



Knowing now matters.™



Alere q™ TB Case Detection and TB Drug Resistance Profile Tests

POC Platform for Microscopy Centers and Beyond

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TB Diagnostics Workshop, NIRT, Chennai

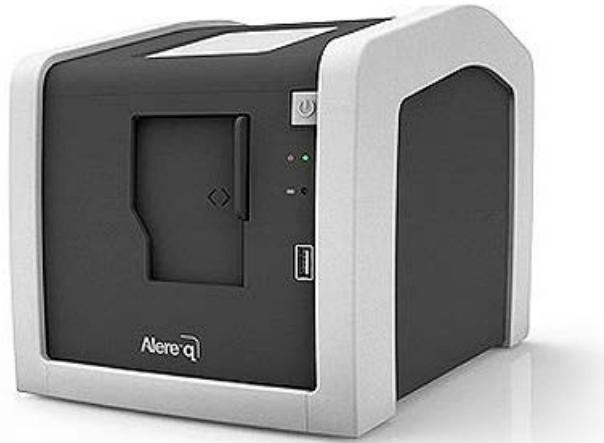
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Intended use settings





Alere's experience with POC settings





Level 1 TB MDx Technology Product Profile

Characteristic	Optimal Design	Alere q TB
Purpose of diagnostic	Diagnosis of active pulmonary TB with full DST profile	✓
Sample type	Sputum	✓
Diagnostic sensitivity	>98% (smear-positive)	✓
Diagnostic specificity	>99%	✓
Analytic sensitivity	<10 ² cfu/ml	✓
Analytic specificity	No cross reactivity including NTM	✓
Drug resistance screening	Detection of RIF, INH, FQ, PZA resistance via reflex cartridge	✓*
Total Time to result	<20 min case ID; <40 min DST profile	✓
Instrumentation	Single device	✓
Sample prep & processing	Fully integrated and automated	✓
Biosafety	No biosafety cabinet, direct disposal of consumable	✓
Reagent integration	All reagents in consumable	✓
Reagent kit Stability	24 months at 40 °C, 70% Relative Humidity	✓
Controls	Internal full-process positive control and negative controls	✓
Electronics and data analysis	Integrated	✓
Results documentation	Electronic and printed, wireless transmission	✓
Power	Optional battery or solar operation	✓
Thermal tolerance	Operation at 40 °C	✓
Training and education needs	< 1 hour, high school diploma or equivalent	✓



Alere™ TB case detection and drug resistance profile cartridges



D 2.0 LVSM cartridge with cup for TB-Test



R1.0 TB resistance profile cartridge



Potential TB Patient Experience

- Counseling, cup, and cap
 - Counseling for potential patient on how to produce best quality sputum sample
 - Potential patient given sputum collection cup and cap

- Potential patient expectorates into cup at proper place and time
 - Can be used for multiple expectorations if necessary

- Threaded screw cap is closed on sample cup until sealed

- Sealed sputum sample cup returned to test operator

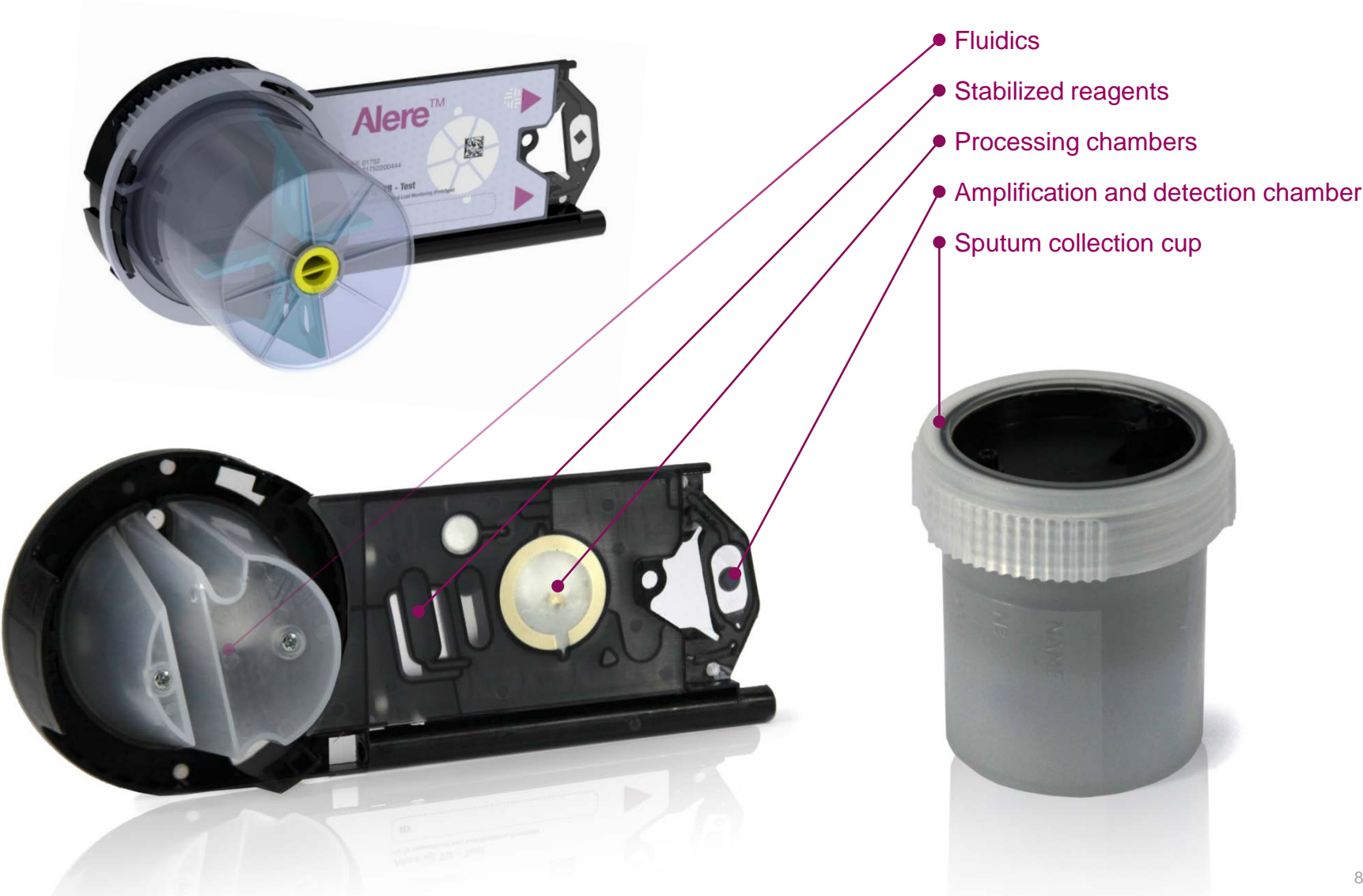


TB MDx Test Operator Experience

- Provide counseling, cup, and cap, to TB suspect
- Collect sealed sample cup with sputum sample
- Attach sample cup to TB test cartridge
- Insert entire cartridge into q Analyzer instrument
- Enter basic patient and operator ID
- Run test
- Wait up to 20 minutes for result
- Collect result by paper, electronic, or wireless method
- Transfer TB-positive DNA sample to DST profile test
- Dispose of sealed TB test cartridge

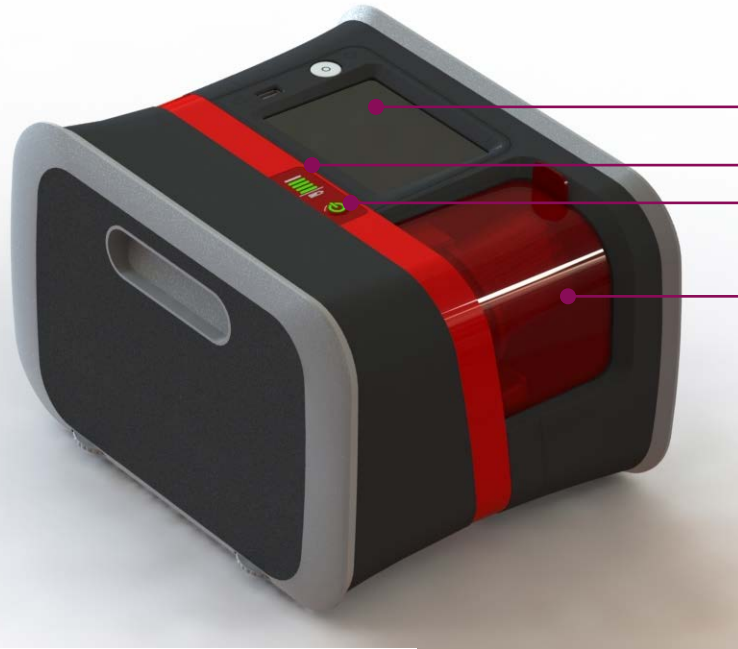


Alere q TB CD cartridge and sample cup





Alere q Analyzer



- touch-screen display
- battery charge indicator
- power ON button
- door for test cartridge (TB cartridge or HIV cartridge)
- Adjustable feet



Power Drum auxiliary battery

- level
- 4 x USB ports

- network connector
- ventilation system
- power switch
- mains power connector





Alere™ TB case detection and drug resistance profile cartridges

Transfer of purified DNA (pre-amplification)
with simple transfer tool to drug resistance profile cartridge

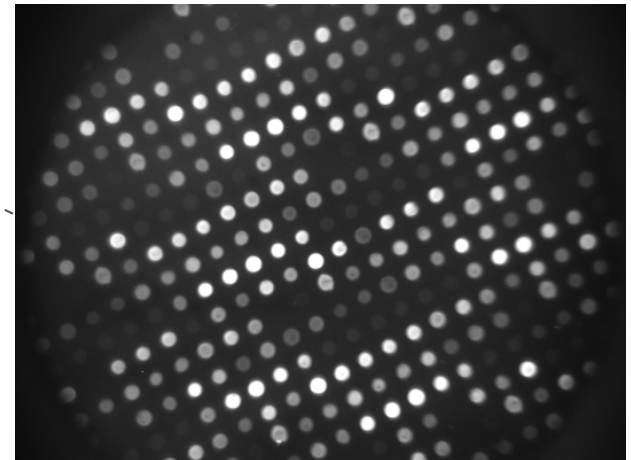
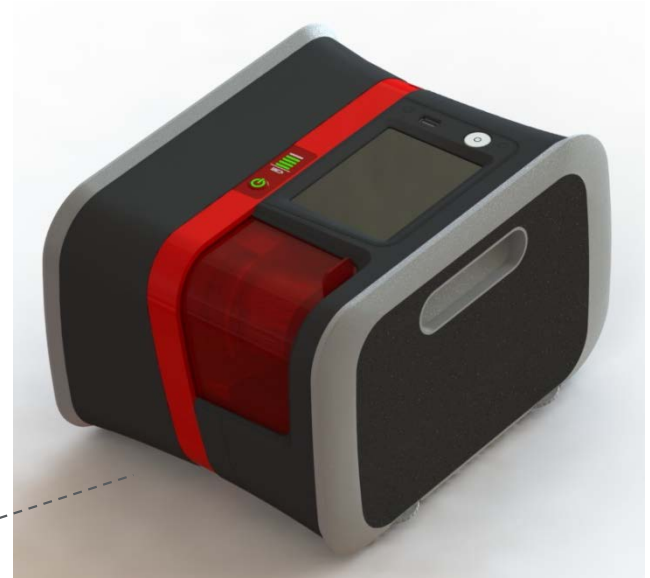
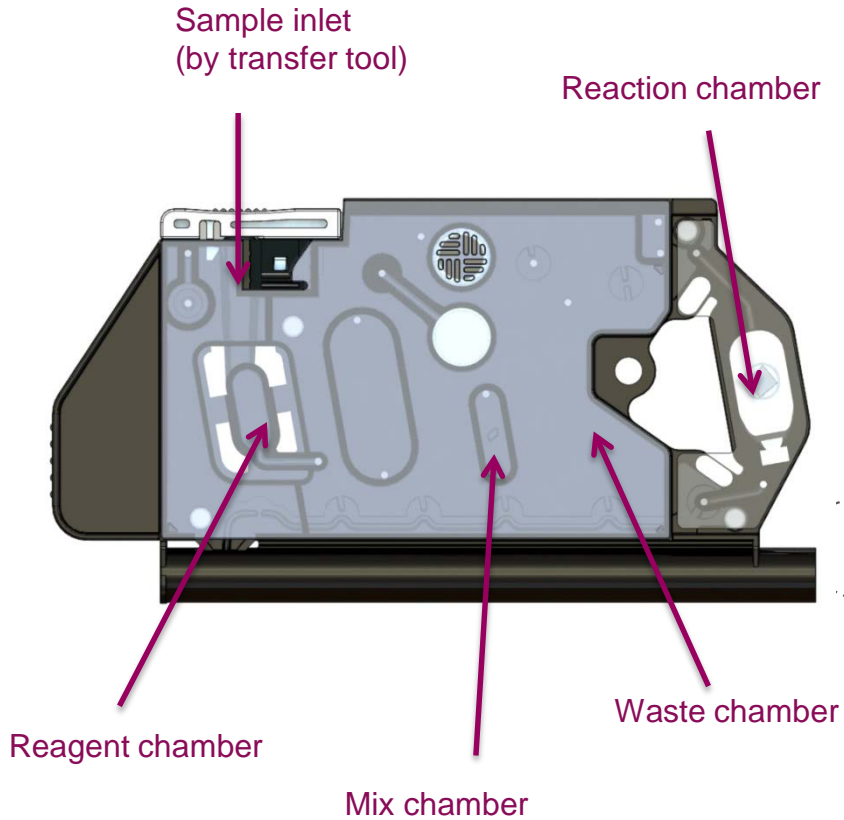


D 2.0 LVSM cartridge with cup for TB-Test

R1.0 TB resistance profile cartridge



Alere q cartridge and analyzer – TB DST Profile



DST Profile – RIF resistance SNPs

Black: implemented, cranberry: planned

Drug	Gene locus/- function/ amplicon size	Codon	Mutation	Substitution	% in resistant strains	Clinical isolate/plasmid library	Reference/Country/Time Period
Rifampin (RIF)	<i>rpoB</i> β-Subunit of RNA- Polymerase 129bp	146	Val146Phe	GTC>TTC	0,6 – 5,9	y/n	
		511	Leu511Pro	CTG>CCG	0,9 - 8,4	y/y	Tatkov et al, 2007, Russia 2000-2005; Afanasev et al, 2007, Russia, 1997-2005.; Huang et al, 2009, Taiwan, 2007-2008; Chan et al, 2007, Hong Kong 1994-2004; Yip et al, 2006, Hong Kong 1999-2003; Sivkov et al, 2006, Russia, 2000-2002; Jou et al, 2005, Taiwan, 1998-2003; Prammananan et al, 2008, Thailand, 2003-2005; Suresh et al, 2006, India, 2001-2003; Miotto et al, 2006, Italy, 2002-2005; Park et al, 2006, Korea, N.S.; Wang et al, 2007, China, N.S.; Tho et al, 2008, Vietnam, 2005; Sun et al, 2009, China, 2005-2006
		513	Gln513Pro	CAA>CCA	0,6	y/n	
			Gln513Leu	CAA>CTA	0,6 – 3,1	y/n	
			Gln513Lys	CAA>AAA	1,25		
		516	Asp516Val	GAC>GTC	1,9 - 9,6	y/y	
			Asp516Tyr	GAC>TAC	0,9 - 4	y/y	
		518	Asn518Ser	AAC>AGC	1 isolate	y/n	
		522	Ser522Leu	TCG>TTG	0,7 - 1,7	y/y	
			Ser522Trp	TCG>TGG	1 isolate	y/n	
			Ser522Gln	TCG>TAG	1,2 - 4		
		526	His526Tyr	CAC>TAC	1,9 - 14,9	y/y	
			His526Asp	CAC>GAC	1 - 14,7	y/y	
			His526Arg	CAC>CGC	0,4 - 10,8	y/y	
			His526Leu	CAC>CTC	0,4 - 10,8	y/y	
			His526Asn	CAC>AAC	0,6 - 3,9	y/y	
			His526Pro	CAC>CCC	1 isolate	y/y	
	His526Cys	CAC>TGC	1,5	y/y			
531	Ser531Leu	TCG>TTG	31,3 - 71,8	y/y			
	Ser531Trp	TCG>TGG	0,5 - 13,4	y/y			
533	Leu533Pro	CTG>CCG	1,5 - 7,4	y/y			
572	Ile572Phe	ATC>TTC	0,6 - 3	y/n			

DST Profile – INH, FQ resistance SNPs

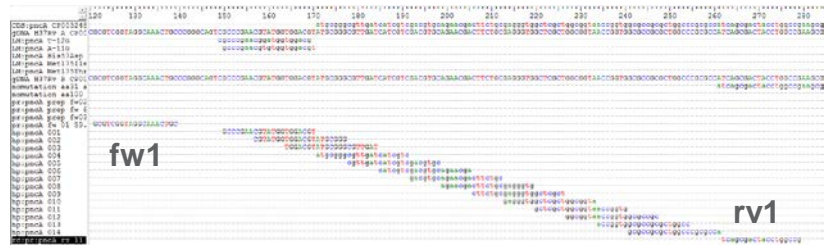
Black: implemented, cranberry: planned

Drug	Gene Locus/ function/ Amplicon Size	Codon	Mutation	Substitution	Percent of resistance	Clinical isolate/plasmid library	Reference/Country/Time Period
Isoniazid (INH)	<i>katG</i>	315	Ser315Thr1	AGC>ACC	31,1 - 90,5	y/y	Hazbón et al, 2006, Multiple countries, 1989-2002; Afanasev et al, 2007, Russia, 1997-2005; Huang et al, 2009, Taiwan, 2007-2008; Chan et al, 2007, Hong Kong 1994-2004; Dalla Costa et al, 2009, Brazil, Peru, Argentina, 2003-2004; Baker et al, 2005, UK, 1998; Miotto et al, 2006, Italy, 2002-2005; Parsons et al, 2005, USA, 1999-2004; Bolotin et al, 2009, Canada, 1999-2001; Hillemann et al, 2005, Kazaksthan, 2004; Park et al, 2006, South Korea, N.S.; Wu et al, 2006, China, 1999-2004; Boonaiaam et al, 2006, Thailand, 2005-2006; Hillemann et al, 2005, Germany, 2001
			Ser315Thr2	AGC>ACA	0,3 - 20,4	y/y	
			Ser315Asn	AGC>AAC	0,6 - 4	y/y	
			Ser315Ile	AGC>ATC	0,6 – 1,5	y/y	
		Ser315Gly	AGC>GGC		y/y		
		<i>inh A</i>					
	Enoyl-ACP- Reductase 130bp	-15		C>T	1,2 - 47,1	y/y	
		-8		T>A T>C	0,6 - 2,9	y/y n/n	
Fluoroquinolone	<i>gyrA</i>	88	Gly88Cys	GGC>TGC		y/n	Shi et al, 2006, China, 2002-2003; Sulochana et al, 2007, India, N.S. AI, N.S.; Chan et al, 2007, Hong Kong 1994-2004; Siddiqi et al, 2002, India, 1995-1998; Antonova et al, 2008, Russia, N.S.; Park et al, 2005, South Korea, 2004; Cheng et al, 2004, Hong Kong, 1991-2000; Lee et al, 2002, Singapore, N.S; Mokrousov et al, 2008, Russia, 2006; Zhao et al, 2004, China, N.S; An et al, 2005, China, N.S.; van Doorn et al, 2008, Vietnam, 2005-2006; Kam et al, 2006*, Hong Kong, 1999-2003
	DNA Gyrase A						
	121bp	89	Asp89Asn	GAC>AAC		y/n	
		90	Ala90Val	GCG>GTG	0 - 54	y/y	
		91	Ser91Pro	TCG>CCG	0 - 11,5	y/y	
		94	Asp94Gly	GAC>GGC	0 - 48,3	y/y	
			Asp94Tyr	GAC>TAC	0 - 18,8	y/y	
			Asp94Asn	GAC>AAC	0 - 28,7	y/y	
			Asp94Ala	GAC>GCC	1,1-15,3	y/y	
			Asp94His	GAC>CAC	1,5-7	y/y	

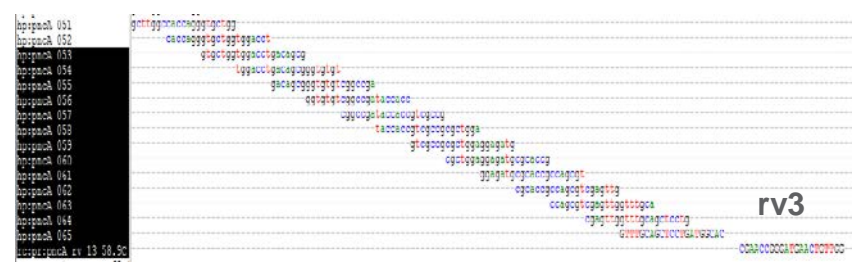
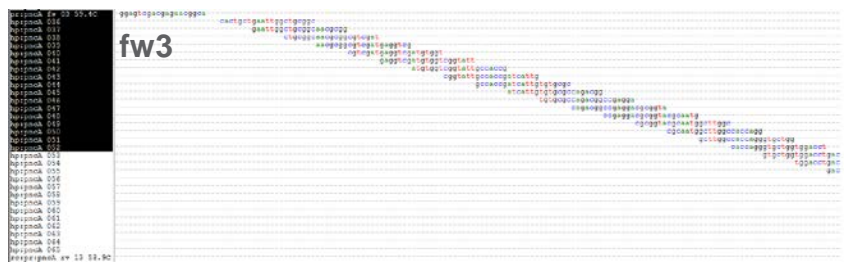
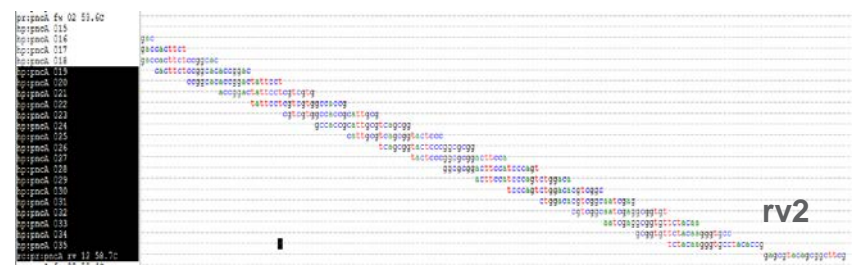
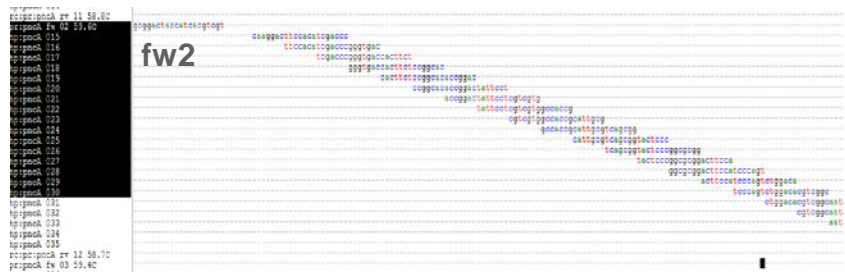


Tiling probe array for *pncA* wild type gene discrimination

65 tiling probes (21 bp length, 14 bp overlap)

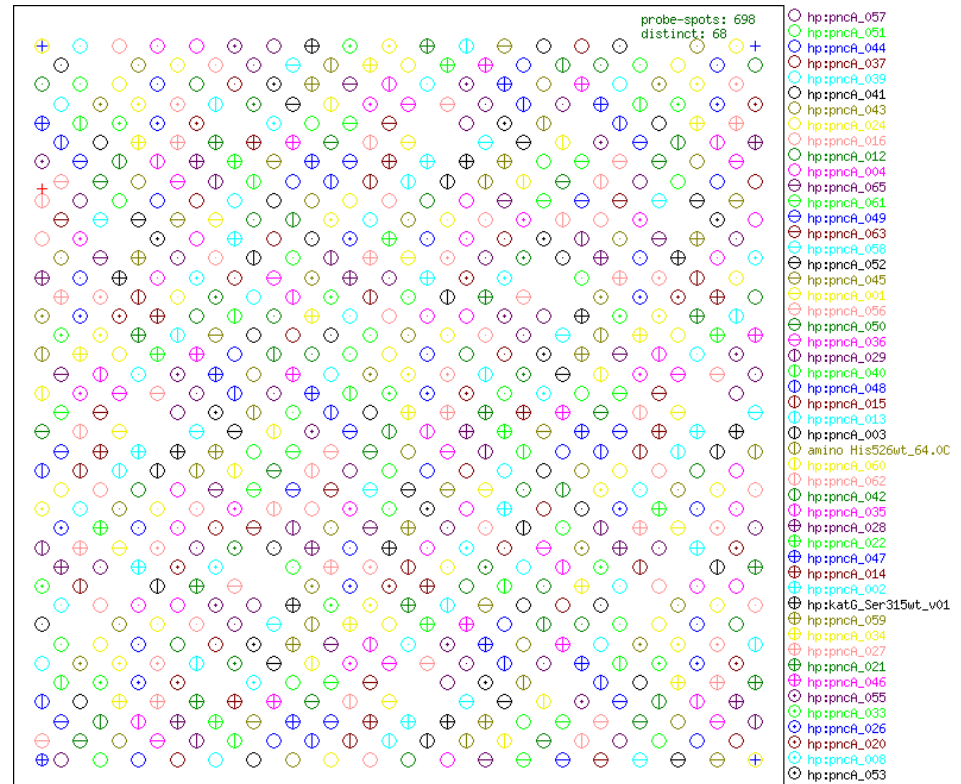
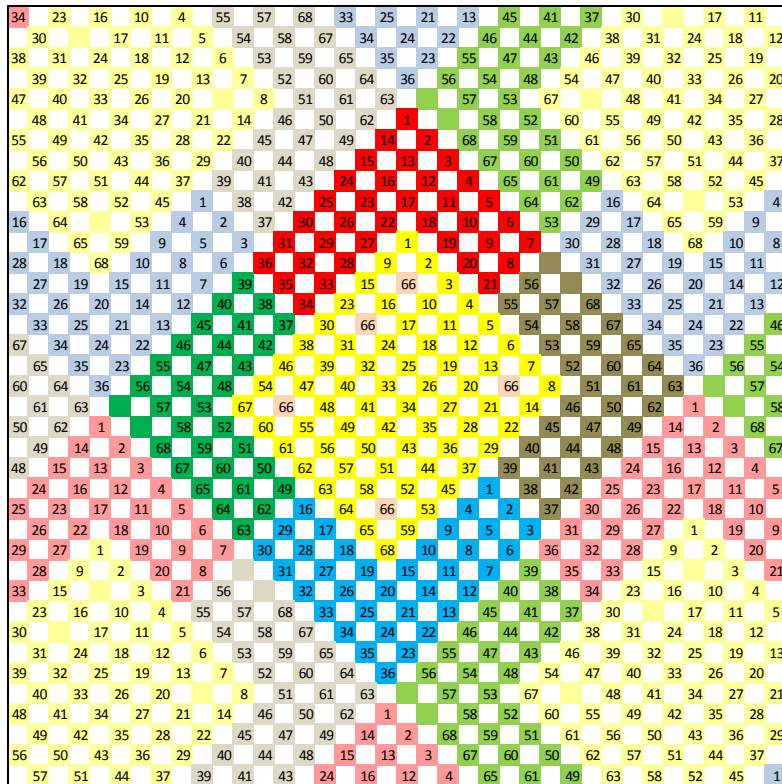


- Amplicon 1 - 159bp
- Amplicon 2 - 205bp
- Amplicon 3 - 270bp



Array layout for *pncA* wild type discrimination

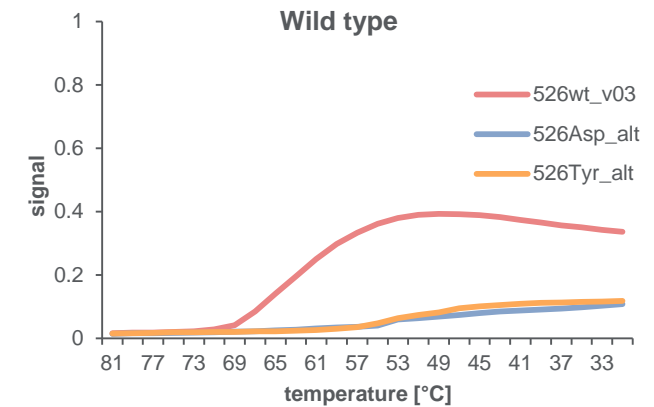
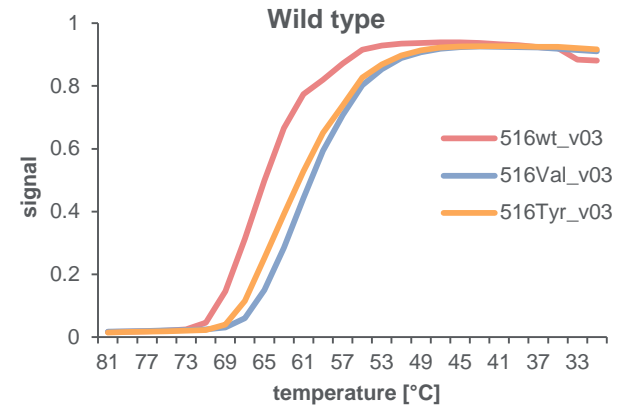
Orthogonal rotation of array for 65 *pncA* probes



Data processing for melt curve analysis

The screenshot shows the Partisan IconoClust software interface. The main window displays a microarray image with several spots highlighted in green and blue. The left sidebar shows a list of parameters for each spot. The bottom-left pane shows a report of the software's execution, including commands like 'Executed CommitImage' and 'Loading Image'. The bottom-right pane shows a table of results for five spots.

Spot ID	Substance	Backgr...	CoGX	CoGY	CoG_x	CoG_y	Confid...	Dis...
001	hp.rpoB_513Pro_v02	0.000	0	0	0.000000	0.000000	0	400
002	hp.rpoB_513Pro_v03	0.000	0	0	0.000000	0.000000	0	400
003	hp.rpoB_516wt_v01	0.000	0	0	0.000000	0.000000	0	400
004	hp.rpoB_572Phe_v01	0.000	0	0	0.000000	0.000000	0	400
005	homoB_572wt_v03	0.000	0	0	0.000000	0.000000	0	400





Alere Data Point Connectivity

Analyzer



USB Modems



Alere SIMs

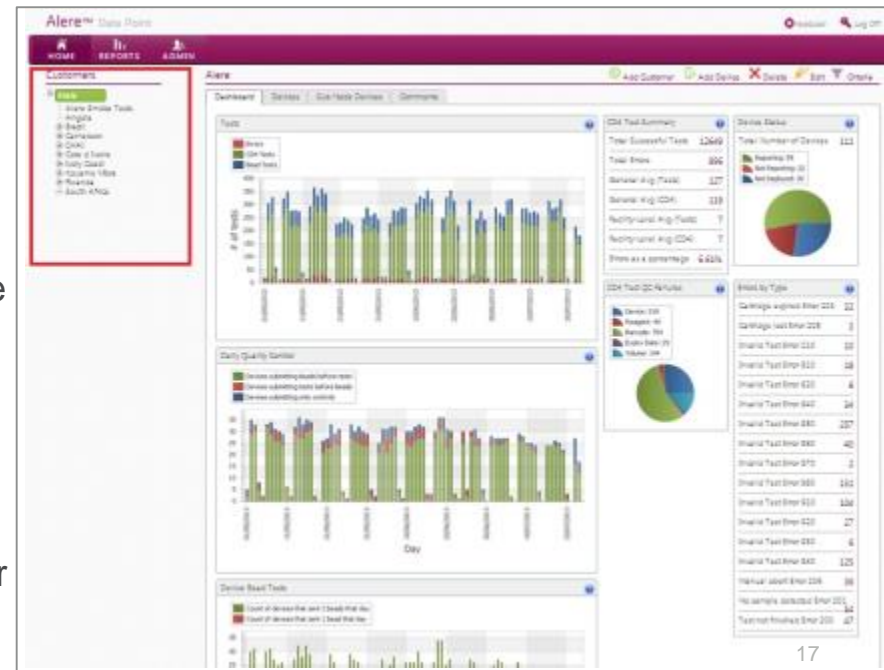


Alere Data Point Portal



Data Point Connectivity offering

- Data Point is the connectivity package that delivers analyser results to a central server enabling customers to access data remotely via the Data Point portal.
- Regardless of how many analyzers are in the field, the portal allows near real-time monitoring of data including usage patterns, device condition & stock management.
- The portal is also enabled with a flexible reporting & alerting system to alert program administrators to activity that is of interest to them on a near real-time or scheduled basis.



Thank You!



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