Quality Assurance Panel

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QA vs QC: American Society for Quality Definitions

- **Quality assurance** consists of that "part of *quality management* focused on providing confidence that *quality requirements* will be fulfilled." The confidence provided by quality assurance is twofold—internally to management and externally to customers, government agencies, regulators, certifiers, and third parties.
- **Quality control** is that "part of *quality management* focused on fulfilling *quality requirements*."

http://asq.org/learn-about-quality/quality-assurance-quality-control/overview/overview.html

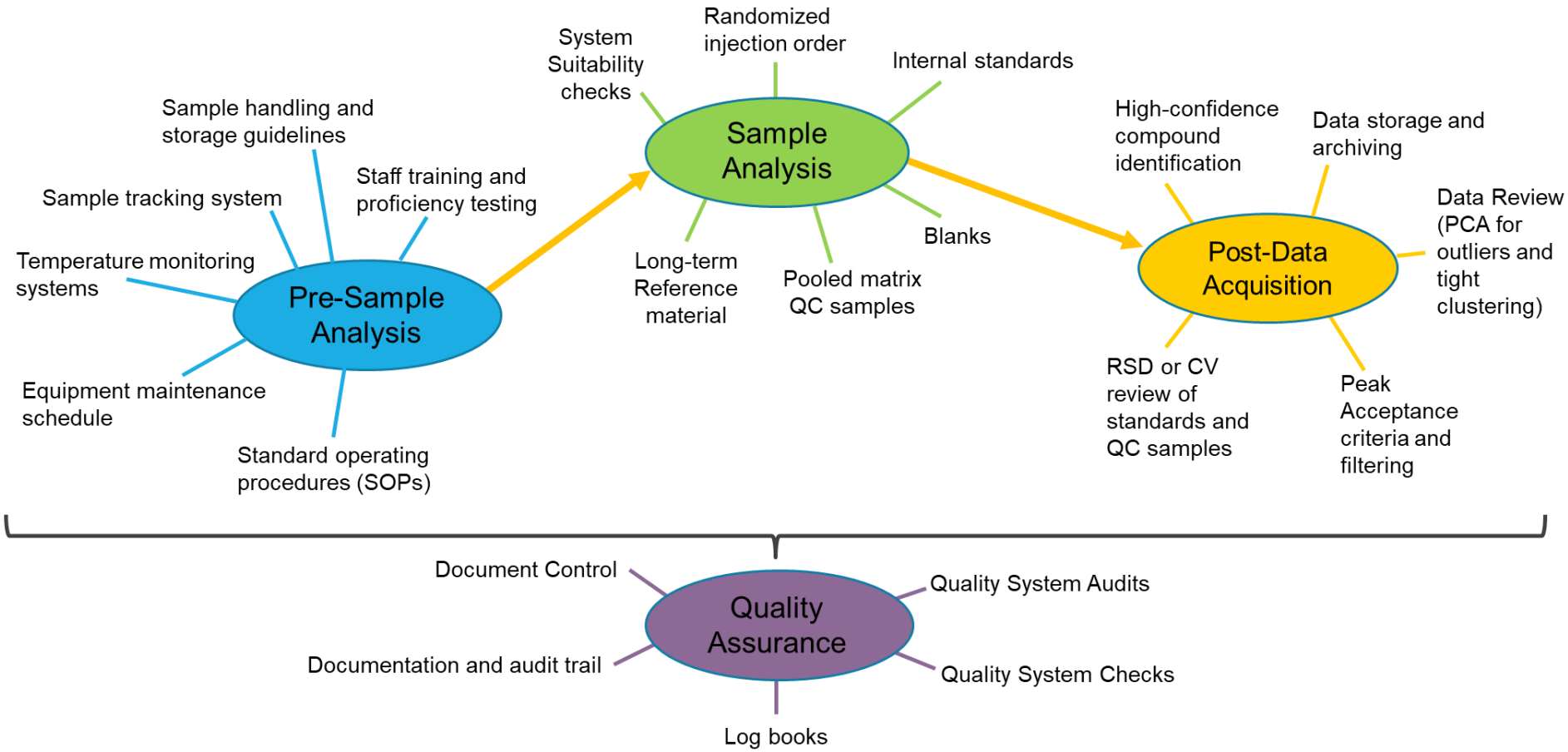
What is QA??

Parameters	Quality Assurance	Quality Control
Definition	QA is a set of activities for ensuring quality in the processes by which products are developed.	QC is a set of activities for ensuring quality in products. The activities focus on identifying defects in the actual products produced.
Focus on	QA aims to prevent defects with a focus on the process used to make the product. It is a proactive quality process.	QC aims to identify (and correct) defects in the finished product. Quality control, therefore, is a reactive process.
Goal	The goal of QA is to improve development and test processes so that defects do not arise when the product is being developed.	The goal of QC is to identify defects after a product is developed and before it's released.

QA Definition Proposed for Workshop

QA is the set of procedures that are performed in advance of analysis of samples that are used to improve data quality (e.g. education, analyst competency, method development and documentation)

Summary of QA/QC procedures



See A. Evans' **Poster:** Session 1 (Monday 5:15pm - 6:45pm) and Session 2 (Tuesday 5:15pm - 6:45pm)

Poster Group: Sample Prep and Quality **Poster Number:** 333

General Ideas

- Keep It Simple Silly – if you have nothing in place, start simply
  - Part of a quality system is to be able to trace what you are doing... if the system is too complicated or too cumbersome people will not follow it and traceability goes to zero.
  - Establish clear criteria
- Check lists are actually pretty useful. They are used in flight cockpits!
- Any person in a group can operate as a QA person at any time. You don't need a dedicated QA person (though this is also an option). "Sure I can review your calculations".

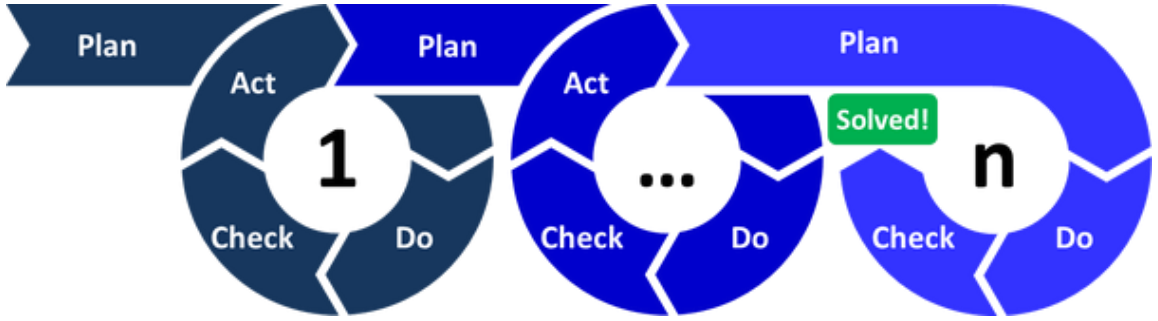
Pre-Analysis Ideas

- Training Instrument Operators
  - Weighing tests
  - Pipet tests
  - Best practices for notebooks
- Instrument Maintenance and Troubleshooting
  - Tuning and calibration
  - Column Pressure Checks
  - Acceptance criteria for benchmarking
  - Checklist – what to do if acceptance criteria are not met
- Standard Operating Procedures (SOP)
  - Maintained in a repository (i.e. needs version control)
  - Cover every step of the analytical process
  - Also for post-analytical processes (e.g. data pre-processing and calculations)

“Document, document, document …”

- Notebooks, Log Books (e.g. instrument, sample storage), Temperature Monitoring Sheets, etc.
- List of SOPs (or Method files) that each individual has signed as “read and understood”
- List of SOPs that the trainer has signed off on for each individual.
  - SOP 001. Laboratory Workflow and Documentation Procedures
  - SOP 002. Balance Calibration
  - SOP 003. Pipette Calibration
  - SOP 004. Processing Urine Samples for Untargeted Metabolomics

Documentation is more than just keeping a lab notebook!



The PDCA Cycle

https://www.allaboutlean.com/pdca/

Interlaboratory Comparison Basics

- **Interlaboratory Study (ILS)**: A study in which several laboratories measure a quantity in one or more identical portions of homogeneous, stable materials under documented conditions, the results of which are compiled into a single report

- **Protocols**
  - Minimum number of laboratories
  - Number and nature of test samples
  - Details of the analysis methods
  - Number of replicate determinations
  - Details of transport, receipt and preservation of test samples
  - Details of statistical analysis (particularly outlier removal)
  - Reporting of final results

- **Types of ILS**
  - Nomenclature of interlaboratory analytical studies, Pure & Applied Chemistry 1994;66(9):1903-1911 https://www.iupac.org/publicaGons/pac/66/9/1903/pdf/index.html
  - Review: Inter-laboratory studies in analytical chemistry, Analytica Chimica Acta 2000;423:145–165 https://doi.org/10.1016/S0003-2670(00)01115-6

Considerations for Ring Trial

- **Agreement**: Establish Agreement on the Purpose and Aims of the Ring Trail using an independent oversight committee
  - Prepare protocol that all labs will follow (e.g., receipt of samples, study goals, how to report the analytical metadata, how to report the results).
- **Samples Distribution:** Use a Central Lab to prepare masked material for distribution to all analytical laboratories to ensure all participants receive the same high quality material.
  - Analyze the biospecimens before distribution, and serially following distribution, to reveal the quality/variation of the prepared material.
  - This central lab needs to ensure that the objectives are possible, samples are uniform, viable, etc.
- **Data Analysis**: Use an independent Centralized Repository for agglomerating, analyzing, and unmasking results.
- **Information Resource**: Ensure that all information about the analytical platforms, sample preparation, and data analysis approaches used by each participating laboratory are well documented via protocols.
  - This will help unravel any differences noted between laboratories.
- **Publication:** Ensure rapid publication with lessons learned.

NIH Common Fund Ring Trial Study Design

Analytical component

- 40 masked spiked-in standards
  - drugs, chemicals, and endogenous compounds
- 5 tubes of pooled plasma with different concentrations

Aims Included: Identification of the 40 masked spike-in standards, with quantitation, or ranking

Demographics Collected
(individual data not provided to cores)

20 Males
Age (41.4 +/- 15.2 yrs, range 20-66)
BMI (28.0 +/- 4.2, range 22-36)

20 Females
Age (39.5 +/- 13.2 yrs, range 22-59)
BMI (33.8 +/- 7.9, range 19-52)

Metabolomics component

- Masked Samples
  - male (20, 5 ml)
  - female plasma (20, 5 ml)
  - pooled samples (10, 5 ml)

Paper in preparation

Aims included

- identification of the pools (to demonstrate that the pool samples were the average of the samples from which they were derived)
- Identification of the samples in each study group, and metabolite differentiators

Case Studies
QA Workshop

Annie Evans

“Keep it real”

“Approval of a data set was delayed significantly because a single person used the wrong date format when they signed off on a final report… i.e. 5/24/18 rather than May 24, 2018. Everyone had to be tracked down again and resign the final report because there was an SOP which stated ‘use this date format’.”

“Keep it real”

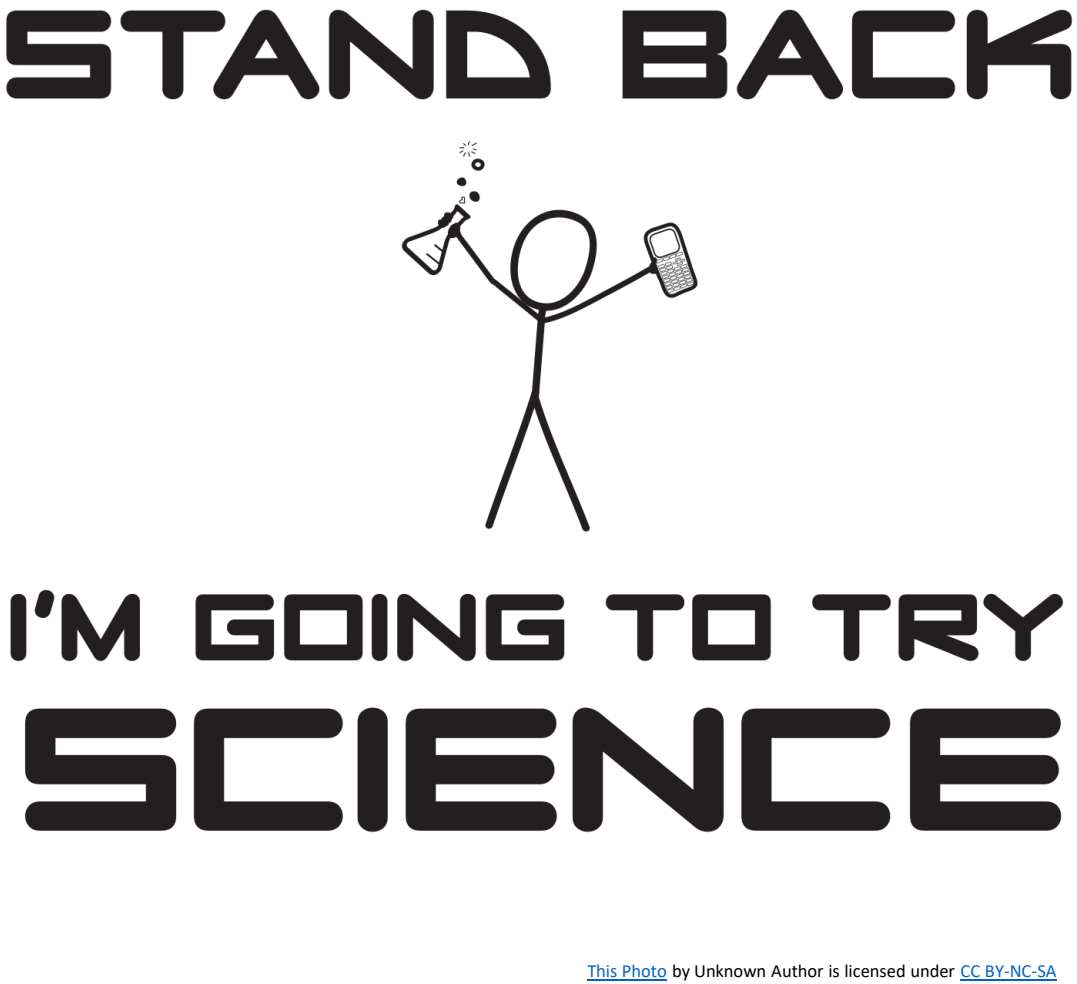
This highlights the need for …

- Distinguishing between what is and is not important
- Keeping it simple!

When starting out with a Quality System, keep it within reason and grow as people become “used to” the process and mind set.

“Sure, I can pipet”

“We noticed a small and seemingly sporadic increase in variability of technical replicates in our QC review of data. We did a little digging and it turns out all the cases of increased variability were linked to a specific person preparing the samples. Turns out the individual was never properly trained on proper use of a pipet and so was pulling varying volumes when doing volume transfers”



"Sure, I can pipet"

This highlights the need for …

- Training and continued proficiency testing
- Employee training logs

Also shows the power of good documentation as the lab was able to track the error back to a single person

“Fear the wrath”

“Analyst saw QA department as predatory…. ‘they are trying to get me in trouble by reporting my errors’. This analyst never documented their deviations from SOP, because they were afraid of being ‘dinged’.”

“Fear the wrath”

There is a helpful mindset with regard to QA and a not so helpful mindset.

- Not so helpful: THEY ARE OUT TO GET ME.. IT WILL GO ON MY RECORD…
- Not so helpful: YOU WILL BE COMPLIANT!!!!

“Fear the wrath”

This highlights the need for …

- A helpful mindset towards QA
- The need to collaborate with PIs on developing SOPs

QA may find things that will improve the process and help out with quality of data, but it is not intended to get in the way of getting science done

“Consistent but wrong”

“A team of scientists was using a standardized excel macro to do a series of calculations to determine concentration. This was great because it built consistency into the workflow and made sure the team was using the same calculations in all their different projects….but no one had double checked the macro and the macro was doing some of the calculations incorrectly.”

“Consistent but wrong”

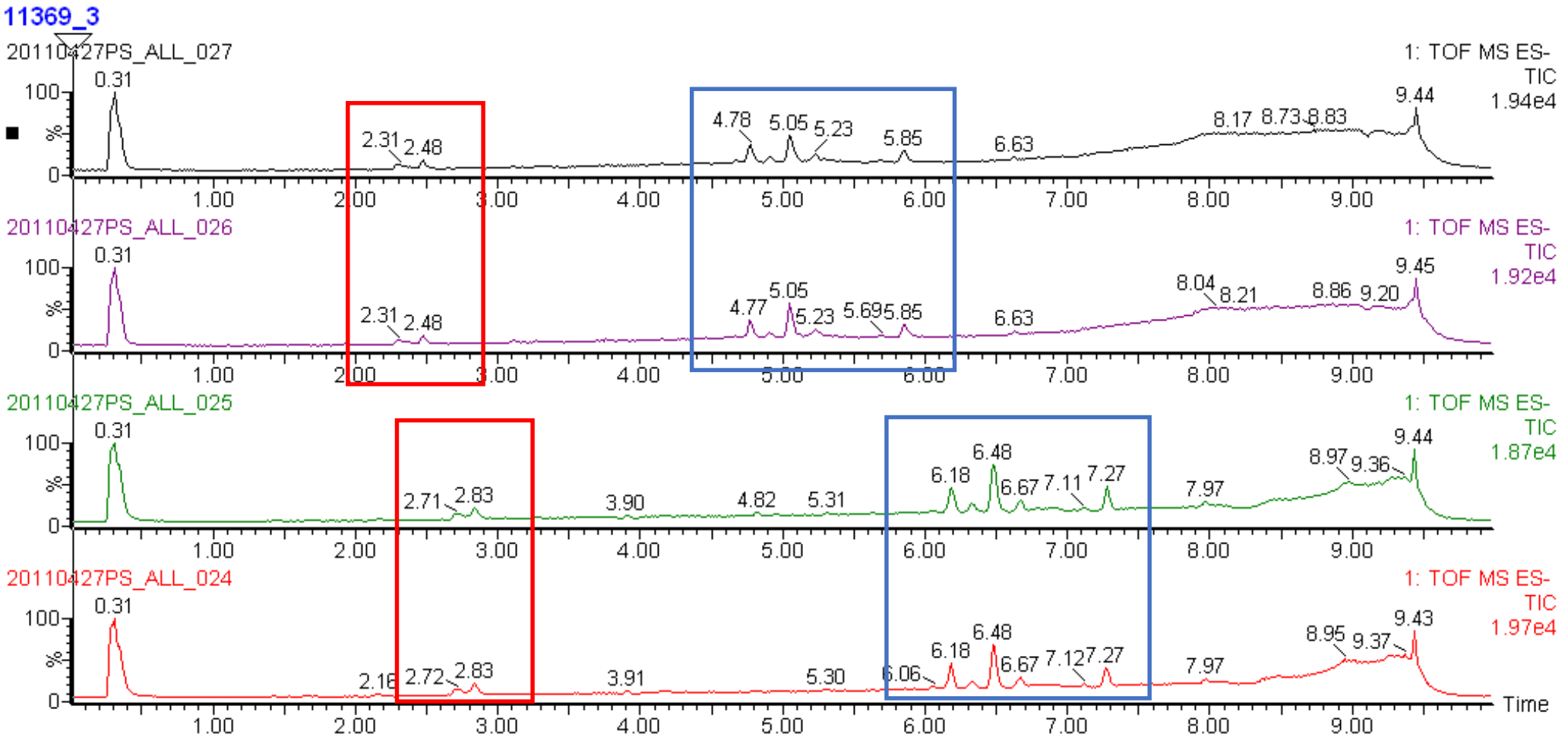
This highlights the need for …

- Properly developed SOPs that include system checks and acceptance criteria
- QA review from an outside perspective

A great mindset for a quality system, in general, is to think of it as a second set of eyes.

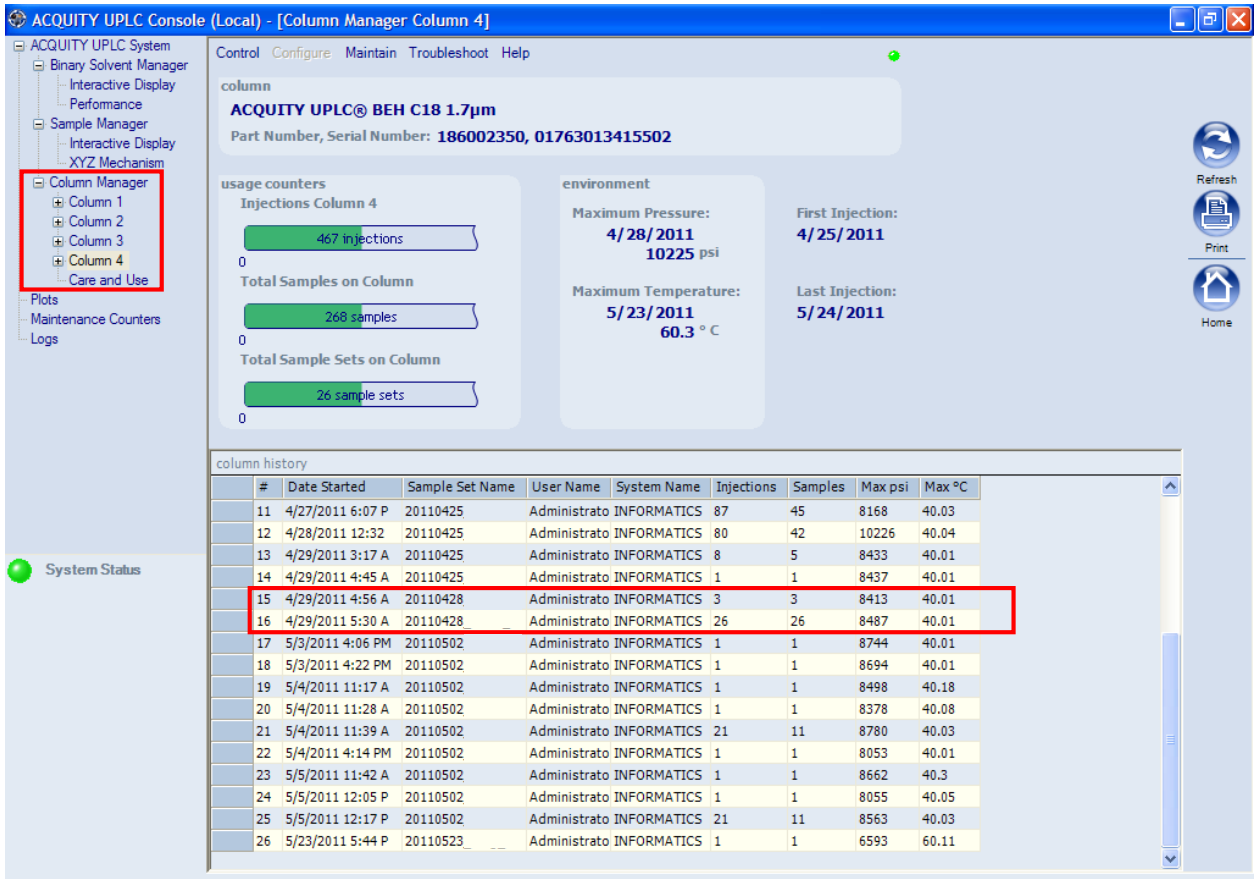
“You get what you pay for…”

“One of the first few studies we did was a large scale study of ~700 human samples trying to identify biomarker from cigarette smoking. Samples were sent to a metabolomics core facility, which hadn’t run many large scale studies. We found several issues from the data…”



Issues with the Retention Time Shift

Switching columns induced a retention time shift between samples

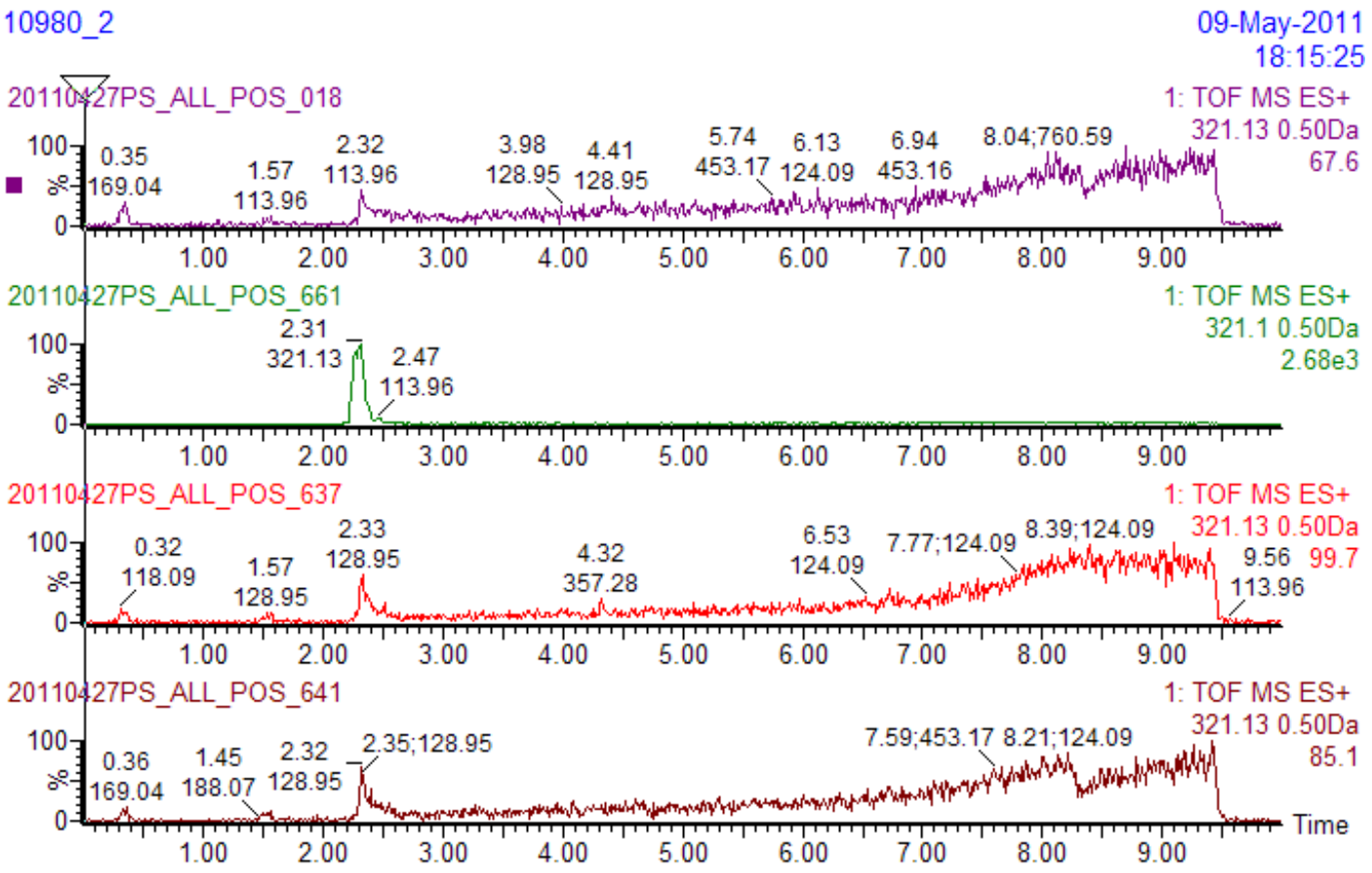


“You get what you pay for…”

This highlights the need for …

- Properly developed SOPs that include system checks and acceptance criteria
- Proper training of instrument operators

At least good documentation allowed researcher to trace problem back to bad columns



10980_1

10980_1_2freeze-thaw-cycle

10980_2

10980_3

Issues in the Freeze-Thaw cycle

First, third and fourth traces are from same sample, freshly made and run. The second is after two freeze-thaw cycles. The ion 321.13 was not found in any of the fresh made samples, but appears after two freeze-thaw cycle.

"You get what you pay for…"

This highlights the need for …

- Properly developed SOPs related to sample handling and storage
- Communication of quality procedures to clients upfront

Overall, the original data, which cost the client $15k, was unusable, and the whole project had to be re-run (at a discounted price…)