

Ensuring sample quality in UK Biobank

Sharing Human Tissue Meeting
15.IX.10



UK Biobank – simultaneous engineering

Research/
design

Production/operations
development

Manufacture
/operate

Facilities design
and commissioning

Process development
Technology design and integration
Systems development



Scientific testing – extensive pilots

PROJECT

OPERATION

Sample processing at UK Biobank is centralised and high throughput

Central

- Increased quality and consistency in processing and processes
- Increased achievable throughput
- Robust data trail
- Cost

- Delay in processing may result in loss of labile species
- Increased shipping costs

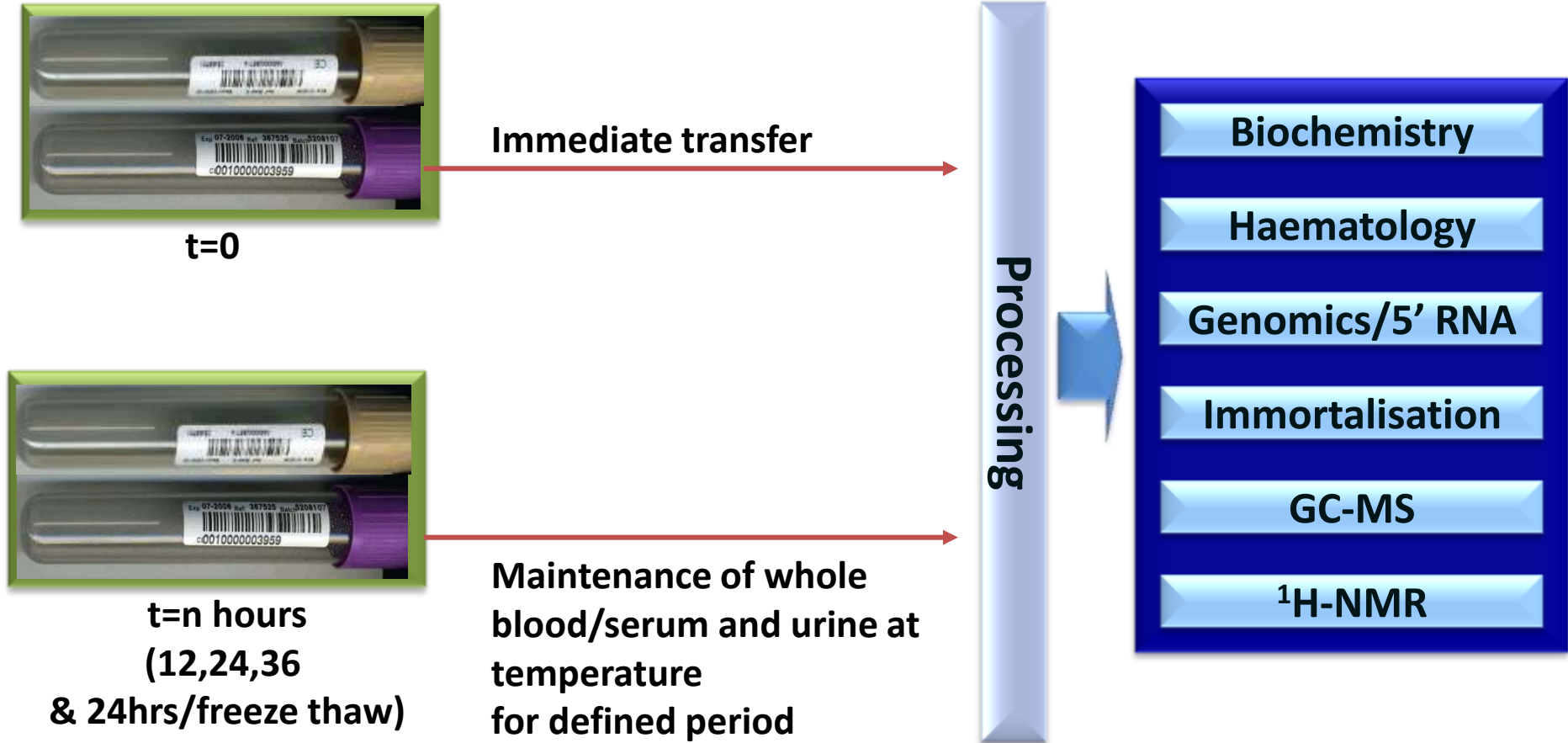
Avoid random, centre specific, non-detectable error

Local

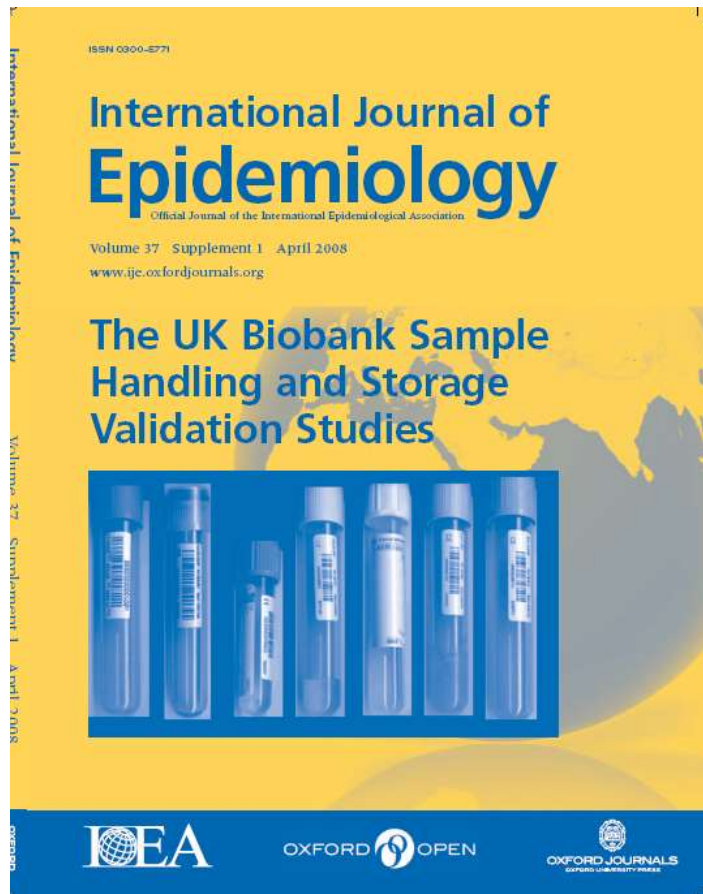
- Processing is as rapid as is achievable – preservation of most species

- QA/QC from manual processing at high throughput
- Robustness of data trail
- Risk to locally stored samples
- Regulatory issues of local storage
- Cost – staff and hardware
- Impact of freeze thaw if samples are not processed

Sample handling pilot – demonstrating fit for purpose



The validation studies have informed laboratory targets



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Design and implementation of a high-throughput biological sample processing facility using modern manufacturing principles

Paul Downey* and Tim C Peakman

Accepted 10 December 2007

Background UK Biobank is a prospective study that is collecting biological samples and health and lifestyle data from 500 000 volunteer

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Designing and implementing a large-scale automated -80°C archive

Justin M Owen* and Peter Woods

Accepted 10 December 2007

Background This article describes an automated facility for storing biological samples at -80°C , designed to meet the needs of The UK Biobank. No store of this size has previously used liquid nitrogen as refrigerant, and so it was important to confirm the storage compartments could achieve and maintain uniform conditions

...and the sample collection protocol

K₂EDTA

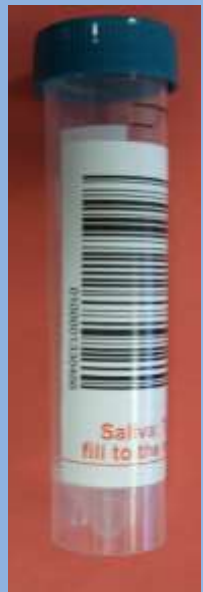
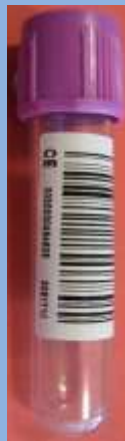
Silica

Li/Hep

Acid citrate
dextrose

K₂EDTA

Tempus
tube



4°C Transport

18°C Transport

4°C Transport

Plasma, Buffy
coat,
Red cells

Serum

Plasma

PBLs

Haematology

Urine
analytes

RNA

Saliva

...and stored in ultra-low temperature archives



UK Biobank – aims and methods



**700
participants
per day**



**6,300
vacutainers
per day**



**25,200 aliquots
per day**

**Reliable, cost effective, capacity
to continually process, store and
retrieve samples and data in a
form suitable for future scientific
research**



**15 million
study aliquots**



UK Biobank – implementing an industrialised approach

Understand the system and its goals and how this will deliver the organization strategy *before* investment is committed

Infrastructure

- supply chain
 - logistics
 - data

Organization

- availability of manpower
 - skill levels
- structure of the organization

Technology

- enabling technology
- technology in parallel activities
- technology equilibrium

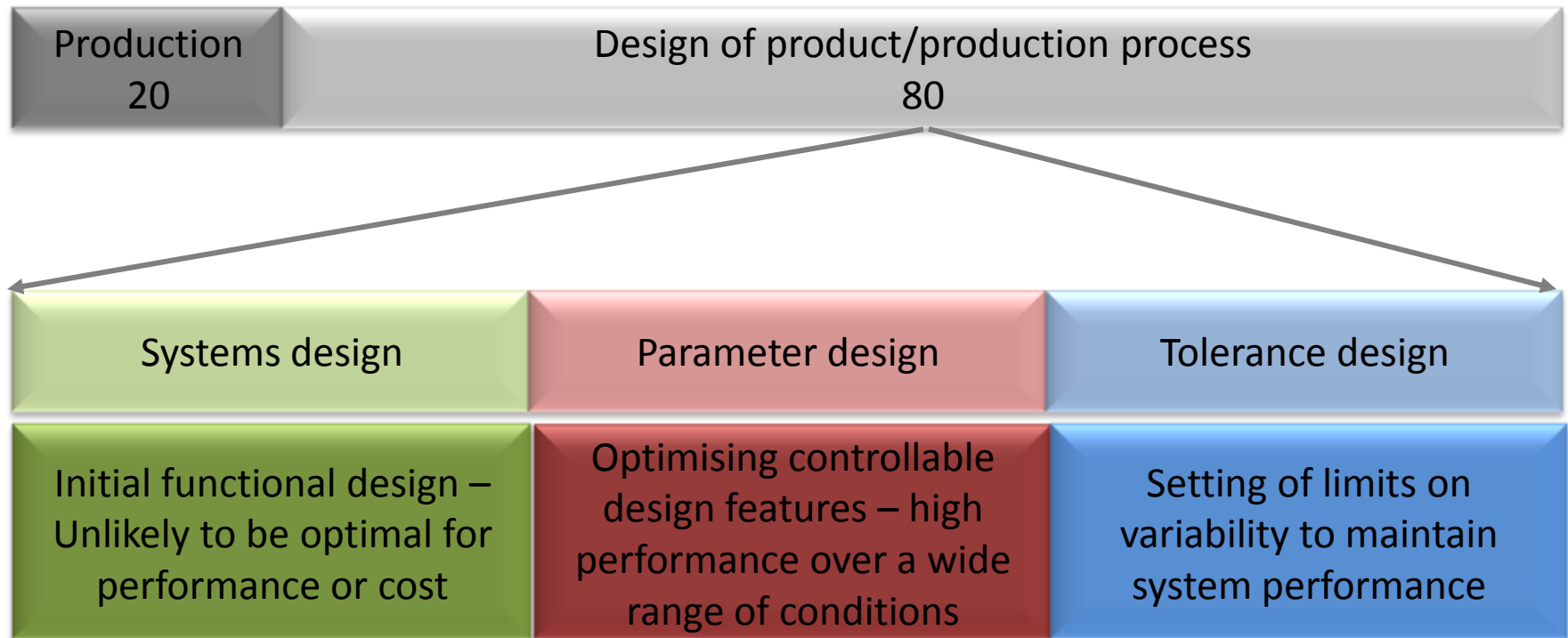
Scientific production methods

- technical specification
- planning and process description
- tolerances and standardisation

Fit for Quality (in design and operation)

Design and prototype – build in process quality

- Taguchi – Robust design
- Whole system quality and in-process control – Poke Yoke
- FMEA



Design and prototype – build in quality – Poke Yoke

- Large complex processes are prone to propagation of small errors
- Zero Quality Management - Poke Yoke

“.....mistakes will not turn into defects if worker errors are discovered and eliminated beforehand” *Shigeo Shingo*, 1986

- Contact defects
- Constant number defects
- Performance sequence defects



Design and prototype - FMEA and Taguchi in UK Biobank

Frequent change

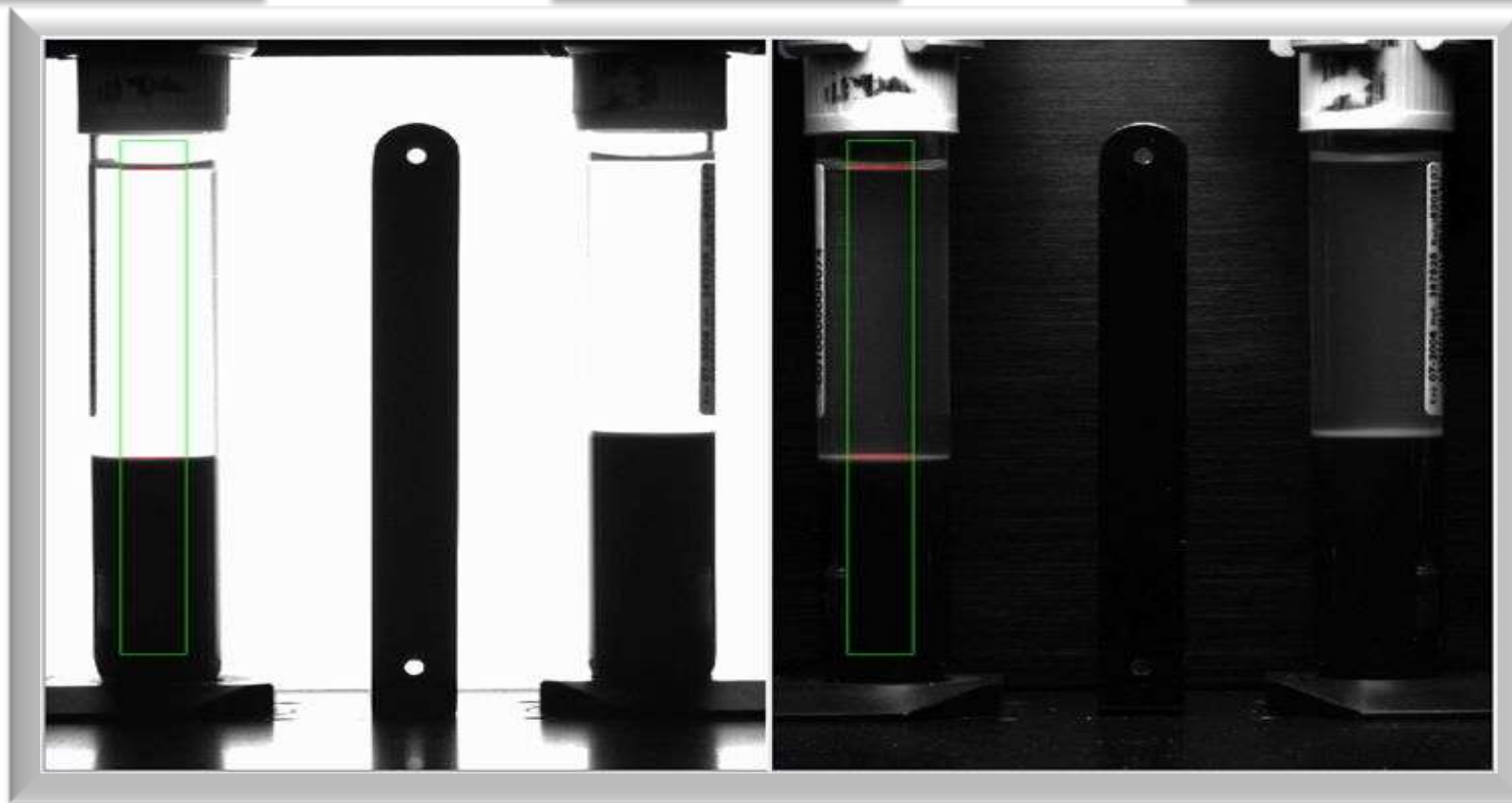
Change possible

Controlled change

Design phase

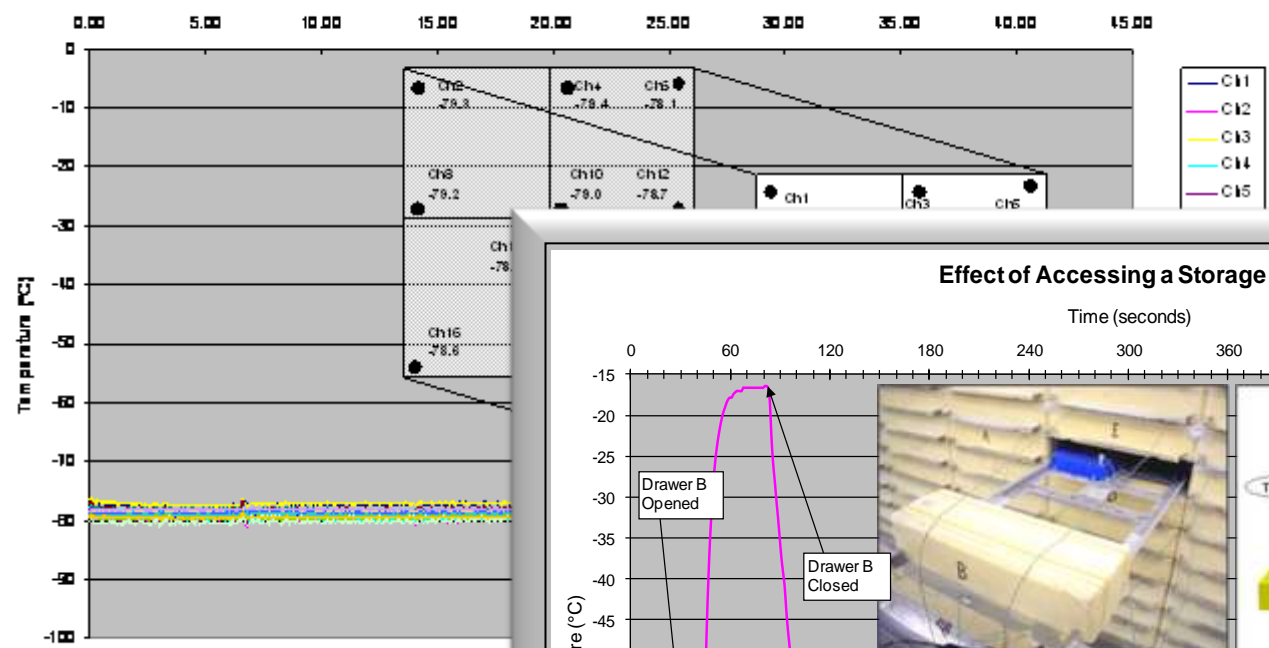
Prototyping
phase

Build and
commission



Prototyping – identify parameters that affect quality

ULTC Spatial Temperature Uniformity



Effect of Accessing a Storage Drawer

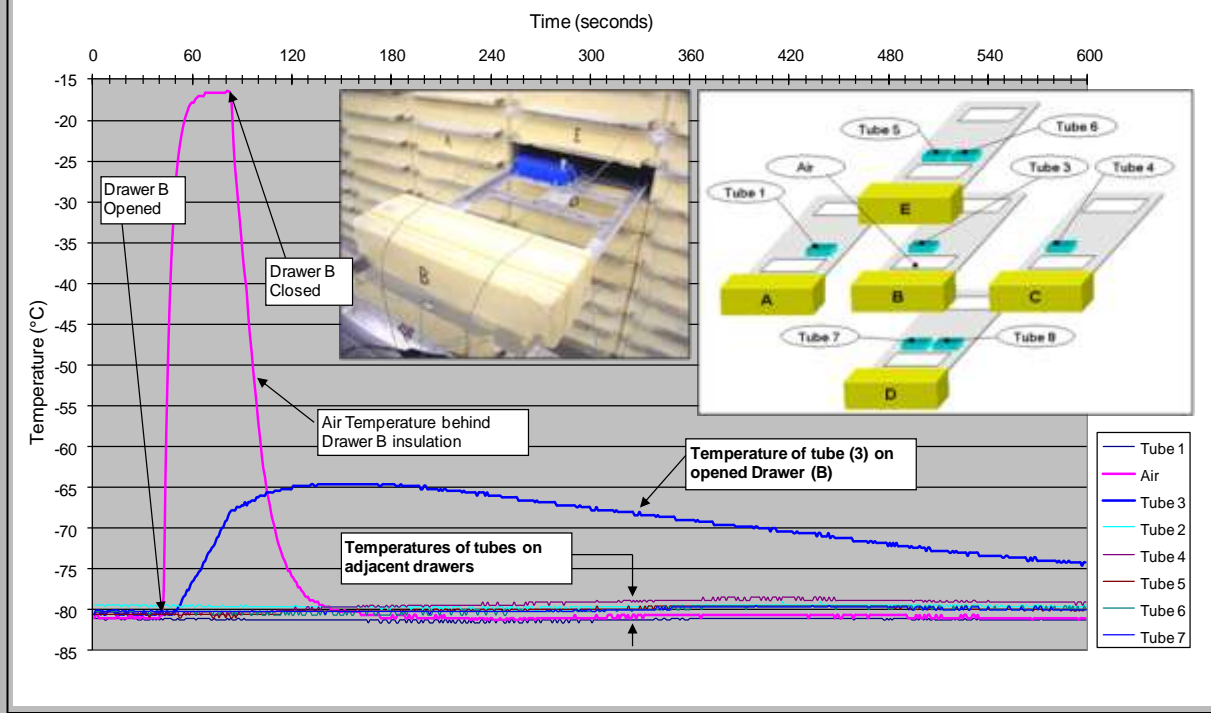
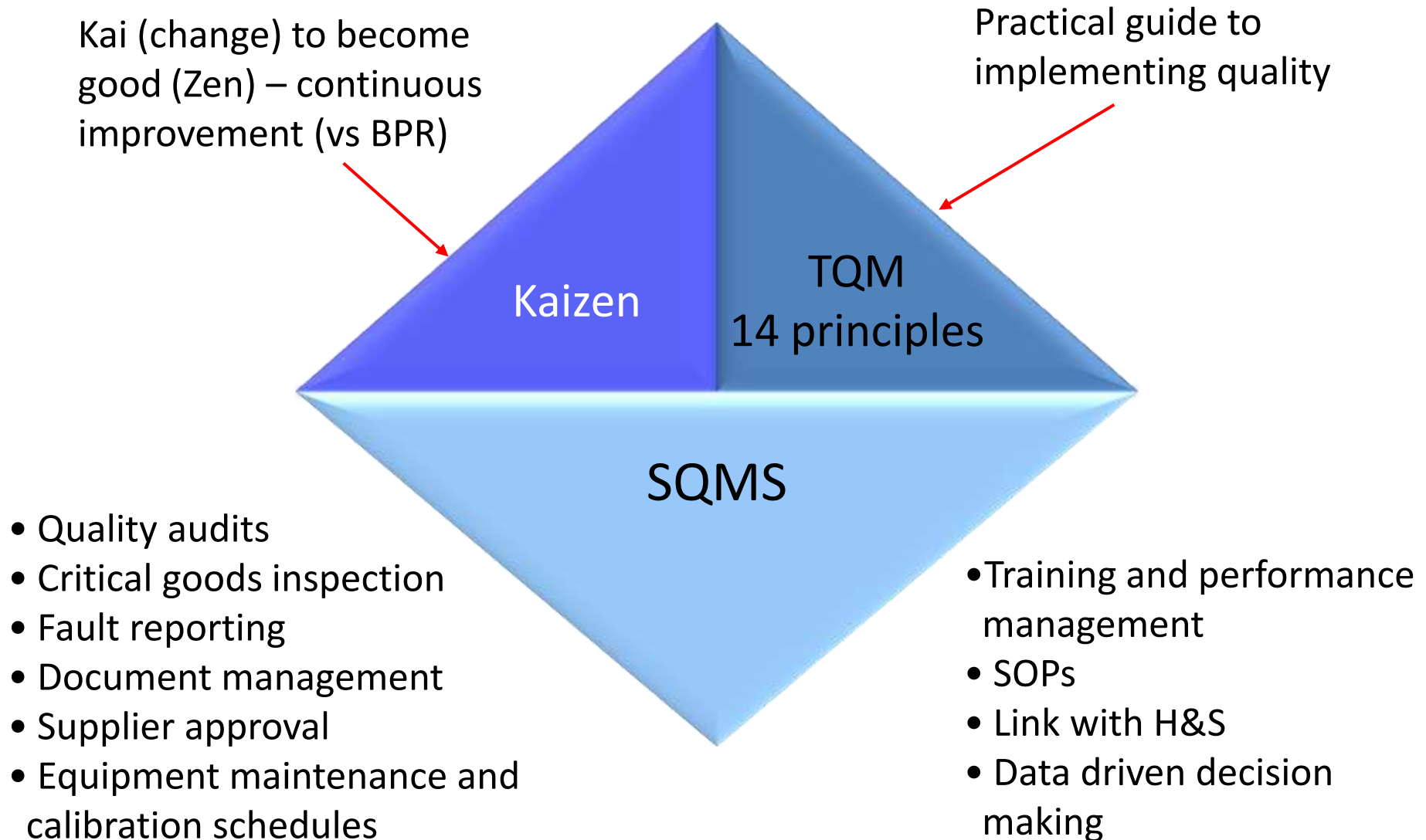


Figure courtesy of Justin Owen – The Automation Partnership

Managing quality during operation



Implementing quality management – continuous improvement through quality circles

- Simple, effective, cheap and pragmatic – the answer is not always more of something
- Listen to the staff and implement suggestions
- Understand what you are trying to achieve and measure the impact
- Be prepared to say no
 - Courier – man in a van – cost of quality
 - Early start to shifts
 - Chelation of serum and plasma
 - Ghosting of PCs
 - Continuous vs batch processing



Kaizen

Impact of SQMS quality circles on sample processing time

	EDTA 1	EDTA 1 - buffy coat	EDTA 1 - plasma	EDTA 1 - red cells	EDTA 2	EDTA 2 - buffy coat	EDTA 2 - plasma	EDTA 2 - red cells	Plasma (PST)	Serum (SST)	Urine	ACD
Average processing time (hours)	25.11	24.98	25.07	25.36	25.34	25.33	25.34	25.33	25.98	26	25.48	25.94
	24.45	24.27	24.41	24.82	24.7	24.81	24.65	24.81	24.63	24.52	24.62	24.97
Standard deviation	2.78	2.76	2.78	2.8	2.81	2.81	2.8	2.81	3.02	3.09	3.2	2.85
	2.03	1.99	2.03	2.07	2.28	2.27	2.29	2.27	1.88	1.94	2.25	1.98

Summary

- Understand the impact of your process on your samples
- Take a systems engineering approach – science leads the process
- Focus on the end product – the what, not the how
- Design fit for quality through all aspects of the study
- Build quality into the process – success by design
- Emphasise QA *and* QC
- Build a SQMS for your study and maintain it

- Support at a senior level