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England

# **Systematic comparison of the ability of commercial cleaning indicators to predict process failures.**

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## Disclaimer

**Ø Opinions expressed are those of the author and not necessarily those of Public Health England, Department of Health, National Institute of Health Research or other funding agencies.**

**Ø The Technology Development Group, develop novel technologies in the field of decontamination and applied infection control.**

**Ø The thermostable adenylate kinase technology was invented, patented and developed in the group and PHE will receive milestone and royalty payments if the tAK indicators system is commercialised.**

**Ø The Technology Development Group, Porton Down has been funded by or has provided services and advice to a number of commercial parties**

Genencor International (co-development of Prionzyme-M™), Advanced Sterilisation Products (ASP), CISA SpA, BES Decon, BiotAK, TSO<sub>3</sub>, Hygiena International, Ecolabs



# Monitoring cleaning efficacy

Why is it important to monitor cleaning efficacy ?

Tests for monitoring cleaning efficacy; qualitative and quantitative

Test models for measuring cleaning efficacy; what do they tell us about protein removal and test devices?

Enzyme indicators in a hospital trial for automated washer disinfectors



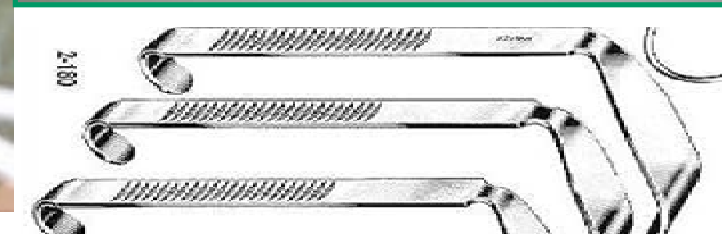
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# How do you tell if something is clean ?



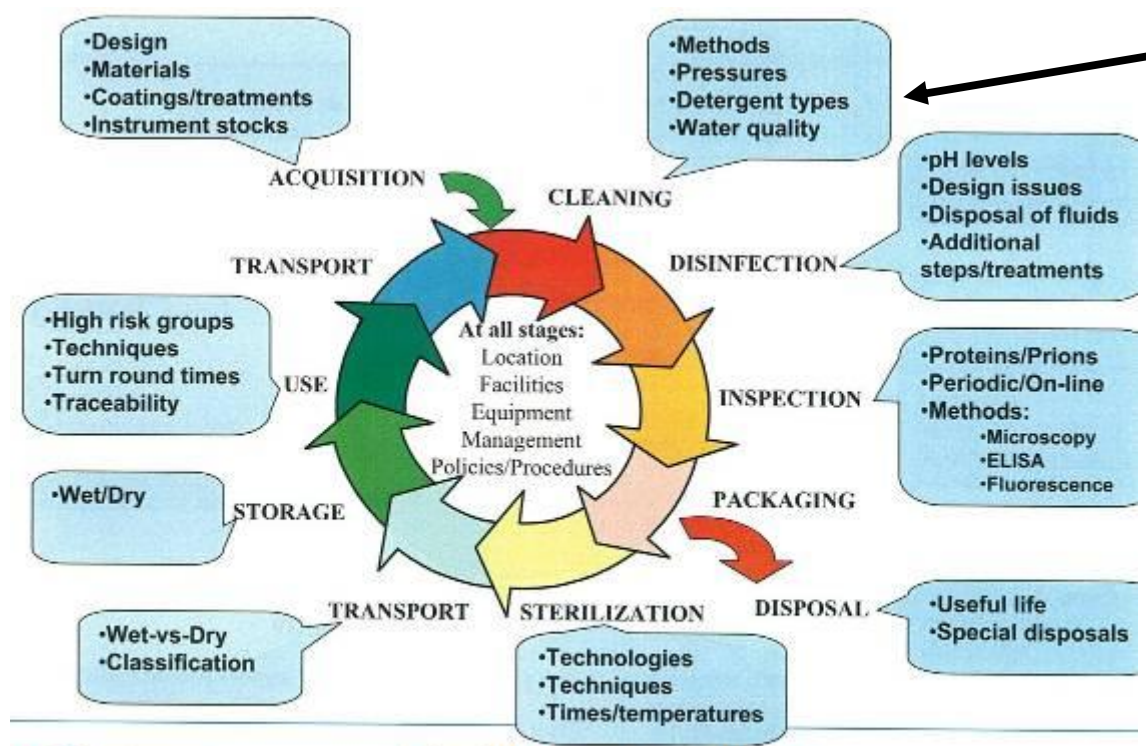


# And where it really matters !





# The life-cycle of a surgical instrument



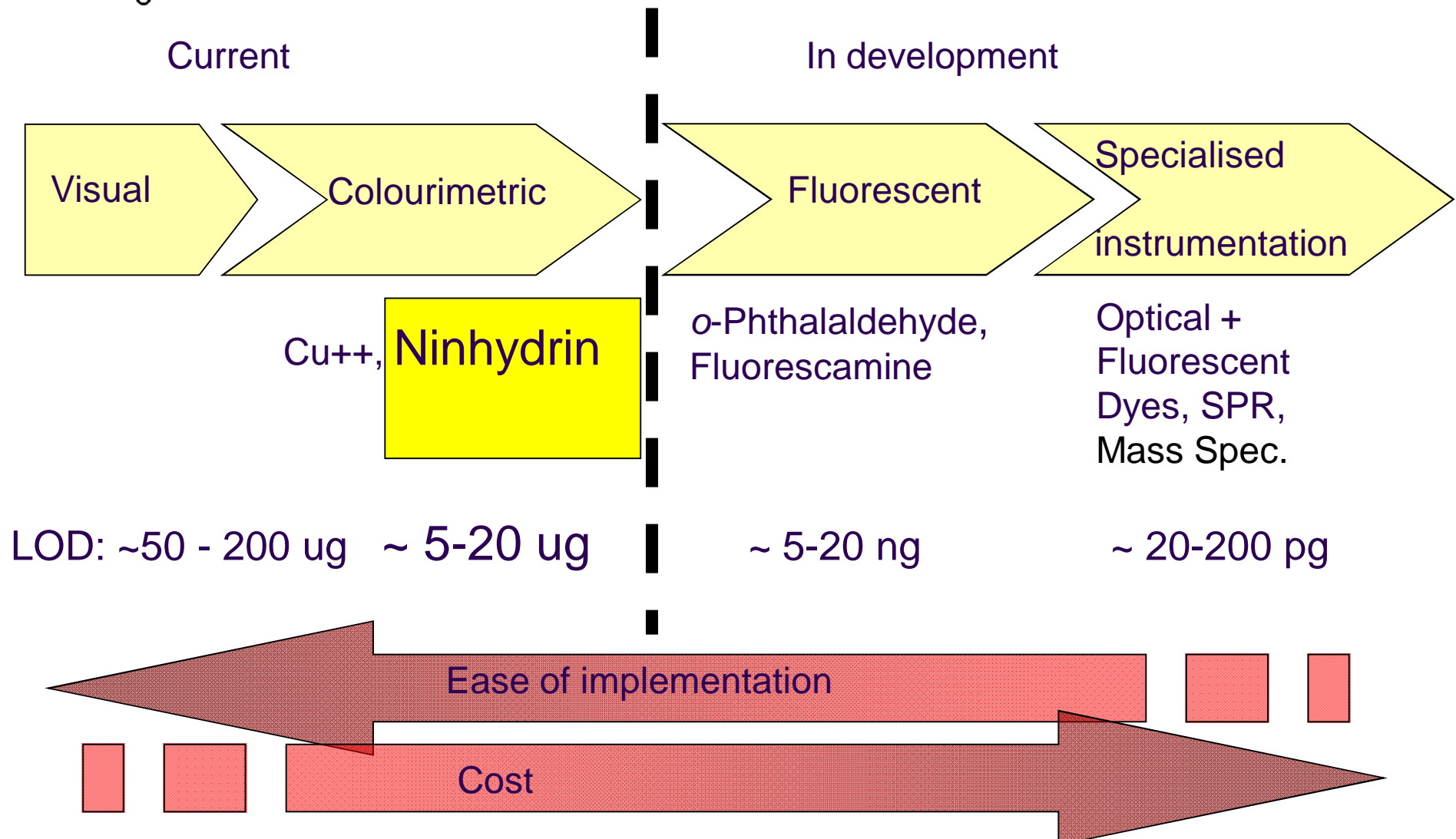
New alkaline or protease cleaning formulations; including several to control prions

Visual inspection

Assessment of protein residue (surrogate for prion removal)



# The challenge: how to quantify cleaning efficacy, sensitively and in real time ?





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# Qualitative measures for assessing process performance: wash

GKE  
level 1-4

Tosi

Valisafe

Steritec

Brownes;  
Load check

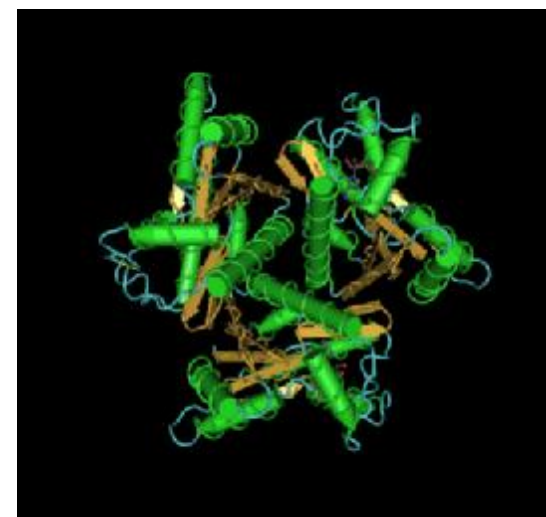
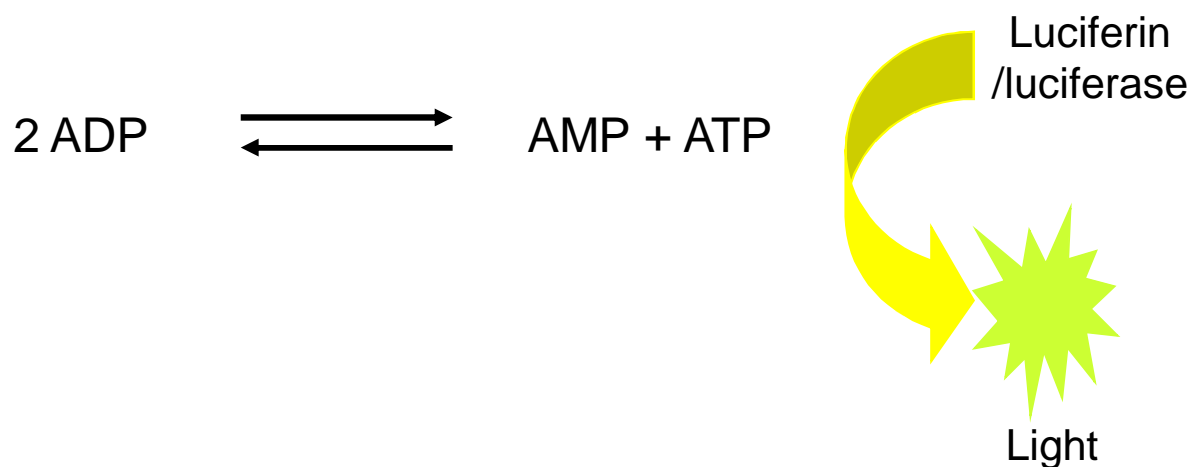






# Basis of rapid detection systems

- Ø Thermostable adenylate kinases (tAKs)
- Ø Isolated from thermophilic bacteria in volcanic springs; *Sulpholobus acidocaldarius*





## Developing a technology - fit for purpose

- Ø Projects have been carried out working closely with NHS staff
- Ø Projects funded by Department of Health (New and Emerging Applications of Technology) and NIHR (Invention for Innovation).
- Ø Carried out in collaboration with Peter Wells, Salisbury District Hospital

### Device needs to be:

Quick and easy to use

ü 2-minute assay by end user

Unambiguous

ü Quantifiable measure - “Pass/Fail”

Sensitive and specific

ü Limit of detection 30pg

Traceable

ü Download to PC to follow trends



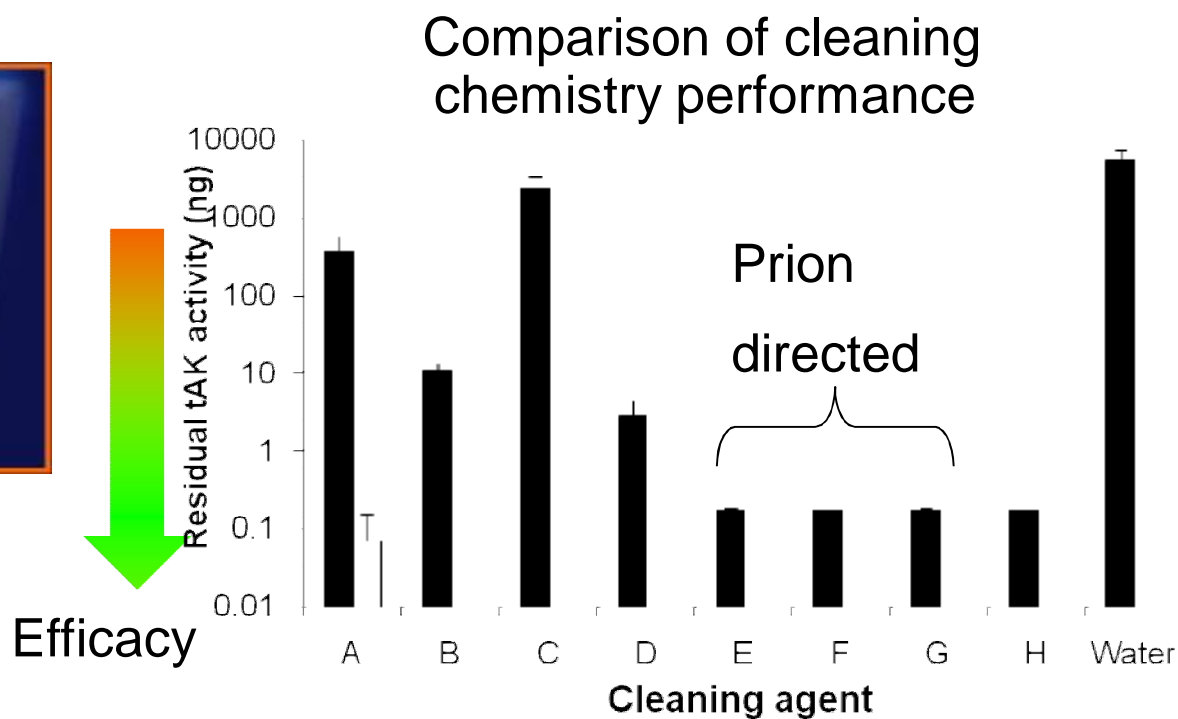
# Quantitative measurement of cleaning efficacy



- ∅ Surrogate measure of cleaning efficacy
- ∅ Test measures tAK enzyme remaining at the end of process
- ∅ Quantifiable measure of cleaning efficacy
- ∅ Various systems for measurement



# Devices used to quantitatively compare cleaning efficacy





# Setting up standardised test rigs for assessing cleaning efficacy: benchmarked against AWDs

## Standard test rig

**Time:** As required in test protocol

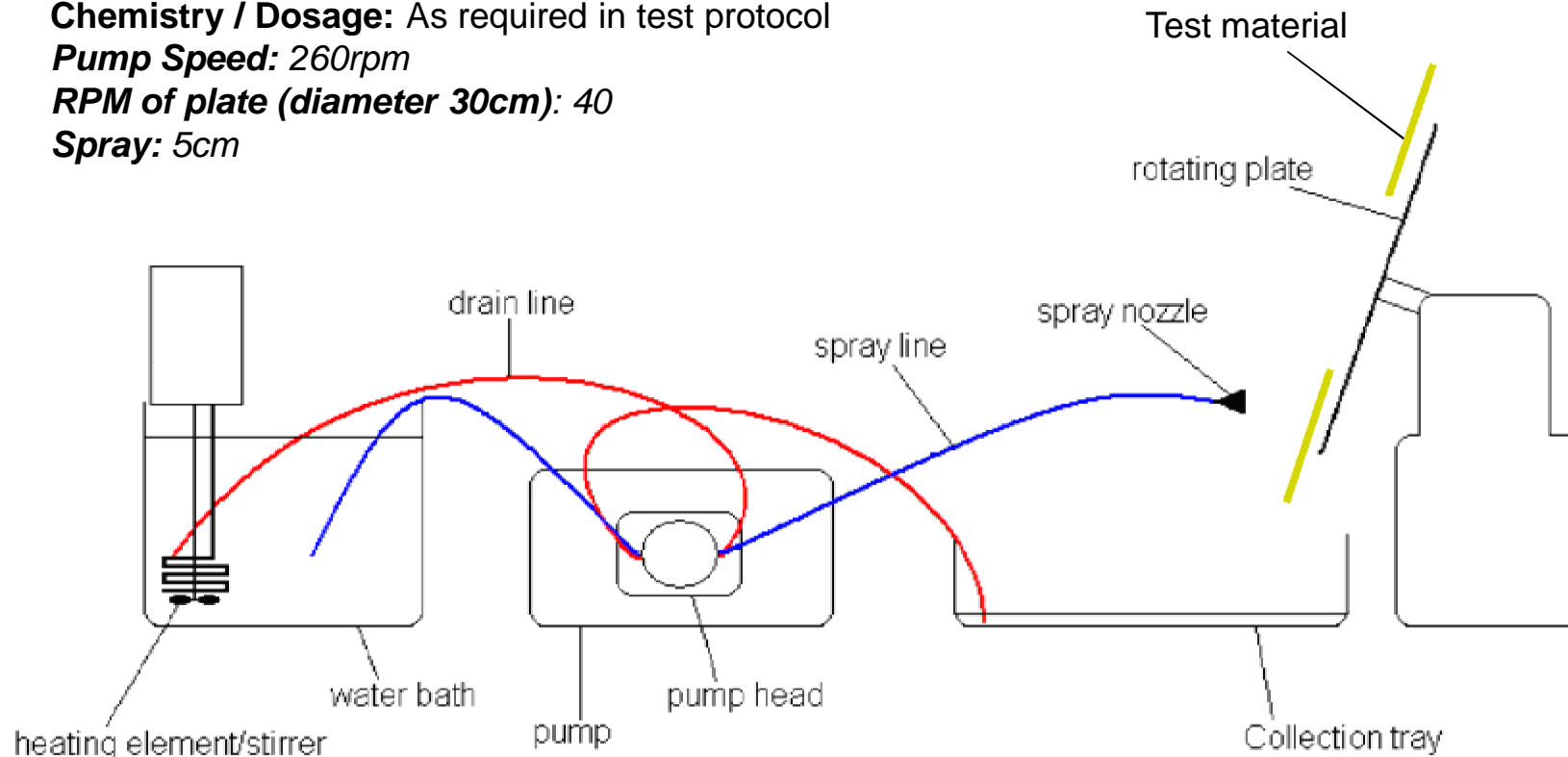
**Temperature of wash:** As required in test protocol

**Chemistry / Dosage:** As required in test protocol

**Pump Speed:** 260rpm

**RPM of plate (diameter 30cm):** 40

**Spray:** 5cm





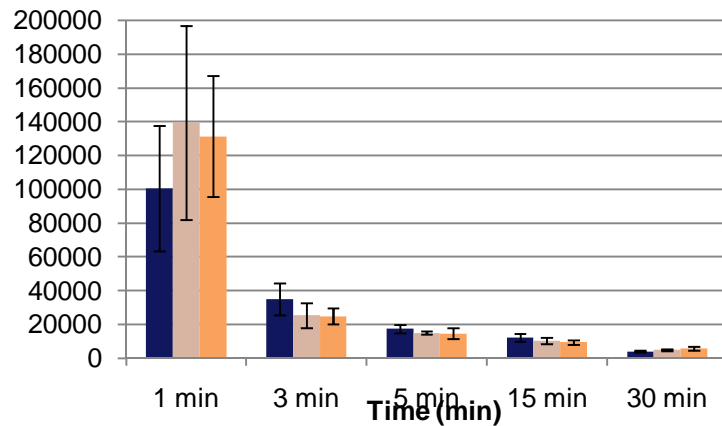
## Critical cleaning parameters: automated washer disinfectors

Test Parameter	Min - Max	Standard setting when not being varied	Number of conditions tested
Main wash time (mins)	0-30 and extended	15	6 (0,1,3,5,15,30)
Water Temp (°C)	ambient-50	40	4 (ambient (recorded),30,40,50)
Detergent Dosing (%)	0 – 150% (100% = manufacture's recommendation)	100%	7 (0,2,5,10,25,50,100,150)



# Defining critical process parameters during a wash process: time.

## Analysis of residual tAK concentration with wash time

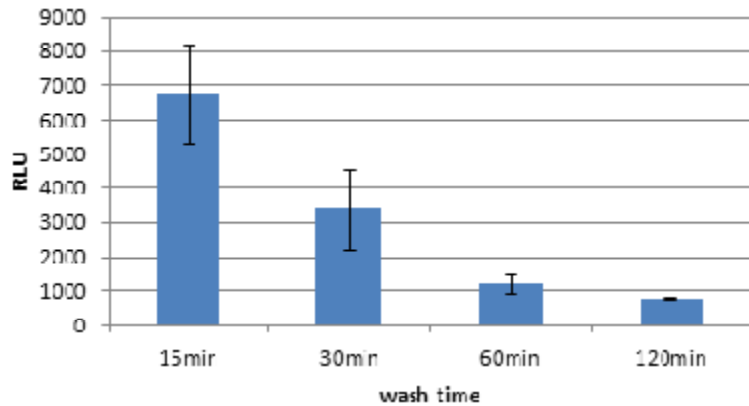


Standard wash;  
15 minutes,  
40°C  
Detergent F; 2ml/l



# Defining critical process parameters during a wash process: time.

## Analysis of residual tAK concentration with extended wash time



Standard wash;  
15 minutes,  
40°C  
Detergent F; 2ml/l

## Commercial indicators; visual scores

		1			2			3					4					
Time		1	3	5	1	3	5	1	3	5	10	15	1	3	5	10	15	30
Te	st	1	*	*	*	*	*	1	1	1	*		1	1	1	1	1	*
		2	*	*	*	*	*	1	1	1	*		1	1	1	1	1	*
Te	st	1	*	*	*	*	*	1	1	1	*	*	1	1	1	1	1	*
		2	*	*	*	*	*	1	1	1	*	*	1	1	1	1	1	*

		5						6				7						8			
Time		1	3	5	10	15	30	1	3	5	10	1	3	5	10	15	30	1	3	5	10
Te	st	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Te	st	1	1	1	*			1	1	1	1	1	1	1	1	1	*	1	1	1	1
		2	1	1	*			1	1	1	1	1	1	1	1	*	1	1	1	1	



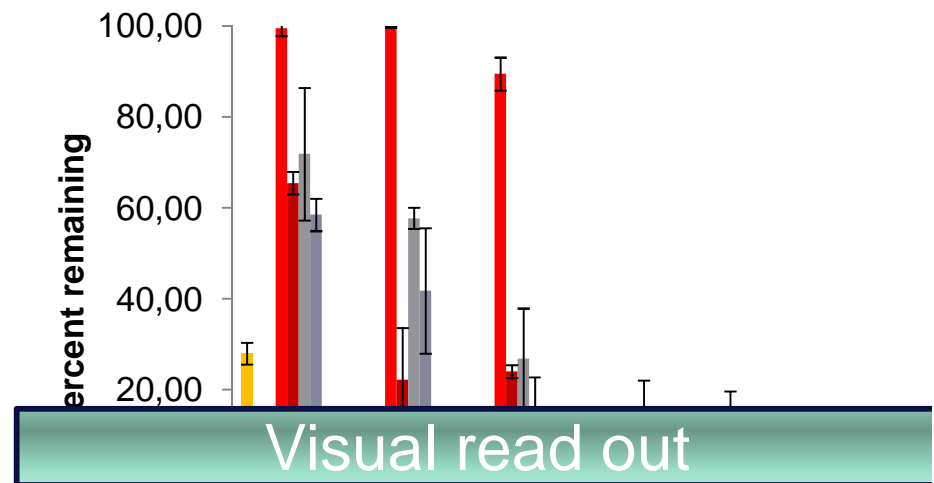


# Defining critical process parameters during a wash process: time.

## Commercial indicators; visual scores

		1			2			3					4					
Time		1	3	5	1	3	5	1	3	5	10	15	1	3	5	10	15	30
Test 1		Red	Green*	Green*	Green*	Green*	Green*	Red	Red	Red	Green*		Red	Red	Red	Red	Red	Green*
		Red	Green*	Green*	Green*	Green*	Green*	Red	Red	Red	Green*		Red	Red	Red	Red	Red	Green*
Test 2		Red	Red	Green*	Green*	Green*	Green*	Red	Red	Red	Red	Green*	Red	Red	Red	Red	Red	Green*
		Red	Red	Green*	Green*	Green*	Green*	Red	Red	Red	Red	Green*	Red	Red	Red	Red	Red	Green*

## Commercial indicators; quantification by densitometry



		5						6				7						8			
Time		1	3	5	10	15	30	1	3	5	10	1	3	5	10	15	30	1	3	5	10
Test 1		Red	Red	Red	Red	Red	Green	Red	Red	Red	Green	Red	Red	Red	Red	Red	Red	Red	Red	Red	Green
		Red	Red	Red	Red	Red	Green	Red	Red	Red	Green	Red	Red	Red	Red	Red	Red	Red	Red	Red	Green
Test 2		Red	Red	Red	Red*	Red*	Red*	Red	Red	Red	Red	Red	Red	Red	Red	Red	Red*	Red	Red	Red	Green
		Red	Red	Red	Red*	Red*	Red*	Red	Red	Red	Red	Red	Red	Red	Red	Red	Red*	Red	Red	Red	Green

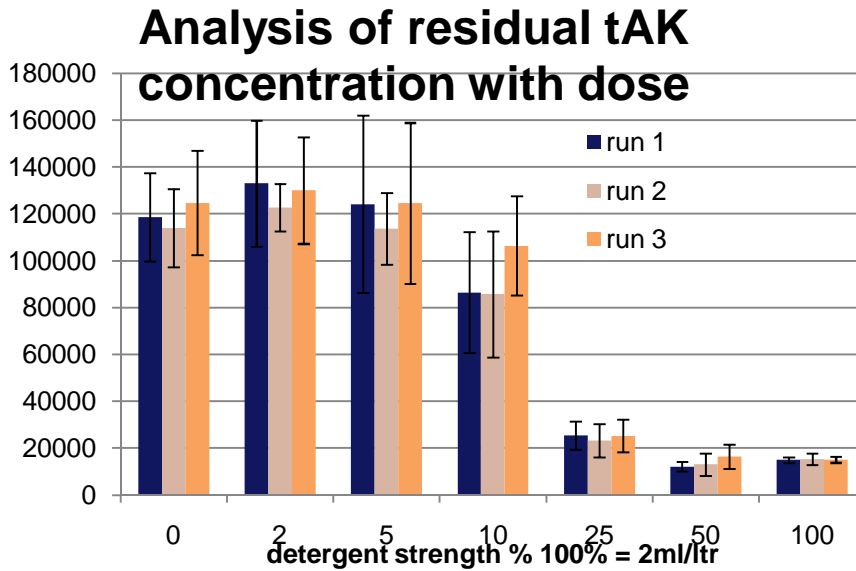


**ImageQuant  
LAS 4000**  
**GE Healthcare**



# Defining critical process parameters during a wash process: dose

## Commercial indicators

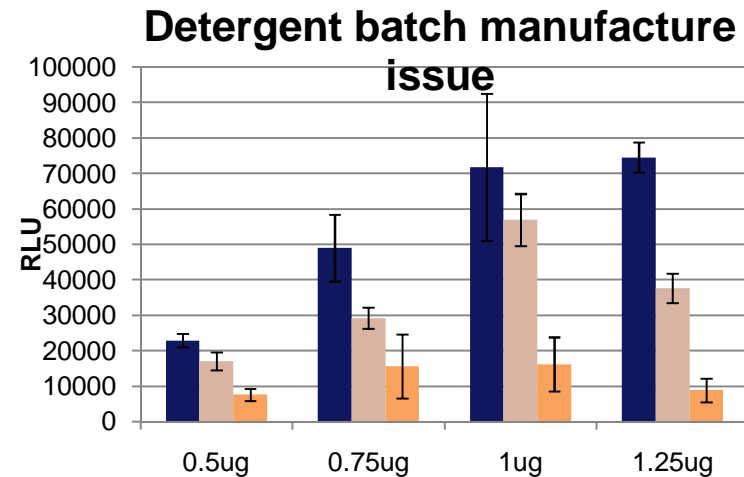


Indicator:	5								6				7					8																										
Detergent:	0	2	5	10	25	50	100	0	2	5	10	0	2	5	10	25	0	2	5	10	25	50	100																					
Test 1	[Red]																						*	[Red]																				
Test 2	[Red]																						*	[Red]																				

Indicator:	1					2			3						4																													
Detergent:	0	2	5	10	25	0	2	5	0	2	5	10	25	50	100	0	2	5	10	25	50	100																						
Test 1	[Red]																						**	[Red]																				
Test 2	[Red]																						**	[Red]																				

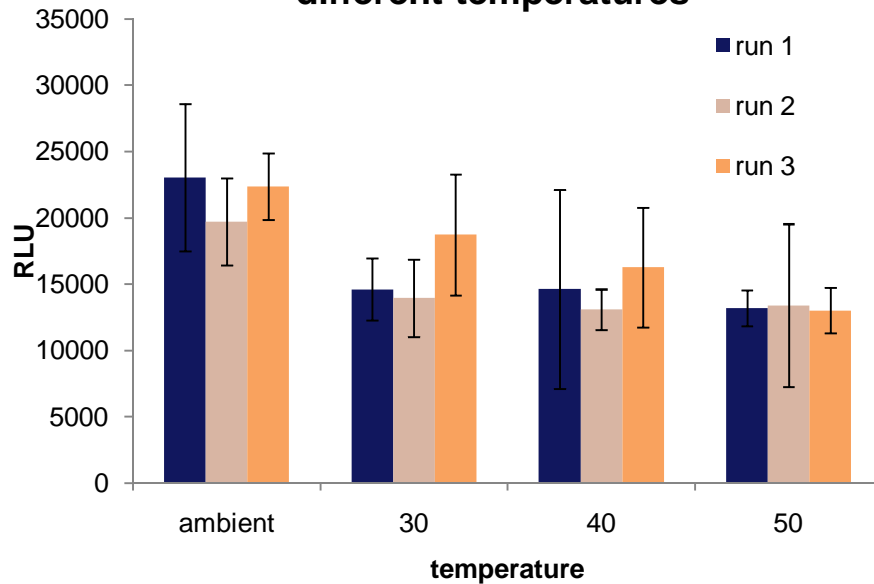
Standard wash  
15 minutes,  
40°C  
Detergent F 2ml/l





# Defining critical process parameters during a wash process: temperature

**Residual tAK activity after washing at different temperatures**



Indicator	1	2	3			4				
Temp (°C)	Amb	Amb	Amb	30	40	50	Amb	30	40	50
Test 1	Rep 1	**	*			**				**
	Rep 2	**	*			**				**
Test 2	Rep 1	**	*			**				**
	Rep 2	**				**				**

Indicator	5				6			7	8		
Temp (°C)	Amb	30	40	50	Amb	30	40	50	Amb	Amb	30
Test 1	Rep 1							*			
	Rep 2							*			
Test 2	Rep 1										
	Rep 2										

Standard wash

15 minutes,

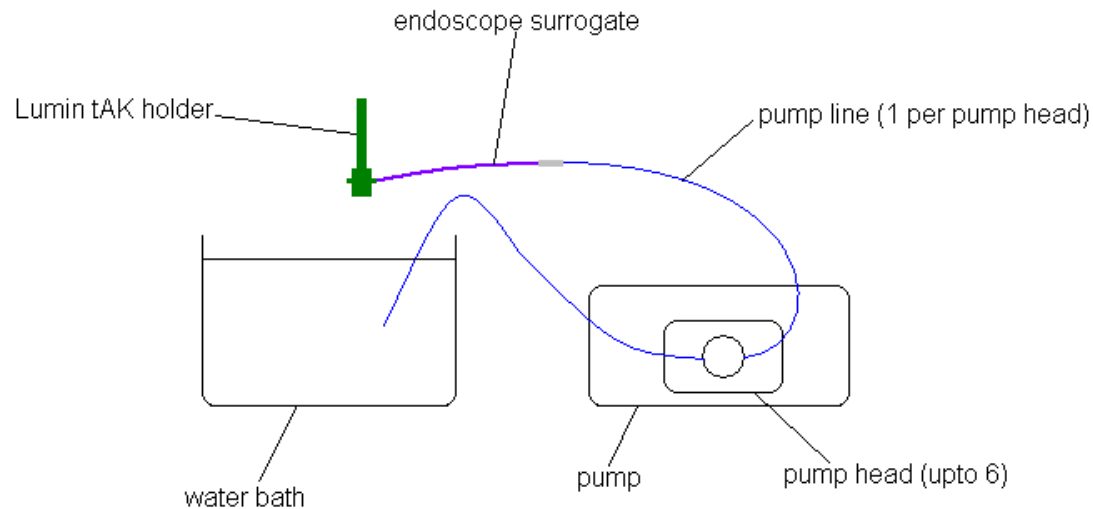
40°C

Detergent F 2ml/l



# Test models for lumen washing

## Schematic of test rig

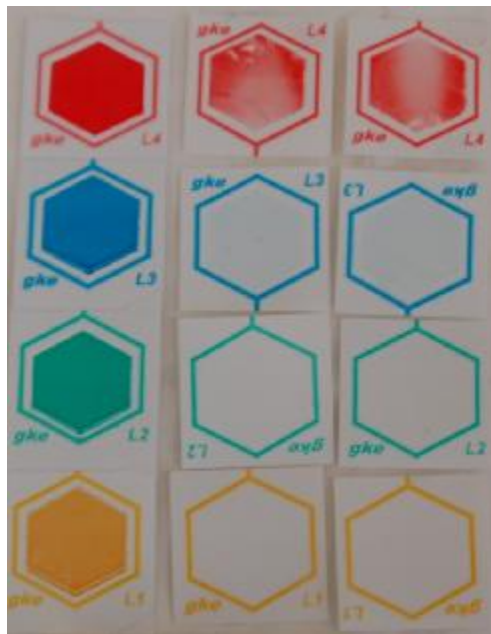


5 minute wash,  
40°C,  
Detergent F; Dose 5ml/l  
Flow rate 375-400ml/min



# Qualitative measures for assessing process performance: endoscope

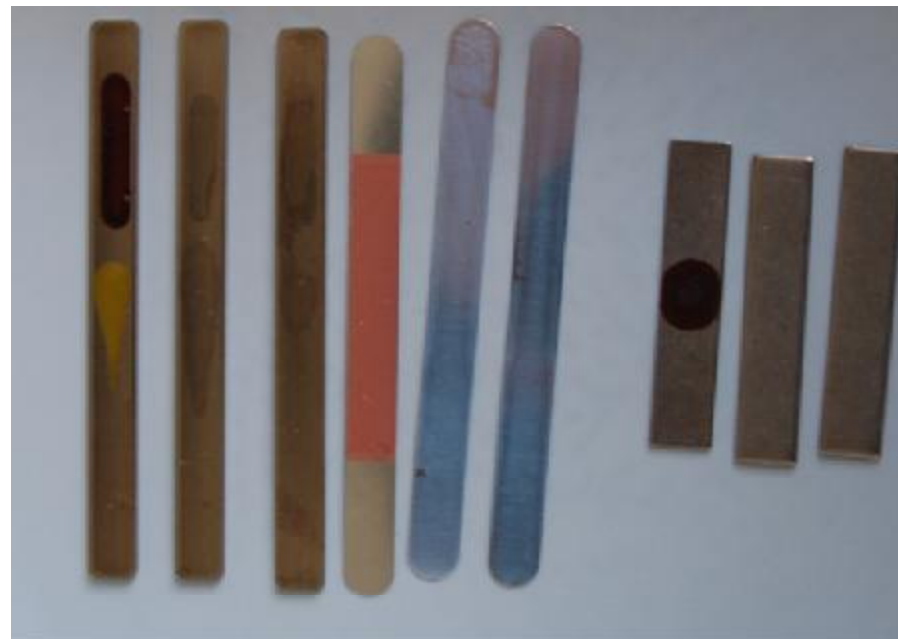
GKE level  
1-4



Tosi  
Lumen

Wash  
Check H

Valisafe





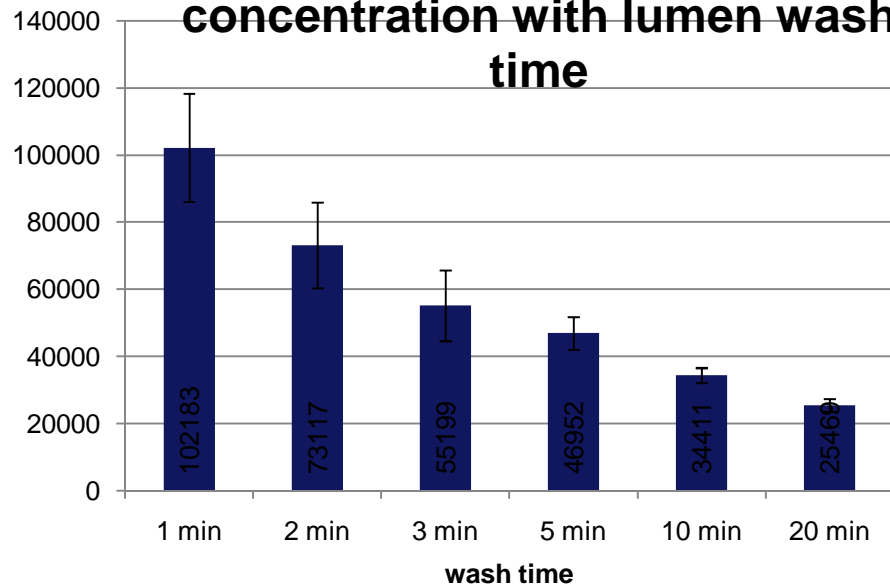
# Critical cleaning parameters: endoscope surrogates

Test Parameter	Min - Max	Standard setting when not being varied	Number of conditions tested
Wash (contact) Time (mins)	5 – 20	5	6 (1, 2, 3, 5, 10, 15, 20)
Water Temp (°C)	ambient - 50	40	4 (ambient (recorded), 30, 40,50)
Detergent Dosing (%)	0 – 100 manufacturer's recommended dose	100%	7 (0,5,10,20,30,50, 100)
Flow rate (ml/min)	0-400	Nominally 375-400	9 (0, 20, 40, 80, 100 150, 200, 250, 400)



# Defining critical process parameters during endoscope washing: time

### Analysis of residual tAK concentration with lumen wash time



Indicator		1					2		3			4					CFPP standard	
		1	2	3	5	10	1	2	1	2	3	1	2	3	5	10		20
Test 1	Rep 1	Red	Red	Red	Red	Green	Green	Green	Green	Green	White	Red	Red	Red	Red	Red	Red	Green
	Rep 2	Red	Red	Red	Red	Green	Red	Green	Green	Green	White	Red	Red	Red	Red	Red	Red	Green
Test 2	Rep 1	Red	Red	Red	Red	Green	Red	Green	Red	Green	White	Red	Red	Red	Red	Red	Red	Green
	Rep 2	Red	Red	Red	Red	Green	Red	Green	Red	Red	White	Red	Red	Red	Red	Red	Red	Green

5 minute wash,  
40°C,  
Detergent F; Dose 5ml/l  
Flow rate 375-400ml/min



# Standardised test rigs and cleaning tests

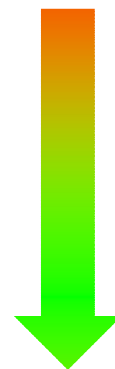
## Summary:

- Ø Standardised test rigs allow critical process parameters to be independently evaluated
- Ø Cleaning is inherently variable and models need multiple test devices to generate statistical data (revolving disk for wash rig)
- Ø For the chemistry shown, wash time and dose were critical process parameters, but changes in temperature had little effect
- Ø Different test devices show altered kinetics of removal (and this differs with chemistry; data not shown)
- Ø Additional value in terms of having a quantifiable measure of cleaning efficacy; e.g. detergent batch issues.



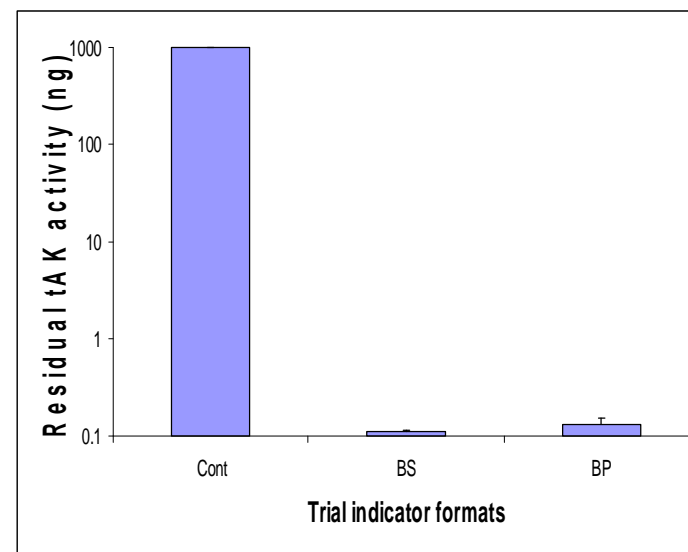


# Can tAK indicator devices provide in-use process validation ?



Efficacy

Validation of  
cleaning

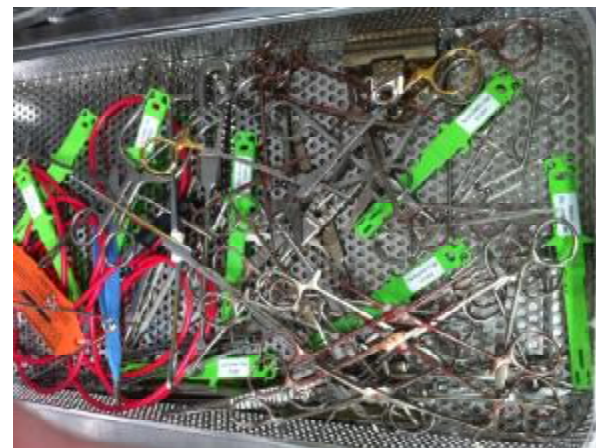




# Extended hospital trials: NIHR I4I

## AWD Field trial

- Ø 6 NHS SSUs and International site in Netherlands (2-processes) agreed to participate in trial.
- Ø Designed as an in-use study with no attempt by the project team to influence the loading of the AWD
- Ø A risk-assessment was performed at each site with SSU and infection control staff.
- Ø Study carried out over 2 days within a single AWD where possible
- Ø 5 wash cycles examined. 8(9) baskets per cycle, 3 test plus 2 blanks
- Ø 3 commercial indicators per basket.



Hospital automated washer disinfector (AWD) wash chemistries and wash cycle parameters

SSD AWD code	AWD model/ manufacturer	Detergent	Detergent pH	Total cycle time $\pm$ SD	Disinfection temperature and time	Drying temperature and time
A1	Steris HAMO T21	Steris Hamo Liquid 52	>12.0	61 $\pm$ 2 min	90–92 °C 2–3 min	111 °C 20 min
A2	Gettinge 8666	Olympic Spray Clean 2000	>12.0	75 $\pm$ 2 min	91–93 °C 2 min	85 °C 17 min
A3	Miele Professional	Neo-Disher Oxi-Vario + Neo-Disher FA alkaline	11.4–11.9	94 $\pm$ 1 min	92–95 °C 5–6 min	111 °C 13 min
A4	Miele Professional	Neo-Disher Medi-clean	8.5–9.5	77 $\pm$ 3 min	92–95 °C 5–6 min	111 °C 13 min
B1	Dekomed (DEKO 2000)	SerChem Delta	12.0–14.0	60 $\pm$ 3 min	92–94 °C 2 min	77 °C 23 min
B2	Steris HAMO T21	Steris Hamo 100	10.5	60 $\pm$ 1 min	91–93 °C 8 min	110 °C 25 min
B3	BHT Innova (M5-ISO)	Steris Prolystica	11.2	61 $\pm$ 2 min	90–92 °C 2–3 min	111 °C 20 min
C1	Dekomed (DEKO 2000)	Steris Renu Klenz	7.3	75 $\pm$ 2 min	91–93 °C 2 min	85 °C 17 min

From: Application of rapid read-out cleaning indicators for improved process control in hospital sterile services departments; J. Hosp Inf Nugent et al 2013.



# Summary of results

§ With the exception of a single test, the commercial test device showed a pass suggesting that cleaning had been adequate

∅ not able to discriminate between the performance of different processes.

§ The tAK indicator device was able to resolve differences in the performance of processes across the different SSUs and within a single site

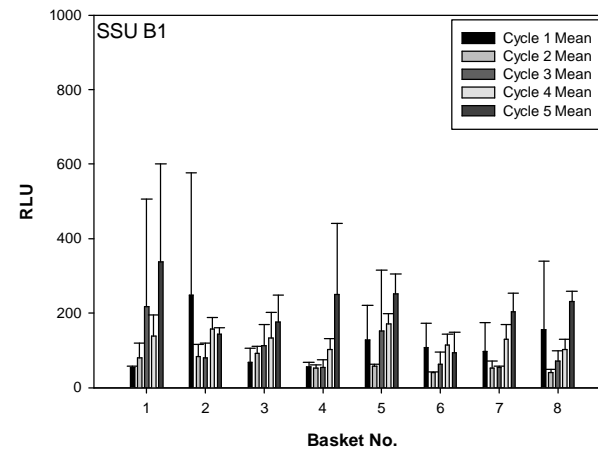
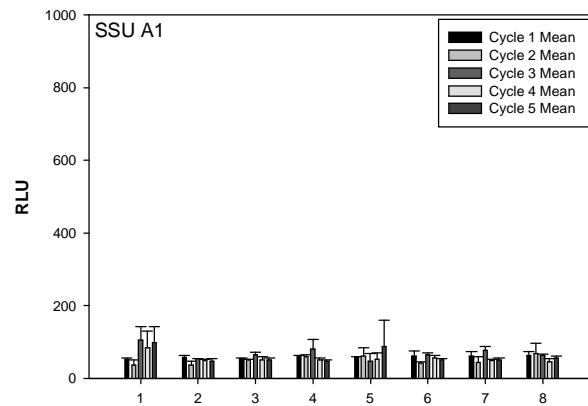
∅ Sites classified as A (>95% indicators below lower limited of detection), B (>60% below LLOD) and C (0% below LLOD) on the basis of cleaning performance

∅ Where the tAK indicator identified that processes cleaned to the limits of detection of the assay (10pg), this demonstrated a greater than 5.69-log removal of the enzyme.

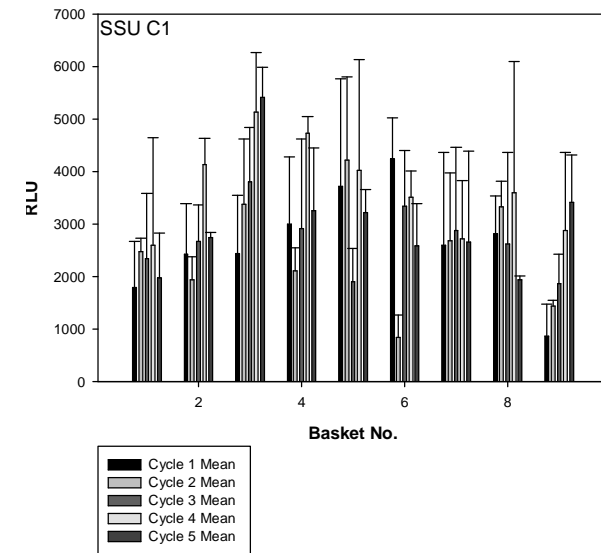
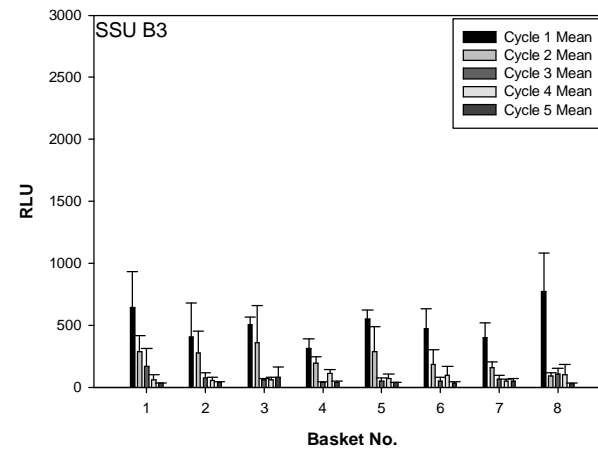


## Group B SSU

## Group A SSU



## Group C SSU





## Next applications: Hydrogen peroxide whole room decontamination



24 to 72 hours to result

Extremely unreliable

Poor quantification

AND  
/ OR



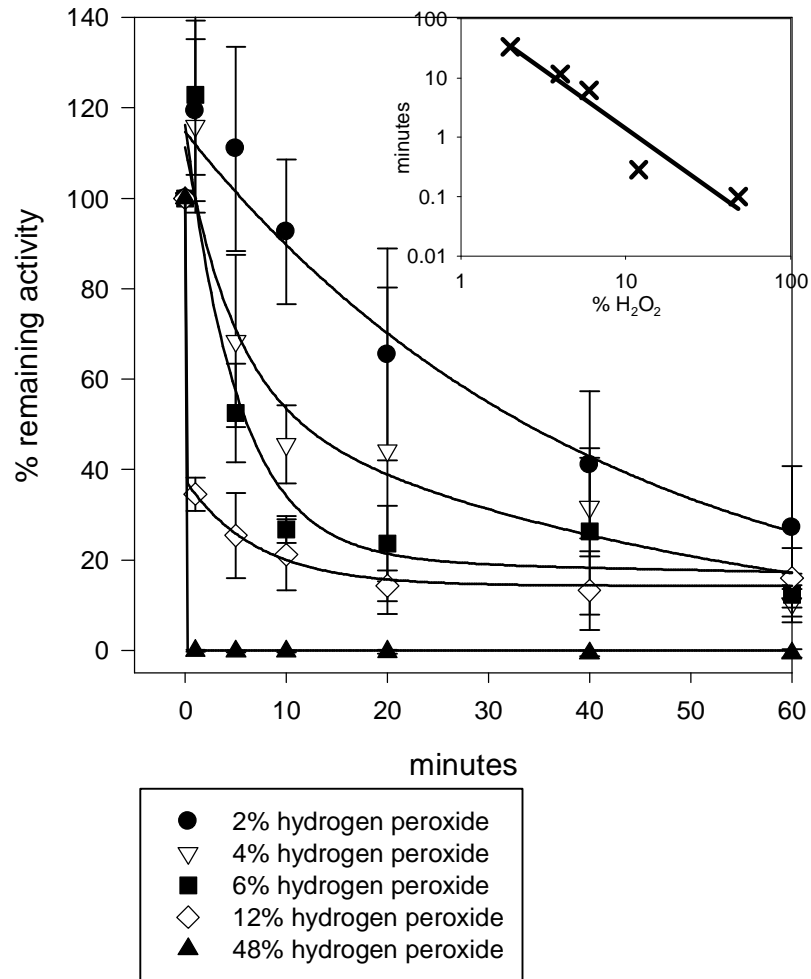
2 minutes

Good reproducibility

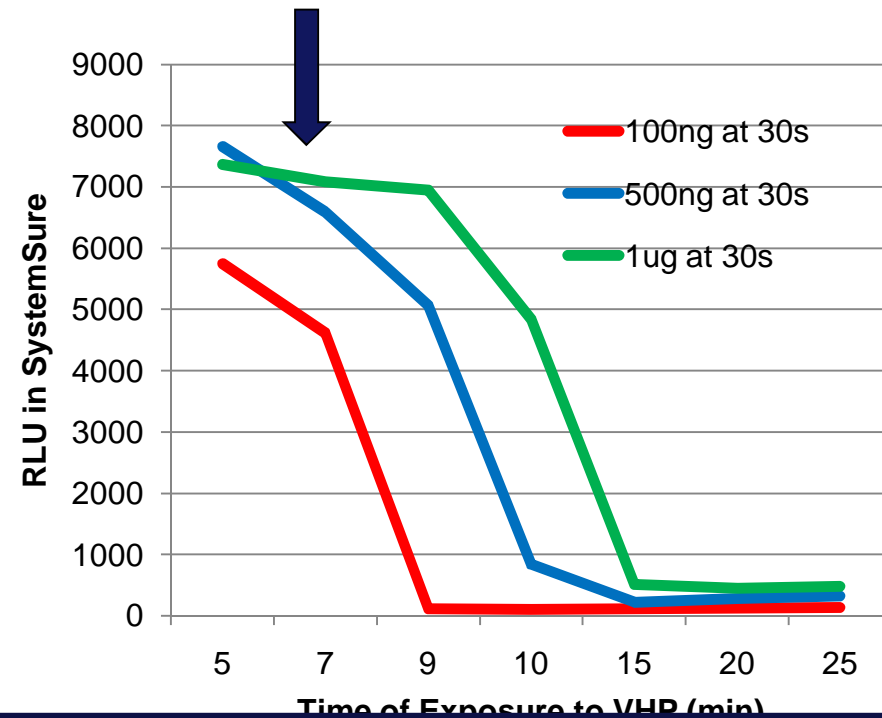
Fully quantifiable / loggable



# Rapid process monitoring with increased security



## 6-log reduction in BI *Geobacillus* *stearothermophilus*



**ü Improved validation of  
decontamination process**  
**ü Better ability to detect failures**  
**ü More robust evaluation of  
penetration of disinfectant vapour**



# What else can you measure with an enzyme on a stick ?

## Removal

- üCleaning
- üSurface modification
- üPlasma systems

## Protein damage

- üProtease
- üCross-linking e.g formaldehyde
- üDry heat
- üOxidation

tAK: 2 minutes

## Disinfectant efficacy

- üChlorine / chlorine dioxide
- üHydrogen peroxide
- üOzone
- üPeracetic acid / peroxygen
- üReactive amides

## “Blue skies”

- No-wash assay format
- Specific metabolites





# Conclusion

- Ø Commercial tests have very different performance levels, some of which are useful
- Ø tAK represents a rapid, simple and sensitive detection system for monitoring cleaning efficacy
- Ø tAK indicators demonstrate differences in cleaning efficacy in both lab settings and hospital trials
- Ø WASHtAK and LUMENtAK to be commercialised by BIOtAK Ltd; **WFHSS Stand 67 for questions**
- Ø Developing further applications for a range of processes; discussions welcome

# Technology Development Group

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**Hygiena International**

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Sharp Laboratories Europe - Jason Hector

University Manchester -Dr Paul Dark, Dr Bruce  
Humphrey

Salford Royal NHS Trust - Dr Geoff Warhurst

**Foresite Diagnostics, Mast Diagnostics**

**University Bath – Dr Toby Jenkins**

## **Biotechnology Funders:**

**NIHR; Invention for Innovation**

Department of Health; Policy

Research Programme

Technology Strategy Board

BBSRC

HPA - Pipeline fund



Removing the need to assume