ThermoFisher SCIENTIFIC

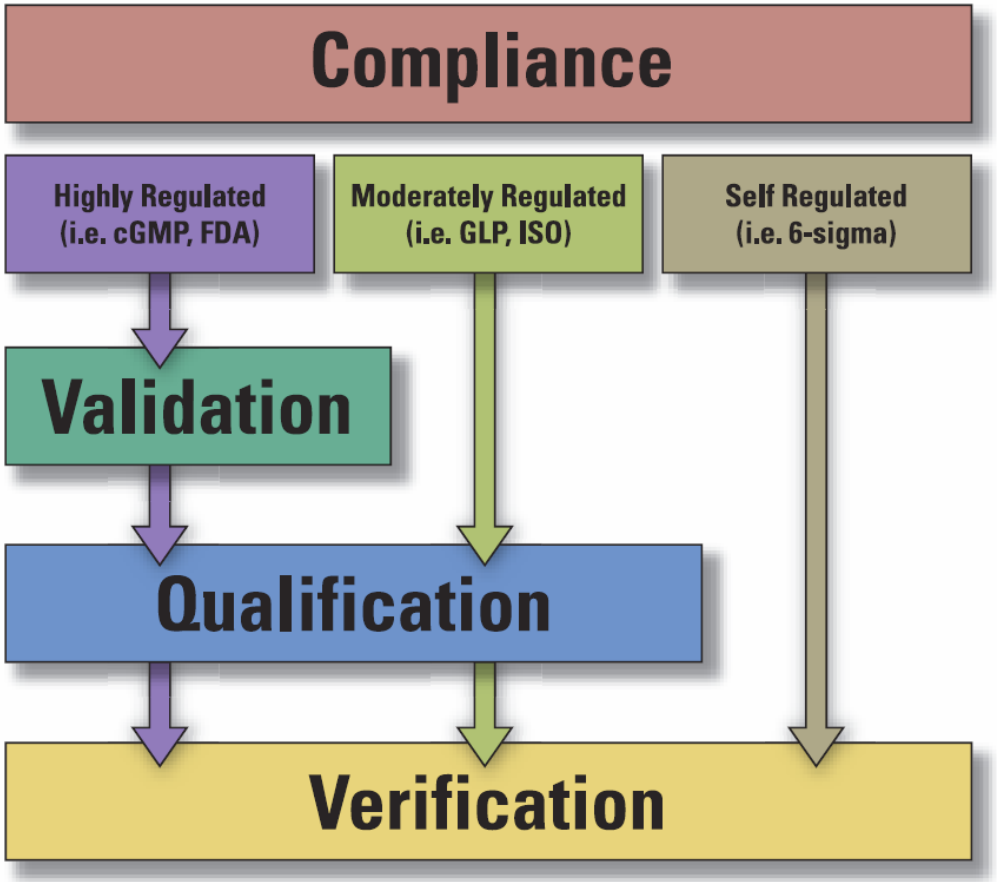
The world leader in serving science

Ensuring Data Quality in Today's Laboratory

Thermo Fisher Scientific's approach to Data Quality

The Compliance Hierarchy

- Verification
  - Demonstrates that the instrument is working properly
- Qualification
  - Provides a high degree of confidence that the instrument has been installed correctly, and is capable of producing the quality of data required
  - Provide documentation for external agencies
- Validation
  - Proves and fully documents that the instrument itself, it's design, installation, and maintenance are 'fit for purpose'
  - Includes details of SOP's, operator training, etc.



AAS Hardware Verification – the iSQ Module

- **Intelligent** – Automatically identifies which instrument it is connected to and which tests are appropriate eg. Polarizer tests on Zeeman instruments. Software automatically runs tests and clearly displays Pass/Fail

- **Spectrometer** – Tests the hardware of the spectrometer it is connected to and helps to diagnose the source of any hardware problems at an early stage

- **Qualification** – Verifies that the instrument is operating entirely within the specifications that it was designed to operate within. Confirming that your analyses will be run on an instrument that is capable of producing sound analytical data.

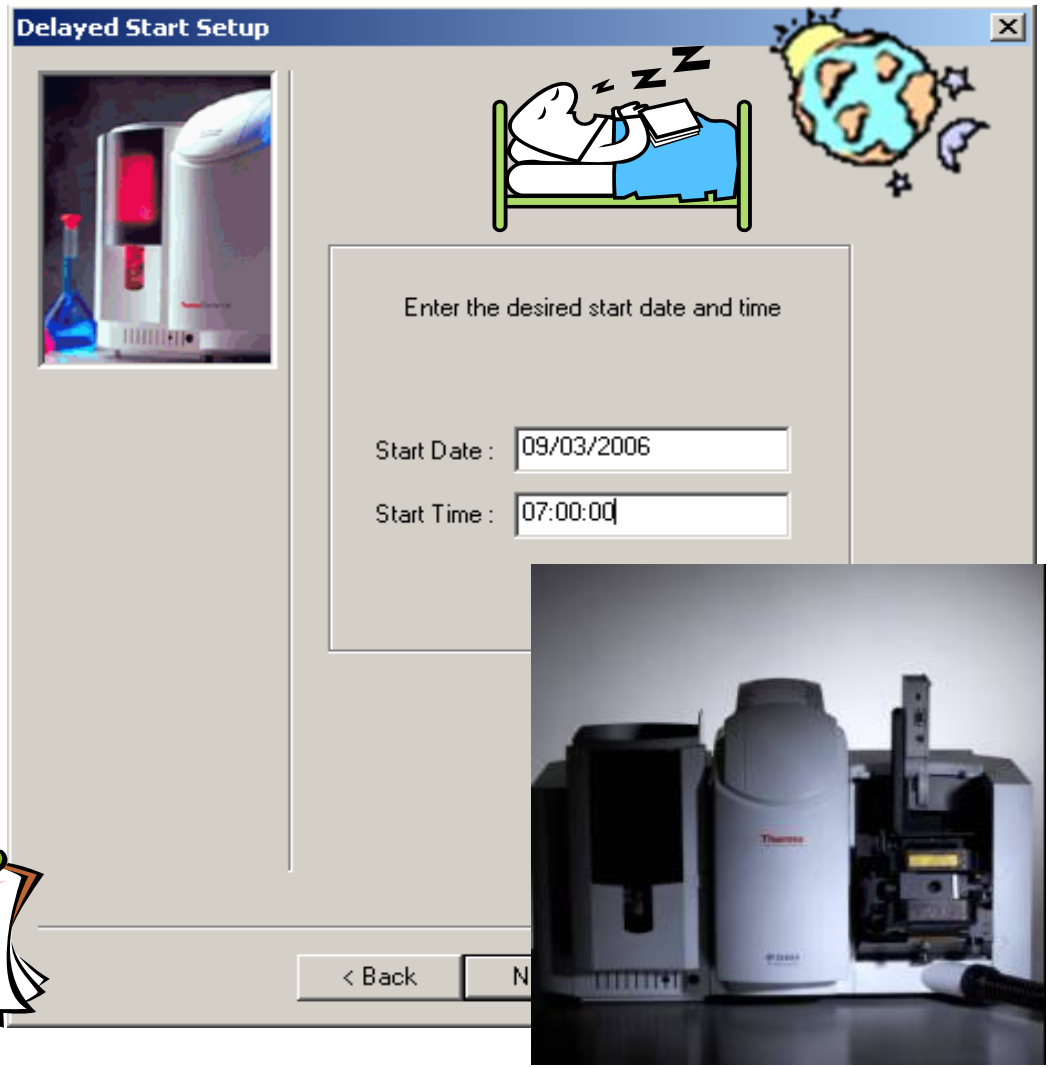
What does iSQ Test ?

Test	Result of a failure
Wavelength Accuracy	Poor sensitivity
Monochromator Resolution	Low sensitivity, increased curvature
Photometric accuracy	Major result errors possible
Photometric Stability	Instrument exhibits Drift
D_2 Background Correction	Inaccurate D_2 BGC
Lamp Peaking	Degraded DL's inaccurate D_2 correction
Beam Selector Movement	Baseline shifts - errors on low conc samples
Polarizer Orientation	Zeeman BGC doesn't work
Polarizer Repeatability	Baseline shifts and inaccurate Zeeman Correction

S*i* and M*i* can wake up before you do!

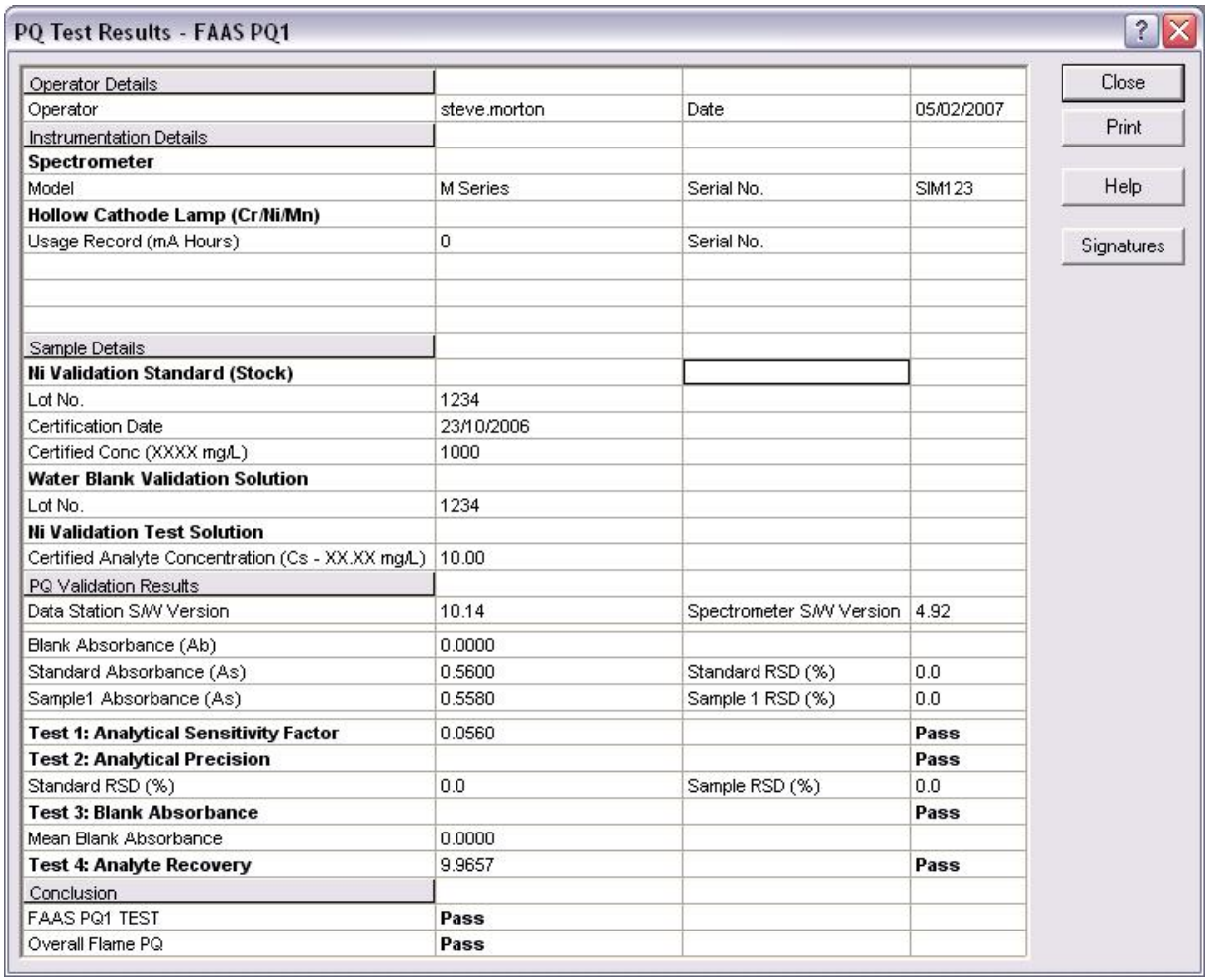
- ‘Wake Up’ function
- Optimizes productivity
- Have the instrument wake up before you do
- It can start the tests before you arrive in the lab
- Arrive to find an on screen report confirming

Good to Go!



AAS Analysis Verification – the PQ Wizard

- Wizard-driven from SOLAAR software
- Proves analytical performance
- Analytical sensitivity / precision
- Blank absorbance
- Analyte recovery
  - Ni (Air/C_2H_2 flame)
  - Cr (N_2O/C_2H_2 flame)
  - Mn (GFAAS, Quadline)
  - Mn (GFAAS, Zeeman)



PQ Test Results - FAAS PQ1

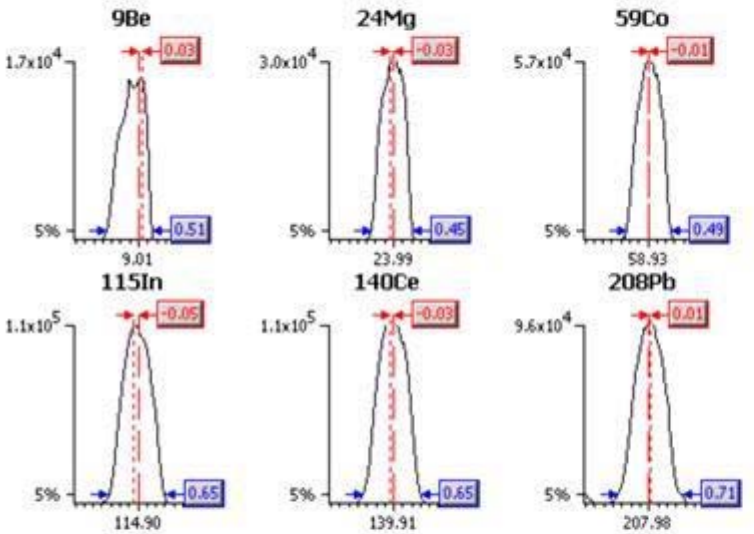
Operator Details			
Operator	steve.morton	Date	05/02/2007
Instrumentation Details			
Spectrometer			
Model	M Series	Serial No.	SIM123
Hollow Cathode Lamp (Cr/Ni/Mn)			
Usage Record (mA Hours)	0	Serial No.	
Sample Details			
Ni Validation Standard (Stock)			
Lot No.	1234		
Certification Date	23/10/2006		
Certified Conc (XXXX mg/L)	1000		
Water Blank Validation Solution			
Lot No.	1234		
Ni Validation Test Solution			
Certified Analyte Concentration (Cs - XX.XX mg/L)	10.00		
PQ Validation Results			
Data Station S/W Version	10.14	Spectrometer S/W Version	4.92
Blank Absorbance (Ab)	0.0000		
Standard Absorbance (As)	0.5600	Standard RSD (%)	0.0
Sample1 Absorbance (As)	0.5580	Sample 1 RSD (%)	0.0
Test 1: Analytical Sensitivity Factor	0.0560		**Pass**
Test 2: Analytical Precision			**Pass**
Standard RSD (%)	0.0	Sample RSD (%)	0.0
Test 3: Blank Absorbance			**Pass**
Mean Blank Absorbance	0.0000		
Test 4: Analyte Recovery	9.9657		**Pass**
Conclusion			
FAAS PQ1 TEST	**Pass**		
Overall Flame PQ	**Pass**		

Close
Print
Help
Signatures

ICP-MS Daily Performance Qualification

Performance Report

Mass Calibration verification



Analyte	Limits			Results	
	Max. width	Min. width	Max. error	Peak width	Peak error
9Be	0.75	0.40	0.10	0.51	0.03
24Mg	0.75	0.40	0.10	0.45	-0.03
59Co	0.75	0.40	0.10	0.49	-0.01
115In	0.75	0.40	0.10	0.65	-0.05
140Ce	0.75	0.40	0.10	0.65	-0.03
208Pb	0.75	0.40	0.10	0.71	0.01

Result : The performance report passed

Sample details
Acquired at : 12/12/2002 14:08:12
Report name : EPA ILM05.2 / 6020A 2.1 [12/12/2002 13:56:01]

Sensitivity and stability results
Acquisition parameters
Sweeps : 180

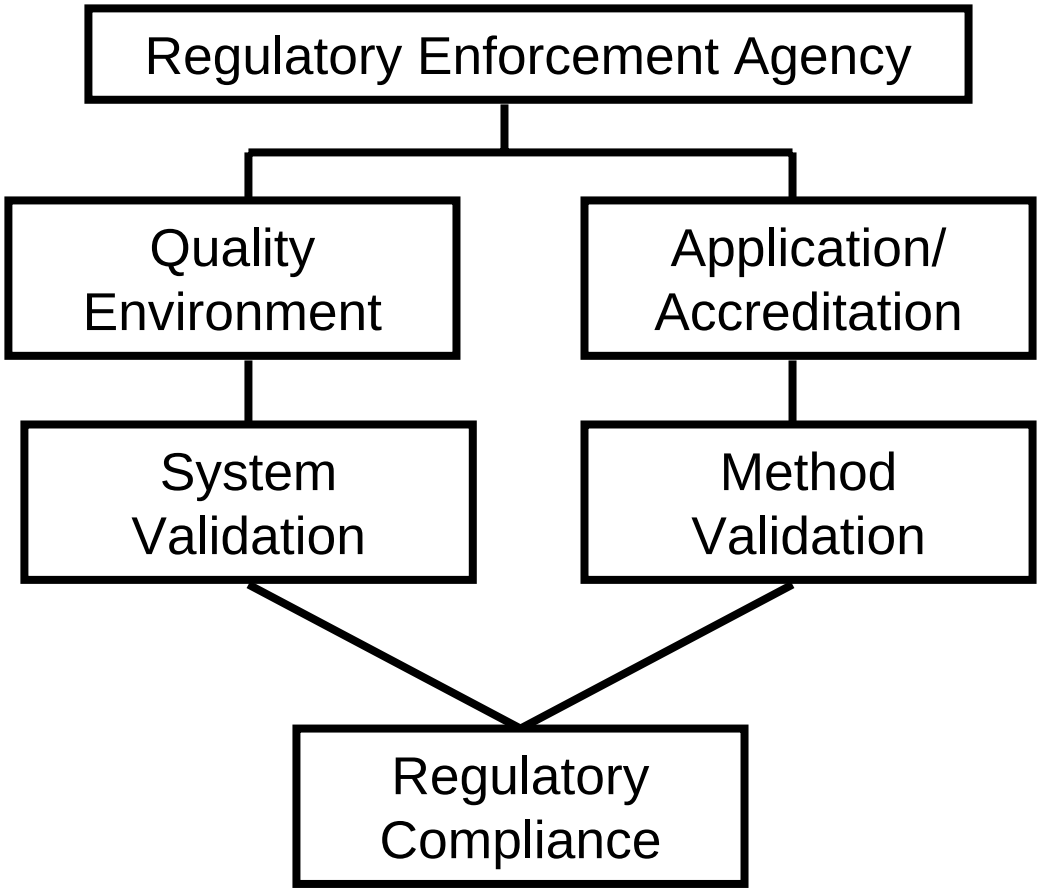
Run	Time	5Bkg	9Be	24Mg	59Co	115In	140Ce	156Ce O	208Pb	220Bkg
Dwell (mSecs)		100.0	10.0	10.0	10.0	10.0	10.0	30.0	10.0	100.0
Limits	%RSD	-	2.0%	2.0%	2.0%	2.0%	2.0%	-	2.0%	-
	Countrate	<2	>5000	>5000	>10000	>50000	>10000	-	>25000	<2
1	14:08:24	0.000	16797	33832	61243	112879	116767	1962	100691	0.222
2	14:09:23	0.000	16640	33338	61235	113079	116573	1935	100713	0.111
3	14:10:23	0.000	16894	33514	61133	113174	117136	1964	100805	0.444
4	14:11:23	0.167	17027	33294	61436	112328	117146	1948	100657	0.000
5	14:12:23	0.056	16536	33001	61020	112235	116563	1998	100517	0.056
x		0.044	16779	33396	61214	112739	116837	1961	100677	0.167
σ		0.07	195	305	153	432	289	23	104	0.18
%RSD		162.980	1.168	0.916	0.252	0.383	0.248	1.209	0.104	105.409

Ratio results

Run	Time	156Ce O/140Ce
Ratio limits		<0.0200
1	14:08:24	0.017
2	14:09:23	0.017
3	14:10:23	0.017
4	14:11:23	0.017
5	14:12:23	0.017
x		0.0168
σ		0.00
%RSD		1.2931

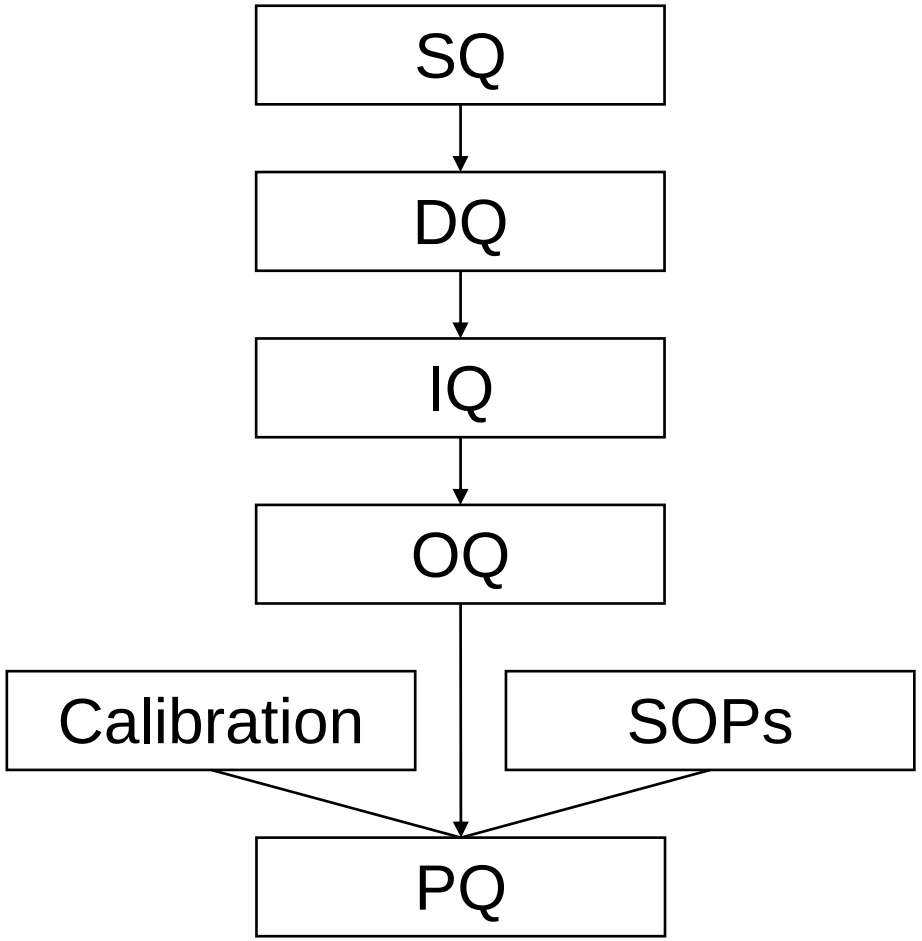
Result : The performance report passed

Validation - The Regulatory Environment



Generic System Validation

- **Specification Qualification (SQ)**
- **Design Qualification (DQ)**
- **Installation Qualification (IQ)**
- **Operational Qualification (OQ)**
  - **System Calibration**
  - **Standard Operating Procedures**
- **Performance Qualification (PQ)**

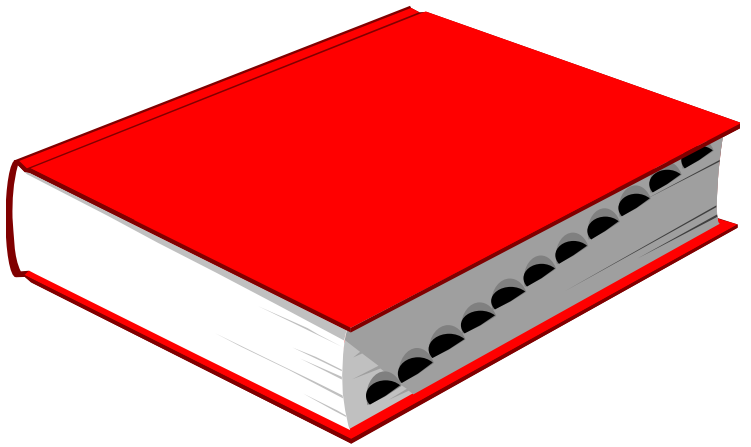


Example: AA Series Validator Accessories

- Contains documentation, SOP's, accessories and consumables to **assist** users in **Validating** and/or **Qualifying** their Thermo Scientific AA Series Atomic Absorption spectrometer.
- Variants for:
  - Flame only systems
  - Graphite Furnace only systems
  - All systems
- Validator$_{plus}$ accessory provides automated OQ functions if required

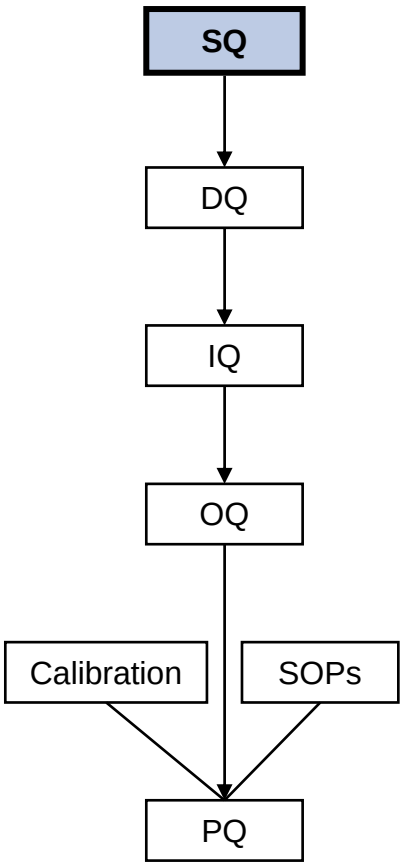
Validator Log Book

- Provides comprehensive documentation, procedures and templates for the entire process
- Chapter Headings
  - Validation Overview
  - Supplier Assessment Questionaire
    - ISO 9001:2000
  - Validation procedures
  - Test criteria
  - SOPs
  - Method Validation Manual
    - Text book on Method Development and Validation Protocols in AAS



Specification Qualification

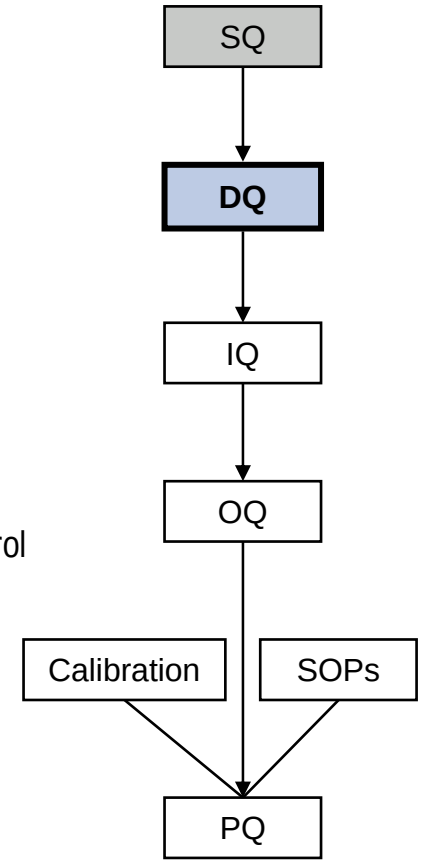
- User Requirements Specification
  - Defines the requirements of the user
  - Produced by the user, often following internal or industry guidelines
- System Specification
  - Defines the features, functions and performance of the system
- Gap Analysis
  - User(s) and Vendors compare these documents
  - Identify gaps (if any)
  - Amend User Requirements Specification and/or System Specification as required
- Final agreement is documented and signed off.



Design Qualification

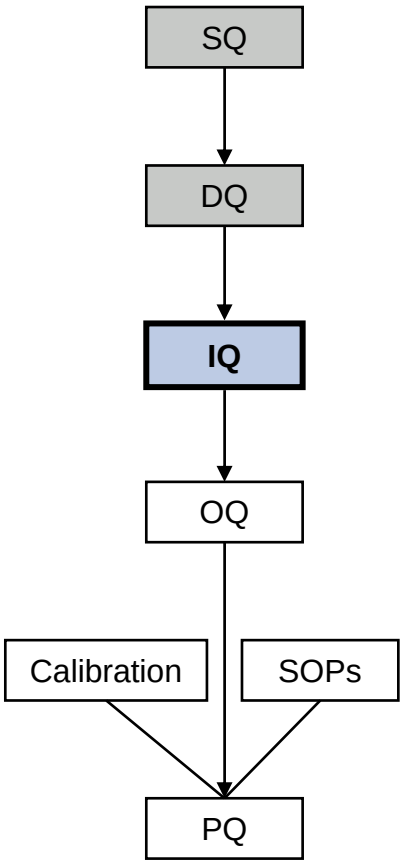
- The process of demonstrating that the system has been designed in such a way that all instruments meet their System Specification
- This is the **Manufacturers** responsibility
- The manufacturer frequently operates under a comprehensive, internationally recognised and externally assessed Quality System
- The manufacturers Quality System must include
  - Formal processes for specifying, designing and developing and manufacturing products to a specified degree of quality
  - Formal testing of each instrument to ensure that it meets the specification in the factory
- The Thermo Scientific Cambridge Site Quality System is certified to ISO 9001:2000, which includes these processes

- Supplier Questionnaire format
  - Vendor Organisation
    - Company
    - Development Team
  - Familiarity with CGMPs
  - Development Practices
    - Software Development
    - Code Development
    - Testing Procedures and Results
    - Security
    - Change Control
  - Customer Support
    - Ongoing evaluation and Change Control
    - Disaster Contingency Plan
  - Document Availability



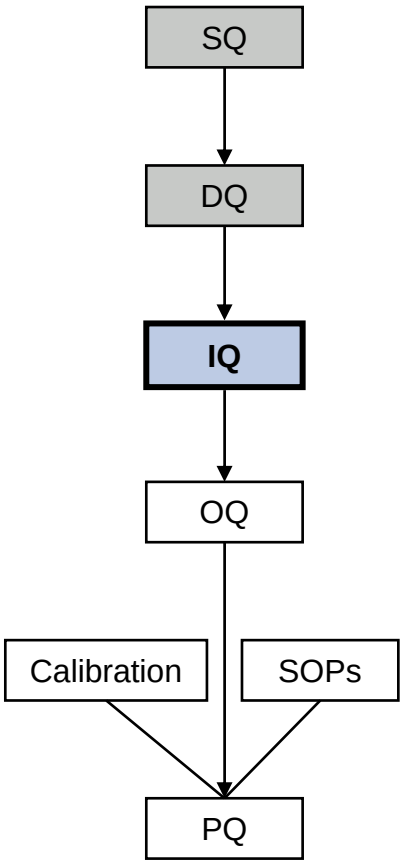
Installation Qualification

- Provides proof of correct system installation to a basic operating level
- Installation can **only** be carried out by a properly trained and certified Thermo Scientific Service Engineer
- Consists of
  - Pre-installation qualification of laboratory services and facilities
  - Deliverables qualification
    - Match the order, permit safe installation and operation
  - Safety instructions
  - Spectrometer installation
  - System and Services interconnections
- Test Record Sheet completed and signed off



Software Installation Qualification

- Provides proof that the system software is the correct version, and has been correctly installed
- Consists of
  - Software deliverables qualification
  - Software installation on data station PC
  - Software functionality
  - System communication
- Test Record Sheet completed and signed off.

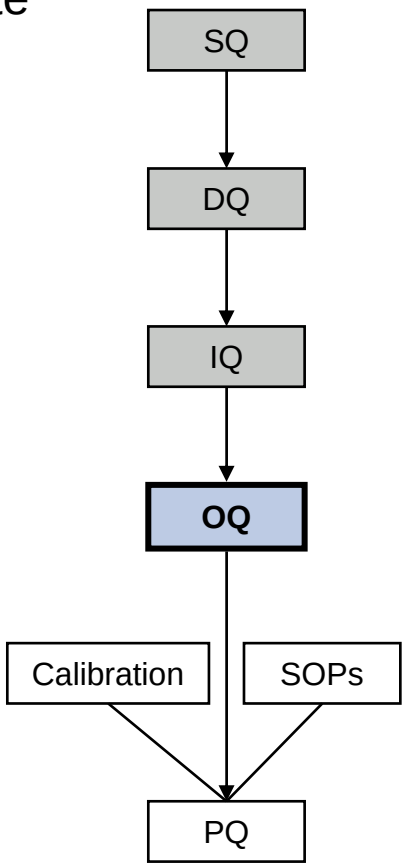


Operational Qualification

- Provides proof that the spectrometer sub-systems and firmware operate correctly
- Performed as part of the IQ process, and at regular intervals for on-going verification
- For AAS requires a Hollow Cathode Lamp with known usage history
  - This is included in the Validator Kits
- Two options:

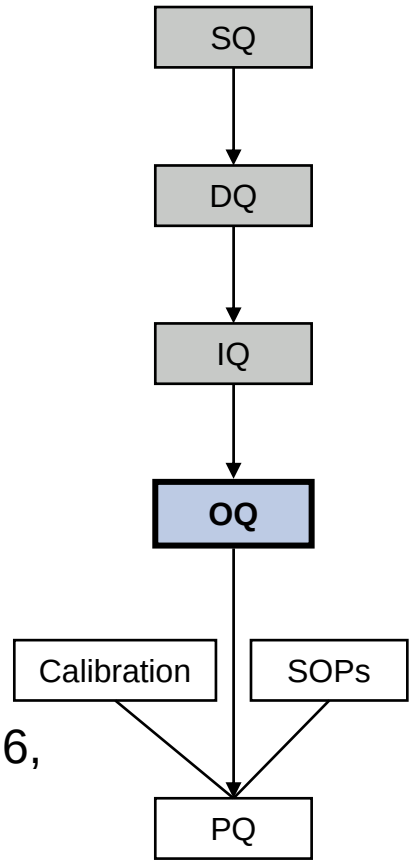
- **Manual OQ**
- Requires calibrated filters
  - Carried by FSE
- Paper documentation completed and signed off

- **Automatic OQ**
- Requires Validator*plus* Calibration Validation Unit
- Results automatically saved in secure OQ Database
- Customised Reports can be printed and signed off if required



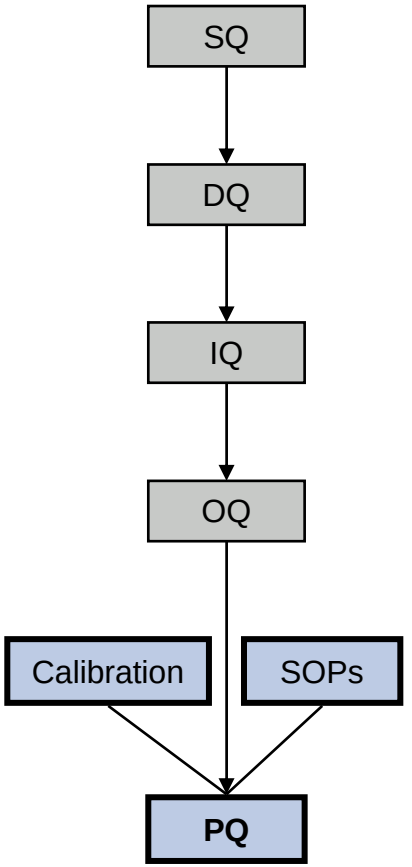
OQ Tests

- Manual Tests
  - Gas Leak test (flame capable system only)
  - Wavelength accuracy
  - Photometric stability
  - Background correction accuracy
- Automatic Tests
  - Gas Leak test (flame capable system only)
  - Wavelength accuracy
  - Monochromator resolution
  - Photometric accuracy
  - Photometric stability
  - Quadline background correction accuracy
  - Lamp peaking
  - Beam selector operation
  - Zeeman Polarizer Orientation (M6, MQZ spectrometers only)
  - Zeeman Polarizer Repeatability (M6, MQZ spectrometers only)



Performance Qualification

- Demonstrates that the system and laboratory is able to make analytical measurements that meet the instrument specification
  - Requires certified reference solutions for preparing sample
  - Requires Hollow Cathode Lamp with know usage history
  - Requires the correct type of graphite cuvette (GFAAS capable system only)
  - All are provided in the Validator Kits
- Performed as part of the IQ process, and at regular intervals for on-going verification
- Performed using the PQ Test Wizard described earlier
- Tests for
  - Analytical sensitivity / precision
  - Blank
  - Analyte recovery
- Results are saved in secure PQ Database
- Hard copy Report can be customized and printed for sign-off if necessary



Continuing System Validation

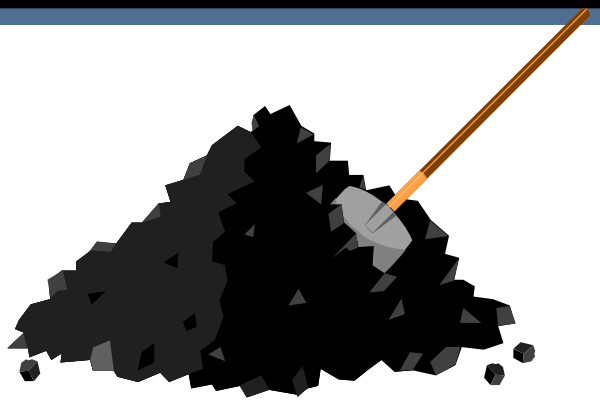
- Following successful Validation on Installation, Validation becomes an on-going, continuous process
- Operational Qualification Tests
  - Can be run by User (Automated version using Validator$_{plus}$ accessory only) or by FSE.
  - May be incorporated into Service Contract
  - Should be run typically at 6 monthly intervals, or when routine or non-routine service is performed
- Performance Qualifications Tests
  - Usually run by User
  - Typically monthly or six monthly intervals, depending on instrument usage
- Log Book includes
  - OQ and PQ Test Record Summary Sheets
  - Test Incident Sheets (Failure/Action)
- PQ and automatic OQ status can be linked to analytical data records
  - Demonstrate that the instrument was performing correctly when the results were measured

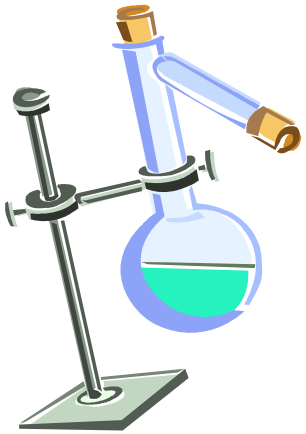
Method Validation

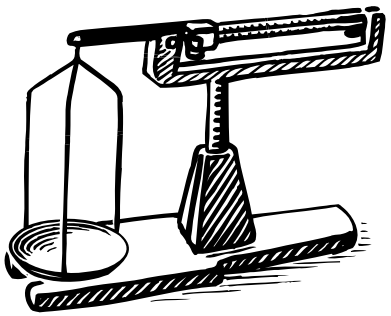
- The analytical instrument itself is just one step in the process required to produce analytical data at a specified quality level
- Other steps may be:
  1. Method Development
  2. Sample Collection
  3. Sample Preparation
  4. Parameter Optimization
  5. Calibration
  6. Analytical Quality Control
  7. Data Reduction
  8. Data Reporting
  9. Data Archiving
- Thermo Scientific can help with the Method Validation by providing:
  - A Method Validation Text Book, included in the Validator Log Book
  - Software tools and features to simplify many of the steps

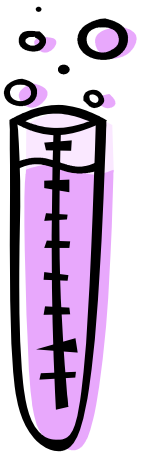
Method Validation Text Book

- The Method Validation Text Book includes chapters covering:
  - Sources of Method Development information
  - Sampling
  - Sample digestion
  - Sample preparation
  - Matrix effects
  - Speciation
  - Literature review
  - Parameter optimization



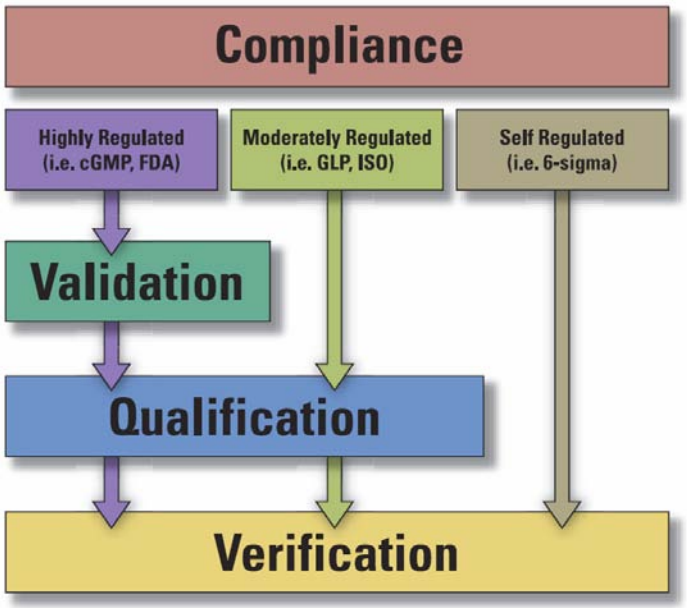






Data Quality – the Thermo Scientific approach

- Analytical Data Quality is assured by compliance with government mandated or self-imposed regulations
- Compliance can be described as a hierarchy
  - Verification – lowest level
  - Qualification – intermediate level
  - Validation – highest level
- Thermo Scientific can supply tools and accessories to demonstrate that your instrument is compliant at each of these levels

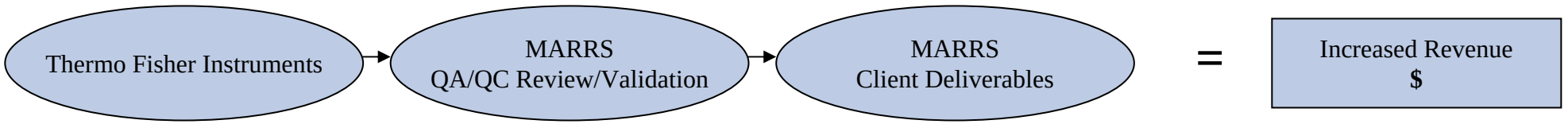


Data review and reporting

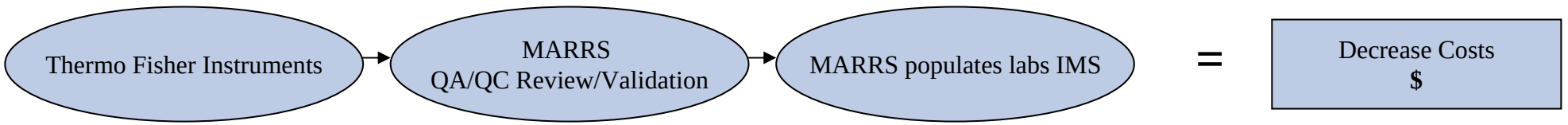
- IQ/OQ/PQ is only enough to get you started
- QC samples will verify the samples ran successfully
- However, clients/sponsors do not pay you to run QC samples
- Review of Data is a significant bottle neck in many laboratories
- Reporting of Data to client deliverable specifications requires flexible reporting capabilities
  - Especially with multiple techniques and protocols

Metals Analytical Review and Reporting Software (MARRS) REVIEW...REPORT…RELAX

- Providing an Integrated Solution
  - Commercial Laboratory - Analytical Production

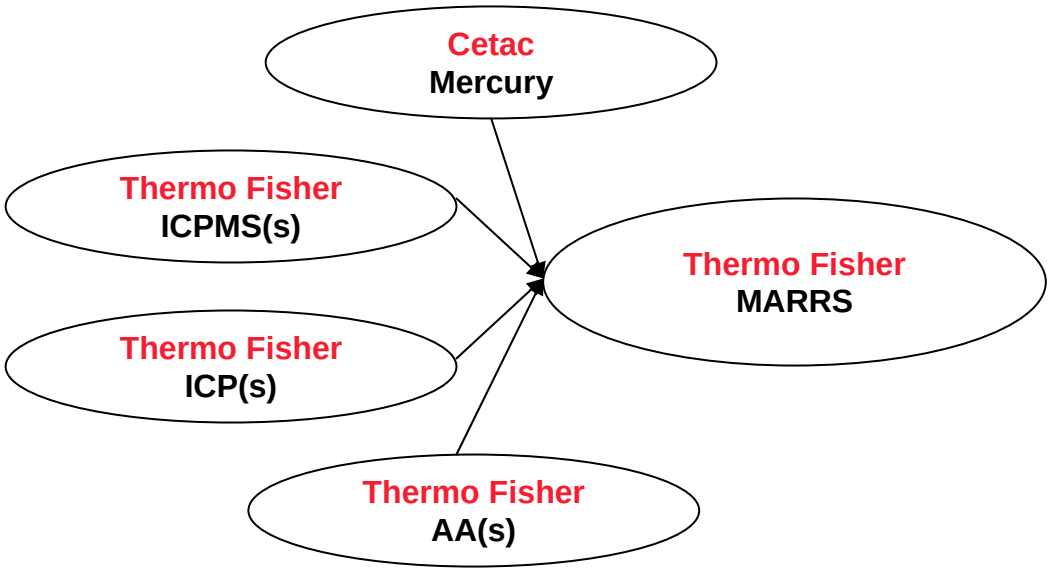


  - Compliance and Process Laboratories - Analytical Production



REVIEW…REPORT…RELAX

- **Thermo Scientific Inorganic Instrumentation Automatically Interface with MARRS**



7 minutes from Instrument to Client Deliverable

DELIVERABLES

IMS Transfer/Interface

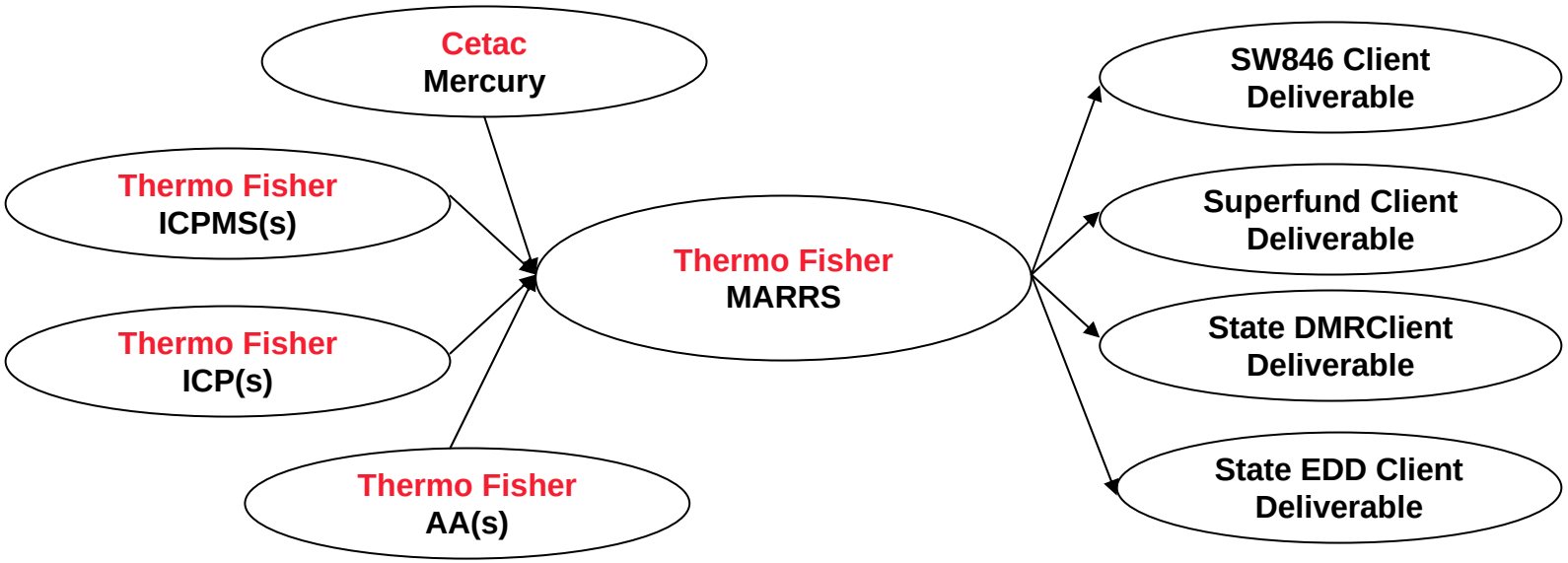
Deliverable Capabilities

- Superfund (all sow's)
- Superfund-Like
- SW846 Reports
- State Form Reports
- NPDES Reports
- Discharge Monitoring Reports
- Geochemical
- Nuclear
- Biomedical
- Health & Safety

EDD Capabilities

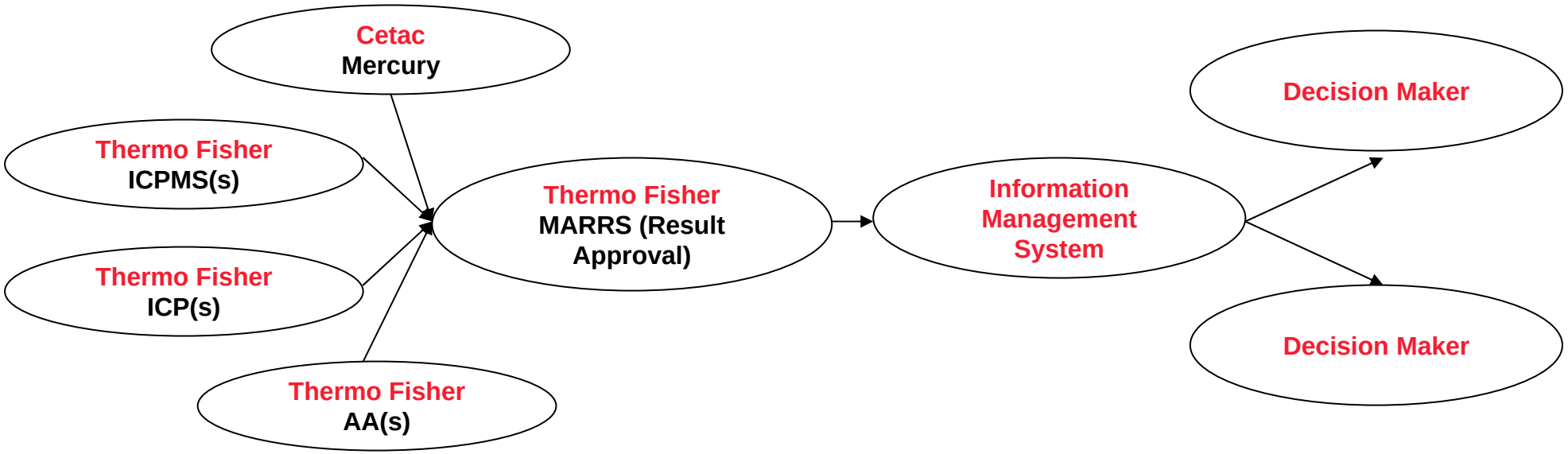
- SEDD - XML Stage 2A, 2B, 3
- All State EDI's
- All other EDD's

- MARRS Flexibility
  - Commercial Laboratory - Interchange Client Deliverables



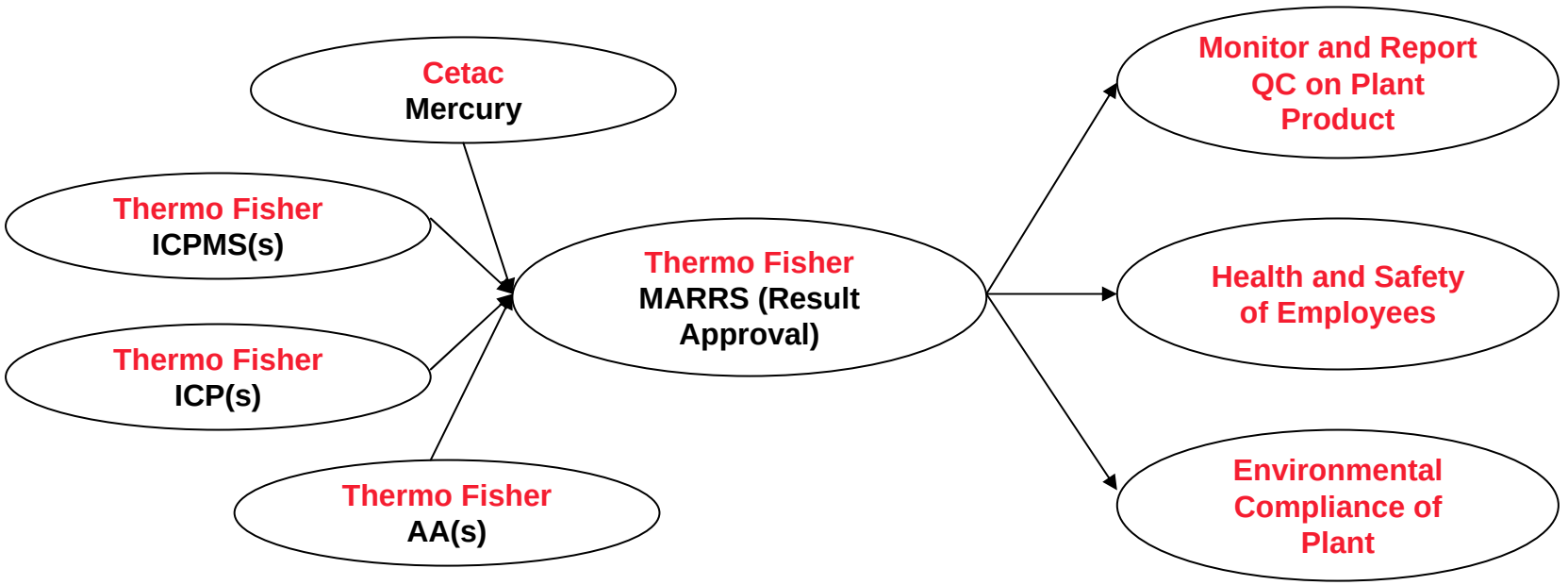
REVIEW…REPORT…RELAX

- MARRS Flexibility
  - Water Laboratory - Automated Quality Assurance System



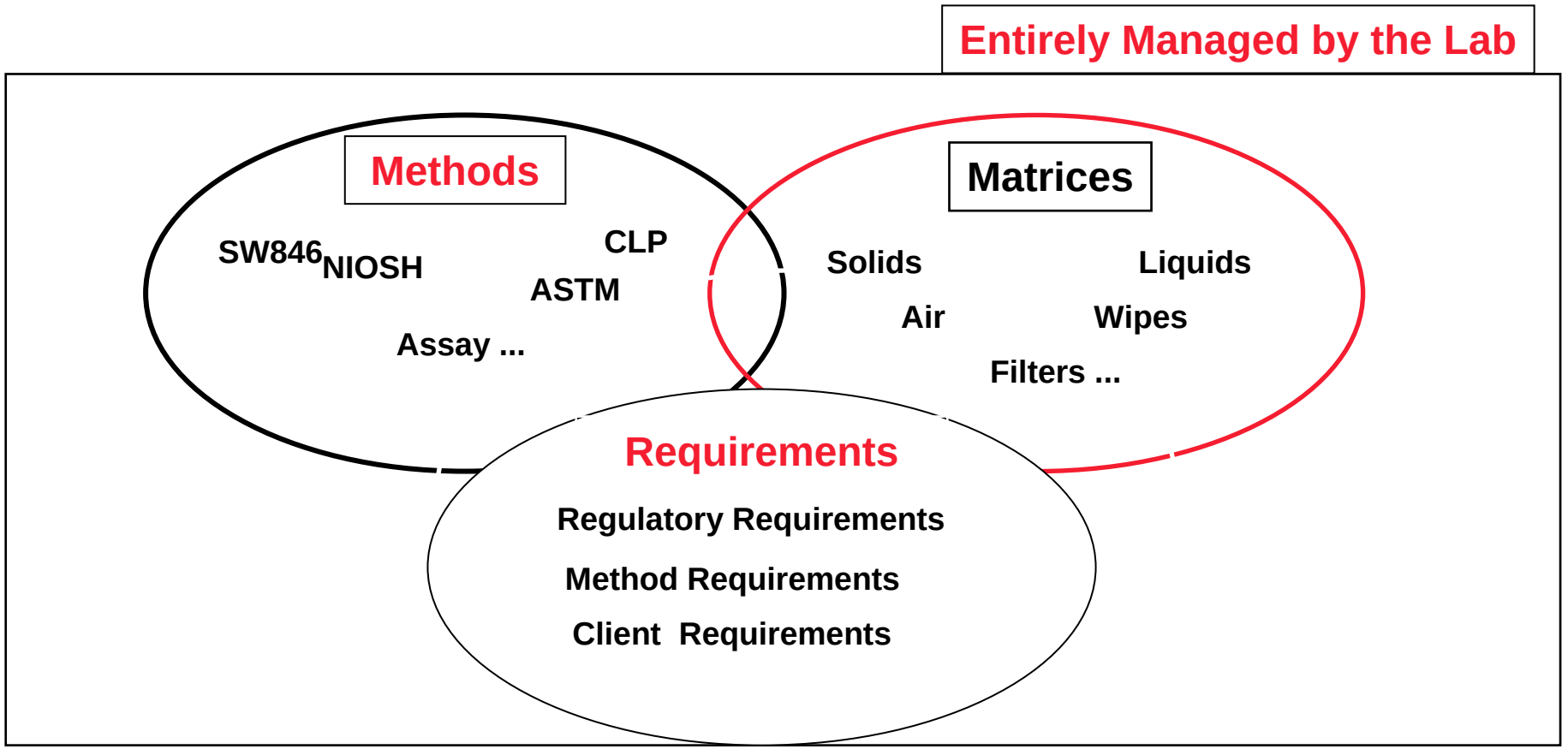
REVIEW…REPORT…RELAX

- MARRS Flexibility
  - Process and Manufacturing Laboratory - MARRS serves multiple purposes



REVIEW…REPORT…RELAX

- MARRS Manageability
  - Provides a union of requirements to produce final analytical product

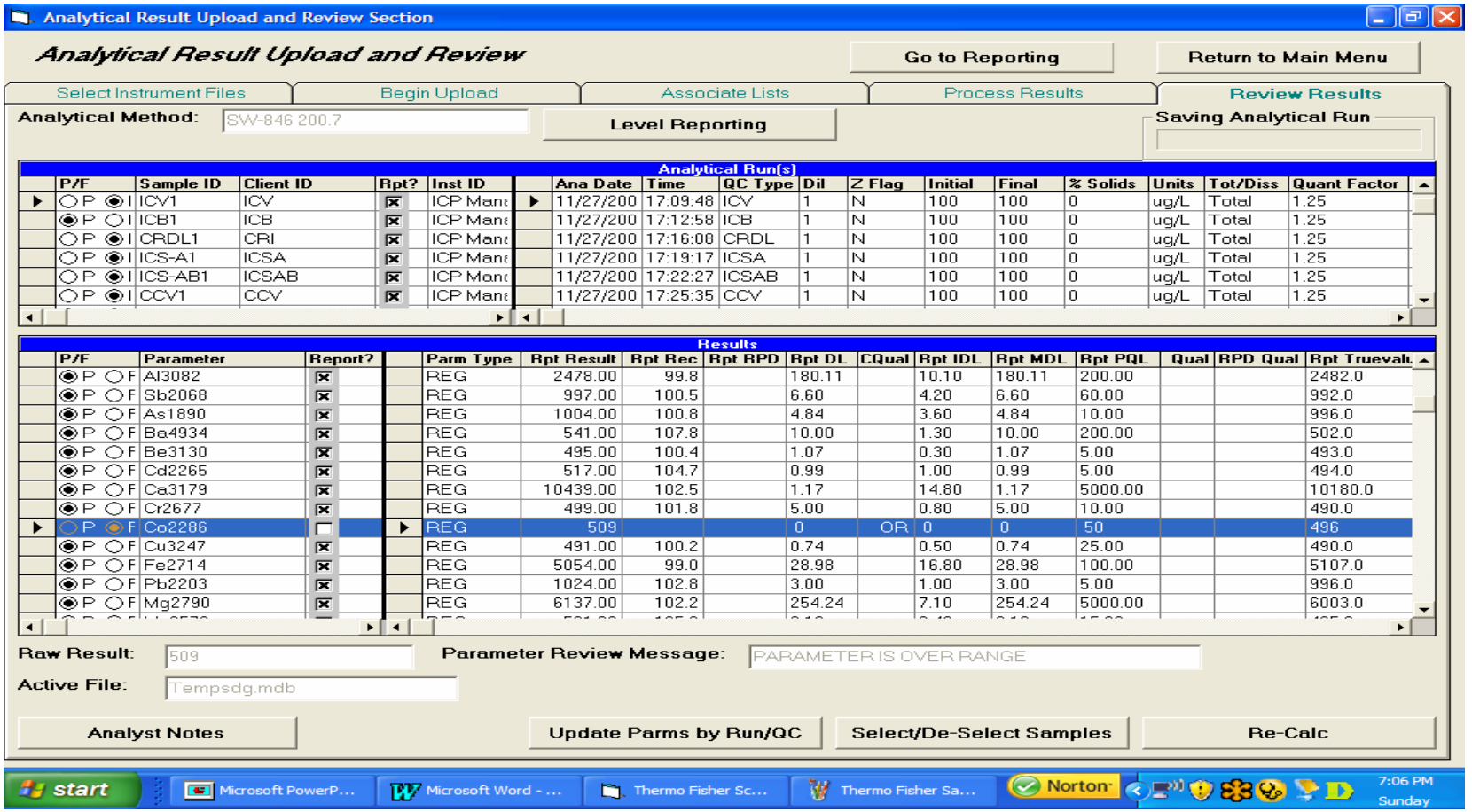


REVIEW…REPORT…RELAX

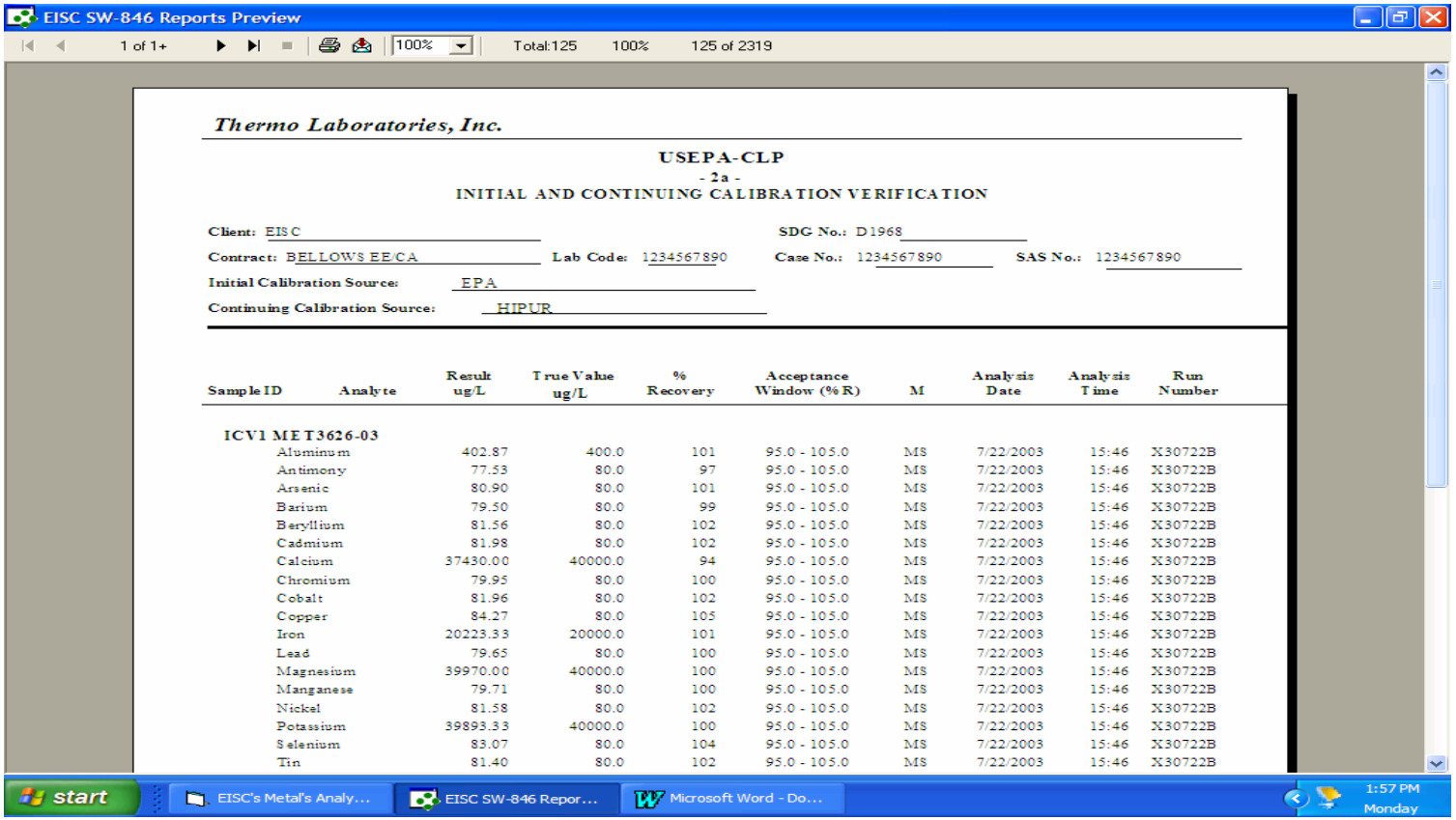
- MARRS Speed
  - Provides a significant increase in laboratory production

REVIEW…REPORT…RELAX

- MARRS Speed
  - Automation of Quality Assurance with interactive review and communication of QA issues against Method, Regulatory and Client Requirements



Metals Analytical Reporting and Review Software (MARRS)



Example of SW846 Report for Initial and Continuing Calibration Verification

- The only scalable software for lab production.
- Automatic analytical review and client specific or regulatory reporting
- Increase production, ensure data quality and integrity and eliminate manual entry, “re-work” and backlog.
  - ICP, ICPMS, Mercury, GFAA Metals, Cyanide and General Chemistry

Quality Summary

- Getting the right result involves three main steps
  - VALIDATION
  - DATA REVIEW
  - DATA REPORTING