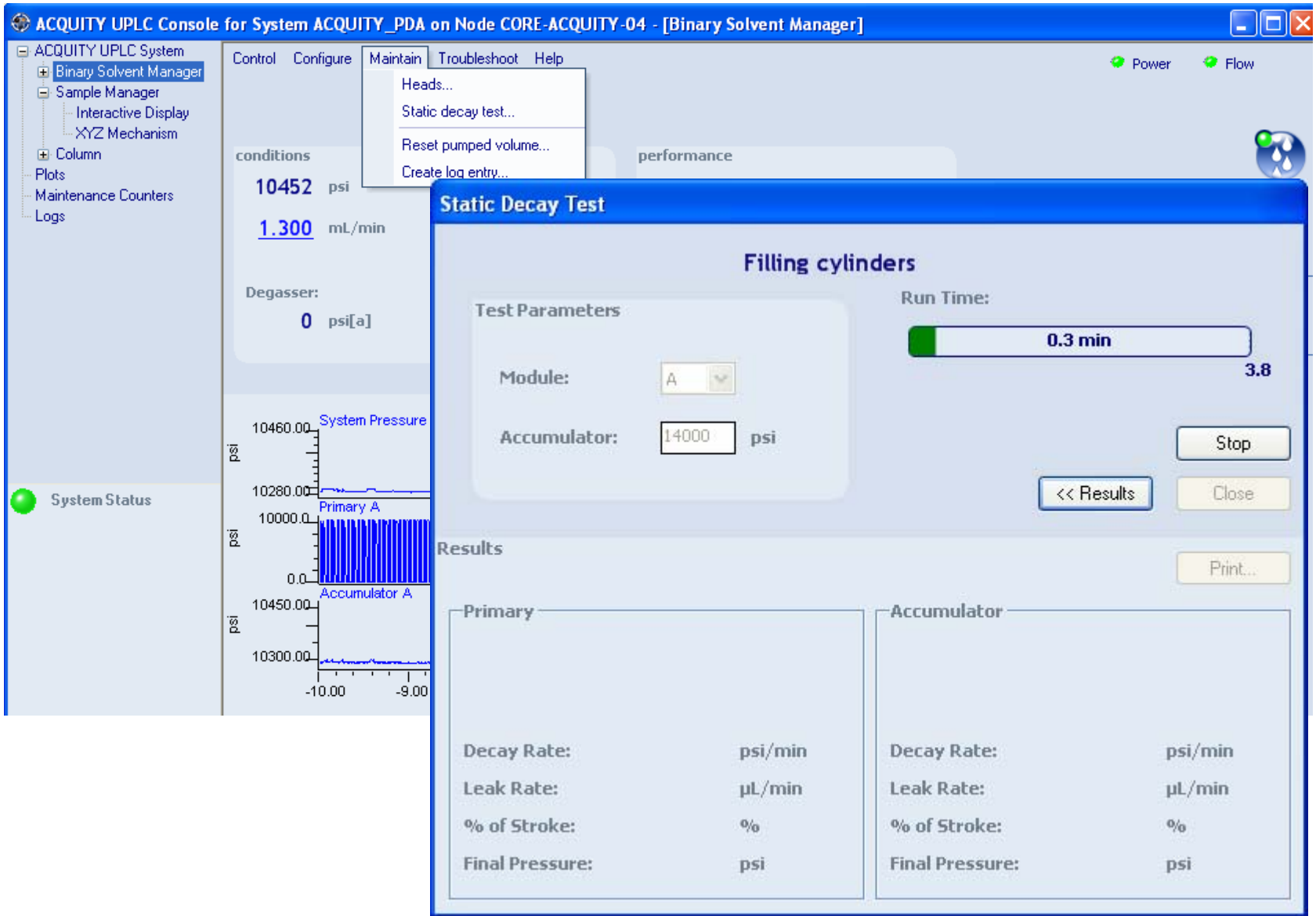

ACQUITY UPLC™ Binary Solvent Manager :
Automated Maintenance & Performance Testing

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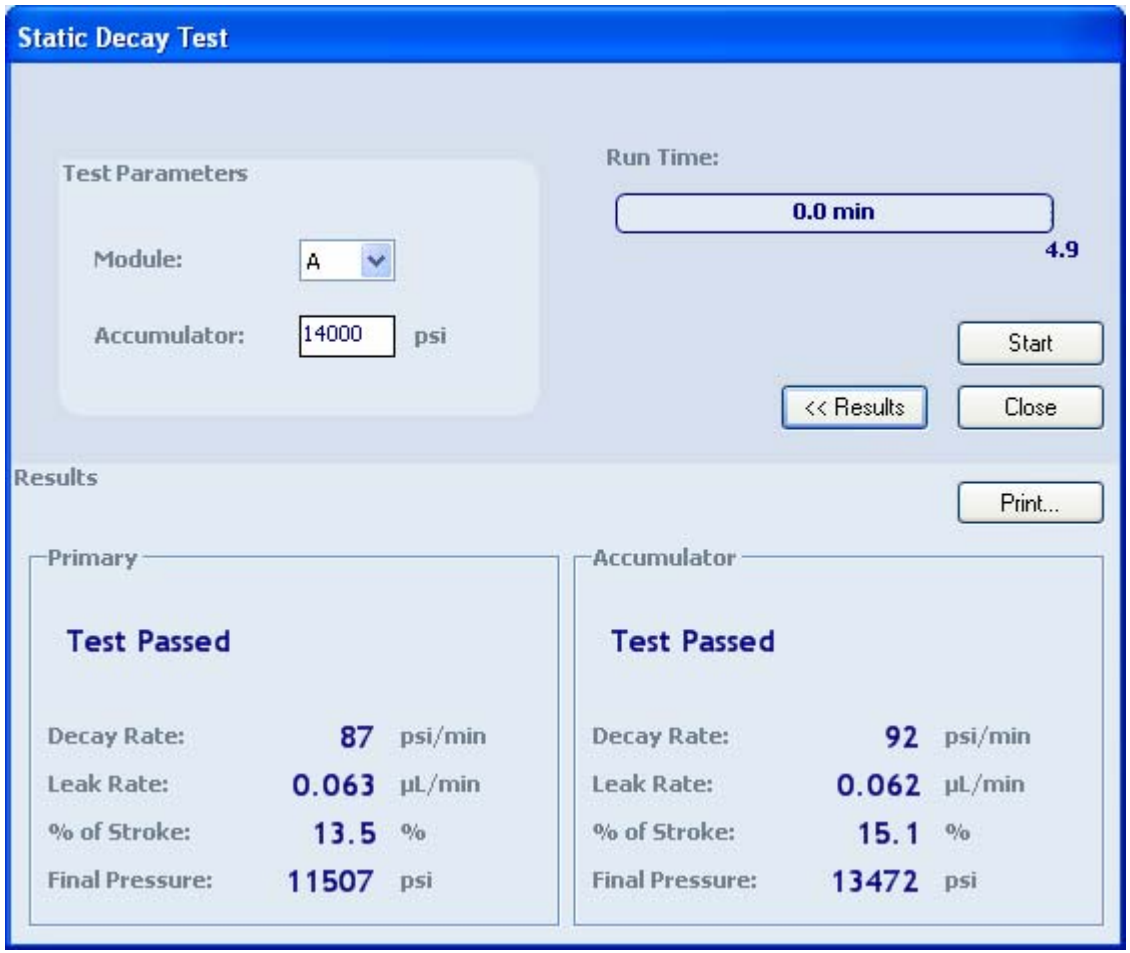

ACQUITY UPLC™ Binary Solvent Manager : *Real Time Interactive Display*

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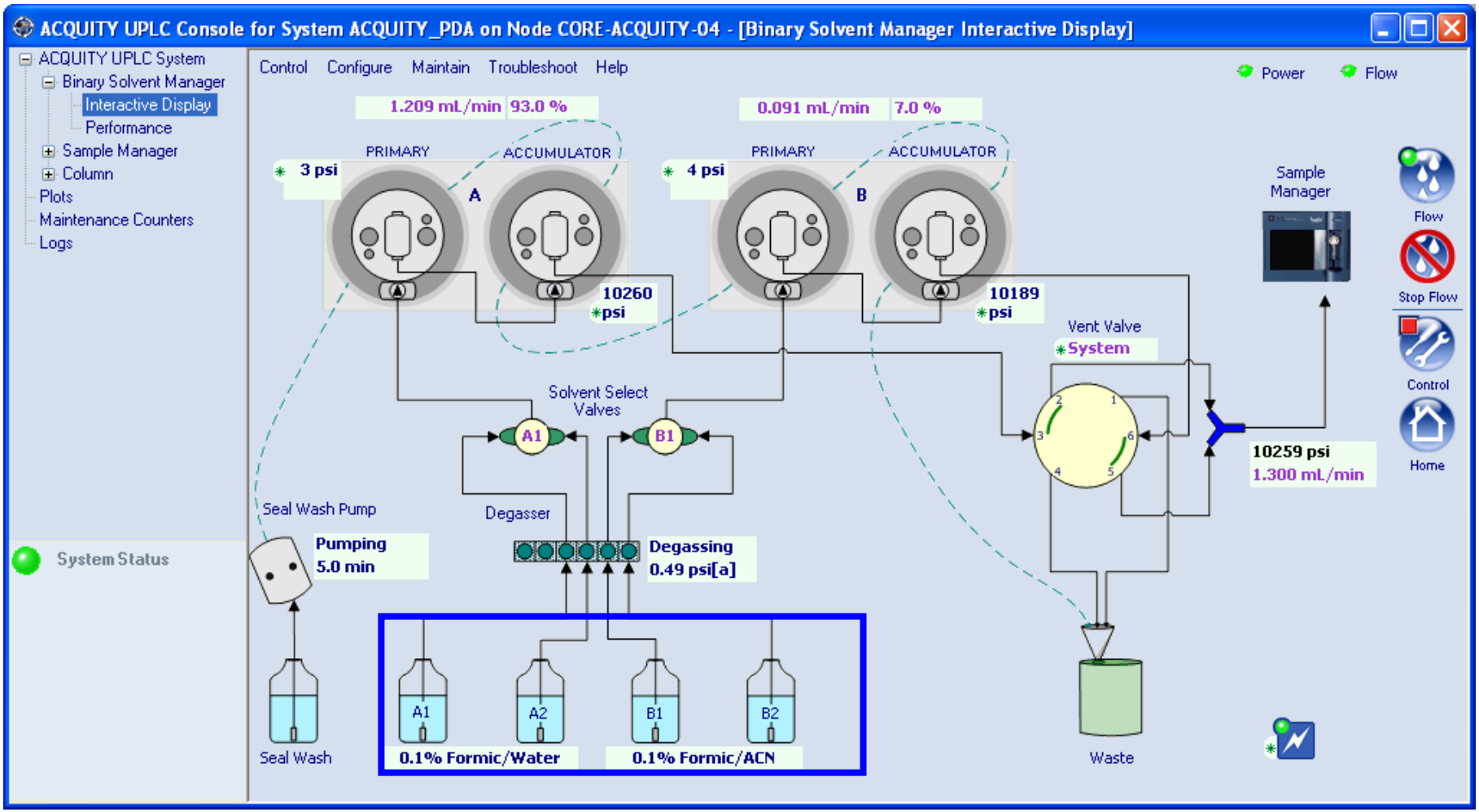

ACQUITY UPLC™ Binary Solvent Manager : *Real Time Performance*

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ACQUITY UPLC™ Sample Manager: *Main Interface*

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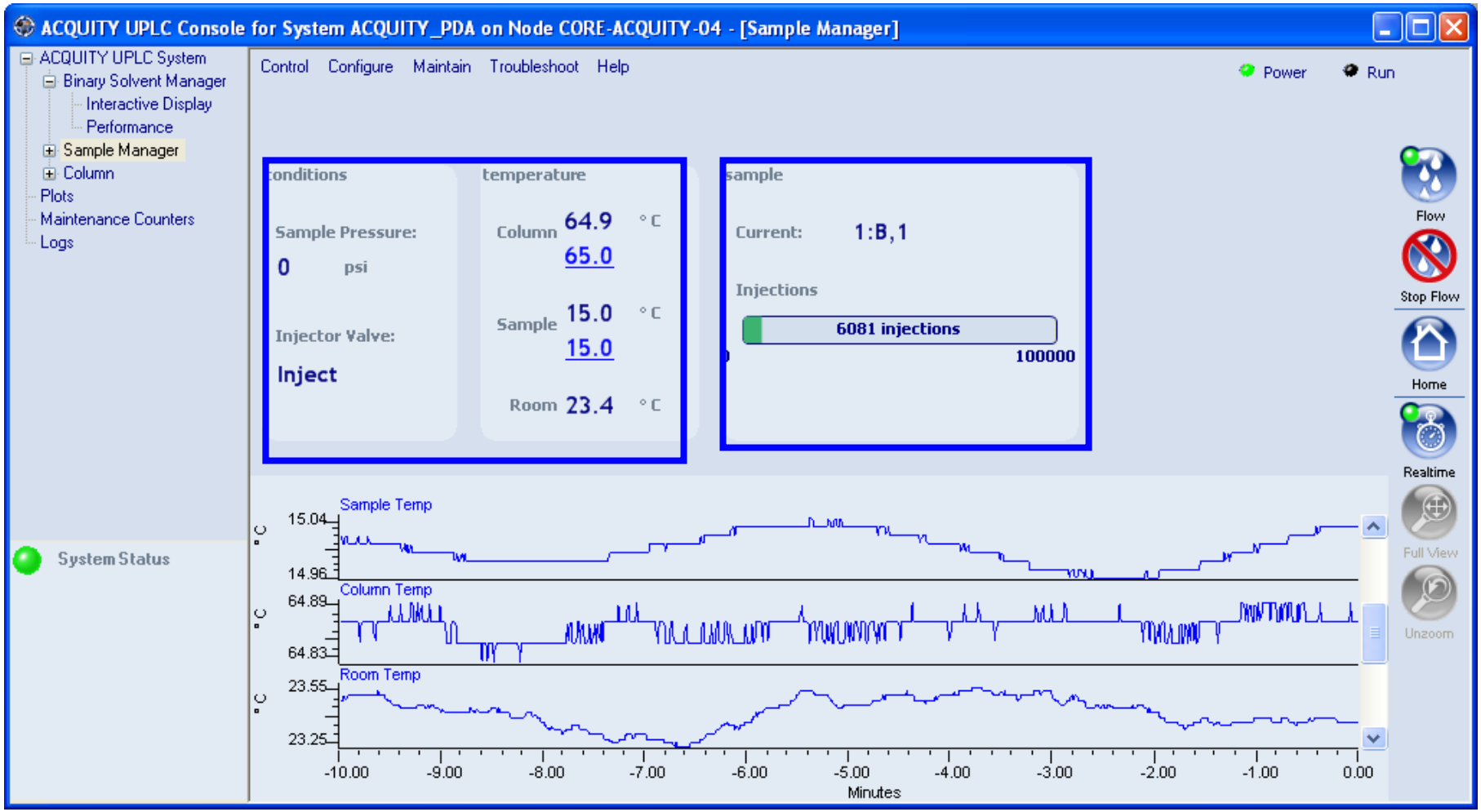

ACQUITY UPLC™ Sample Manager: *Real Time Interactive Display*

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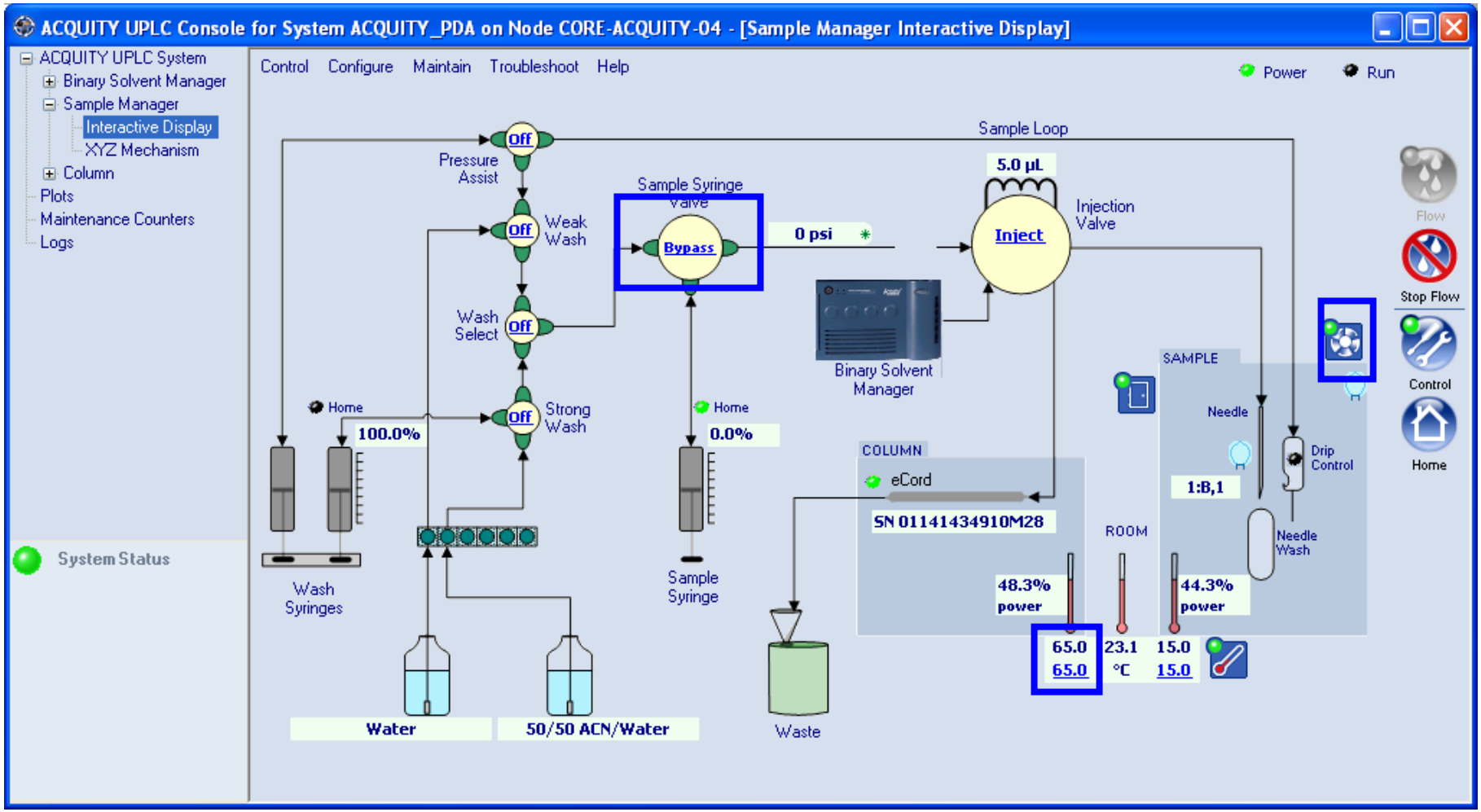

ACQUITY UPLC™ Sample Manager: *Real Time Interactive Display*

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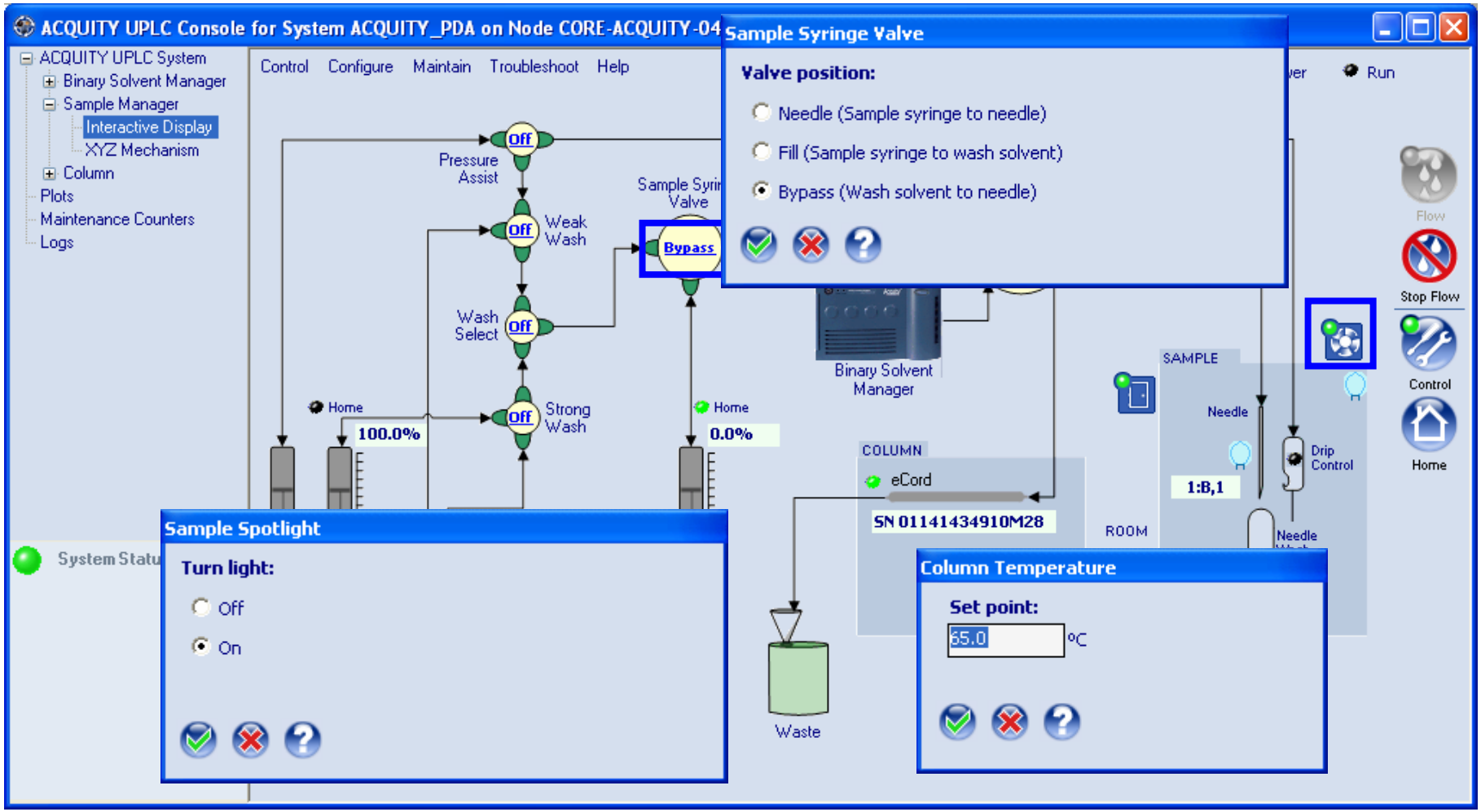

ACQUITY UPLC™ Sample Manager:
Characterization, *Maintenance and Testing Functions*

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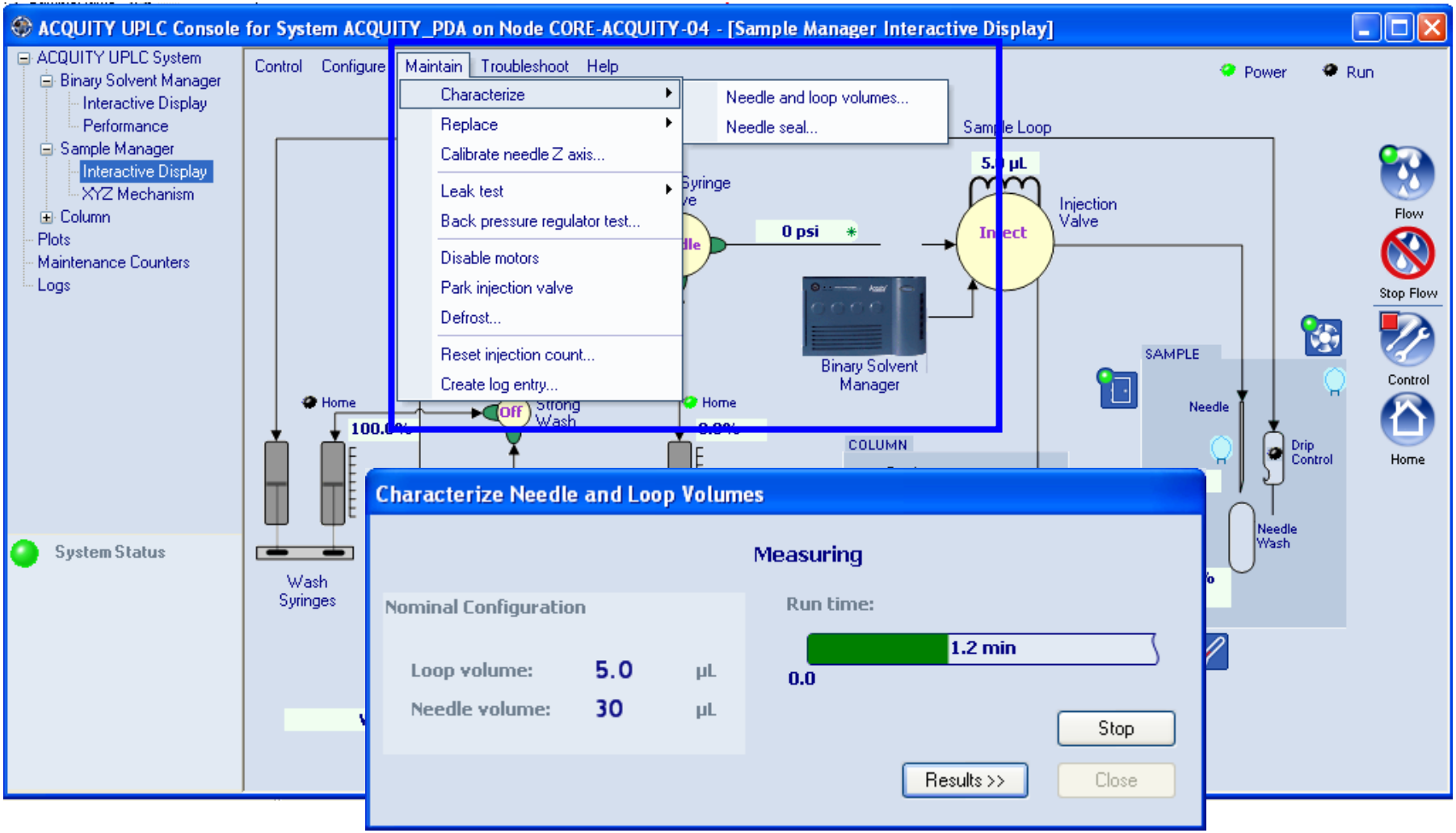

ACQUITY UPLC™ Sample Manager:
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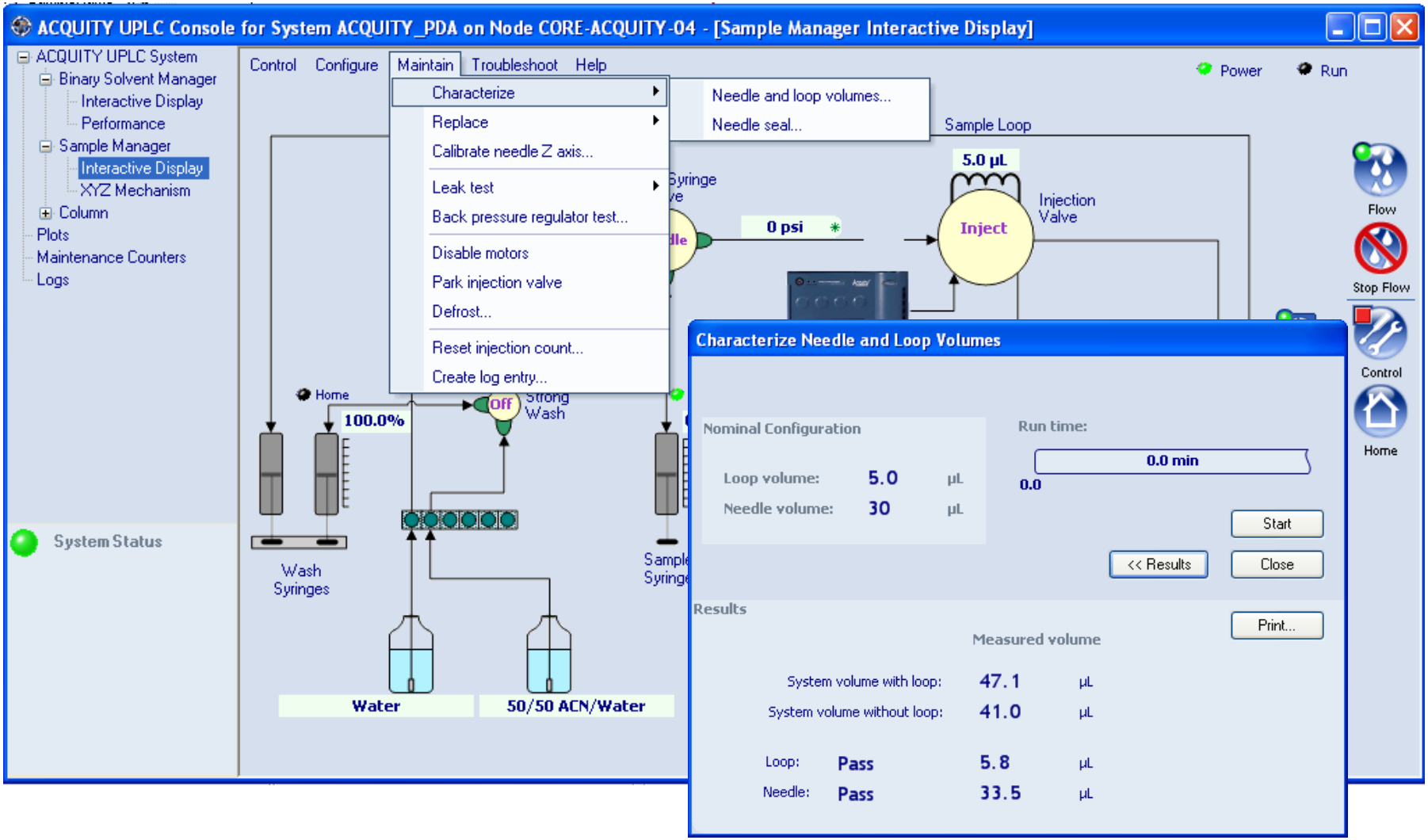

ACQUITY UPLC™ Sample Manager:
*Characterization, **Maintenance** and Testing Functions*

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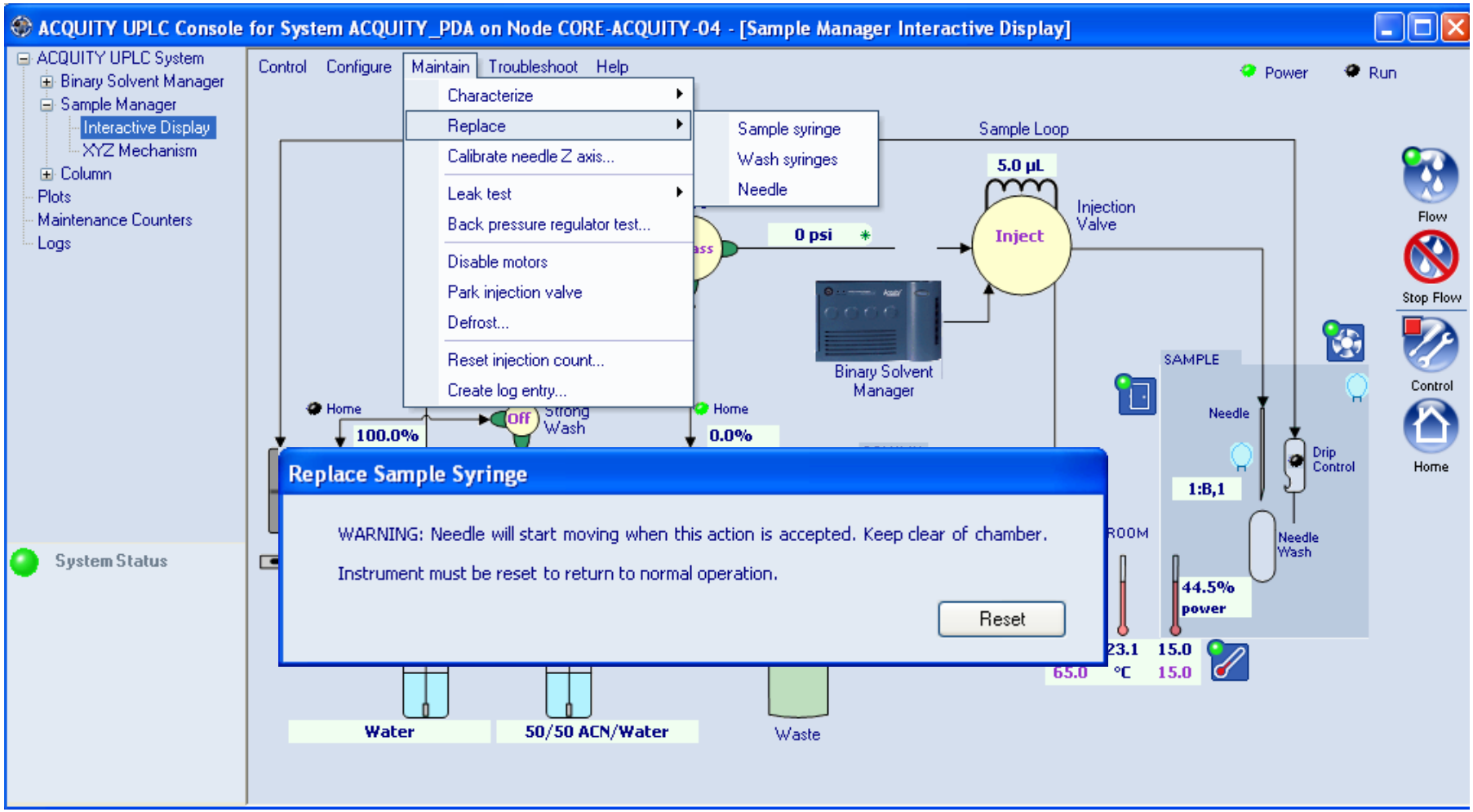

ACQUITY UPLC™ Sample Manager:
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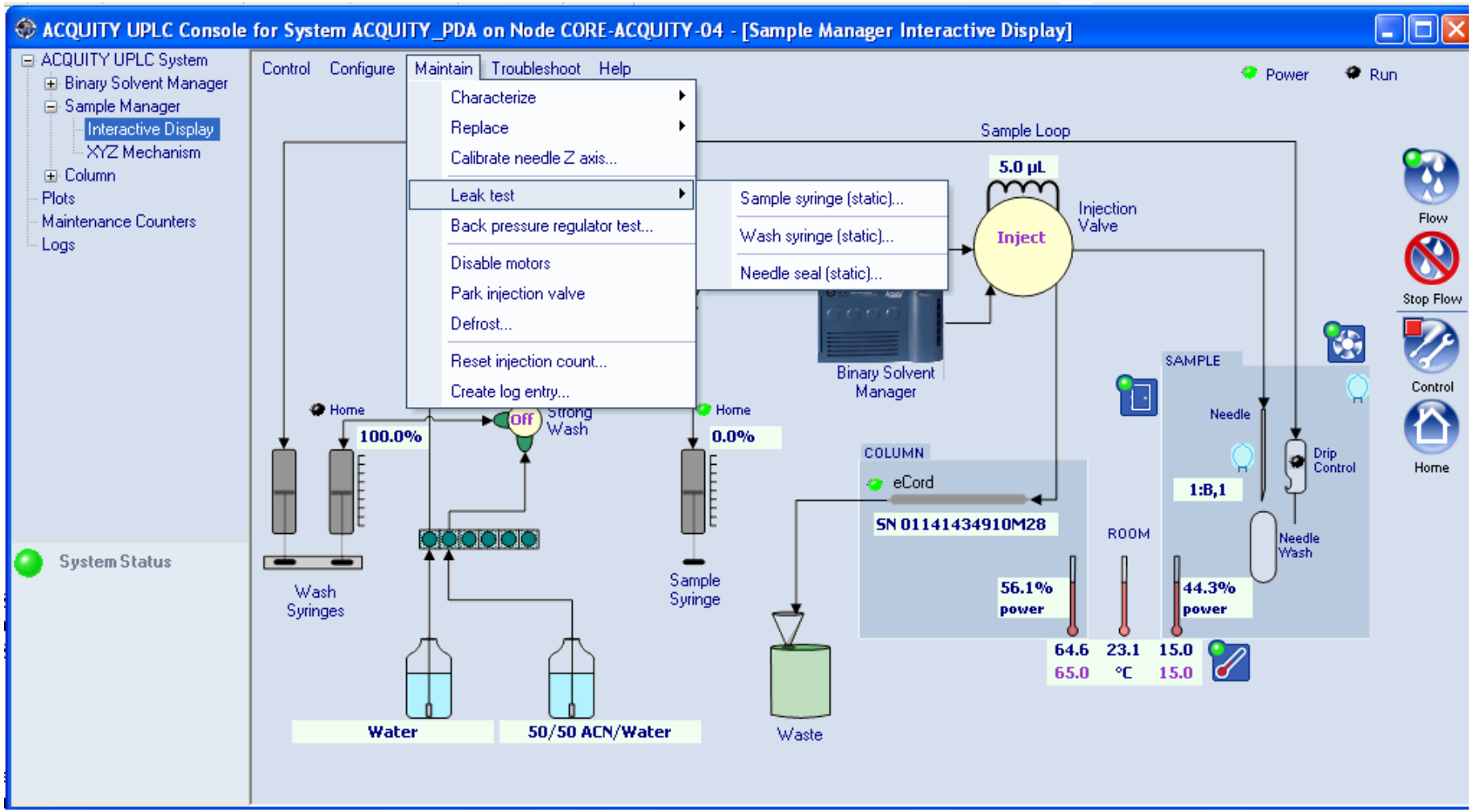

ACQUITY UPLC™ Sample Manager: *Sample Manager XYZ Mechanism*

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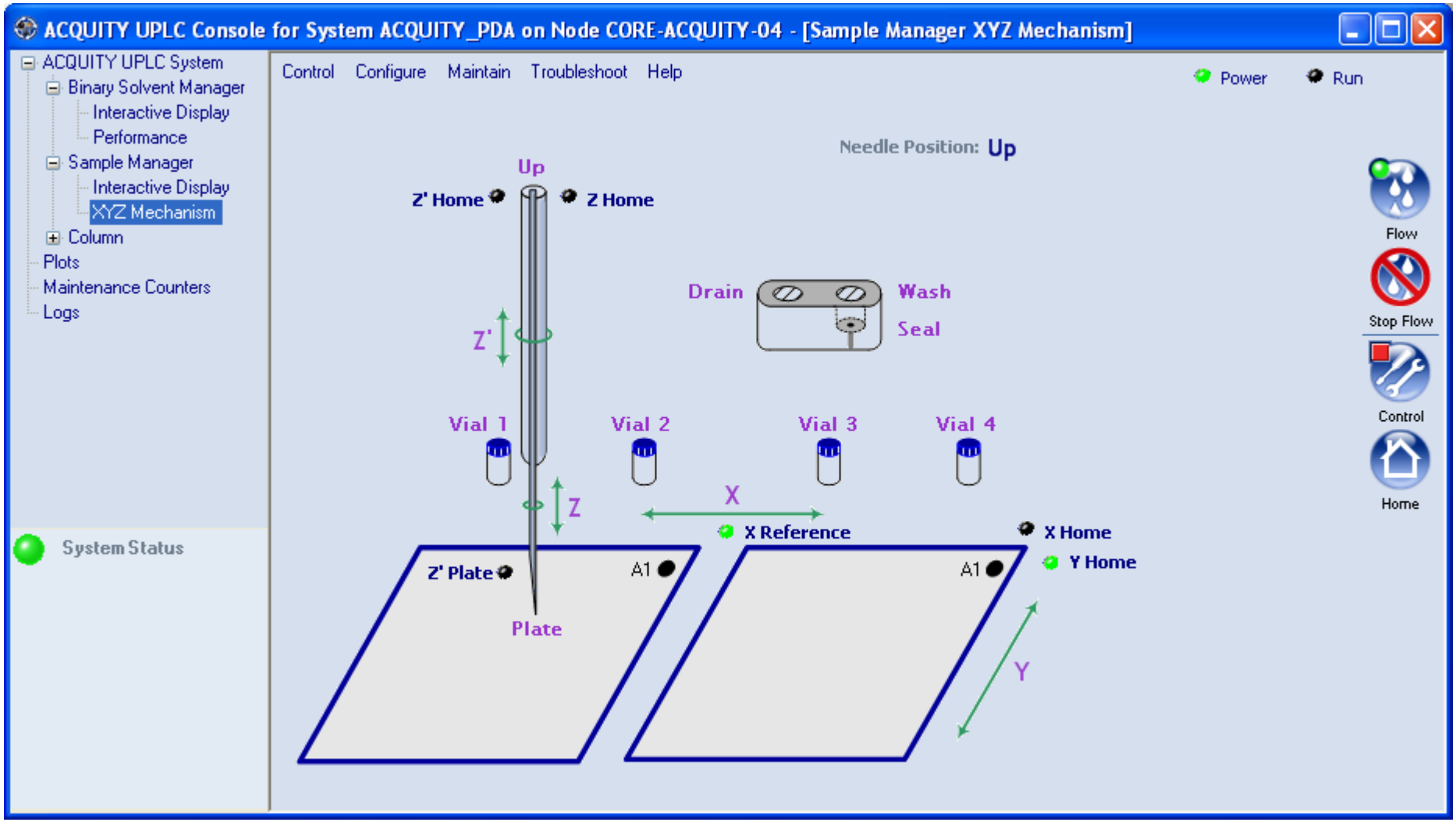

ACQUITY UPLC™ Sample Manager: *Sample Manager XYZ Mechanism*

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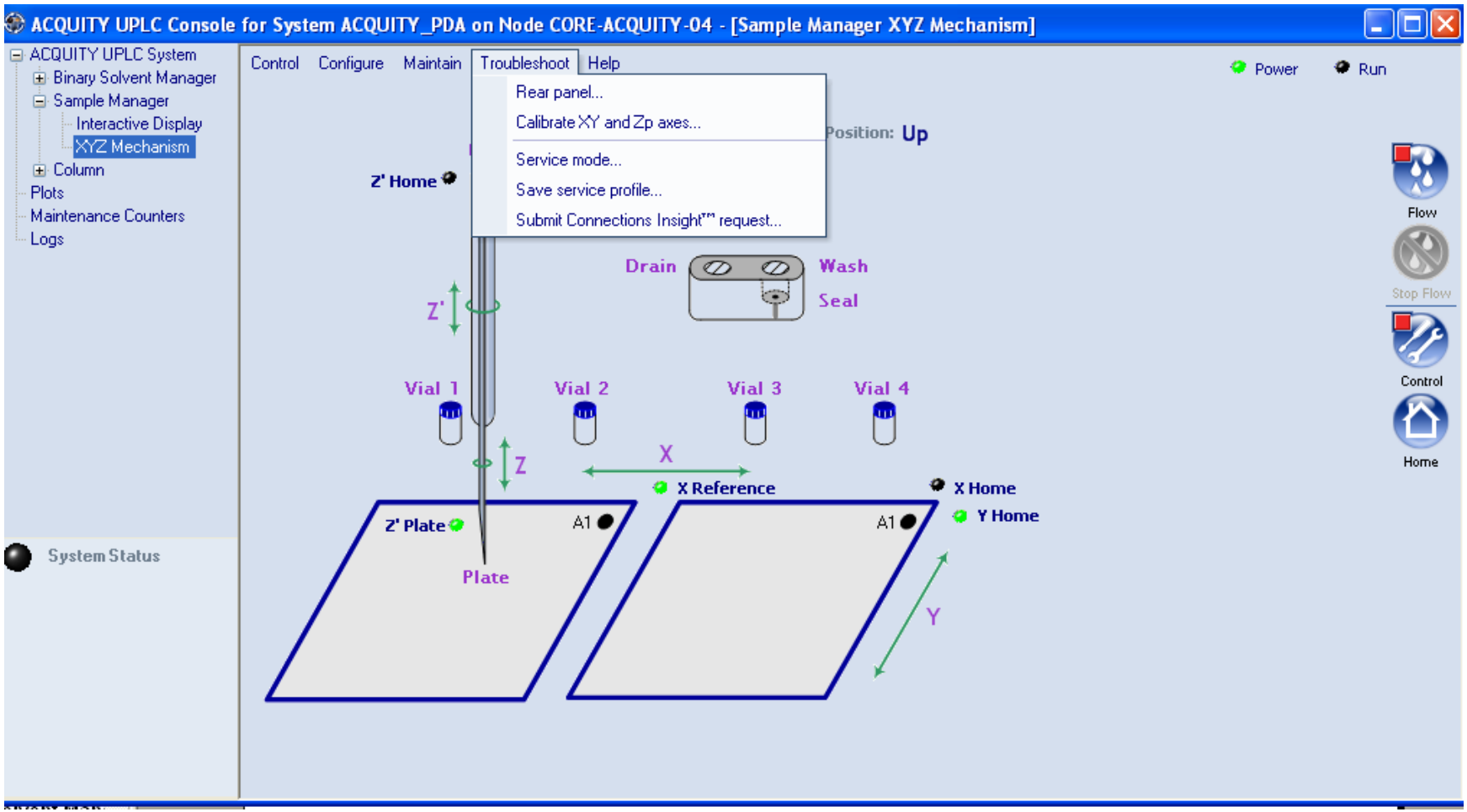

ACQUITY UPLC™ TUV Detector
Interactive Display

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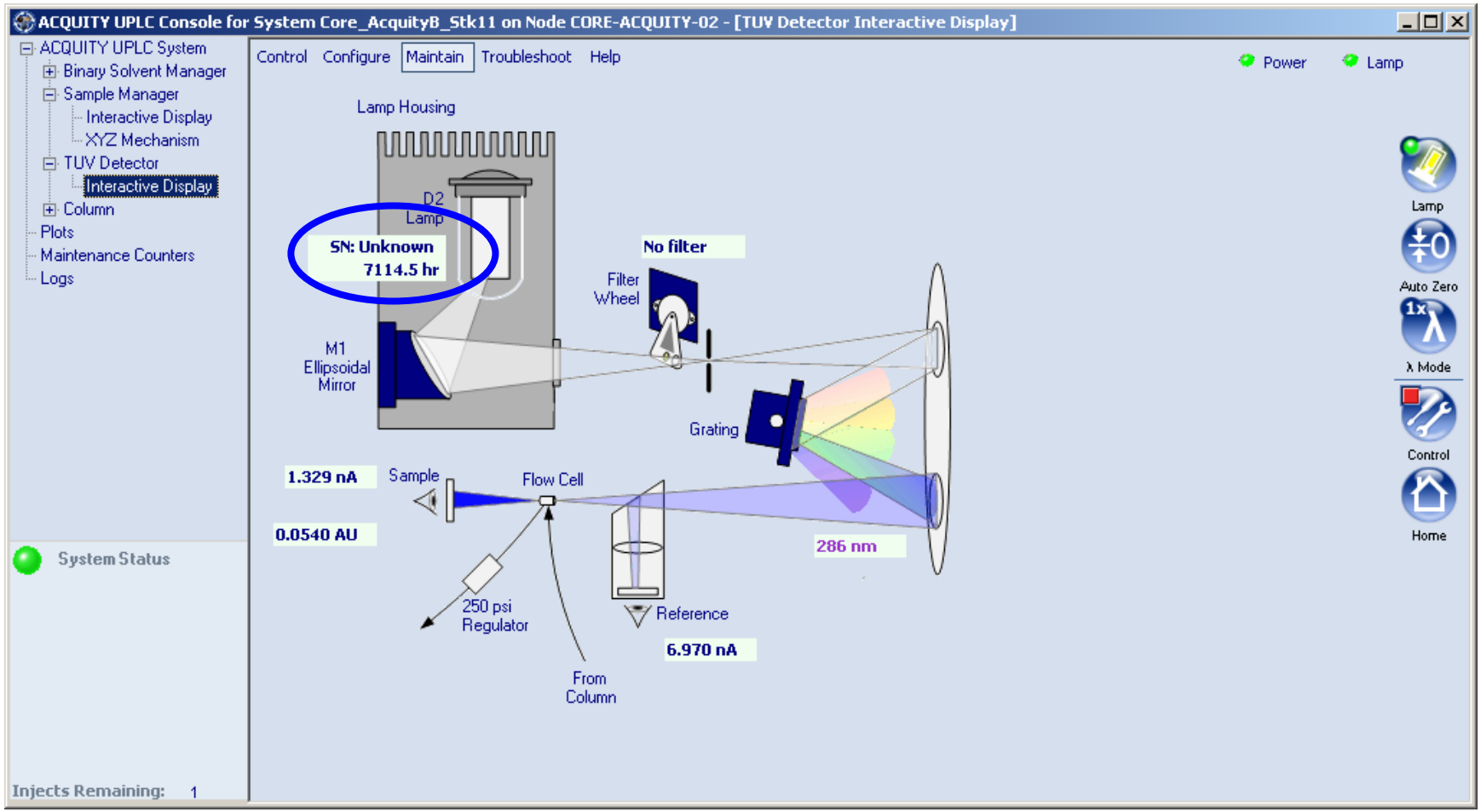

ACQUITY UPLC™
96 hours of performance information

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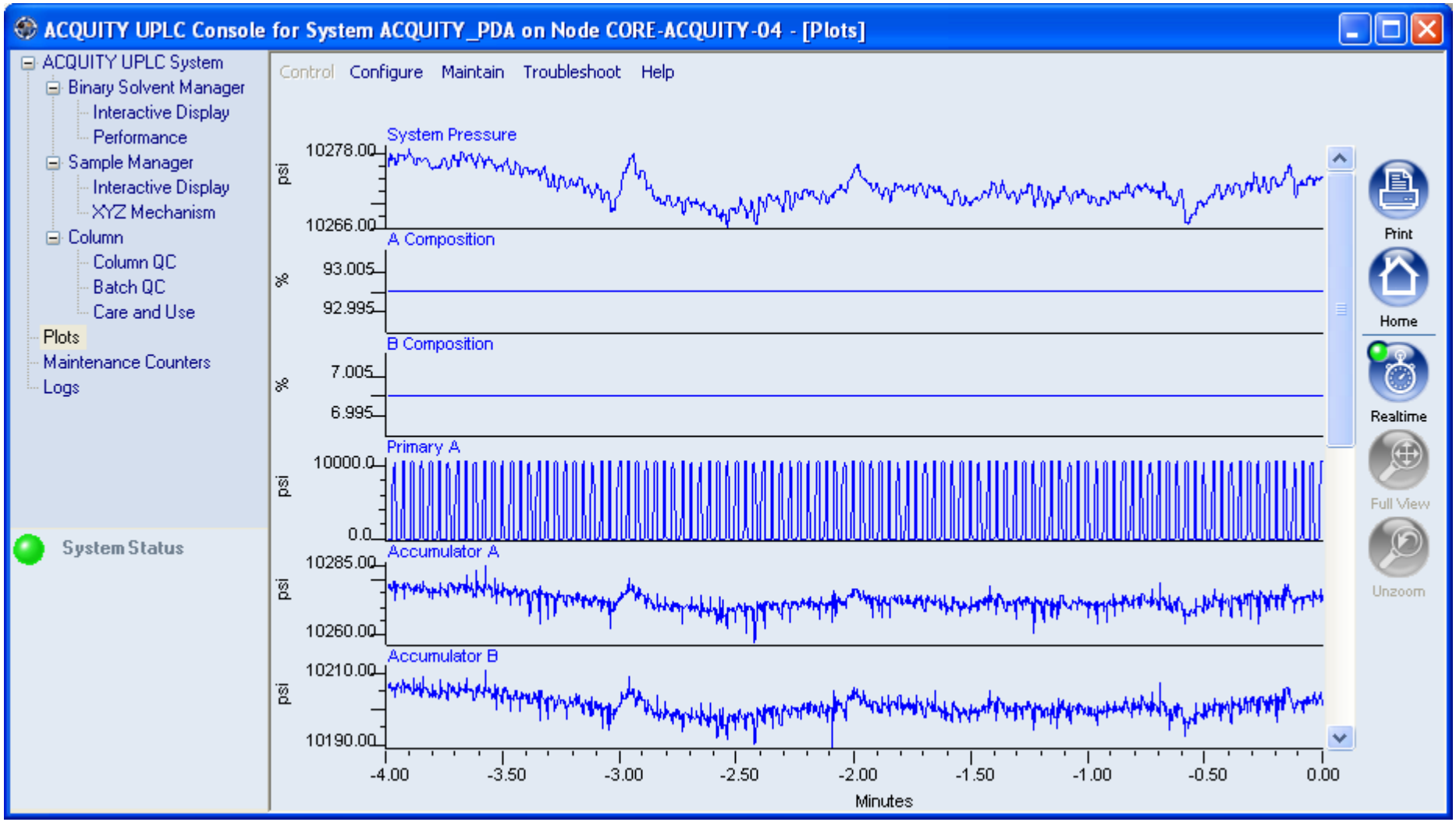

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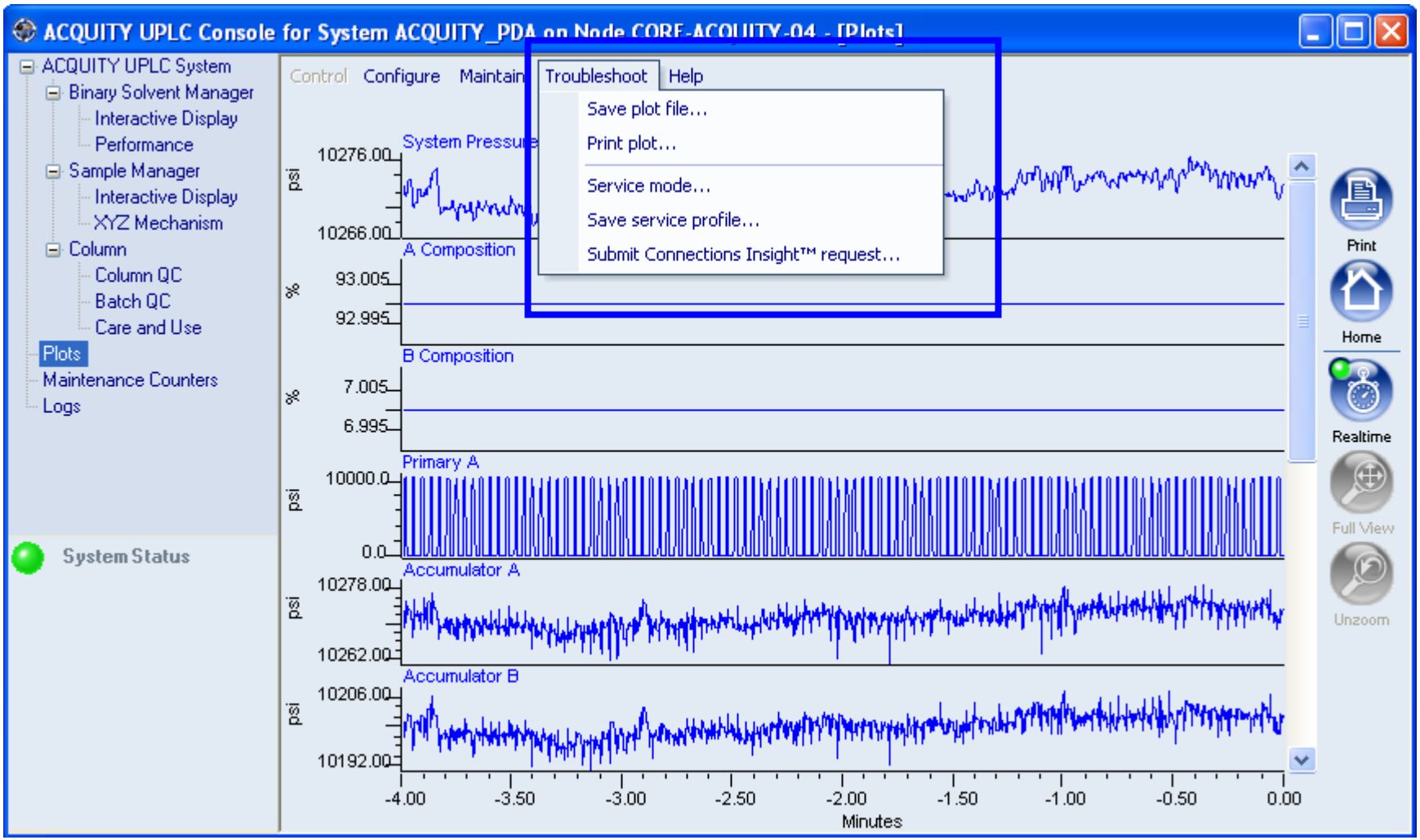

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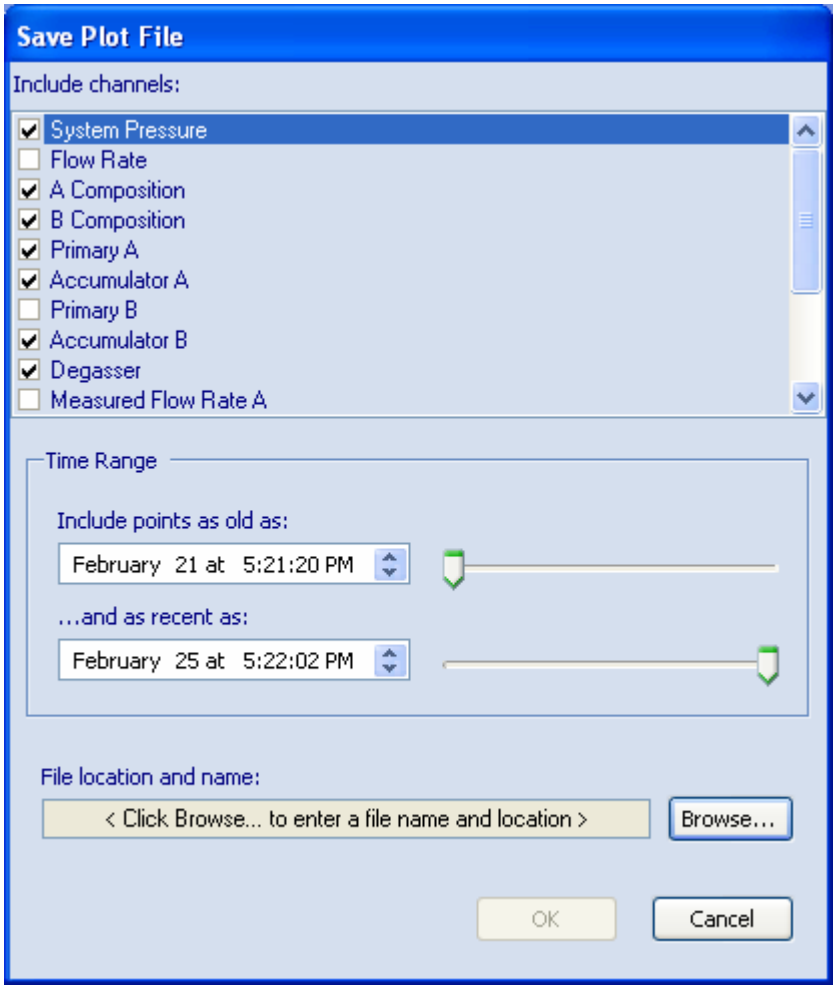

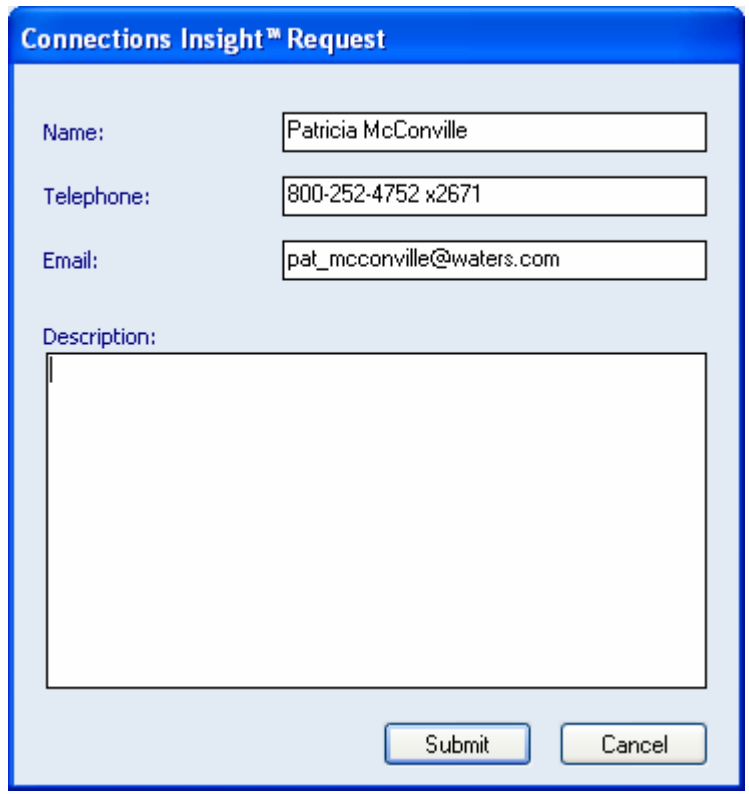

ACQUITY UPLC™ Maintenance Counters: *User defined "warning" levels*

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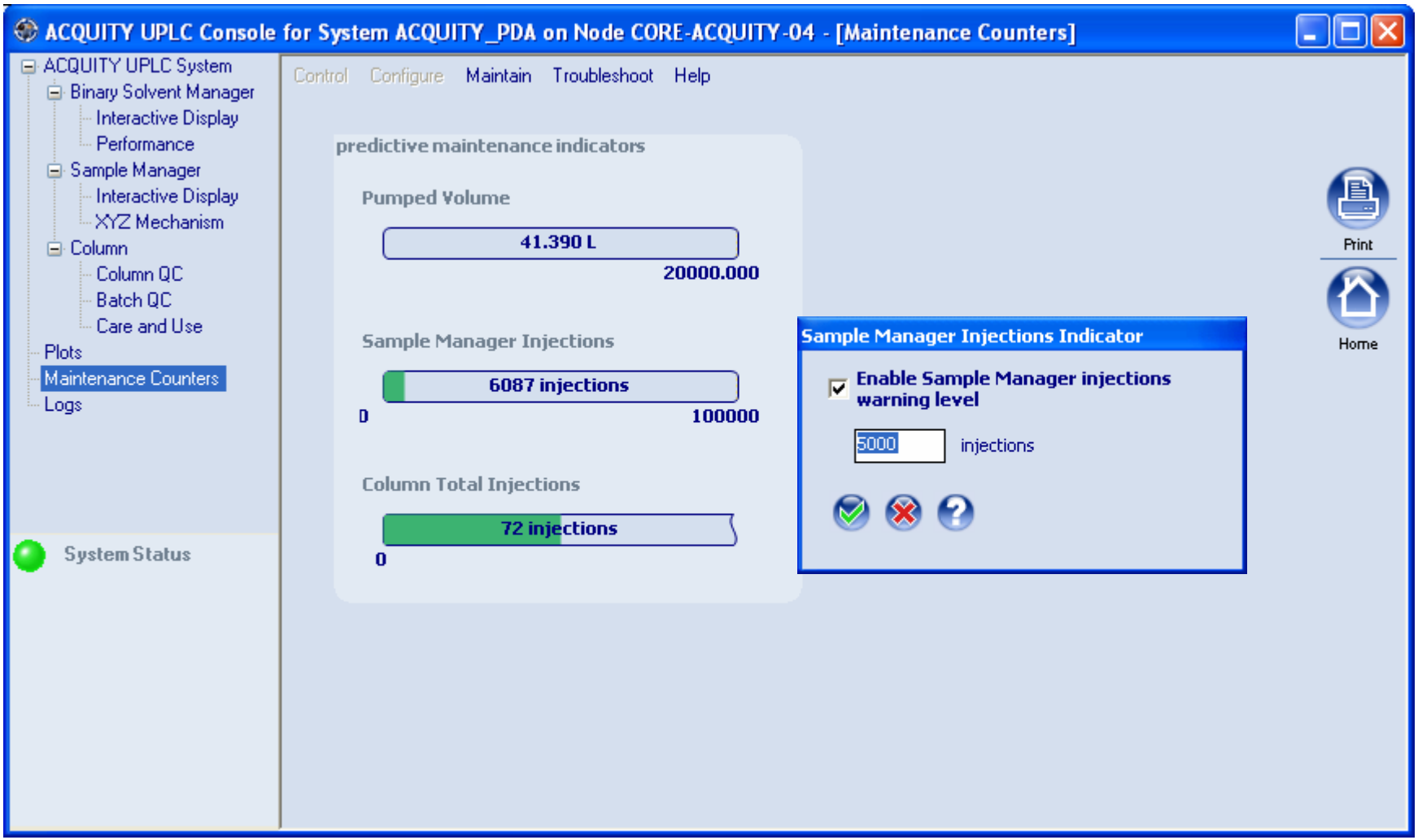

ACQUITY UPLC™ Maintenance Counters: *Notification when "warning" level exceeded*

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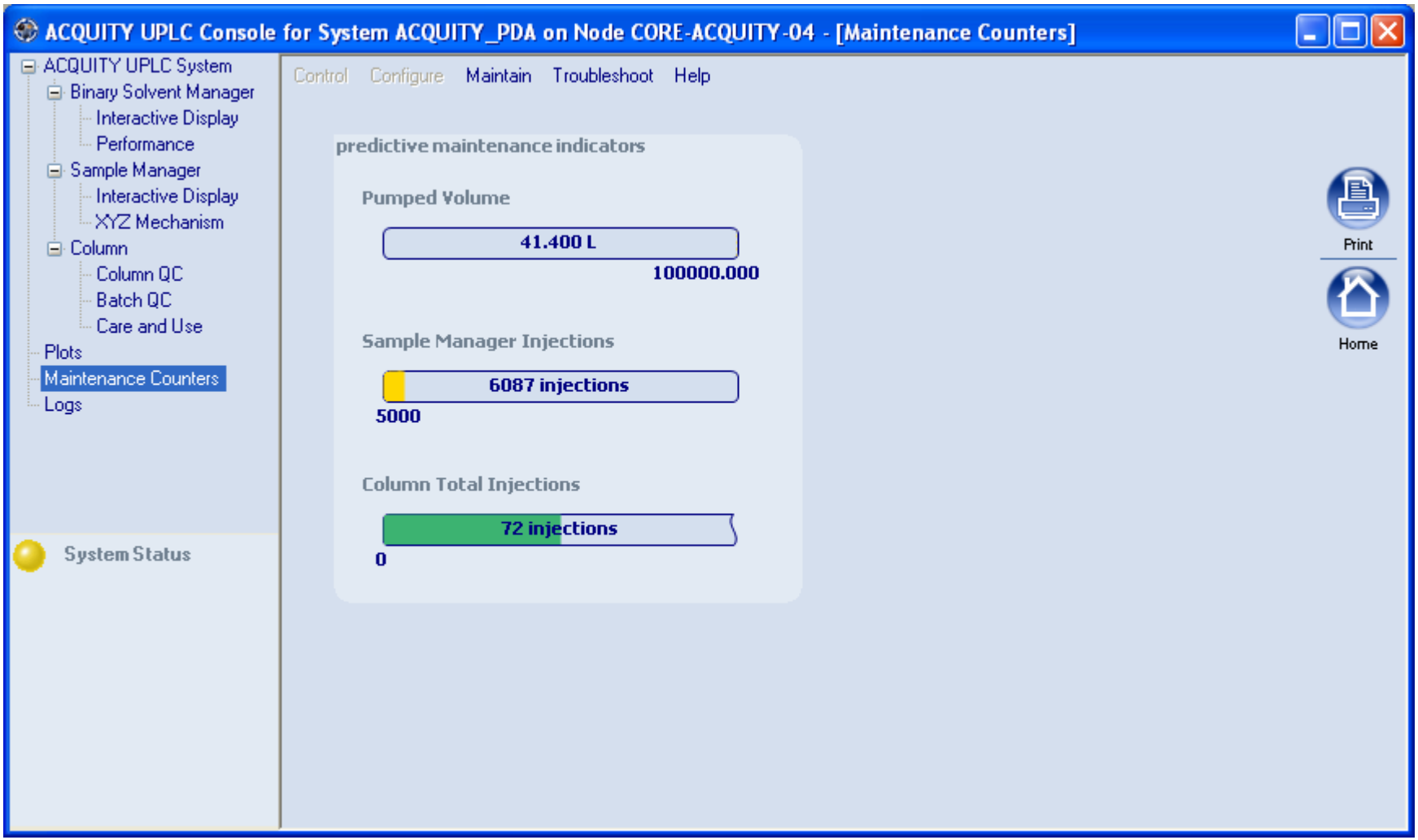

ACQUITY UPLC™
Logs

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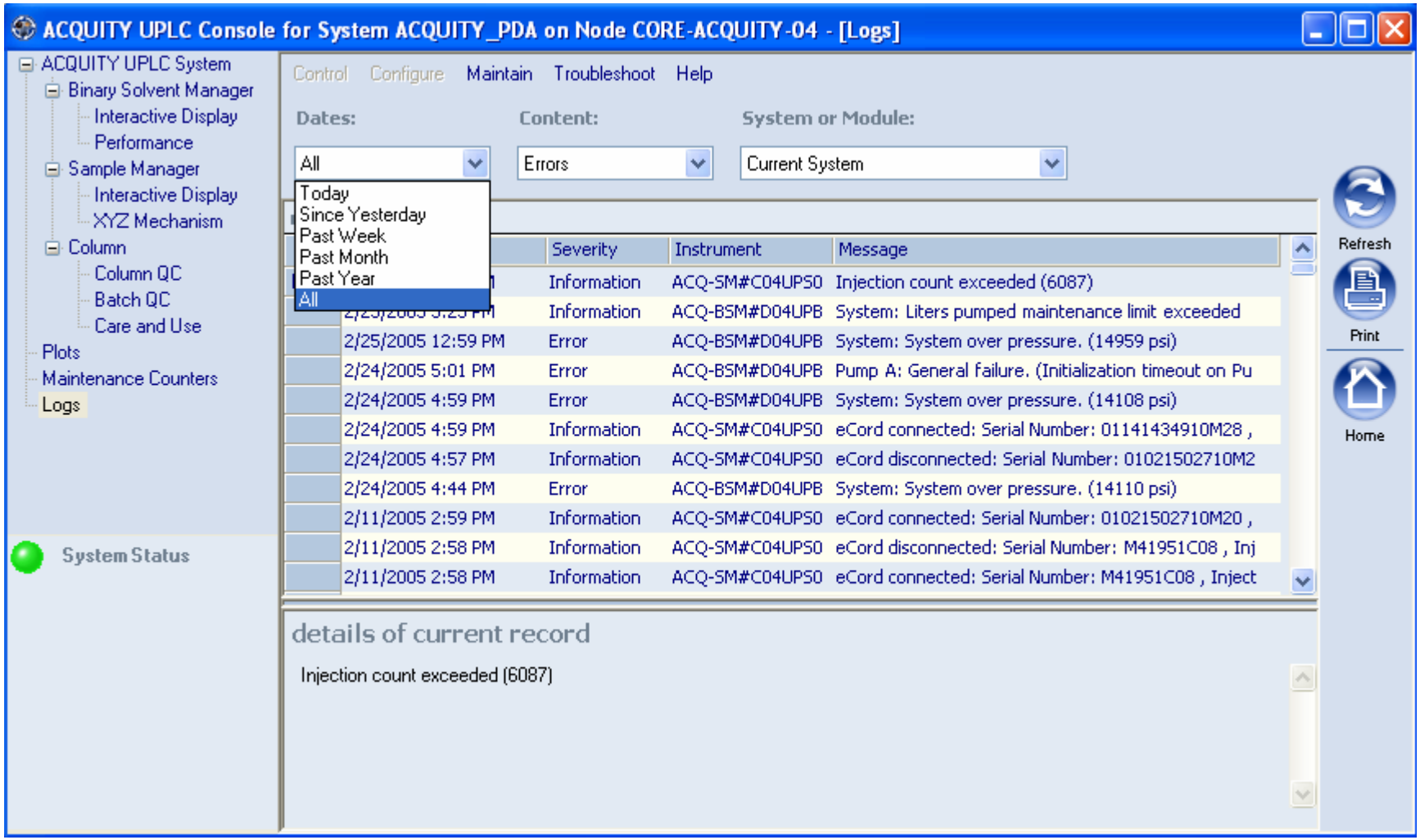

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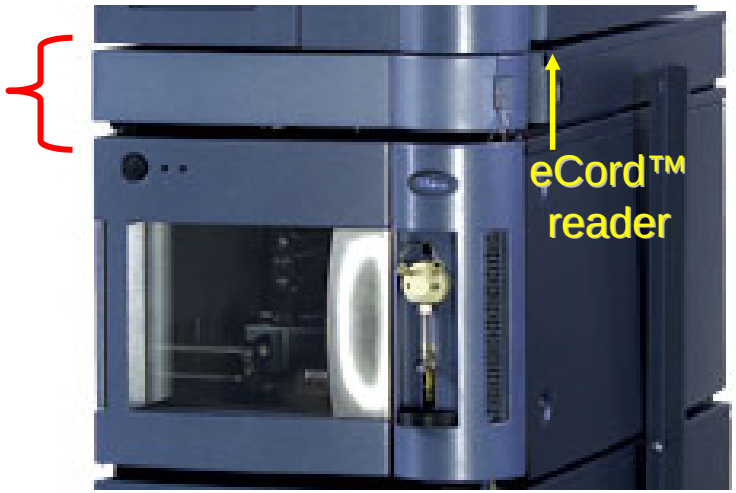
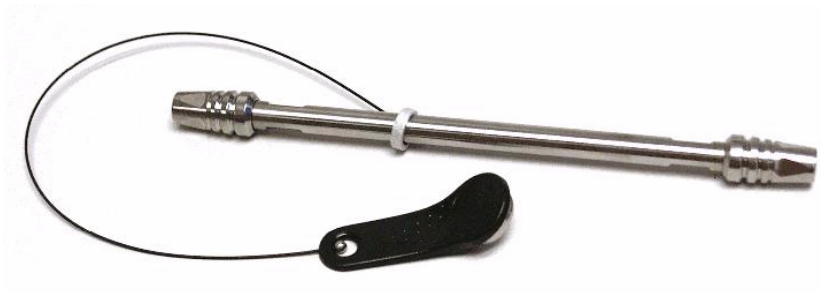
eCord™ Technology

- Column Information
  - Certificate of Analysis
- Column Usage History
  - Total number of samples
  - Injections
  - Pressure/Temperature history
  - And much more…





eCord™

ACQUITY UPLC™ Column:
Complete Column Record View in Console

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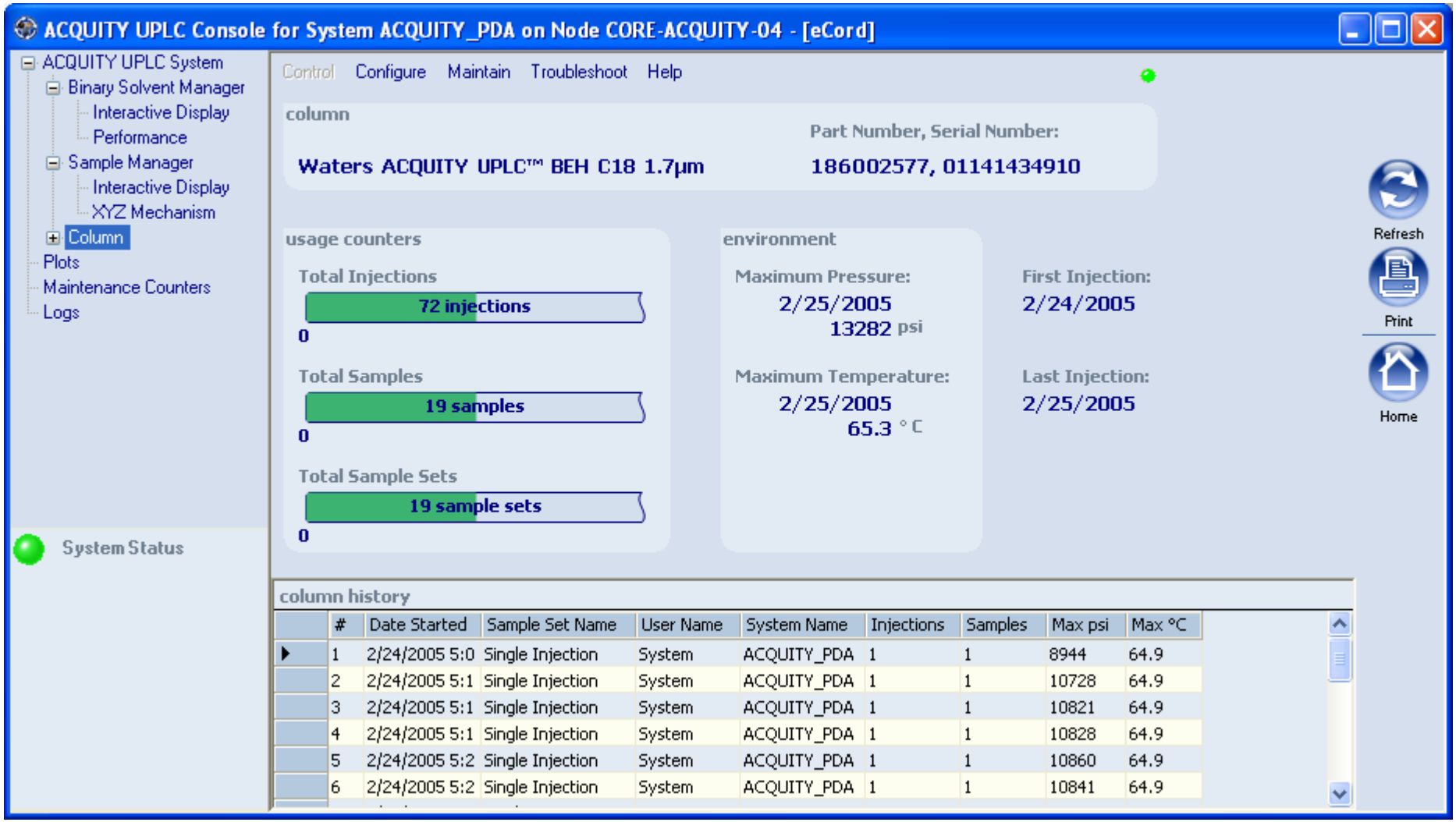

#	Date Started	Sample Set Name	User Name	System Name	Injections	Samples	Max psi	Max °C
1	2/24/2005 5:0	Single Injection	System	ACQUITY_PDA	1	1	8944	64.9
2	2/24/2005 5:1	Single Injection	System	ACQUITY_PDA	1	1	10728	64.9
3	2/24/2005 5:1	Single Injection	System	ACQUITY_PDA	1	1	10821	64.9
4	2/24/2005 5:1	Single Injection	System	ACQUITY_PDA	1	1	10828	64.9
5	2/24/2005 5:2	Single Injection	System	ACQUITY_PDA	1	1	10860	64.9
6	2/24/2005 5:2	Single Injection	System	ACQUITY_PDA	1	1	10841	64.9

ACQUITY UPLC™ eCord™ Column QC

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ACQUITY UPLC Console for System test on Node CORE-ACQUITY-01 - [Column QC]

ACQUITY UPLC System
- Binary Solvent Manager
  - Interactive Display
  - Performance
- Sample Manager
  - Interactive Display
  - XYZ Mechanism
- Column
  - Column QC
  - Batch QC
  - Care and Use
- Plots
- Maintenance Counters
- Logs

System Status

Control Configure Maintain Troubleshoot Help

Waters ACQUITY UPLC™ BEH C18 1.7µm P/N: 186002350 S/N: M41681E01

Print

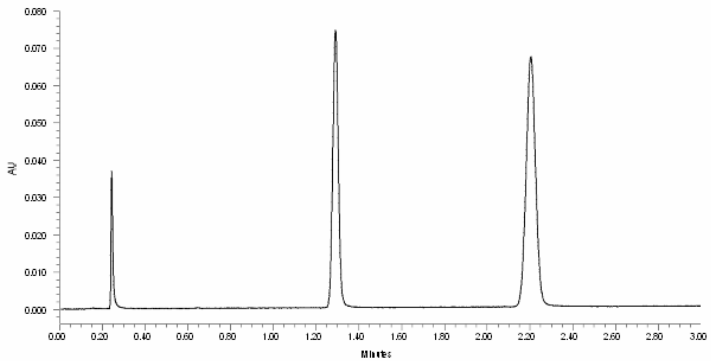
Home

Acquity Ultra Performance LC™

Part Number: 186002350
Column Dimension: 2.1mm x 50mm
Name: Waters ACQUITY UPLC™ BEH C18 1.7µm

Column Serial No: M41681E01 Batch Number: 105

Test Method
Eluent: Acetonitrile-Water 55:45 (v/v)
Sample:
1. Thiourea 0.01mg/mL
2. Naphthalene 0.05mg/mL
3. Acenaphthene 0.2mg/mL
Flow Rate: 0.43 mL/min
Detection: 254 nm
Temperature: Ambient
Injection Volume: 1.2 µl



Test Results For: Acenaphthene Retention Time (min.): 2.20

USP Tangent Efficiency: 11363 Retention Factor: 8.07

USP Tailing: 1.03 Accepted By: SJS

Pressure (psig): 5011 Date: 6/16/2004 7:35:57 AM

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ACQUITY UPLC™ eCord™ Certificate of Analysis

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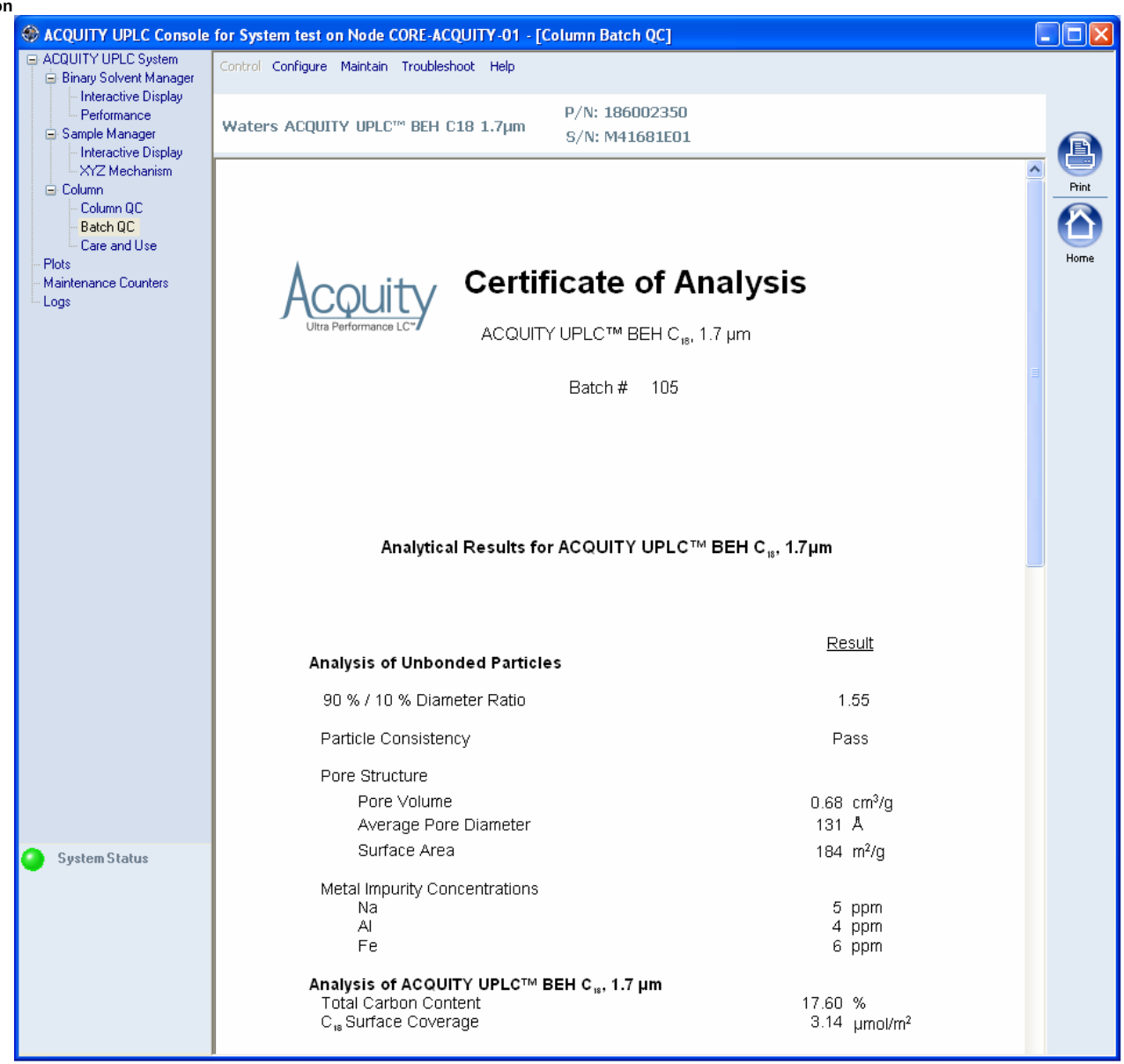

ACQUITY UPLC™ eCord™ Column Care and Use Instructions

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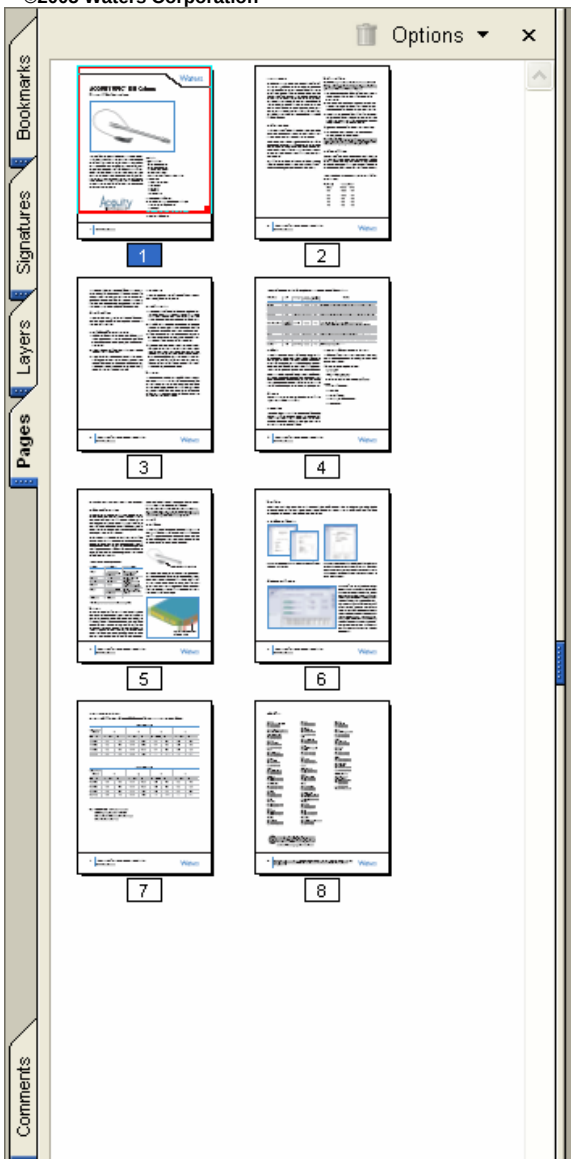
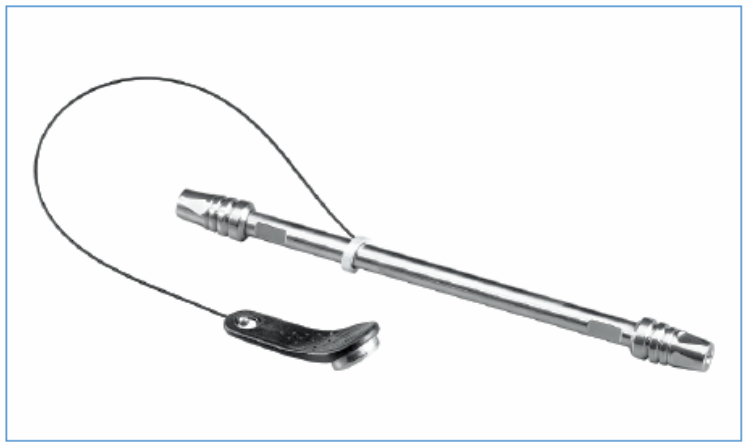


Waters

ACQUITY UPLC™ BEH Column

Care and Use Instructions



Thank you for choosing a Waters ACQUITY UPLC™ BEH column. The ACQUITY UPLC™ BEH packing materials were designed specifically for use with the Waters ACQUITY UPLC™ system and are manufactured in a cGMP, ISO 9002 certified plant using ultra pure reagents. Each batch of ACQUITY UPLC™ BEH material is tested chromatographically with acidic, basic and neutral analytes and the results are held to narrow specification ranges to assure excellent, reproducible performance. Every column is individually tested and a Performance Chromatogram and Certificate of Batch Analysis are provided on the eCord™ intelligent chip.

Contents

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Table 2. Buffer Recommendations for Using ACQUITY UPLC™ BEH Columns from pH 1 to 12

Additive/Buffer	pKa	Buffer range	Volatility (±1 pH unit)	Used for Mass Spec	Comments
TFA	0.3		Volatile	Yes	Ion pair additive, can suppress MS signal, used in the 0.02-0.1% range.
Acetic Acid	4.76		Volatile	Yes	Maximum buffering obtained when used with ammonium acetate salt. Used in 0.1-1.0% range.
Formic Acid	3.75		Volatile	Yes	Maximum buffering obtained when used with ammonium formate salt. Used in 0.1-1.0% range.
Acetate (NH_4CH_3COOH)	4.76	3.76 – 5.76	Volatile	Yes	Used in the 1-10 mM range. Note that sodium or potassium salts are not volatile.
Formate (NH_4COOH)	3.75	2.75 – 4.75	Volatile	Yes	Used in the 1-10 mM range. Note that sodium or potassium salts are not volatile.
Phosphate 1	2.15	1.15 – 3.15	Non-volatile	No	Traditional low pH buffer, good UV transparency.
Phosphate 2	7.2	6.20 – 8.20	Non-volatile	No	Above pH 7, reduce temperature/concentration and use a guard column to maximize lifetime.
4-Methylmorpholine	~8.4	7.4 – 9.4	Volatile	Yes	Generally used at 10 mM or less.
Ammonia (NH_4OH)	9.2	8.2 – 10.2	Volatile	Yes	Keep concentration below 10 mM and temperatures below 30 °C.
Ammonium Bicarbonate	10.3 (HCO_3^-) 9.2 (NH_4^+) 6.3 (H_2CO_3)	6.8 – 11.3	Volatile	Yes	Used in the 5-10 mM range (for MS work keep source >150 °C). Adjust pH with ammonium hydroxide or acetic acid. Good buffering capacity at pH 10. Note: use ammonium bicarbonate (NH_4HCO_3), not ammonium carbonate ($(NH_4)_2CO_3$).
Ammonium (Acetate)	9.2	8.2 – 10.2	Volatile	Yes	Used in the 1-10 mM range.
Ammonium (Formate)	9.2	8.2 – 10.2	Volatile	Yes	Used in the 1-10 mM range.
Borate	9.2	8.2 – 10.2	Non-Volatile	No	Reduce temperature/concentration and use a guard column to maximize lifetime.
CAPSO	9.7	8.7 – 10.7	Non-Volatile	No	Zwitterionic buffer, compatible with acetonitrile, used in the 1-10 mM range. Low odor.
Glycine	2.4, 9.8	8.8 – 10.8	Non-Volatile	No	Zwitterionic buffer, can give longer lifetimes than borate buffer.
1-Methylpiperidine	10.2	9.3 – 11.3	Volatile	Yes	Used in the 1-10 mM range.
CAPS	10.4	9.5 – 11.5	Non-Volatile	No	Zwitterionic buffer, compatible with acetonitrile, used in the 1-10 mM range. Low odor.
Triethylamine (as acetate salt)	10.7	9.7 – 11.7	Volatile	Yes	Used in the 0.1-1.0% range. Volatile only when titrated with acetic acid (not hydrochloric or phosphoric). Used as ion-pair for DNA analysis at pH 7-9.
Pyrrolidine	11.3	10.3 – 12.3	Volatile	Yes	Mild buffer, gives long lifetime.

ACQUITY UPLC™ eCord™ Column Care and Use Instructions

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c. Solvents

To maintain maximum column performance, use high quality chromatography grade solvents. Filter all aqueous buffers prior to use. Pall Gelman Laboratory Acrodisc® filters are recommended. Solvents containing suspended particulate materials will generally clog the outside surface of the inlet distribution frit of the column. This will result in higher operating pressure and poorer performance.

Degas all solvents thoroughly before use to prevent bubble formation in the pump and detector. The use of an on-line degassing unit is also recommended. This is especially important when running low pressure gradients since bubble formation can occur as a result of aqueous and organic solvent mixing during the gradient.

d. Pressure

ACQUITY UPLC™ BEH columns can tolerate pressures of up to 15,000 psi (1034 bar or 103 Mpa).

III. SCALING UP/DOWN ISOCRATIC METHODS

The following formulas will allow scale up or scale down, while maintaining the same linear velocity, and provide new sample loading values:

If column i.d. and/or length are altered:

$$F_2 = F_1 (r_2/r_1)^2$$

$$Load_2 = Load_1 (r_2/r_1)^2(L_2/L_1)$$

$$Injection\ volume_2 = Injection\ volume_1 (r_2/r_1)^2 (L_2/L_1)$$

Where:

r = Radius of the column

F = Flow rate

L = Length of column

1 = Original, or reference column

2 = New column

Next Generation Instrument Design:
Synergistic Design: Hardware and Software

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- Integrated hardware and software
  - Visual system status indicators on hardware
  - Instrument Control Panel
- Instrument Console
  - A customizable *Instrument Console* enables operators to easily stay in control of all system functionality including instrument control, interactive system monitoring, status monitoring, and user diagnostic capabilities.
- eCord™ Technology
  - Accurate permanent record of column history
- Connections® INSIGHT™ remote monitoring capabilities

Today's Service Delivery Model

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- Customer calls Waters asking for support
- Customer describes system problem

- Support Engineer asks a series of questions
  Name, Location, Serial #, Verify entitlement
- Engineer tries to work through the problem

- Support Engineer believes all the information he needs is correct and dispatches Field Engineer to Customer site.

- Field Engineer is now onsite, but finds a completely different problem, consequently, parts and tools he brought will not work for this repair

Process Results In:

- Increased Repair time
  - Challenges in getting info
  - Difficulties in diagnosing problem
- Increased instrument downtime & lower productivity
- Lower Customer Satisfaction

Today's Laboratory Challenges

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- Minimize instrument downtime
- Reduce time to assess & diagnose problems

- Increase laboratory productivity
- Lower support costs

Meeting today's challenges demands proactive and timely service

Connections® INSIGHT™ …a Proven Technology

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- Connections® INSIGHT™ uses proven Intelligent Device Management (IDM™) technology that has been successfully implemented in highly regulated, maximum security medical devices and medical records environments
- Connections® INSIGHT™ leverages the Internet to proactively and securely connect the ACQUITY ULPC™ system to Waters' service experts
- Connections® INSIGHT™ creates the "virtual presence" of a service Engineer in the customer lab that monitors the ACQUITY UPLC™ system to ensure its maximum uptime and system performance

What Does Intelligent Device Management™ Do ?

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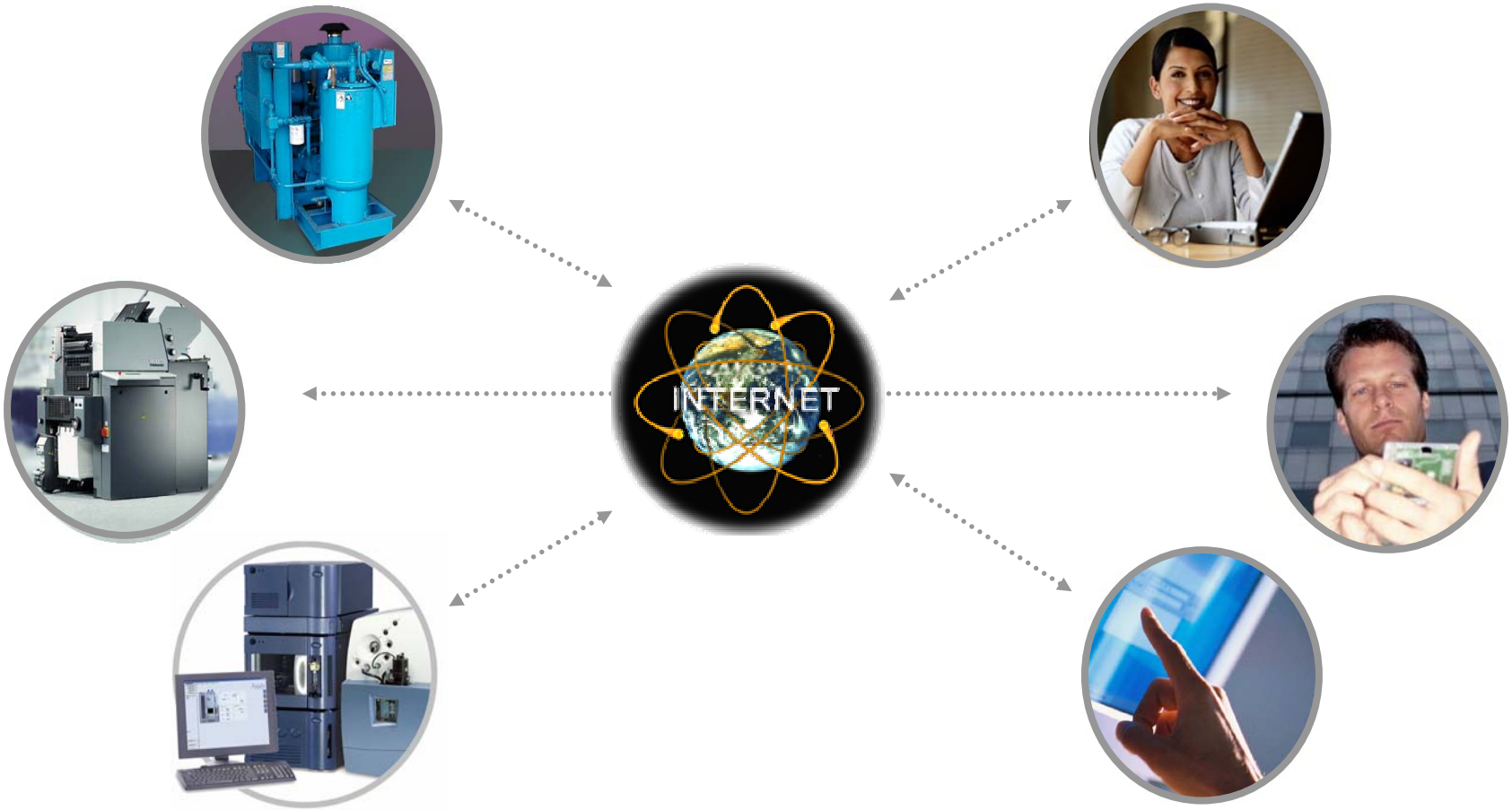

Connections® INSIGHT™ Solution Architecture

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One-way Communication

Key System Performance Parameters Tracked

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Temperature has exceeded threshold

Operating Performance (Status)

System Pressure & over Pressure Conditions

Lost remote communication

Troubleshooting

Injections Per column

Liters Pumped

Lamp Hours

System Injections

# of Cycles & PM Cycles

Diagnostics

Column

Lamp

Replenishment (parts/consumables)

“Connections® INSIGHT™Request” Feature

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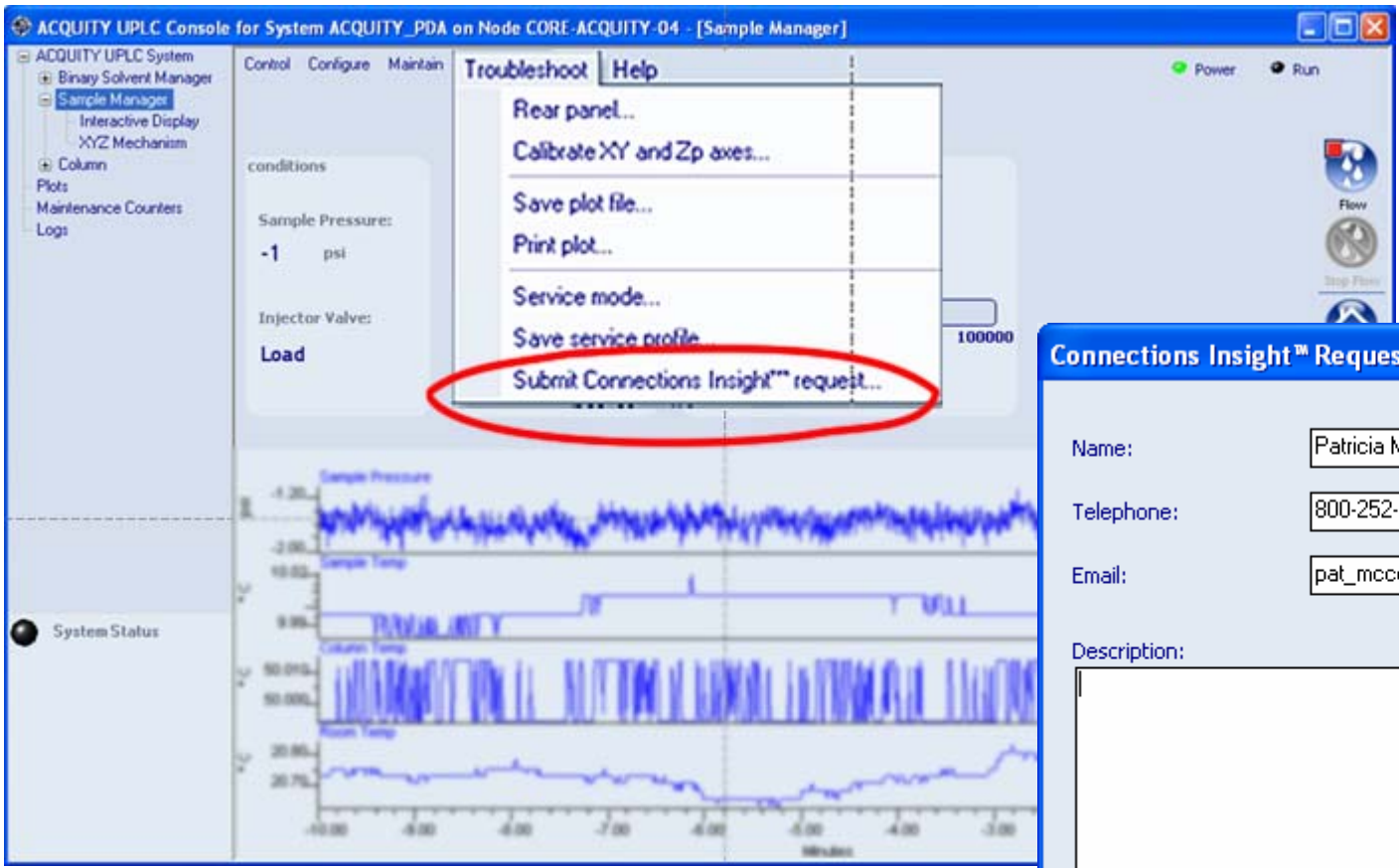

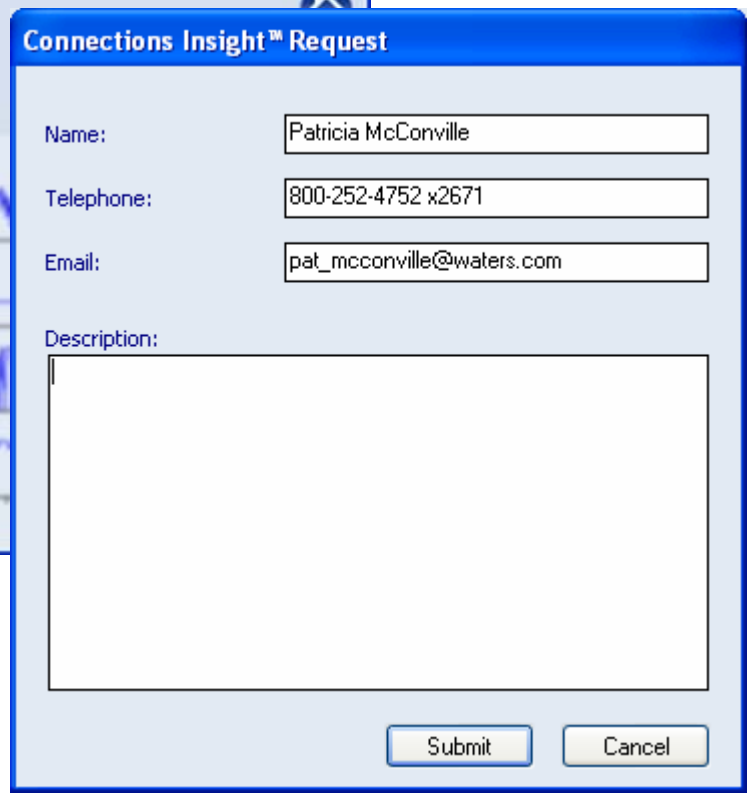

Log File Example

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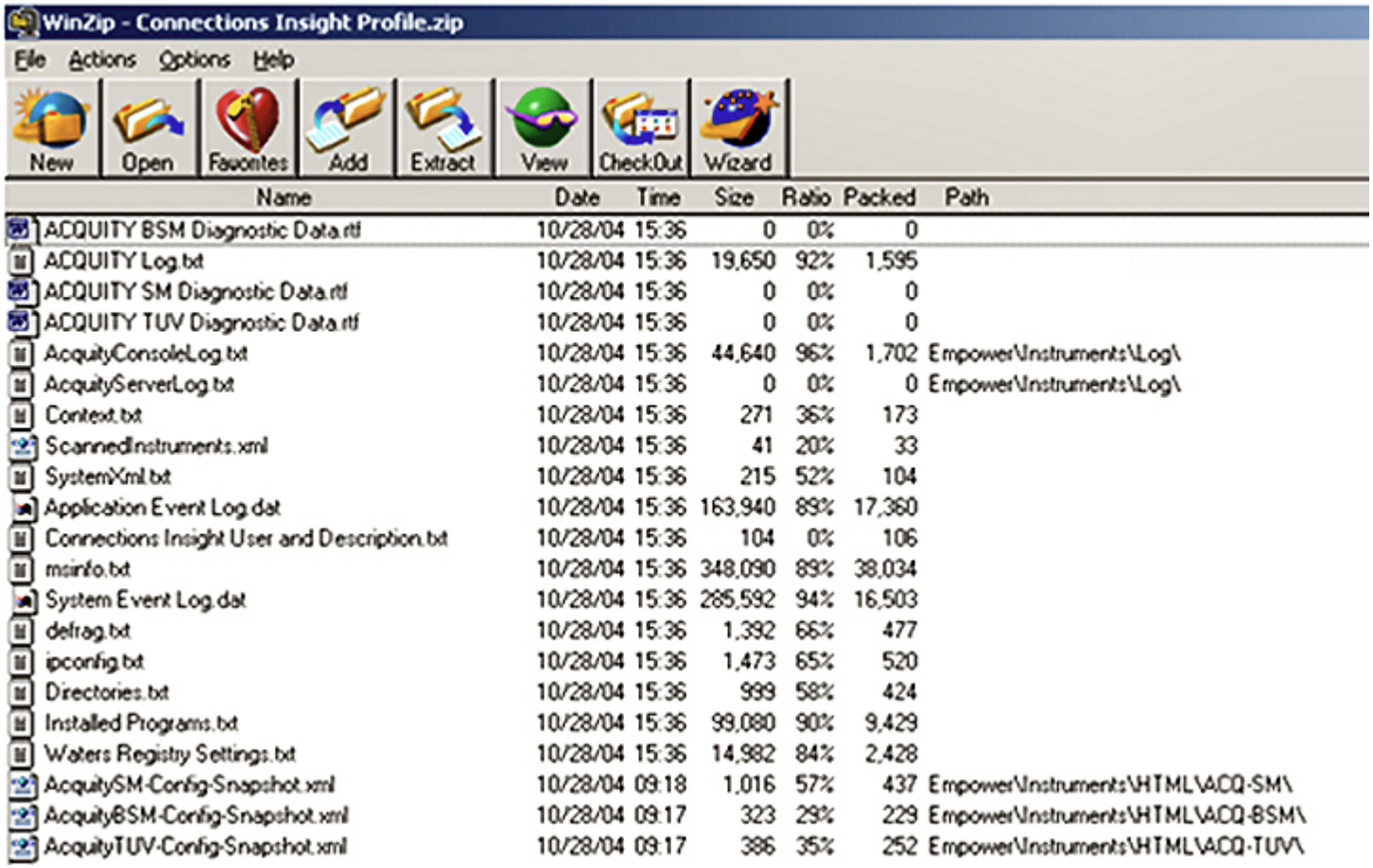
This is a portion of the contents of the “zipped” log file that is received and analyzed in Milford



Name	Date	Time	Size	Ratio	Packed	Path
ACQUITY BSM Diagnostic Data.rtf	10/28/04	15:36	0	0%	0	
ACQUITY Log.txt	10/28/04	15:36	19,650	92%	1,595	
ACQUITY SM Diagnostic Data.rtf	10/28/04	15:36	0	0%	0	
ACQUITY TUV Diagnostic Data.rtf	10/28/04	15:36	0	0%	0	
AcquityConsoleLog.txt	10/28/04	15:36	44,640	96%	1,702	Empower\Instruments\Log\
AcquityServerLog.txt	10/28/04	15:36	0	0%	0	Empower\Instruments\Log\
Context.txt	10/28/04	15:36	271	36%	173	
ScannedInstruments.xml	10/28/04	15:36	41	20%	33	
SystemXml.txt	10/28/04	15:36	215	52%	104	
Application Event Log.dat	10/28/04	15:36	163,940	89%	17,360	
Connections Insight User and Description.txt	10/28/04	15:36	104	0%	106	
msinfo.txt	10/28/04	15:36	348,090	89%	38,034	
System Event Log.dat	10/28/04	15:36	285,592	94%	16,503	
defrag.txt	10/28/04	15:36	1,392	66%	477	
ipconfig.txt	10/28/04	15:36	1,473	65%	520	
Directories.txt	10/28/04	15:36	999	58%	424	
Installed Programs.txt	10/28/04	15:36	99,080	90%	9,429	
Waters Registry Settings.txt	10/28/04	15:36	14,982	84%	2,428	
AcquitySM-Config-Snapshot.xml	10/28/04	09:18	1,016	57%	437	Empower\Instruments\HTML\ACQ-SM\
AcquityBSM-Config-Snapshot.xml	10/28/04	09:17	323	29%	229	Empower\Instruments\HTML\ACQ-BSM\
AcquityTUV-Config-Snapshot.xml	10/28/04	09:17	386	35%	252	Empower\Instruments\HTML\ACQ-TUV\

Connections® INSIGHT™ Alarm Email Example

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Example of an alarm email initiated by customer

This message would be sent to the Engineer monitoring the system

---

To: john_d_walsh@waters.com
cc:
From: john_d_walsh@waters.com
Date: 10/29/2004 04:26:03 PM AST
Subject: Acquity Request #1395 for asset JohnWalsh_AS01_Z04UPS9999M

Dear walshj,

The following alarm has been generated by asset JohnWalsh_AS01_Z04UPS9999M:

Alarm Name = Fault generated by Asset
Alarm Description = C:\ConnectionsInsight/Connections Insight Profile.zip
Alarm Detail = Uploaded new file: C:\ConnectionsInsight/Connections Insight Profile.zip
Generated At = 2004-10-29T16:26:23 EDT

Alert Name = AcquityAssistance
Asset Name = JohnWalsh_AS01_Z04UPS9999M
Error Code = NEW_FILE
Abstract = FILE_UPLOAD
Alarm Event ID = 1425
Alarm ID = 1
Alarm Extension =
Force Reason =

This message can be customized by adding a content prefix to the associated alert.

==========

Connections® INSIGHT™ has a Robust Security System

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Security at system, network and enterprise server levels…

- Uses SSL (Secure Sockets Layer), a multi-level authentication standard that is the same technology used for credit card transactions
- Only diagnostic parameters are transmitted – Waters has no visibility to customers' data (one-way communication)
- Utilizes customers' existing security infrastructure – no special network requirements needed (VPNs, modem pools)
- Initiates all communications from behind customers' firewall (system contacts us)
- Supports multiple network protocols

Implementation Benefits

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Why Would You Want to Implement This?

- Maximizes system uptime and productivity by proactively scheduling maintenance
- Gain confidence in the accuracy and quality of your results
- Predict potential problems by monitoring component and consumable usage
  - Avoid problems
  - Decrease time to repair
- Lower operating expenses through increased instrument utilization

Why Waters Want to Have This Implemented?

- Deliver proactive service to customers
  - Detect or predict problems before they occur or escalate
- Increase instrument uptime
  - Shorten the service response time
- Shorten MTTR (Mean Time to Repair)
  - Arrive on-site with the correct parts the first time
- Highest customer satisfaction

How Is It Available?

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- Connections® INSIGHT™ is available for the Waters' ACQUITY UPLC™ System
- Available at **no additional** charge to customers who are under an ACQUITY UPLC™ warranty during the first year of service
- Value-added feature of ACQUITY UPLC™ Total Assurance Plans and Warranties
- Customer Requirements:
  - ACQUITY UPLC™ must have Empower or Masslynx software installed
  - Customer's PC will need access to the Internet

More Information?

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- Contact –Tina Ferreira, 508.482.3558
  - Questions/issues about Connections® INSIGHT™
  - Coordinate with the appropriate experts to get solutions
  - Arrange customer visits
  - Schedule webcasts

Summary

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- ACQUITY UPLC™ System is synergistically designed…chemistry, hardware and software developed hand-in-hand to deliver outstanding performance, up-time and ease of use.
- Connections® INSIGHT™ provides remote monitoring and proactive troubleshooting capabilities for fast service and support allowing both Waters Service and our Customers to be always alert to any system issues
- ACQUITY UPLC™ :
  - Taking Liquid Chromatography to a whole new level

Waters

©2005 Waters Corporation

Acquity™
Ultra Performance LC

connections® Insight™

Thank you for your time.

Acknowledgements

©2005 Waters Corporation

- Tina Ferreira: Product Manager for Connections Insight
- Elizabeth Robertson: Product Manager for ACQUITY UPLC™
- John Morawski: Project Manager for ACQUITY UPLC™
- Tanya Jenkins: Sr. Applications Chemist
- Eric Grumbach: Sr. Applications Chemist