ThermoFisher SCIENTIFIC

Preparing Your Lab for USP Chapters <232> and <233>

Pharma & Biopharma Tours | 2016

Simon Nelms

Introduction to USP Chapters <232> and <233>

- Concerned with testing of elemental impurities in pharmaceutical products
- New USP Chapters introduced to replace <231>
  - <232> Elemental Impurities – Limits
  - <233> Elemental Impurities – Procedure
  - <2232> Elemental Contaminants in Dietary Supplements

- Chapter 232 sets out the limits for 15 elements
  - 'Big Four' arsenic, cadmium, lead and mercury – must test for these
  - Remainder are commonly used as catalysts – must test if thought to be present
- Chapter 233 describes two analytical procedures:
  - Procedure 1 – ICP-OES
  - Procedure 2 – ICP-MS
  - Acceptance criteria for alternative procedures

Status of Chapters <232> and <233>

- USP has...
  - Deferred introduction of both chapters in May 2013
  - Both chapters have undergone revision to be aligned with ICH Q3D
  - Both chapters became official in August 2015, and implemented (for new pharmaceutical products) in December 2015
  - Both chapters will be implemented for all existing pharmaceutical products on **January 1st 2018** in alignment with ICH Q3D

- ICH Q3D...
  - Step 4 ICH guideline issued on December 16th, 2014
  - Final implementation (Step 5) set for January 1st 2018

- Other regulatory bodies like the European Medicines Agency (EMA)...
  - Delayed implementation dates for compliance for e.g. marketed products

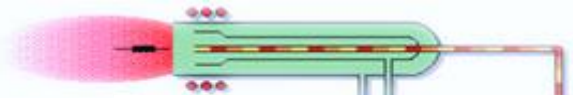
Instrumentation

ICP-OES
Procedure 1

ICP-MS
Procedure 2

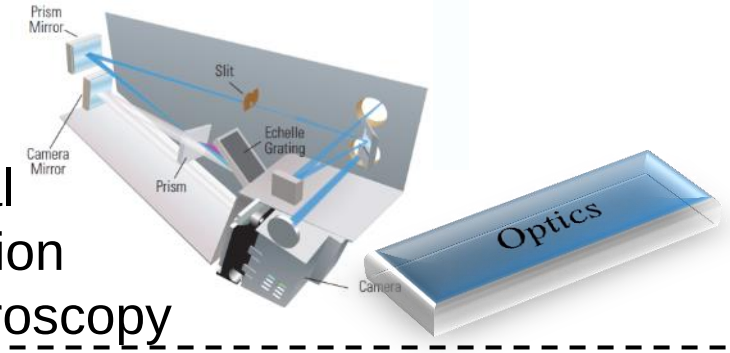
ThermoFisher SCIENTIFIC

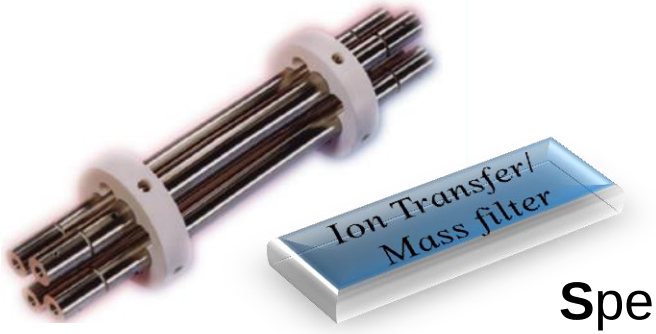
ICP – Optical Emission and Mass Spectrometry



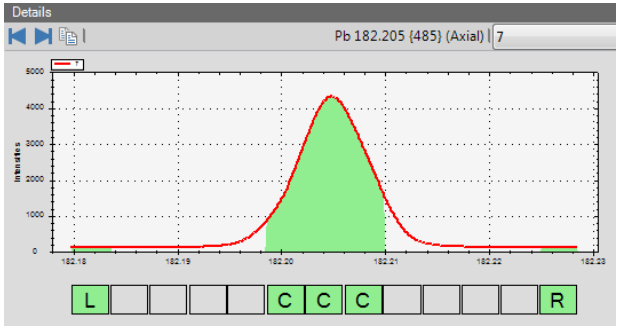
Sample introduction and Plasma

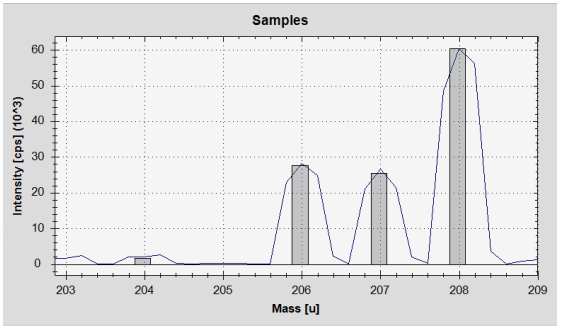
ICP-
Optical
Emission
Spectroscopy





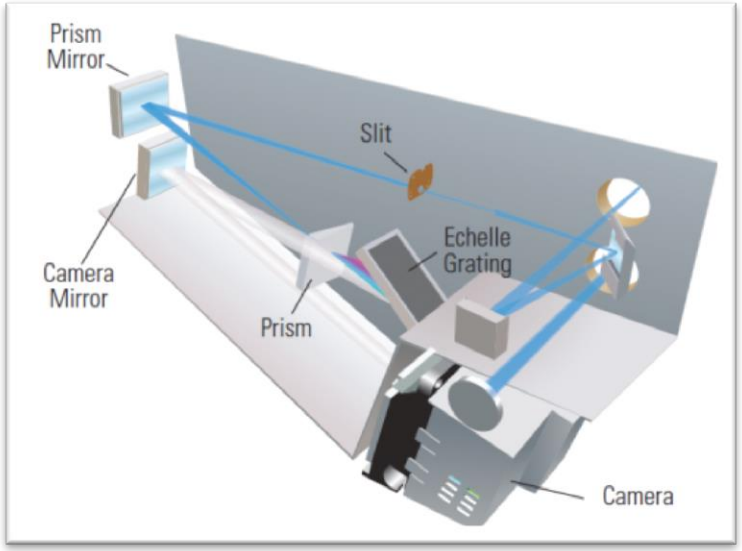
ICP-
Mass
Spectrometry





ThermoFisher SCIENTIFIC

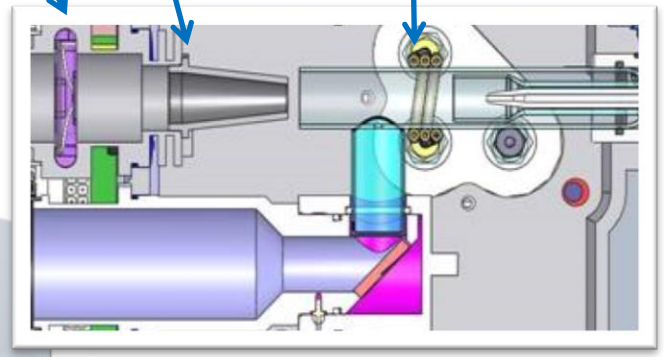
Schematic of an ICP-OES



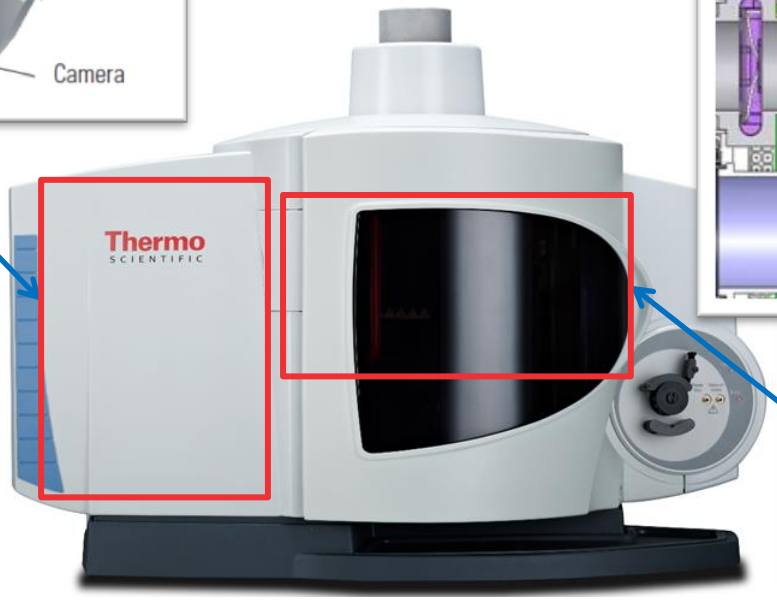
POP window

Purged optical pathway

Plasma Generation



Optical tank

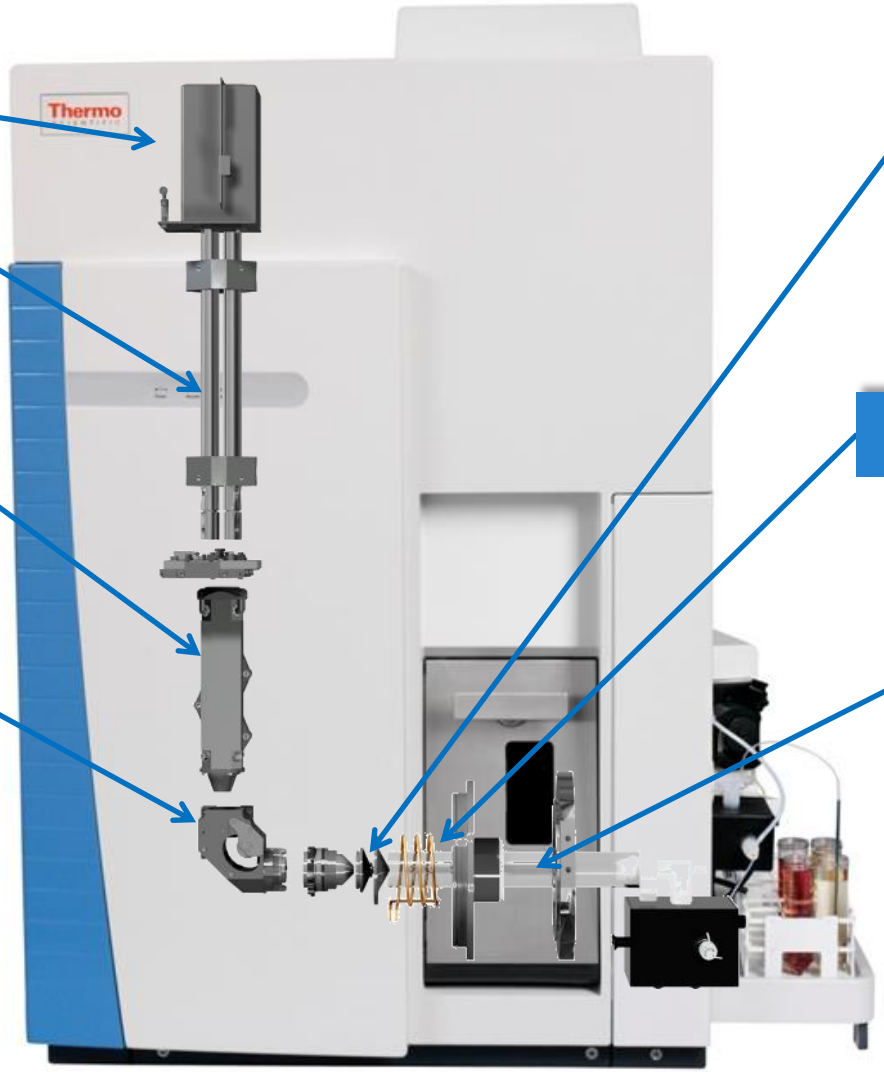


Torch box

DRIVEN BY QTEGRA ISDS

ThermoFisher SCIENTIFIC

Schematic of an ICP-MS



Detector

Quadrupole mass filter

Collision cell

Removal of neutral gas molecules

Interface

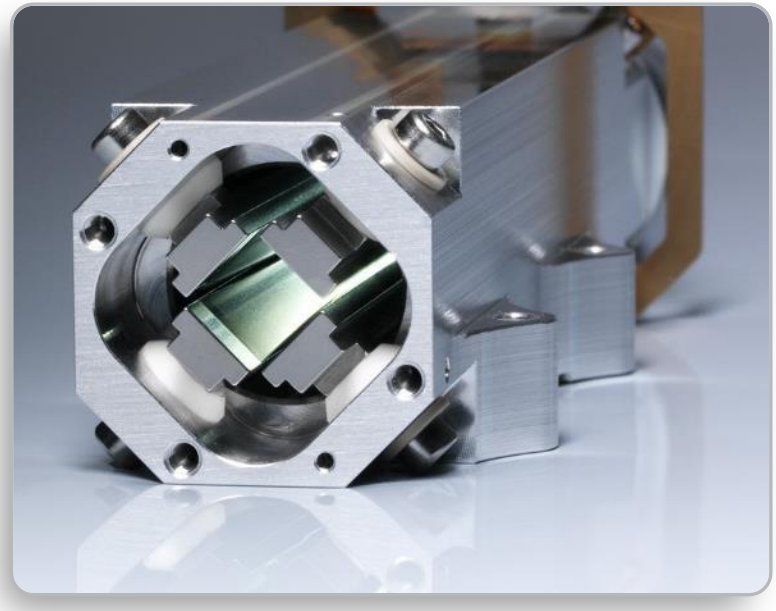
Plasma Generation

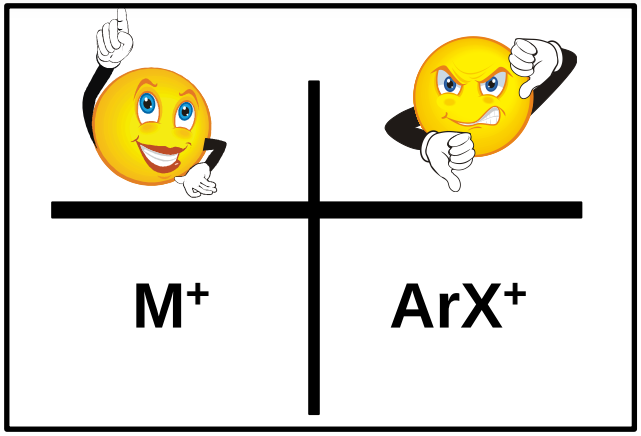
Torch

ThermoFisher SCIENTIFIC

Interference Removal by Collision/Reaction Cell

- Collision/Reaction Cell
  - A multipole (e.g. flatapole) enclosed in a chamber
  - Controlled flow of gas into the cell (usually pure He)
  - Interaction of ions with the gas mainly by collisions
  - Preferred approach: Kinetic Energy Discrimination (KED)
    - This filters out unwanted interference signals on the basis that these ions have lower KE than the isotopes with which they interfere
  - If reactive gas used, reactions occur
    - All cells are reaction cells





Requirements to Operate an ICP-OES or ICP-MS

- Power
  - ICP-OES
  - ICP-MS

  Typically single phase 30 A

- Gases
  - ICP- OES — Argon (grade 4.6 or better)
  - ICP-MS — Argon (grade 4.6 or better) + He (CCT - grade 5.0 or better)

- Extraction
  - ICP-OES
  - ICP-MS

  Typically 5 to 15 m/s

Analysis time for both instruments = typically 2 to 3 mins per sample

Purchase Decision of an Instrument

Expected amount of analysis

- ✓Sample Throughput
- ✓Automation

Instrument performance

- ✓Detection Limits
- ✓Measurement range

ICP-OES or ICP-MS ?

Cost of ownership

- ✓Installation Requirements
- ✓Bench space requirements

Operator skills

- ✓Automation
- ✓Automated software routines

Typical Instrument Implementation Process

X

- Purchase of an instrument
  - ICP-OES or ICP-MS

4-8 Weeks

- System Delivery and Installation
  - Installation- and Operation Qualification (IQ/OQ)

6-8 Weeks

- Method Development
  - Direct analysis, summation?
  - Generation of SOP

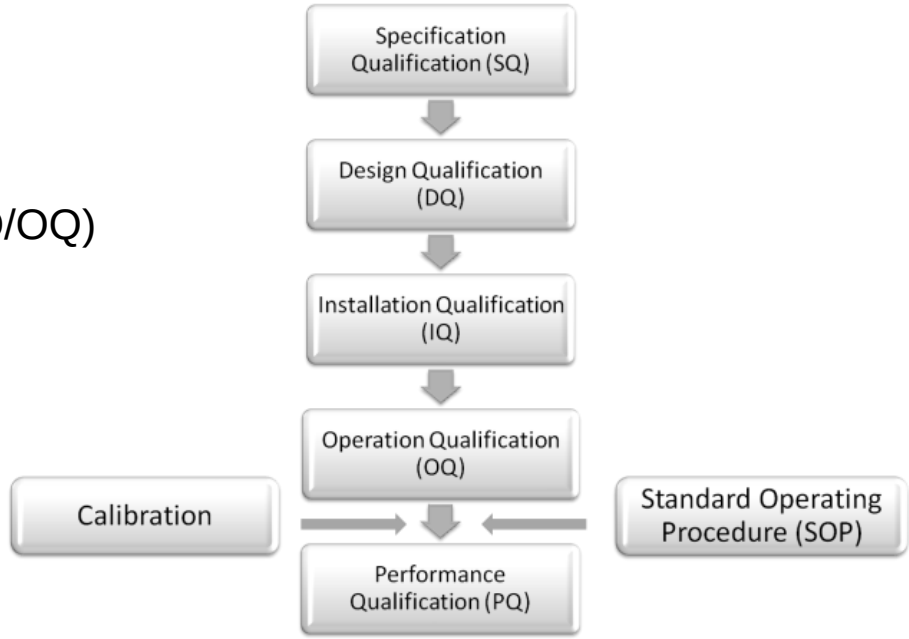
6-8 weeks

- Method Validation and Implementation into Routine Analyis

- Enforcement of new Regulations by FDA, EP etc.

Validation, Software and FDA Compliance

- System qualification includes:
  - Specification Qualification (SQ)
  - Design qualification (DQ)
  - Installation and operational qualification (IQ/OQ)
  - Performance qualification (PQ)
  - Periodic Requalification (RQ)



- System qualification covers:
  - Instrument Hardware and Software

- Compliance with federal regulations is critical
  - Part 11 in Title 21 of the US code of Federal Regulations (21 CFR Part 11)
    - Governs food and drugs in the United States
    - Includes Federal guidelines for storing and protecting electronic records
    - Must contain electronic signatures etc.

The Thermo Scientific™ iCAP™ Qualification Kit

- Available for ICP-OES and ICP-MS
- Contains all necessary documentation for IQ/OQ .... And more!

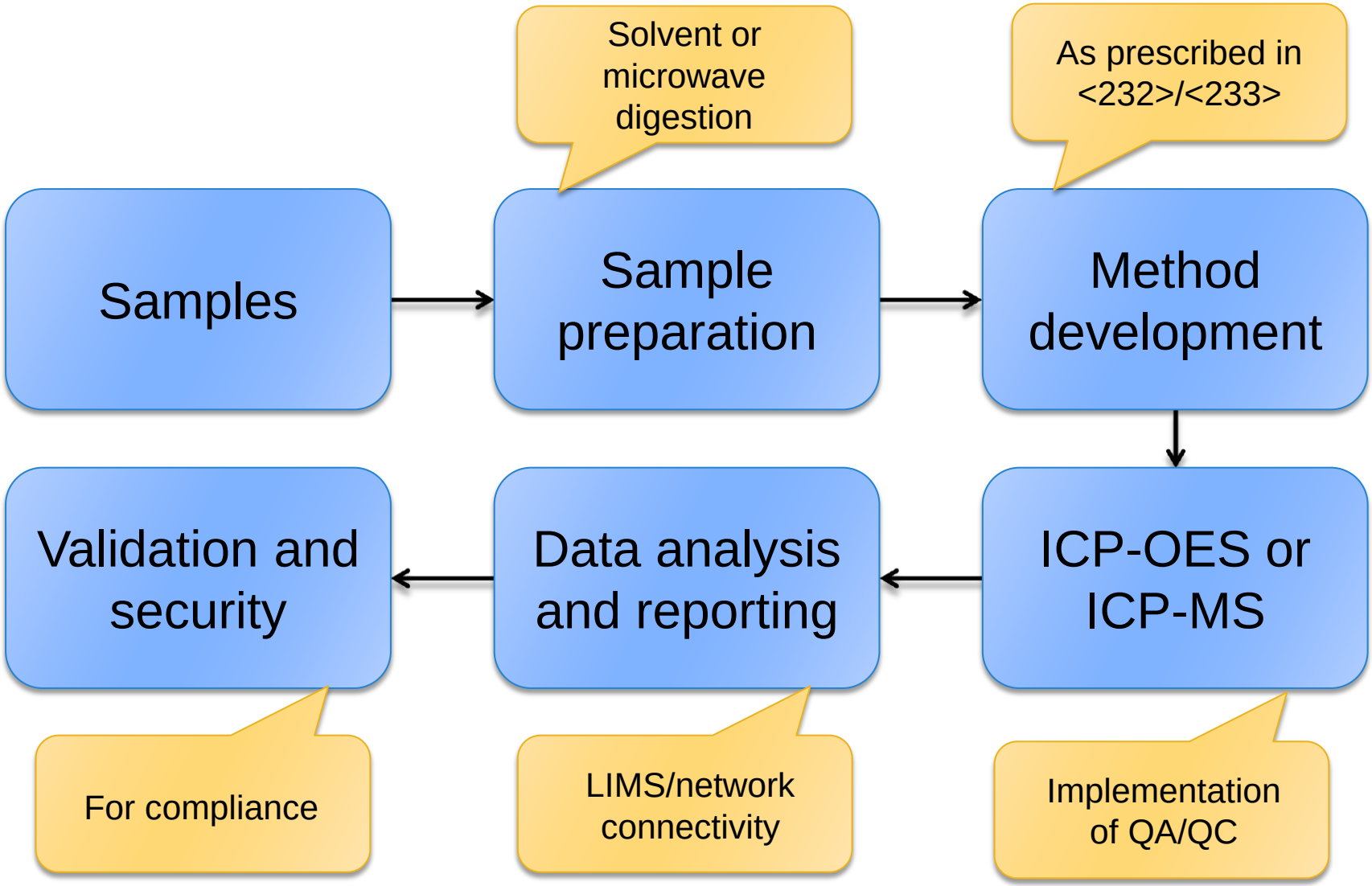
✓ Description of all necessary steps for fast and reliable implementation of a system in your lab

✓ Manuals and Application Notes for a quick start

✓ Documentation for IQ/OQ, Preventive Maintenance and Requalification (RQ) carried out by a service engineer

✓ Best Practices Guide, useful information provided by Application Chemists for new users

Work flow for Metals Analysis



Sample Preparation

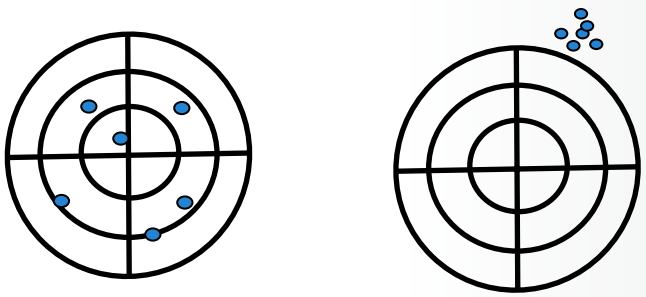
- A typical drug can be described as an API (active pharmaceutical ingredient) + an excipient.
- Common excipients are:
  - Binders e.g. xanthan gum
  - Glidants and lubricants e.g magnesium stearate
  - Disintegrants e.g. crospolividone (E1202)
  - Sweeteners e.g. sucrose
  - Flavourings e.g. fruit
  - Pigments e.g. titanium dioxide
  - Preservatives e.g. methylparaben
  - Coating e.g. shellac or gelatine

- For USP <233> three sample preparation options:

1. Direct Aqueous
   - Dissolution in an aqueous matrix
   - Not all excipients soluble e.g. TiO_2
2. Direct Organic
   - Dissolution in an organic matrix
   - Not all excipients soluble e.g. Magnesium stearate
   - Example with DMSO and ICP-OES
3. Indirect Solution
   - Closed vessel digestion
   - See ICP-MS section for an example
   - **Most universal method**

Method Validation Criteria

- Accuracy
  - Closeness of the result to the true value
- Precision
  - Degree of agreement between individual tests of multiple samples



- Specificity
  - Unequivocal assessment of the analyte in presence of other compounds
- Ruggedness
  - Capacity to be unaffected by small but deliberate changes in the procedure
- LoD, LoQ, Range, Linearity
  - Analytical figures of merit

Required Tests from <233>

- #1 Calibrate the system, analyze a sample containing 0.5J and 1.5J three times each
  - Definition of J:
  - Example:
  - Oral administration;
  - Dose: 10g/day

Concentration (w/w) of the Target limit, appropriately diluted to the working range of the instrument

	As	Cd	Hg	Pb
Target Value [µg/day]	1.5	25	15	5
Target limit [µg/g]	0.15	2.5	1.5	0.5
Dilution factor for ICP-MS	1000	1000	1000	1000
J [ng/g]	0.15	2.5	1.5	0.5
0.5 J [ng/g]	0.075	1.25	0.75	0.25
1.5 J [ng/g]	0.225	1.875	1.125	0.375

Required Tests from <233>

- #1 Calibrate the system, analyze a sample containing 0.5J and 1.5J three times each

→Determined spike recovery 70-150% (Accuracy)

Test implemented in the Qtegra software QC repertoire

→Calculation of LoD/LoQ, Range and Linearity

Qtegra ISDS automatically generates LOD data and correlation coefficient

→Specificity indicated by correct spike recovery result

→Alternative: Monitor two isotopes for one element

Required Tests from <233>

- # 2 Calibrate the system, analyze 6 times a sample spiked with 1J

  → Precision; RSD between all measurements not more than 20%

- # 3 Repeat #2 (6 times J) on either:

  - Two different days
  - Two different analysts
  - Two different systems

  → Intermediate precision, ruggedness; RSD between all not more than 25%

Total: 24 analyses + 1 for unspiked sample

ICP-OES – Procedure 1 USP Chapter <233>

The key benefits of ICP-OES

- Easy to use, learn & maintain
- Fast multi-element capability
- Robust plasma and flexibility for complex sample matrices

- Ability to analyse multiple matrix types in a single method
  - → Axial and radial plasma observation
  - → Robust RF generator
  - → Easy handling of organic solvents using Organics Kit

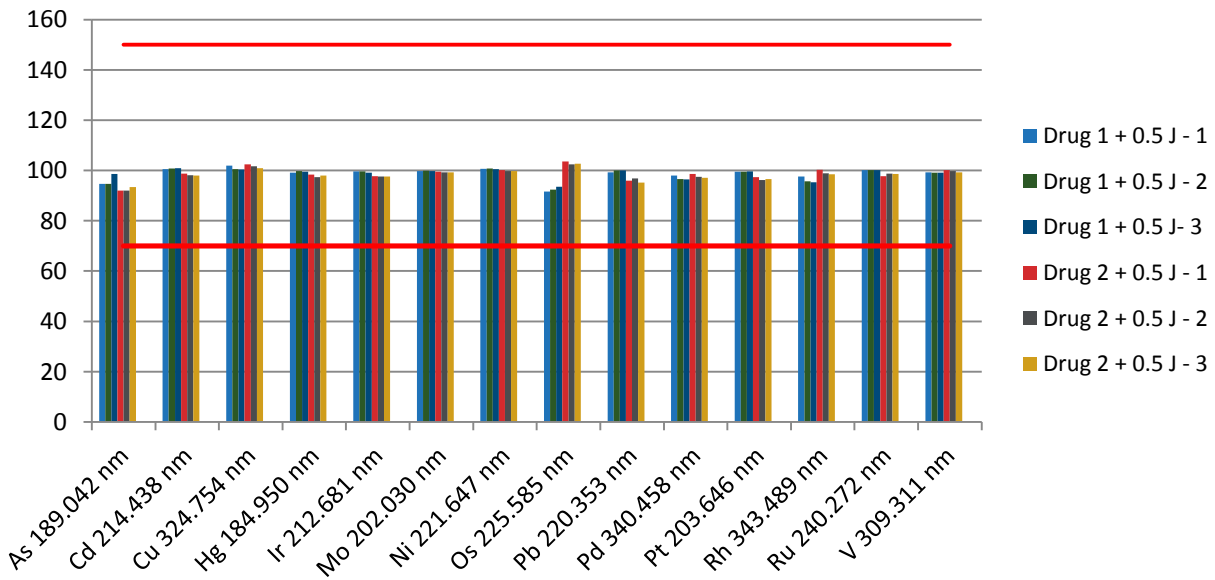
As, Cd, Hg and Pb	'The big four'
Cr, Cu, Mn, Mo, Ni, Pd, Pt, V, Os, Rh, Ru, Ir	Common catalysts

Analysis of Two Over-the-Counter Medicines

- Preparing samples in DMSO
  - DMSO (dimethyl sulfoxide) is a very strong solvent
  - Less toxic than DMF (dimethylformamide)
  - High-boiling point
- Drawbacks of using DMSO
  - Require silicone pump tubing
  - O-rings on spray-chamber require changing more often
  - Will not dissolve all excipients
    - For example: silica, titanium dioxide

Analysis of Two Over-the-Counter Medicines contd.

- Two over-the-counter medicines were tested according to USP <233>
  - Drug 1 – anti-inflamatory
  - Drug 2 – antihistamine
- 0.5 g of dehydrated sample was dissolved in 25 g of DMSO
  - J defined as the w/w concentration of analyte at Target Limit <u>after</u> dilution
  - Target Limit > MDL; recoveries tested at the 0.5J and 1.5J



Elements	0.5 J (µg/kg)
Cadmium	125
Lead	25
Inorganic As	7.5
Inorganic Hg	75
Iridium	500
Osmium	500
Palladium	500
Platinum	500
Rhodium	500
Ruthenium	500
Molybdenum	500
Nickel	2500
Vanadium	500
Copper	5000

Analysis of Two Over-the-Counter Medicines contd.

- Precision
  - Determined by analyzing six individual samples
  - Samples spiked at J
  - USP acceptance criteria < 20%

Elements	Drug 1 Run 1 µg/L	Drug 1 Run 2 µg/L	Drug 1 Run 3 µg/L	Drug 1 Run 4 µg/L	Drug 1 Run 5 µg/L	Drug 1 Run 6 µg/L	RSD %
Cadmium	232.4	232.7	234.7	239.1	235.6	229.9	1.4
Lead	45.9	45.2	44.6	47	46.6	43	3.2
Inorganic arsenic	12.1	12.7	12.8	14	12.9	11.4	6.9
Inorganic mercury	130.7	130.8	132,5	136.5	131.8	127.4	2.3
Iridium	944.5	941.3	948.2	963.7	950.9	924.5	1.4
Osmium	954.8	952.7	959	974.9	960.5	940	1.2
Palladium	918.8	914.7	914.6	928.6	929.4	890.6	1.5
Platinum	924.4	917.6	931.5	949.9	934.6	910.7	1.5
Rhodium	921.5	907.2	907.5	917.6	915.8	874.9	1.9
Ruthenium	955.5	966.5	953.6	972.8	967.5	932.7	1.5
Molybdenum	956.8	952	959.6	974	959.5	937.7	1.2
Nickel	4669	4666	4706	4787	4718	4610	1.3
Vanadium	962.5	952.9	945.5	960.1	961.7	928.9	1.4
Copper	9680	9590	9522	9666	9668	9318	1.5

ICP-MS – Procedure 2 USP Chapter <233>

- The key benefits of ICP-MS relative to ICP-OES are:
  - Improved detection limits:
    - Up to 1000x lower for USP regulated elements such As, Cd, Hg and Pb
  - Able to access a broader elemental package
  - Wider dynamic range, ppt to ppm
  - Straightforward interfacing to speciation techniques (IC etc.)

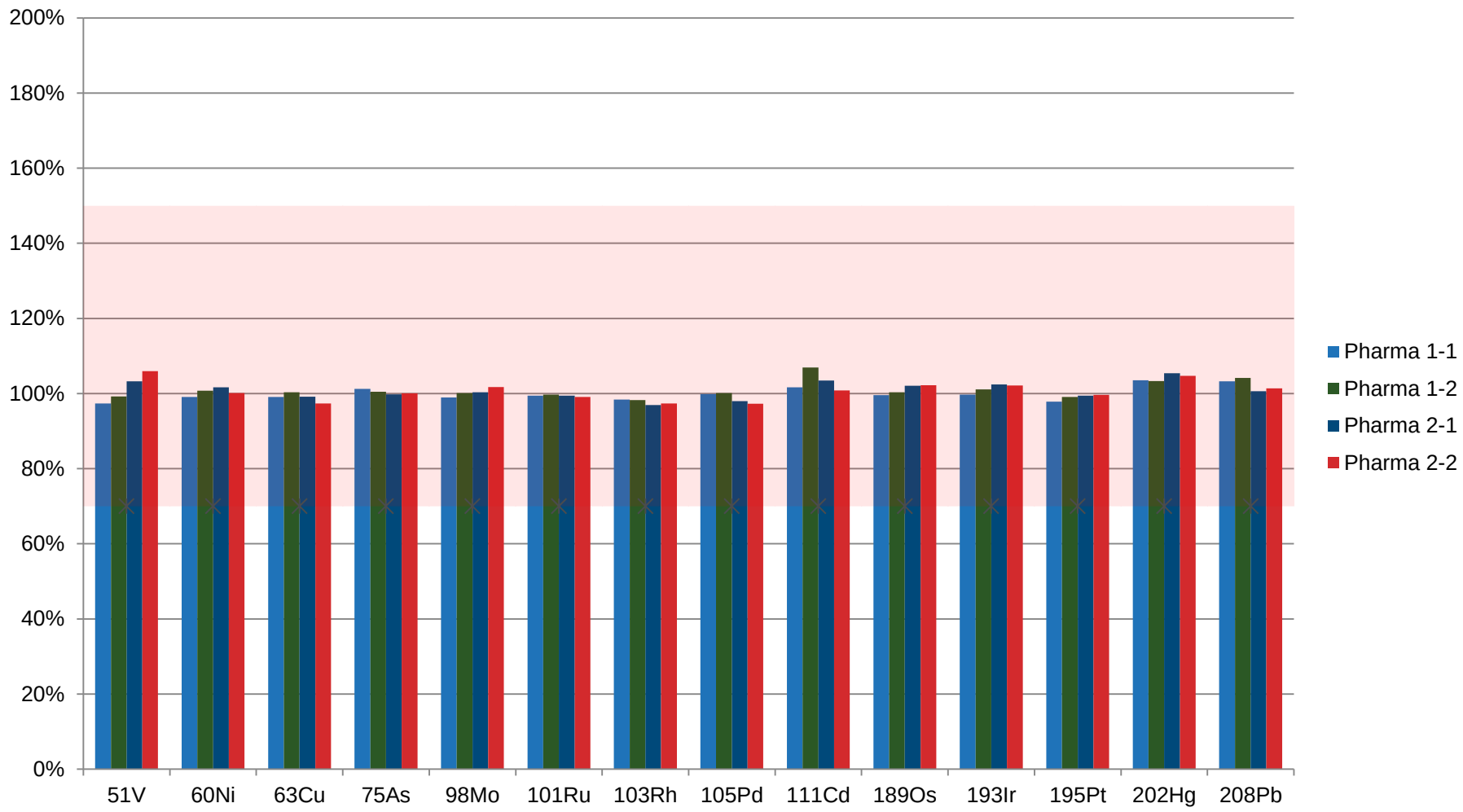
Microwave Sample Preparation

- Four over-the-counter products were locally sourced
- Two samples of each were weighed into 15 ml disposable glass vials
- 3 ml of conc. HNO_3 was added to each vial
- System was closed, and pressurized with N_2 at 40 bar
- Microwave digestion recipe:

Step	Time (min)	Temperature (℃)	Power (kW)
1	15	200	1.5
2	10	200	1.5

- When <60 ℃, the digest was transferred to a polypropylene vial and made up to 50 ml with 1% HCl
- Samples were further diluted before analysis (with high purity 2% HNO_3) to give total dilution factors of between *100 and *1000

Results: Spike Recoveries (0.5 J)



ThermoFisher SCIENTIFIC

ICP-MS Detection Limits Compared to Maximum Daily Dose

Element	Instrumental Detection Limit (ng/mL)	Method Detection Limit (µg/g)	Concentration Limit Max. Daily Dose of ≤10 g/day (µg/g)
Cadmium	0.0001	0.0001	0.5
Lead	0.0005	0.0005	0.5
Inorganic arsenic	0.0005	0.0005	1.5
Inorganic mercury	0.003	0.003	1.5
Iridium	0.002	0.002	10
Osmium	0.0006	0.0006	10
Palladium	0.0008	0.0008	10
Platinum	0.0005	0.0005	10
Rhodium	0.0007	0.0007	10
Ruthenium	0.001	0.001	10
Molybdenum	0.003	0.003	18
Nickel	0.003	0.003	60
Vanadium	0.006	0.006	12
Copper	0.009	0.009	130

Qtegra ISDS: A Simple Workflow to Quality Results

1. **Dashboard**
   "Get Ready"

2. **LabBook**
   "Create LabBook"

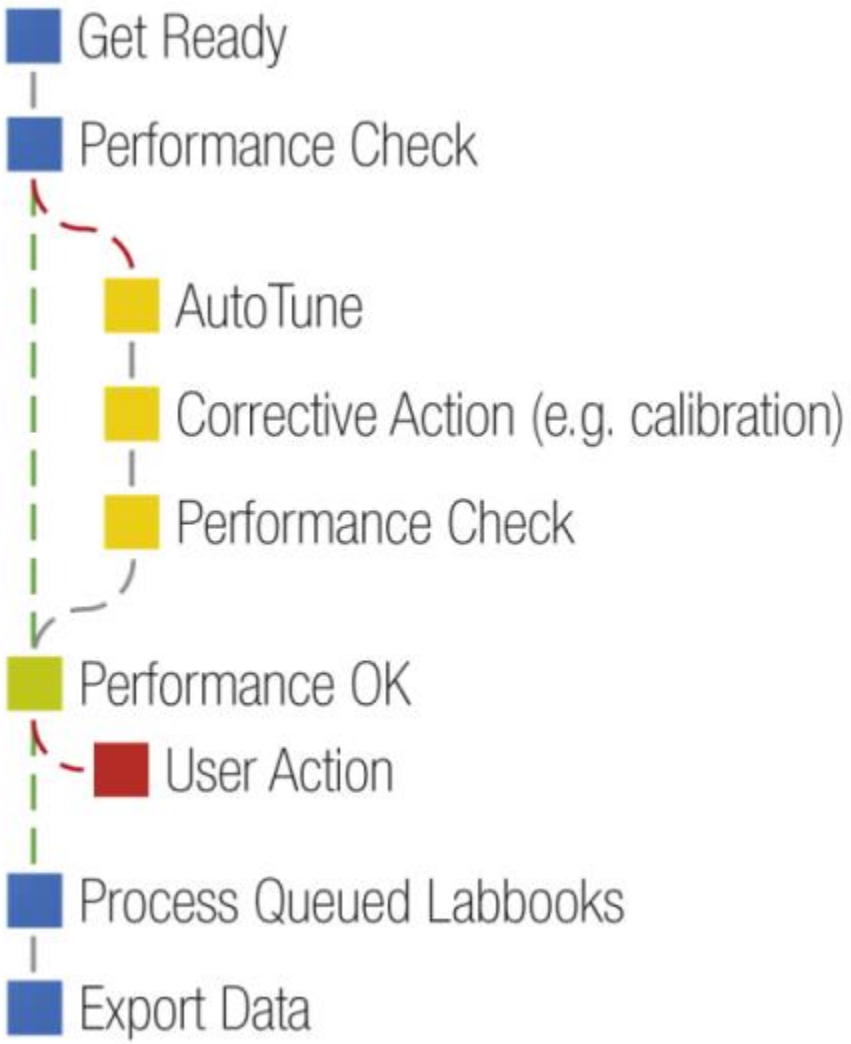
3. **LabBook**
   Results and report

Template
Experiment method and QA/QC protocol

Sample Details
Manual
LIMS
Bar / QR Code

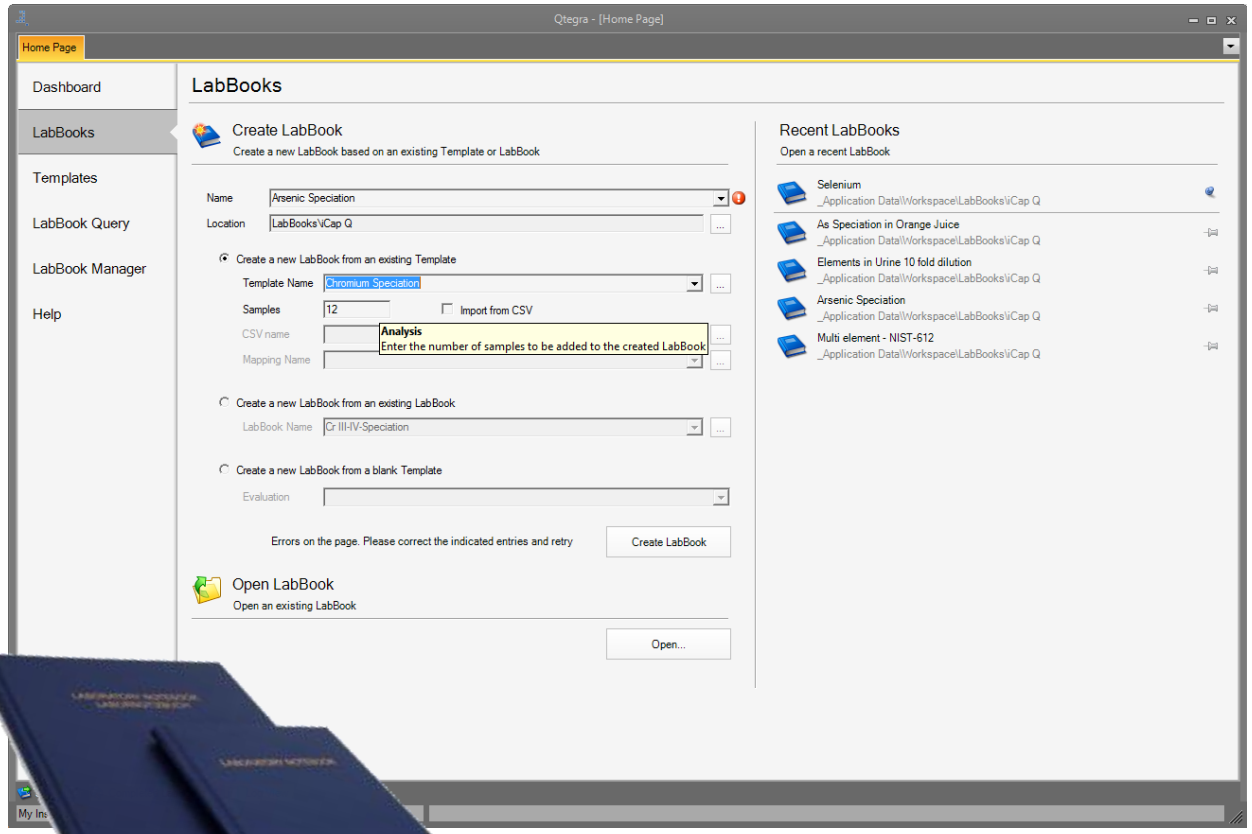
LIMS

Qtegra ISDS: Get Ready



ThermoFisher SCIENTIFIC

Qtegra ISDS: LabBook



- Prepared in just five clicks

- Method
- QA/QC Protocol
- Sample List
- Results
- Report
- Audit trail

ThermoFisher SCIENTIFIC

Qtegra ISDS: Reporting

- Flexible tool for on-line generation of printable records
  - Can be printed online with data acquisition
  - Password protected .pdf files can be generated
- Tables are completely customizable
  - Information about Instrument, LabBook, Method Parameters
- Filtering options for reporting of specific samples
  - Sample name, Sample type, Analyst etc.
  - Individual tables for subsamples in a bigger batch
  - Filtering across all acquired data sets is possible to generate e.g. history recors of QA/QC samples

Qtegra ISDS Reporting – Example 1

Report Precision

4/29/2014 2:22:40 PM

QTEGRA

Summary:

Labbookname	Acquired by	Computer name
Test Labbook Calibration + QC MXS 2.imexp	409865J	409865J-PC

Instrument Information

Filename	Instrument	Serial
Test Labbook Calibration + QC MXS 2.imexp	iCAP Q	Undefined

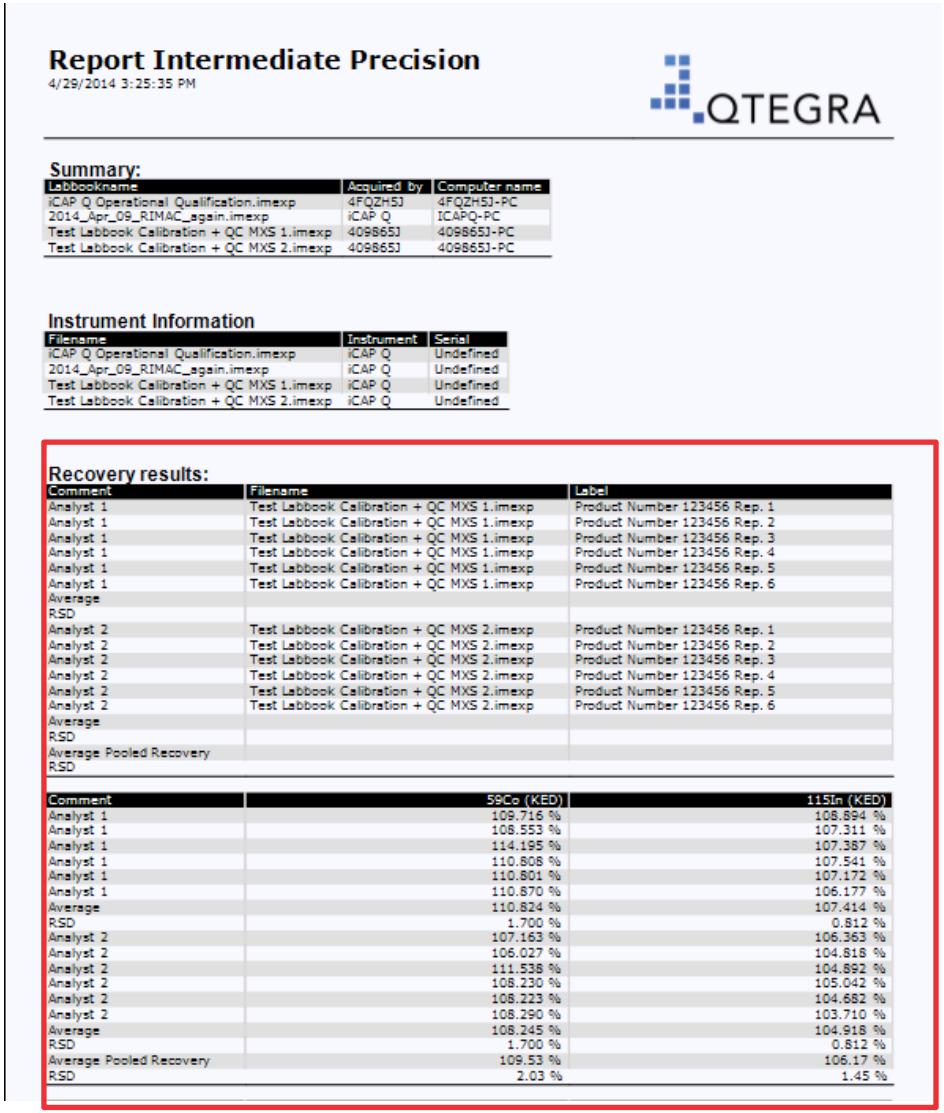
Recovery results:

Label	Index	59Co (KED)	115In (KED)	140Ce (KED)	238U (KED)
Sample XYZ Rep. 1	6	107.163 %	106.363 %	107.952 %	103.087 %
Sample XYZ Rep. 2	7	106.027 %	104.818 %	105.113 %	103.419 %
Sample XYZ Rep. 3	8	111.538 %	104.892 %	107.229 %	105.646 %
Sample XYZ Rep. 4	9	108.230 %	105.042 %	106.404 %	107.043 %
Sample XYZ Rep. 5	10	108.223 %	104.682 %	107.288 %	104.578 %
Sample XYZ Rep. 6	11	108.290 %	103.710 %	105.569 %	107.320 %
Average		108.245 %	104.918 %	106.592 %	105.182 %
RSD		1.700 %	0.812 %	1.029 %	1.706 %

LabBook information:
Created by, Acquired by,
Last changed by,...

Customized table:
Direct overview on precision test for Sample XYZ,
Average Recovery and RSD are automatically calculated

Qtegra ISDS Reporting – Example 2



Report Intermediate Precision
4/29/2014 3:25:35 PM

QTEGRA

Summary:

Labbookname	Acquired by	Computer name
iCAP Q Operational Qualification.imexp	4FQZH5J	4FQZH5J-PC
2014_Apr_09_RIMAC_again.imexp	iCAP Q	ICAPQ-PC
Test Labbook Calibration + QC MXS 1.imexp	409865J	4098655J-PC
Test Labbook Calibration + QC MXS 2.imexp	4098655J	4098655J-PC

Instrument Information

Filename	Instrument	Serial
iCAP Q Operational Qualification.imexp	iCAP Q	Undefined
2014_Apr_09_RIMAC_again.imexp	iCAP Q	Undefined
Test Labbook Calibration + QC MXS 1.imexp	iCAP Q	Undefined
Test Labbook Calibration + QC MXS 2.imexp	iCAP Q	Undefined

Recovery results:

Comment	Filename	Label
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 1
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 2
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 3
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 4
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 5
Analyst 1	Test Labbook Calibration + QC MXS 1.imexp	Product Number 123456 Rep. 6
Average		
RSD		
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 1
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 2
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 3
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 4
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 5
Analyst 2	Test Labbook Calibration + QC MXS 2.imexp	Product Number 123456 Rep. 6
Average		
RSD		
Average Pooled Recovery		
RSD		

Comment	59Co (KED)	115In (KED)
Analyst 1	109.716 %	108.894 %
Analyst 1	108.553 %	107.311 %
Analyst 1	114.195 %	107.387 %
Analyst 1	110.808 %	107.541 %
Analyst 1	110.801 %	107.172 %
Analyst 1	110.870 %	106.177 %
Average	110.824 %	107.414 %
RSD	1.700 %	0.812 %
Analyst 2	107.163 %	106.363 %
Analyst 2	106.027 %	104.818 %
Analyst 2	111.536 %	104.892 %
Analyst 2	108.230 %	105.042 %
Analyst 2	108.223 %	104.682 %
Analyst 2	108.290 %	103.710 %
Average	108.245 %	104.918 %
RSD	1.700 %	0.812 %
Average Pooled Recovery	109.53 %	106.17 %
RSD	2.03 %	1.45 %

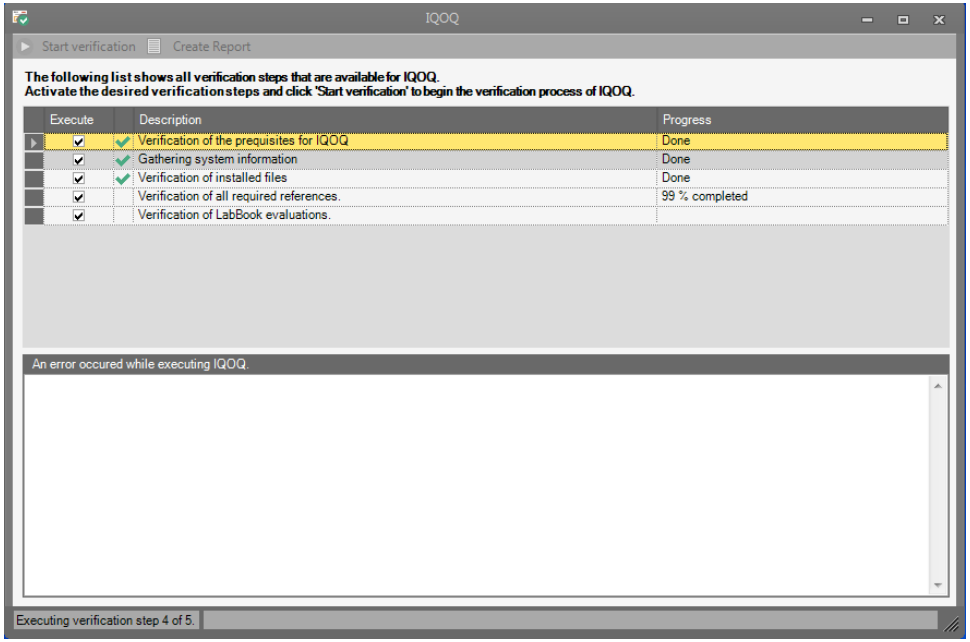
Report Intermediate Precision Test:

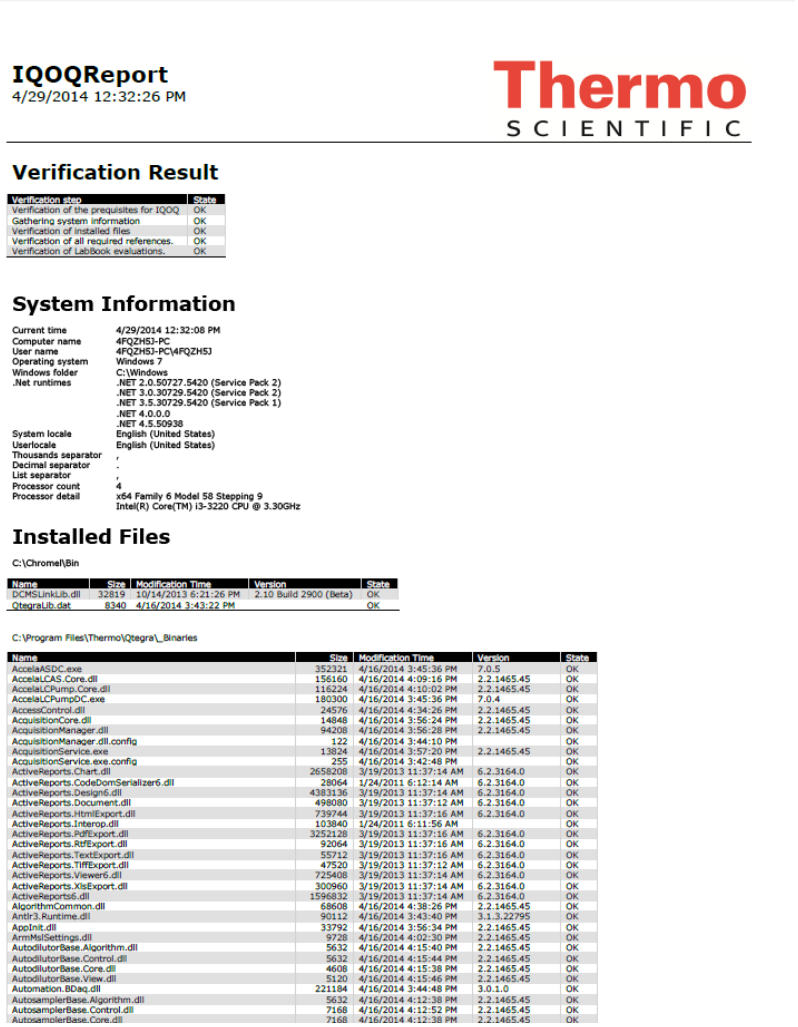
✓Results obtained by two operators are summarized in one table

✓Average value and RSD are calculated

✓Every individual LabBook as datasource can be indentified and history can be displayed

Qtegra ISDS: IQ/OQ





IQOQReport
4/29/2014 12:32:26 PM

Thermo SCIENTIFIC

Verification Result

Verification step	State
Verification of the prequisites for IQOQ	OK
Gathering system information	OK
Verification of installed files	OK
Verification of all required references.	OK
Verification of LabBook evaluations.	OK

System Information

Current time	4/29/2014 12:32:08 PM
Computer name	4FQZH5J-PC
User name	4FQZH5J-PC\4FQZH5J
Operating system	Windows 7
Windows folder	C:\Windows
.Net runtimes	.NET 2.0.50727.5420 (Service Pack 2) .NET 3.0.30729.5420 (Service Pack 2) .NET 3.5.30729.5420 (Service Pack 1) .NET 4.0.0.0 .NET 4.5.50938
System locale	English (United States)
Userlocale	English (United States)
Thousands separator	,
Decimal separator	.
List separator	,
Processor count	4
Processor detail	x64 Family 6 Model 58 Stepping 9 Intel(R) Core(TM) i3-3220 CPU @ 3.30GHz

Installed Files

C:\Chromel\Bin

Name	Size	Modification Time	Version	State
DCMSLinkLib.dll	32819	10/14/2013 6:21:26 PM	2.10 Build 2900 (Beta)	OK
QtegraLib.dat	8340	4/16/2014 3:43:22 PM		OK

C:\Program Files\Thermo\Qtegra_Binaries

Name	Size	Modification Time	Version	State
AccelaASDC.exe	352321	4/16/2014 3:45:36 PM	7.0.5	OK
AccelaLCAS.Core.dll	156160	4/16/2014 4:09:16 PM	2.2.1465.45	OK
AccelaLCPump.Core.dll	116224	4/16/2014 4:10:02 PM	2.2.1465.45	OK
AccelaLCPumpDC.exe	180300	4/16/2014 3:45:36 PM	7.0.4	OK
AccessControl.dll	24576	4/16/2014 4:34:26 PM	2.2.1465.45	OK
AcquisitionCore.dll	14848	4/16/2014 3:56:24 PM	2.2.1465.45	OK
AcquisitionManager.dll	94208	4/16/2014 3:56:28 PM	2.2.1465.45	OK
AcquisitionManager.dll.config	122	4/16/2014 3:44:10 PM		OK
AcquisitionService.exe	13824	4/16/2014 3:57:20 PM	2.2.1465.45	OK
AcquisitionService.exe.config	255	4/16/2014 3:42:48 PM		OK
ActiveReports.Chart.dll	2658208	3/19/2013 11:37:14 AM	6.2.3164.0	OK
ActiveReports.CodeDomSerializer6.dll	28064	1/24/2011 6:12:14 AM	6.2.3164.0	OK
ActiveReports.Design6.dll	4383136	3/19/2013 11:37:14 AM	6.2.3164.0	OK
ActiveReports.Document.dll	498080	3/19/2013 11:37:12 AM	6.2.3164.0	OK
ActiveReports.HtmlExport.dll	739744	3/19/2013 11:37:16 AM	6.2.3164.0	OK
ActiveReports.Interop.dll	103840	1/24/2011 6:11:56 AM		OK
ActiveReports.PdfExport.dll	3252128	3/19/2013 11:37:16 AM	6.2.3164.0	OK
ActiveReports.RtfExport.dll	92064	3/19/2013 11:37:16 AM	6.2.3164.0	OK
ActiveReports.TextExport.dll	55712	3/19/2013 11:37:16 AM	6.2.3164.0	OK
ActiveReports.TiffExport.dll	47520	3/19/2013 11:37:12 AM	6.2.3164.0	OK
ActiveReports.Viewer6.dll	725408	3/19/2013 11:37:14 AM	6.2.3164.0	OK
ActiveReports.XlsExport.dll	300960	3/19/2013 11:37:14 AM	6.2.3164.0	OK
ActiveReports6.dll	1596832	3/19/2013 11:37:14 AM	6.2.3164.0	OK
AlgorithmCommon.dll	68608	4/16/2014 4:38:26 PM	2.2.1465.45	OK
Antlr3.Runtime.dll	90112	4/16/2014 3:43:40 PM	3.1.3.22795	OK
AppInit.dll	33792	4/16/2014 3:56:34 PM	2.2.1465.45	OK
ArmMsiSettings.dll	9728	4/16/2014 4:02:30 PM	2.2.1465.45	OK
AutodilutorBase.Algorithm.dll	5632	4/16/2014 4:15:40 PM	2.2.1465.45	OK
AutodilutorBase.Control.dll	5632	4/16/2014 4:15:44 PM	2.2.1465.45	OK
AutodilutorBase.Core.dll	4608	4/16/2014 4:15:38 PM	2.2.1465.45	OK
AutodilutorBase.View.dll	5120	4/16/2014 4:15:46 PM	2.2.1465.45	OK
Automation.BDaq.dll	221184	4/16/2014 3:44:48 PM	3.0.1.0	OK
AutosamplerBase.Algorithm.dll	5632	4/16/2014 4:12:38 PM	2.2.1465.45	OK
AutosamplerBase.Control.dll	7168	4/16/2014 4:12:52 PM	2.2.1465.45	OK
AutosamplerBase.Core.dll	7168	4/16/2014 4:12:38 PM	2.2.1465.45	OK

- ✓Verification of all installed files
- ✓Checksums to verify consistency
- ✓Verification of data evaluation algorithms
- ✓Executable whenever required

ThermoFisher SCIENTIFIC

Comparison ICP-OES – ICP-MS

Technology		
	ICP-OES	**ICP-MS**
Detection Power (USP)	+	+++
Dynamic Range	++	+++
Speciation Capabilities	+	+++
Lab Requirements	+++	+++
Operating Cost	++	++
Software	+++	+++
Investment	+++	++
Future Proof (USP)	+	+++

Implementing ICP-OES or ICP-MS for USP compliance can be pain free

- ICP-OES and ICP-MS provide multi-elemental determination of heavy metal impurities below the limits listed in USP <232>
- Recent developments have simplified user experience, increased throughput speed and reduced maintenance
- Software advances offer intuitive method development and ensure 21CFR part 11 compliance