Automation in a CRO environment: the challenge to invest, implement and integrate

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12th EBF Open Symposium 2019

Types of Automation

Overview

- Liquid handlers/sample manipulators
- Black box platforms
- Software?

The big winners

- Repetition!

But not Flexibility

Courtesy of Paul Harper, AstraZeneca

Species

Mouse

Rat

Rabbit

Cat

Dog

Pig

Monkey

Human

Matrix

Plasma 77%
Serum
Urine (AAA / stabilisers)
PBMC Lysate
BALF (AM and ELF)
CSF
Bile
Whole Blood
Sputum
Various Tissues
Dialysis Fluid
Saliva
SAM strips
Faeces
VAMS
Seminal Fluid
Synovial Fluid

Anti-coag. / Stabiliser

EDTA

Heparin

EGTA

Oxalate

Citrate

Metabisulphate

Purpose

PK
PD
ADA
- Screen
- Conf
- Titre
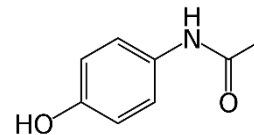- nAbs

Technology

LC-MS

LBA

- Kits?
- ELISA
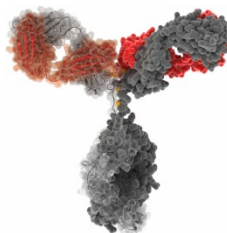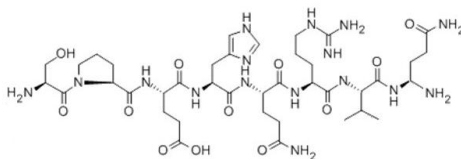- AlphaLISA
- MSD
- Gyrolab
- Luminex
- Quanterix

Flow Cytometry

Method Transfer?

LGC

3

Molecules supported

Small molecule drugs

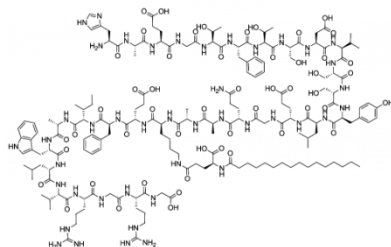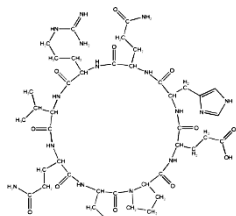**Biomarkers**
- Apolipoproteins
- Complement Proteins
- Coagulation Factors
- Growth Factors

Standard amino acid linear peptides
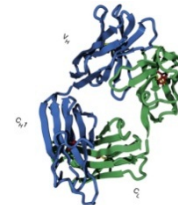
Standard mAb proteins

Partial mAb/Fusion Proteins
- FAb
- Fc

Modified peptides
- Non standard amino acid incorporation
- Palmitoylation
- Cyclic
- Pegylated
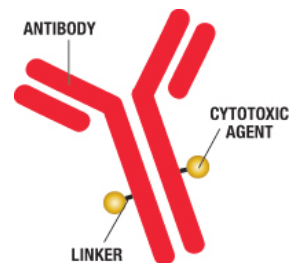
ADC
- Full mAb conjugate
- Fc conjugates

ANTIBODY

CYTOTOXIC AGENT

LINKER

Other challenges

Different Tube types

& Reduced time to plan

- CRO Logistics/Liaising with Central Lab
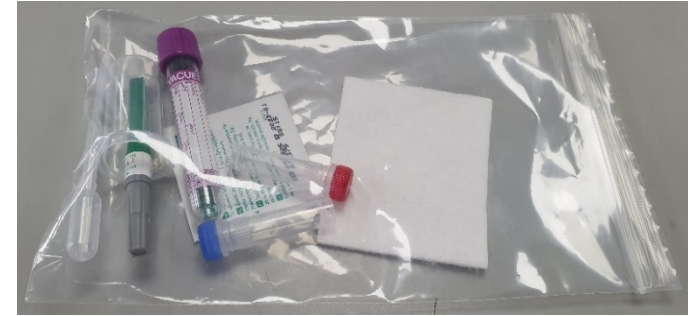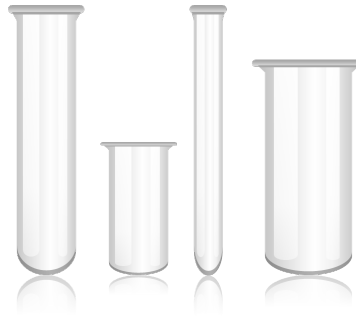
Cost of re-aliquoting & F/T

- ASM

Barcode based workflow?

Sample volume

- ↑ dead vol.

A balancing act

Total Process Automation?

A mixture of study sizes

Small <500 samples

Mid 500-2000 samples

Large 2000+

Mid-Sized Study

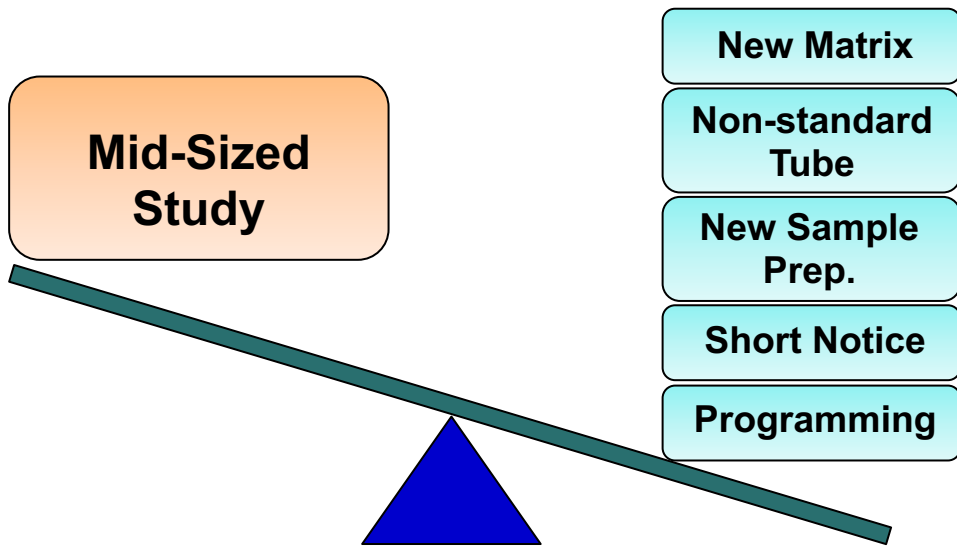| New Matrix |
| Non-standard Tube |
| New Sample Prep. |
| Short Notice |
| Programming |

Forcing flexibility can impact robustness

Total process automation is only as strong as the weakest link

- Broken component = loss of the whole system?

Islands of Automation

Refined Technology that automates a step in the process

- Simpler programming

- Lower cost

- Reduction not replacement

- Less notice required

1° Pipetting

Bead-based manipulation

SPE/ SLE

Dilution/ Plate stamping

Workflow 1 | **Workflow 2** | **Workflow 3**

LC-MS and LBA

Platform Expertise > Assay Expertise

8 opposable thumbs not 2

Simpler from a 21 CFR Pt11 point of view

What is new? Software

LGC

Traditionally

> Low Flexibility = simple software
> High Flexibility = complex software

We want flexibility but….

Complex software is a challenge to implementation and integration

> Changing?

Dedicated automation scientists/engineers

Data Integrity (21 CFR Pt 11 Compliance)

Application of ALCOA principles

> Admin & user roles
> Detailed audit trail
> Database records that enable file archiving
> Or automated file outputs into protected folders

However, "write once, read only" can hamper functionality

CSV Team involvement from the start

Black Box Technology

LC-MS – (Cascadian/CLAM) Unmet need for Bioanalysis?

LBA -Drivers – Lock down liquid handling

Challenges to invest

- 21CFR Part 11 compliant?

- Robustness vs redundancy

- Location of engineers

Moravec's Paradox (1988)

"It is easy to make computers exhibit adult level performance on intelligence tests or playing checkers,

And difficult or impossible to give them the skills of a one-year-old when it comes to perception and mobility"
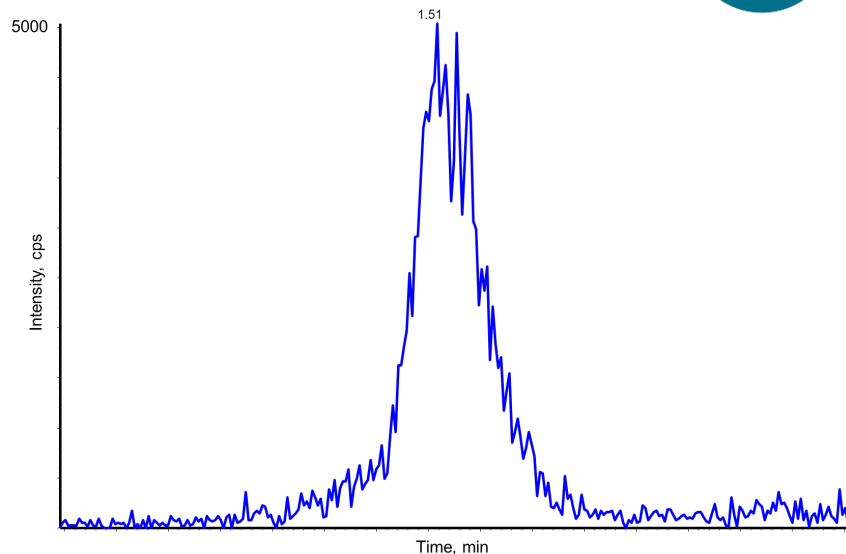
Chromatographic Peak Processing
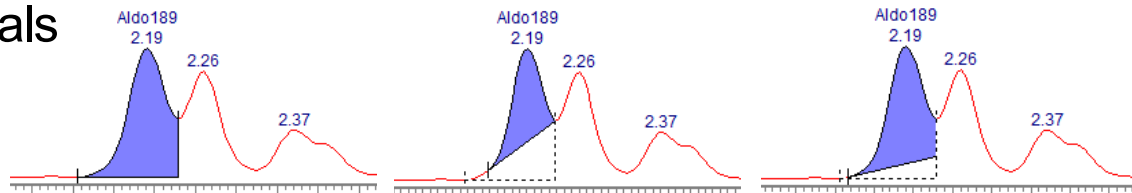
The problem?

Real-world chromatography is complex & data systems sometimes cannot find the right peak.

- Smooth the raw data correctly
- Determine the start and end of the peak
- Determine where the baseline is
- Peak area in the case of co-elution
- Handle deviations in RT and Peak shape

Consistency between individuals

Peak blindness

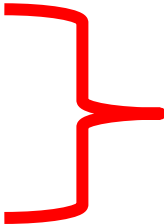# Algorithm to look at the data – not draw lines between dots for a human…

In-house vs **Off the Shelf**

- Dynamic Data Interrogation
  - > Statistical Algorithm driven
  - > Modelling approach
  - > RT derived by equation
  - > Global chromatographic baselines
    - Peak Distortion
    - Saturation/Ion Suppression
    - Peak overlap and co-elution
  - > Better than human eye?

- Vendor Independent?

- Automated rules (e.g. peak integration, peak scoring and IS mapping)

- Manual exception review
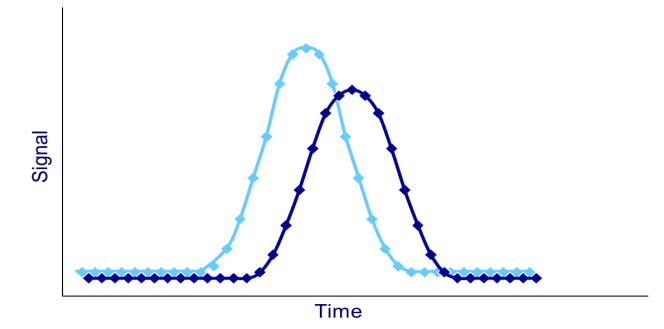
Barriers (real and perceived)

- **Price**

- **Cloud Based**

- **Hosted Software as Service**

- **Subscription Model**

- **Target Market?**

- **Out of control?**
  - > Due diligence
  - > Contracts on ownership of data
  - > Change management
  - > QA unit audits

Automation in a CRO - Invest, implement and integrate?

Cost savings & higher throughput are off-set against:

- Variability of matrix (+ tubes), technology and study type
- Reduced time to plan
- Method Transfers

What do we look for?

- Return on investment
- 21 CFR Pt 11 compliance
- Flexibility
- Robustness or redundancy
- Closely located engineers

What are the barriers?

- Priority?
- Factor in cost of CSV team and delay to installation
  - Get CSV team to speak to vendors first

Questions?

Science
for a safer world

LGC