

Screening Strategies: Serology/NAT screening algorithms

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NRL, Melbourne, Australia

IPFA 4rd Workshop on Plasma Quality and Supply
Hanoi, Vietnam

NRL

- Established in 1985
- Not-for-profit organisation that exists to support laboratories that perform testing for the diagnosis and management of human infectious disease
- Contracts with the Australian Government

NRL – Major Activities

- NRL Evaluations
- NRL Quality Assurance
 - EQAS
 - QC Program
 - Specificity Monitoring
- NRL Training
- NRL Testing
- NRL Workshop

Insight into donor screening

- How does NRL gain insight into donor screening?
 - NRL provides QC and EQAS to the majority of donor screening laboratories
 - Globally – over 1000 participants
 - ‘The Region’
- NRL has a leading role in ‘The Region’
 - Not just provision of Quality Assurance programs
 - Laboratory Strengthening
 - Training (QMS, testing algorithms, QA programs)
- WHO Collaborating Centre for Diagnostics and Laboratory Support for HIV and AIDS and other Blood-Borne Infections

What is 'The Region'?

- The Asia Pacific Region comprises two regions as defined by WHO
 - South-east Asia Region (SEARO)
 - Western Pacific Region (WPRO)

20 countries in NRL QA programs

“The Region” – SEARO



Bangladesh



Bhutan



Democratic People's Republic of Korea



India



Indonesia



Maldives



Myanmar



Nepal



Sri Lanka



Thailand



Timor-Leste



“The Region” – SEARO



Bangladesh



Bhutan



India



Indonesia



Maldives



Myanmar



Nepal



Sri Lanka



Thailand



“The Region” - WPRO



“The Region” - WPRO

	American Samoa		Macao (China)		Philippines
	Australia		Malaysia		Pitcairn Islands (UK)
	Brunei Darussalam		Marshall Islands		Republic of Korea
	Cambodia		Micronesia, Federated States of		Samoa
	China		Mongolia		Singapore
	Cook Islands		Nauru		Solomon Islands
	Fiji		New Caledonia (France)		Tokelau* (New Zealand)
	French Polynesia (France)		New Zealand		Tonga
	Guam (USA)		Niue		Tuvalu
	Hong Kong (China)		Northern Mariana Islands		Vanuatu
	Japan		Palau		Viet Nam
	Kiribati		Papua New Guinea		Wallis and Futuna
	Lao People's Democratic Republic				

“The Region” - WPRO



Australia



Cambodia



Hong Kong (China)



Japan



Macao (China)



Malaysia



Mongolia



New Zealand



Papua New Guinea



Philippines



Republic of Korea



Singapore



Viet Nam

Asian Region

- Has about one third of world population
- Disproportionate burden of disease
- Geographically disparate
 - Large land masses
 - Archipelagos
 - Small island nations
- Vast differences in economies, political stability
- 10 million units
- >3,500 blood banks in eleven countries*

WHO Recommendations

- Each country should have a **national policy** on blood screening
- National programme for blood screening which sets out the **strategy** for screening, with **algorithms that define the actual tests** to be used in each screening facility
- Where feasible, blood screening should be **consolidated in strategically located facilities**

WHO Recommendations

- Screening of all blood donations should be mandatory for
 - HIV 1 and HIV 2
 - HCV
 - HBV
 - Syphilis

WHO Recommendations

- Adequate resources, including sufficient number of qualified and trained staff be available
- A national system for the evaluation, selection and validation of all assays
- The minimum evaluated sensitivity and specificity levels of all assays used for blood screening should be as high as possible and preferably not less than 99.5%.
- Quality-assured screening of using serology should be in place before nucleic acid testing are considered

Blood Screening in the Region



Blood Screening in the Region



Examples of Blood Transfusion Services

Country	No of labs	Centralised services	Type of services	National policies
Australia	4	Yes	Red Cross	Yes
Bhutan	27	Yes	Hospital	Yes
Bangladesh	>100	No	Private/Red crescent	Yes
China (mainland)	>400	Partial	Government	Yes
India	>2750	No	Provincial, hospital, private, charitable, government	Yes (+/-)
Indonesia	>200	No	Red cross, hospital	?
Malaysia	14	Yes	Government	Yes
Myanmar		Yes	?	Yes
Nepal	~70	?	Hospital, district	Yes
New Zealand	2	Yes	Red Cross	Yes
Thailand	13	Yes	Red Cross	Yes
Timor-Leste	1 +/-	Yes	Government	Yes
Sri Lanka	~80	Yes	Hospital, private	Yes

Serology Screening – anti-HIV

Assay	Sensitivity	Specificity
Abbott Architect	100%	99.62%
Abbott PRISM	100%	99.98%
DiaSorin Liaison XL	100%	99.69%
DiaSorin Murex EIA	100%	99.91%
Ortho VITROS	100%	99.92%
Roche Elecsys (combi PT)	100%	99.88%
Siemens ADVIA Centaur	100%	99.74%
Siemens Enzygnost EIA	100%	99.3 – 100%

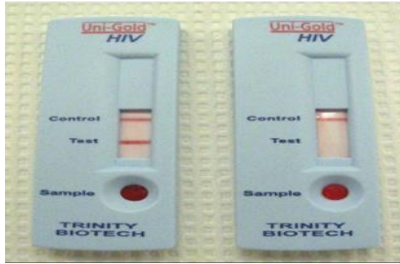
Serology Screening



Serology Screening – anti-HIV

Rapid Tests used in NRL EQAS	WHO Prequalified
ACON HIV 1/2 Ultra Rapid Test Device (Serum/Plasma)	No
Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test	Yes
Alere Determine HIV-1/2 Rapid Test	Yes
Bio Focus BioTracer HIV 1/2 Rapid Card	No
Blue Screen HIV 1/2/O Tri-line HIV Rapid Test Device (WB/S/P)	No
Core Diagnostics Core HIV 1&2	No
Green Cross GENEDIA HIV 1/2 Rapid 3.0	No
Human HEXAGON HIV Rapid Test	No
Organics ImmunoComb II HIV 1 & 2 CombFirm	No
PMC FIRST RESPONSE HIV 1-2.O Rapid Card test (v.3.0)	No
Standard Diagnostics SD Bioline HIV-1/2 3.0 Rapid Test	Yes
J. Mitra HIV TRI-DOT	No
Wondfo One Step HIV 1/2 WB/S/P Rapid Cassette Test (2 Lines)	No

Serology Screening



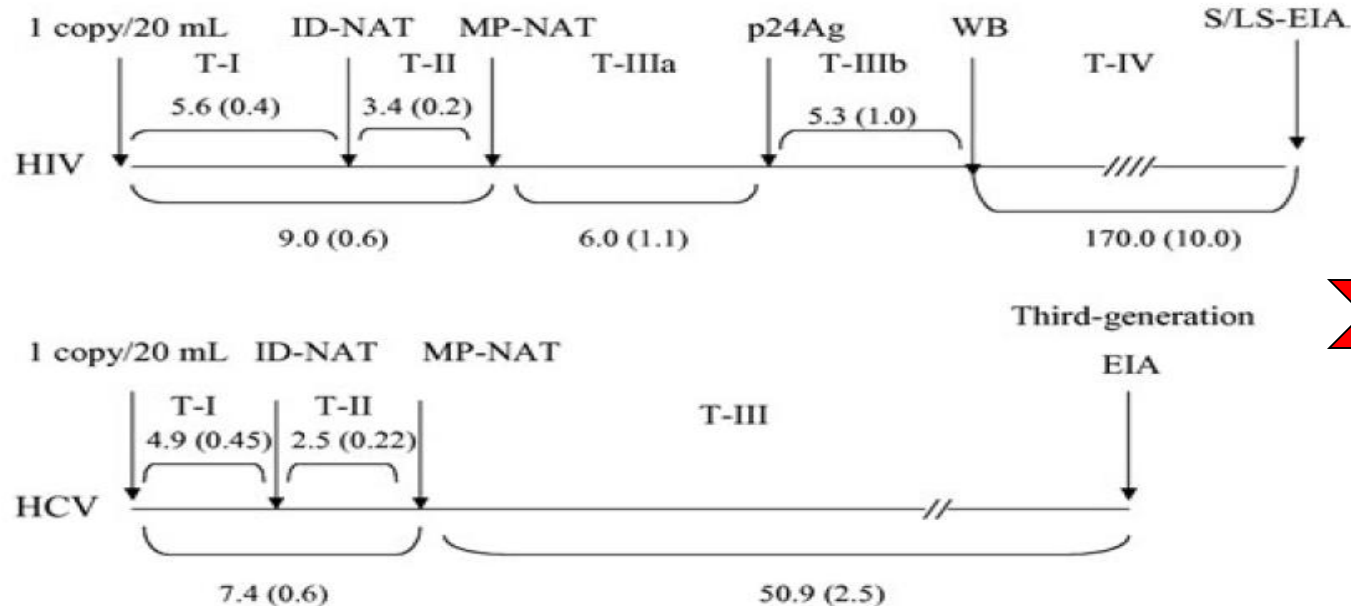
Testing Reported in NRL EQAS

Country	Serology	Nucleic Acid Testing
AUSTRALIA	ChLIA, EIA, Blot, PAA	Yes
BANGLADESH	ChLIA, EIA,	No
BHUTAN	EIA , PAA	No
CHINA (mainland)	ChLIA, EIA, Blot, PAA	Yes
INDIA	ChLIA, EIA, Blot, PAA, RTD	Partial
INDONESIA	ChLIA, EIA, Blot	Yes
JAPAN*	ChLIA, EIA, Blot, PAA	
MALAYSIA	ChLIA, Blot, PAA	Yes
MONGOLIA	ChLIA, EIA, Blot, PAA, RTD	Yes (+/-)
NEPAL	EIA, RTD	No
NEW ZEALAND	ChLIA	Yes
VIETNAM	ChLIA, PAA, RTD	Yes

Testing Reported in NRL EQAS

Country	Serology	Nucleic Acid testing
PR OF CHINA	ChLIA, EIA, Blot, PAA, RTD	Yes
PHILIPPINES	ChLIA, EIA, Blot, PAA, RTD	
REPUBLIC OF KOREA	ChLIA, EIA, Blot, PAA,	Yes
REPUBLIC OF MALDIVES	ChLIA	
REPUBLIC OF SINGAPORE	ChLIA, PAA	Yes
SRI LANKA	ChLIA, EIA, Blot	
THAILAND	ChLIA, EIA, Blot, RTD	Yes
UNION OF MYANMAR	ChLIA, EIA, RTD	
VIETNAM	ChLIA, EIA, Blot, PAA, RTD	Yes

Window Period for HIV and HCV



Busch, M. *et al* Transfusion 2005; 45:254-264

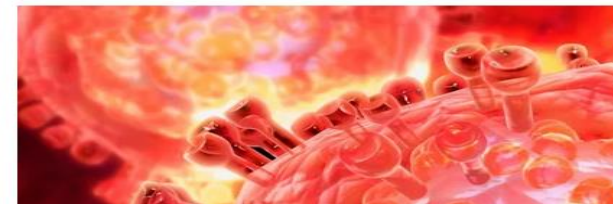
Testing Strategies in Asia Pacific

- Diverse
- Dangerous
- Difficult
- Developing

12,000 Chinese blood plasma treatments contaminated with HIV

- Traces found in batch used for immune deficiencies caused by illnesses including leukaemia, hepatitis and rabies
- Hospitals advised to report their stocks of the treatment and closely monitor patients already treated

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UPDATED : Tuesday, 12 February, 2019, 5:26pm



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Bad blood: 2,234 get HIV after transfusion

Vidya Krishnan

NEW DELHI, MAY 31, 2016 00:31 IST
UPDATED: SEPTEMBER 15, 2016 09:48 IST

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COMMENTS: 45

In India, Blood Transfusions Have Caused Thousands of HIV Infections

The data suggest screening procedures may not be adequate, though a government official says progress has been made.

Nepal | March 13, 2018

The Himalayan

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Bloody hell! Transfusion happening without testing blood for deadly diseases

NO HOSPITAL IN NEPAL HAS KIT TO TEST HIV DURING THE 'WINDOW PERIOD'

Published: June 14, 2017 5:31 am On: [Nepal](#)



Serology

- More common – RTD and PAA used for screening
 - Multiple instances in HIV, HCV and HBsAg RTDs
- Anti-HIV only tests (3rd Gen)
 - Many participants use these with HIV combo as dual screen
 - Some performed anti-HIV only and risk not detecting early infection
 - Many laboratories using RTDs in this situation
- Evidence EQAS is commonly used but QC is not!!!

QC in the Region

Pros

- Vast number of results reported
 - Both serology and NAT
- Overall laboratory performance – Good
- Data generated supports quality improvements
- Often the only positive samples seen frequently

Cons

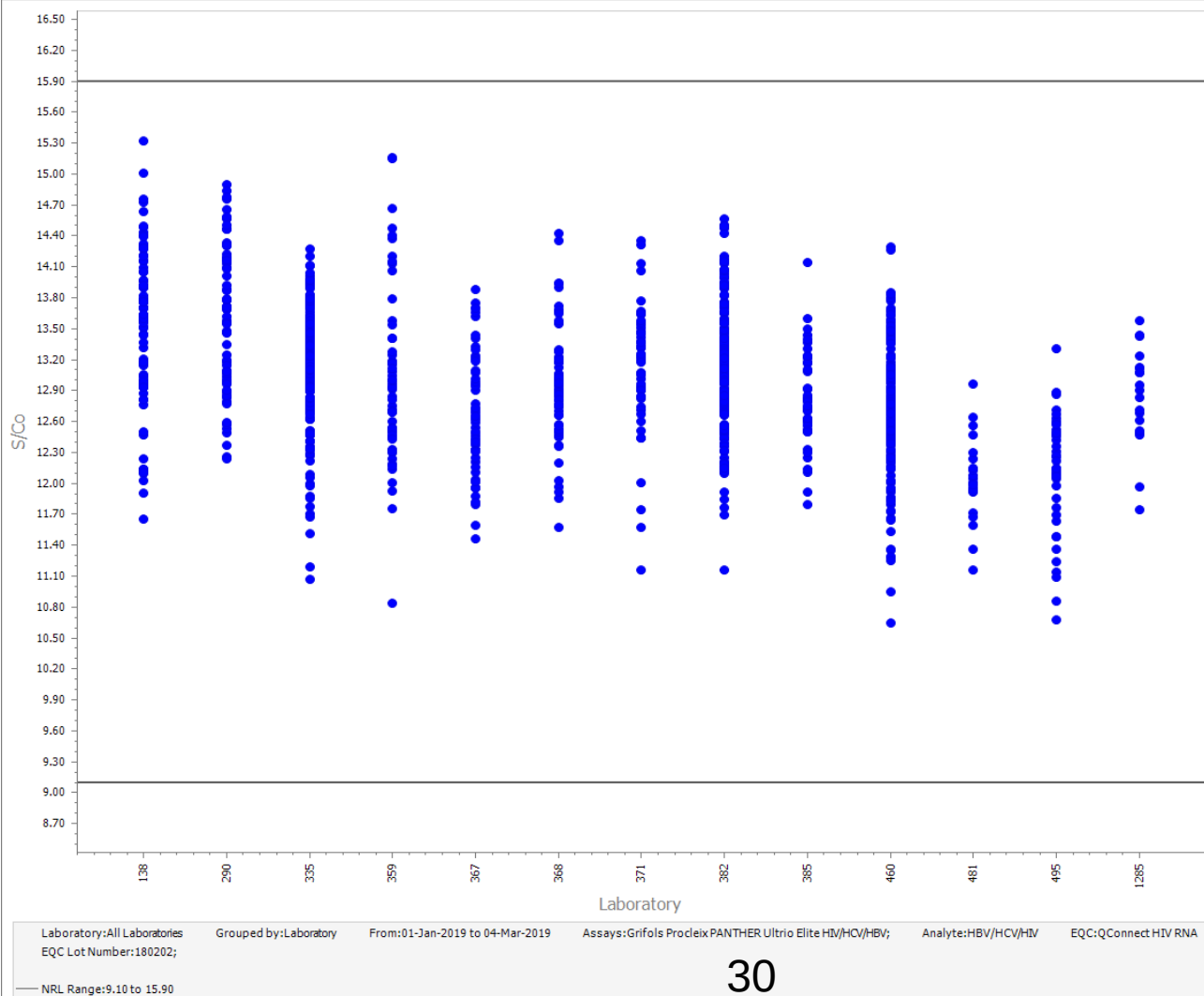
- Not enough participants for IVDs in resource limited labs
- Reports of in-house QC use – common
- Commercial QC cost-prohibitive – a major issue

QConnect Donor Screening NAT

- Two types of QC provided
 - Single viral NAT QC for Grifols
 - QConnect HIV RNA
 - QConnect HCV RNA
 - QConnect HBV DNA
 - Multiplex NAT QC for Roche
 - QConnect TriScreen

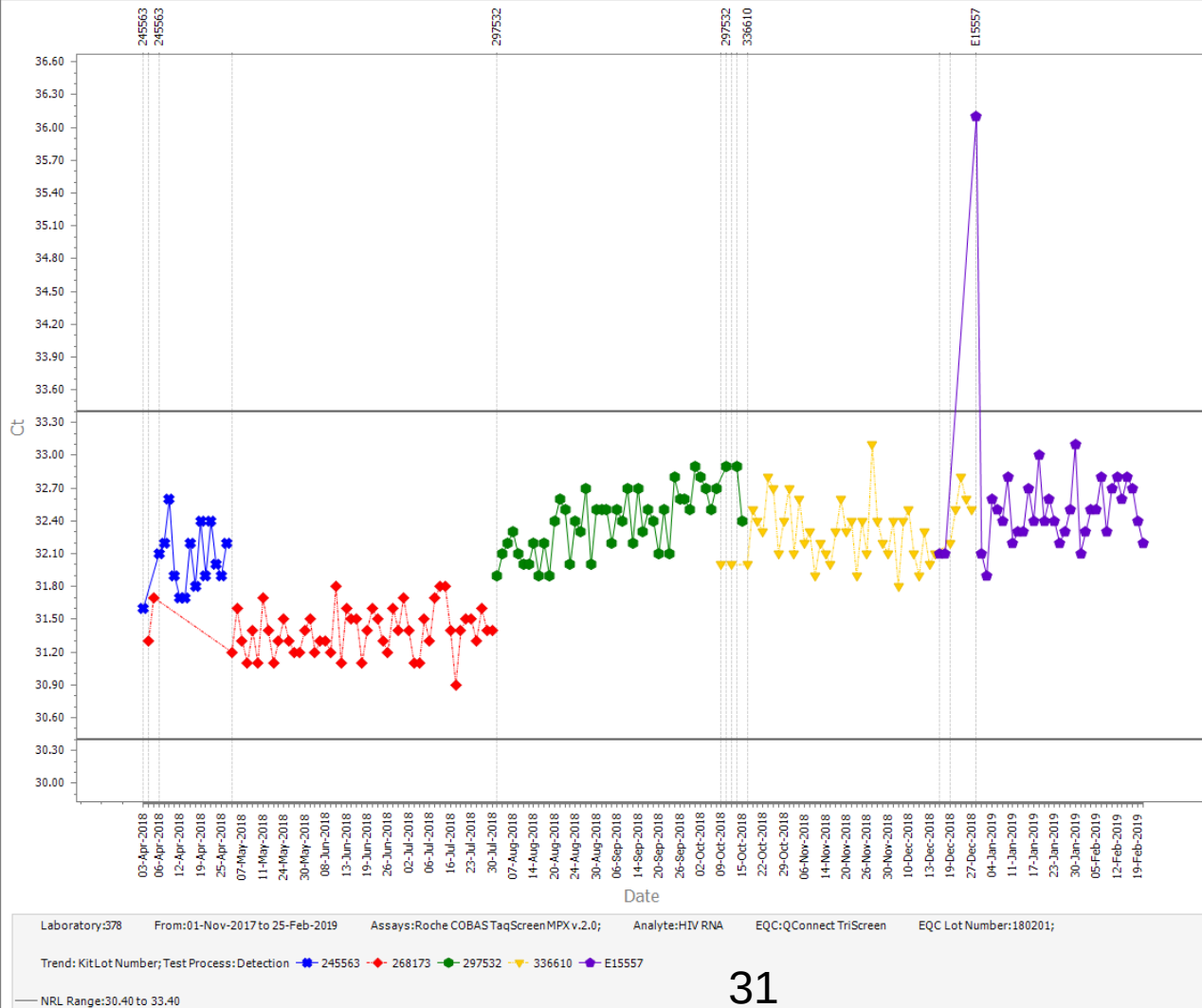
HIV RNA

- Peer Group Data by Lab
- Grifols Ultrio Elite on Panther



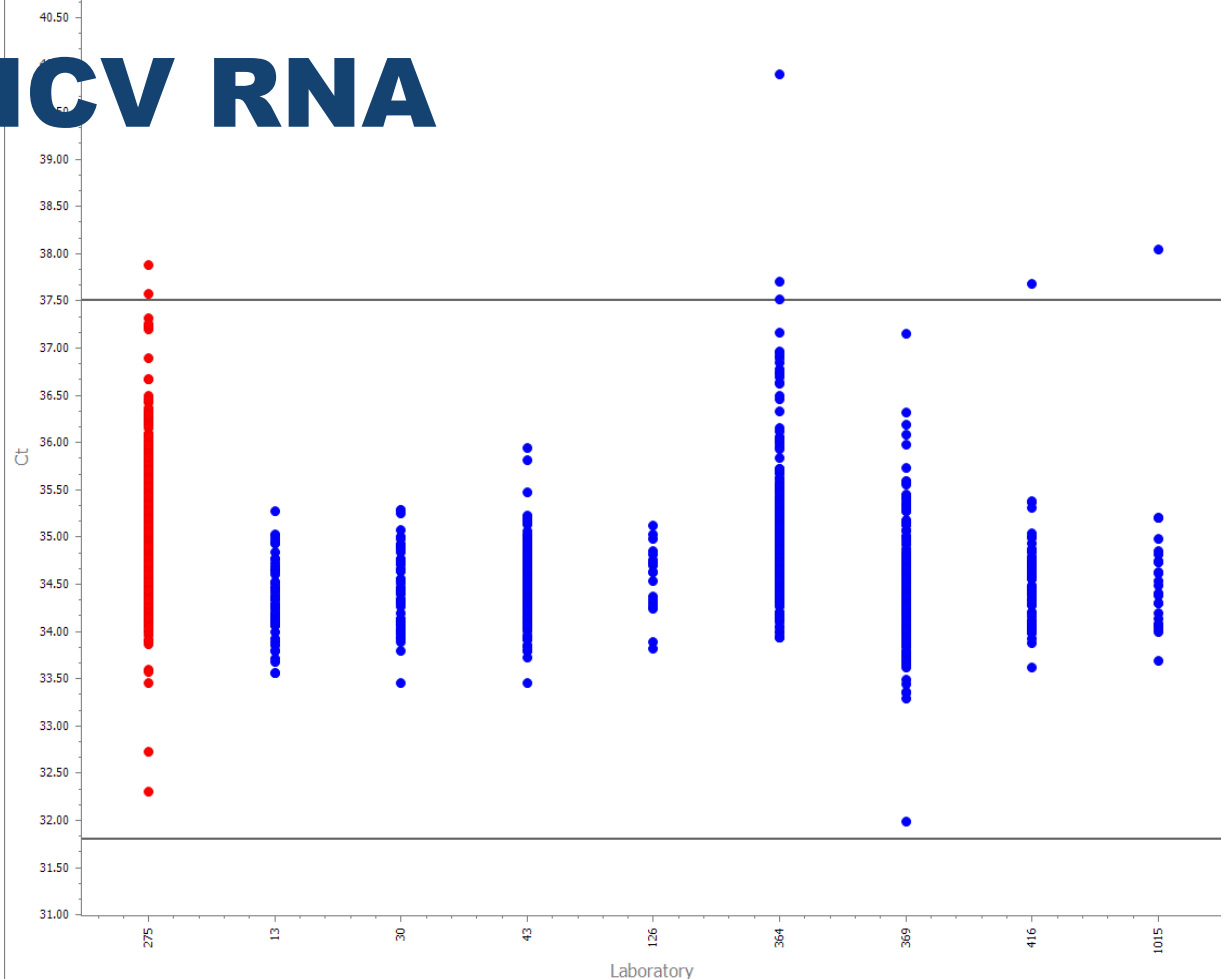
HIV RNA

- Roche cobas MPX v2.0
- Data by reagent lot
- Typical Lot Variation



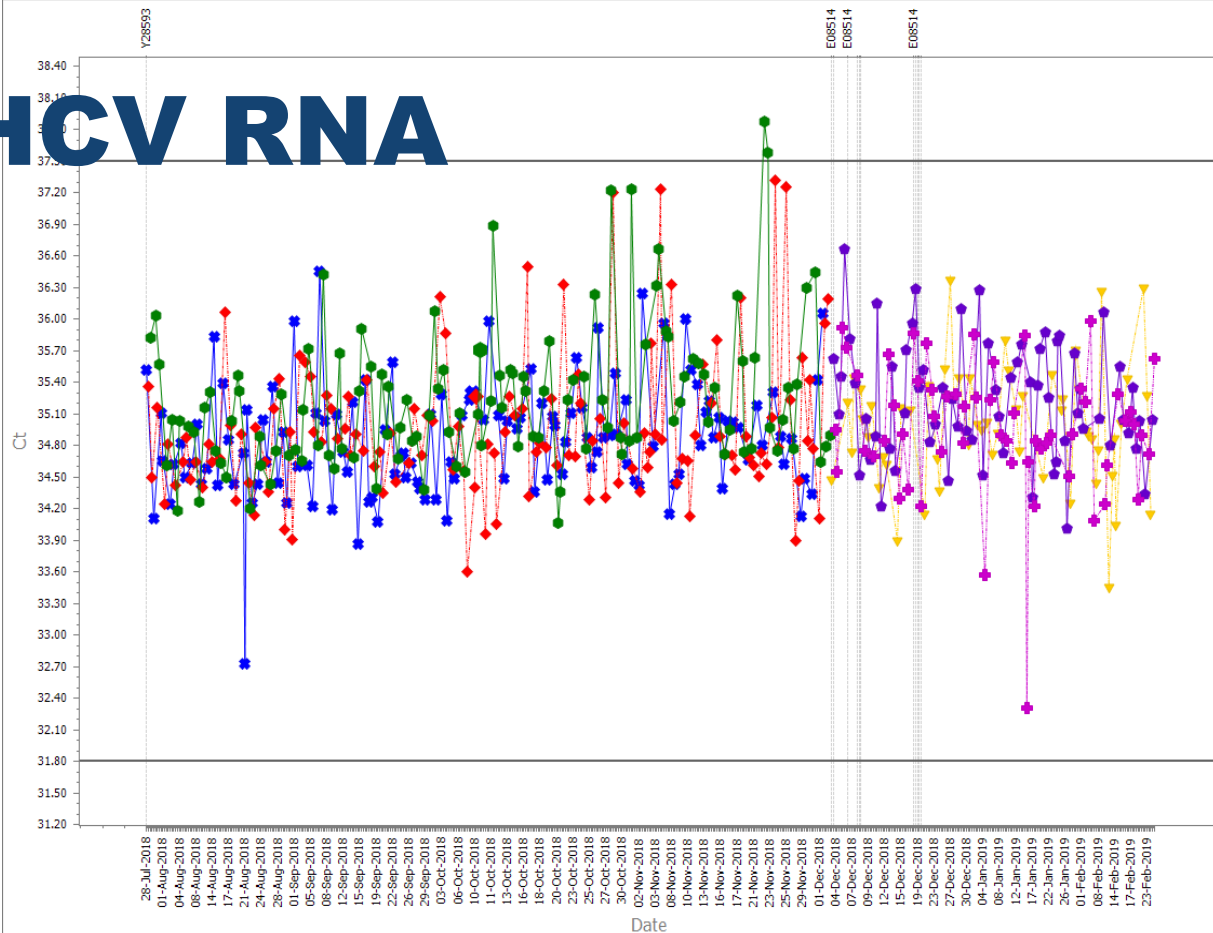
Lab 275 - HCV RNA

- Peer Group Data by Lab
- Roche cobas MPX



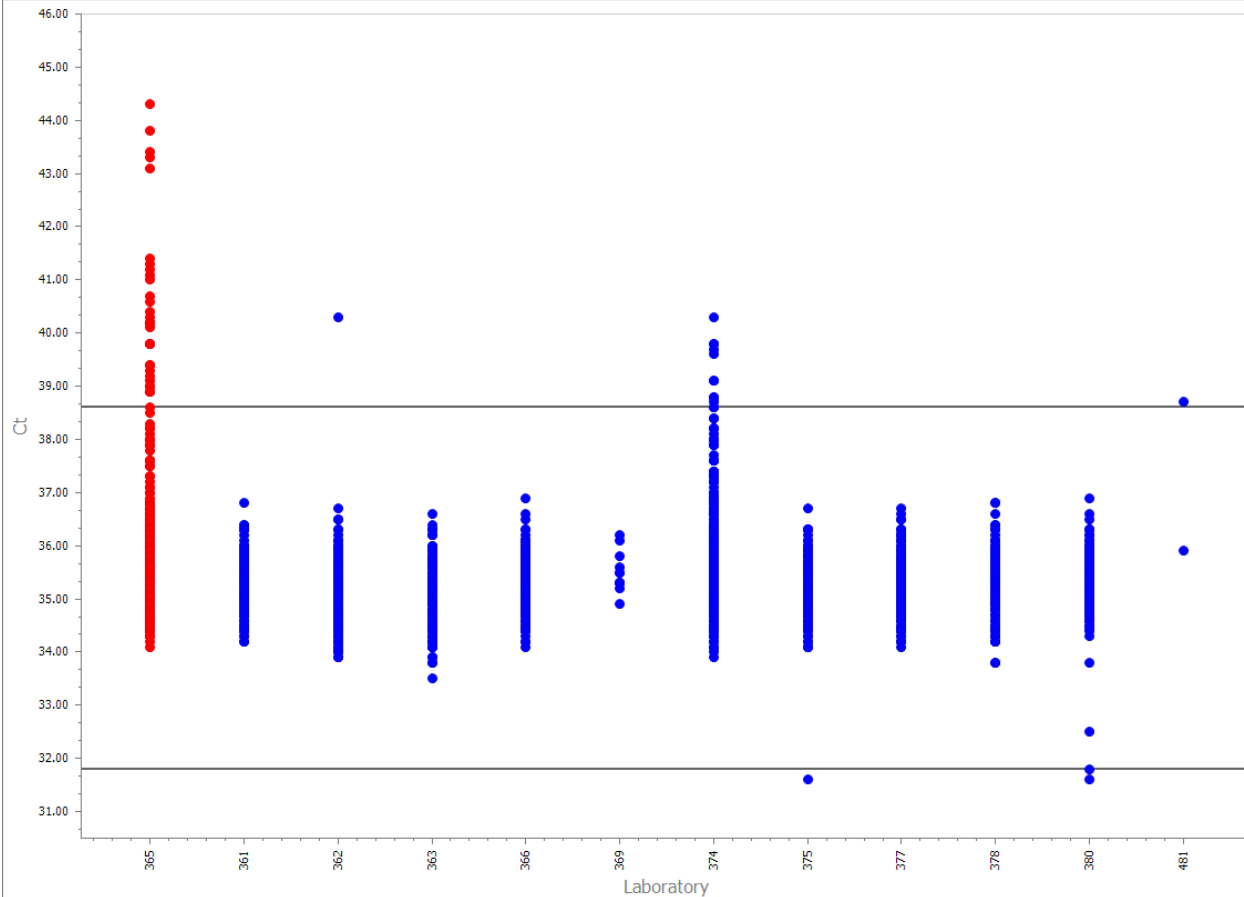
Lab 275 – HCV RNA

- Roche cobas MPX
- Data by Instrument
- Spikes caused by pooling of left over QC samples



HCV RNA

- Roche cobas MPX v2.0
- Peer Group Data
- Unusually high Ct values for Lab 365



Laboratory:365

Grouped by:Laboratory

From:01-Nov-2017 to 25-Feb-2019

Assays:Roche COBAS TaqScreen MPX v.2.0;

Analyte:HCV RNA

EQC:QConnect TriScreen

EQC Lot Number:180201;

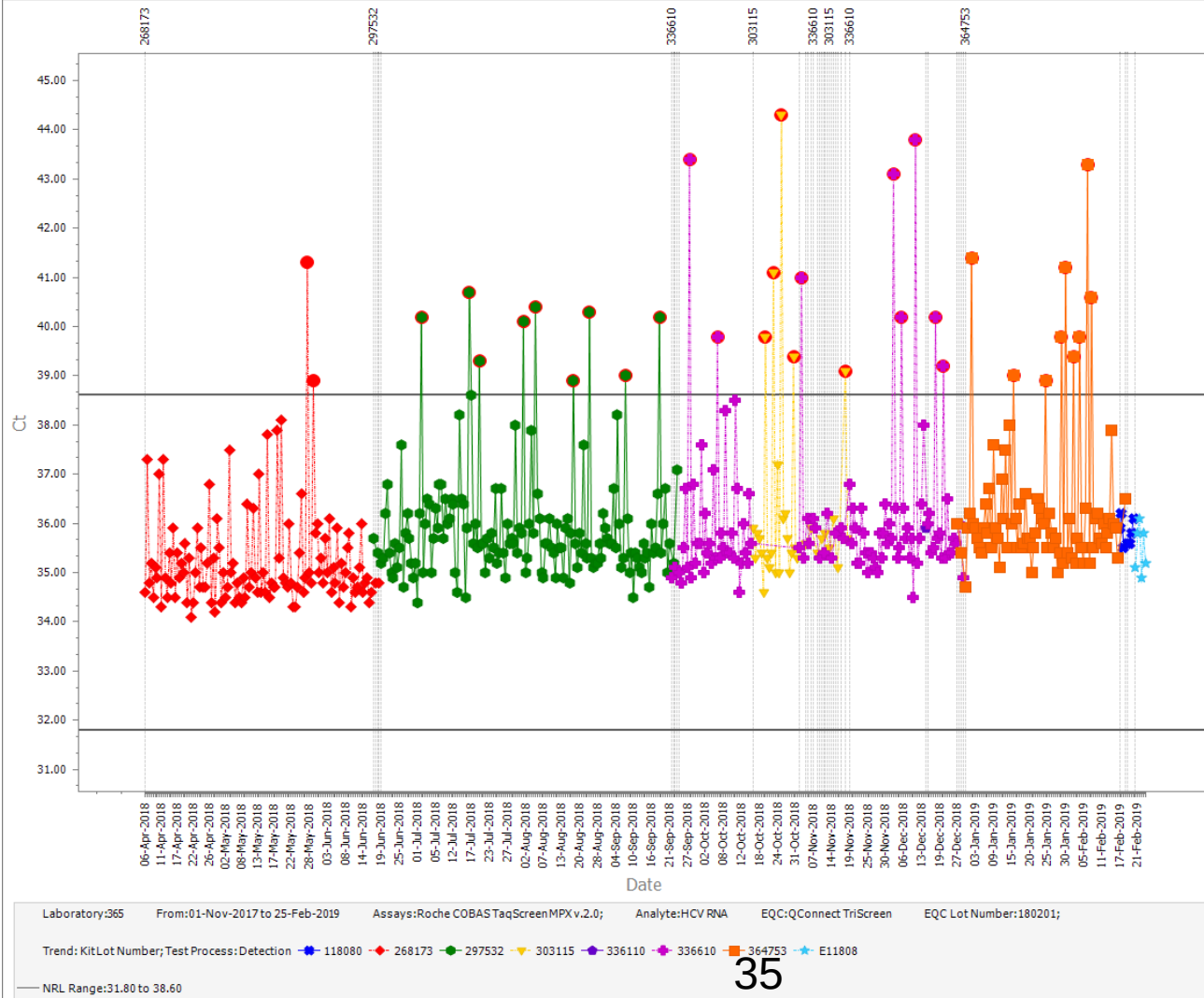
NRL Range:31.80 to 38.60

Note: Custom Y Axis range used.

WARNING: Possible hidden points lower than the chart range.

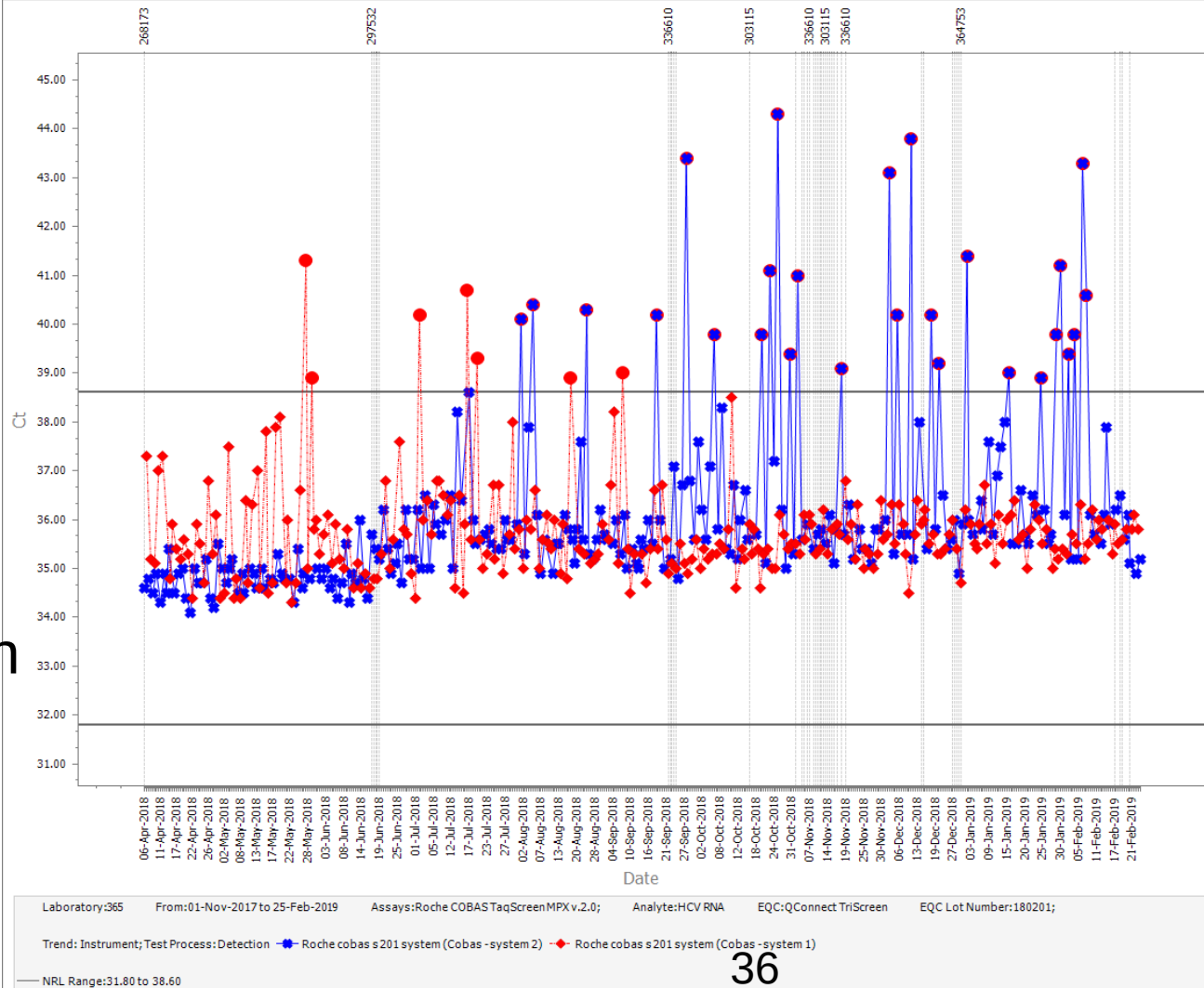
Lab 365

- Roche cobas MPX v2.0
- Data by reagent lot
- Spikes in Ct values



Lab 365

- Roche cobas MPX v2.0
- Data by Instrument
- Spikes in Ct values – switch in instruments reported?



TriScreen Study

- Multi-site, multi-country study on suitability of TriScreen to monitor Roche cobas MPX and cobas TaqScreen MPX v2.0

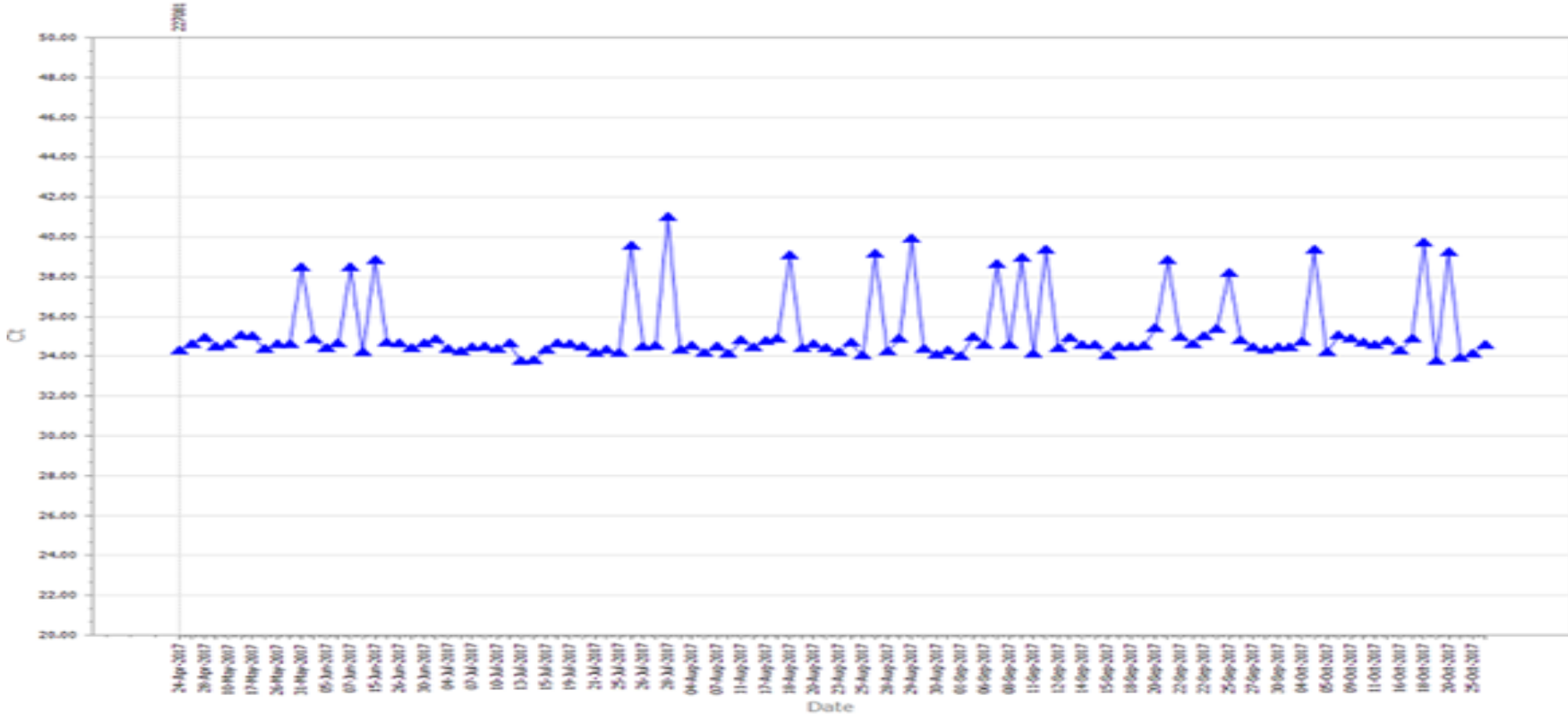
**EVALUATION OF A
MULTIMARKER QUALITY
CONTROL SAMPLE FOR
MONITORING THE
PERFORMANCE OF
MULTIPLEX BLOOD
SCREENING NUCLEIC
ACID TESTS**

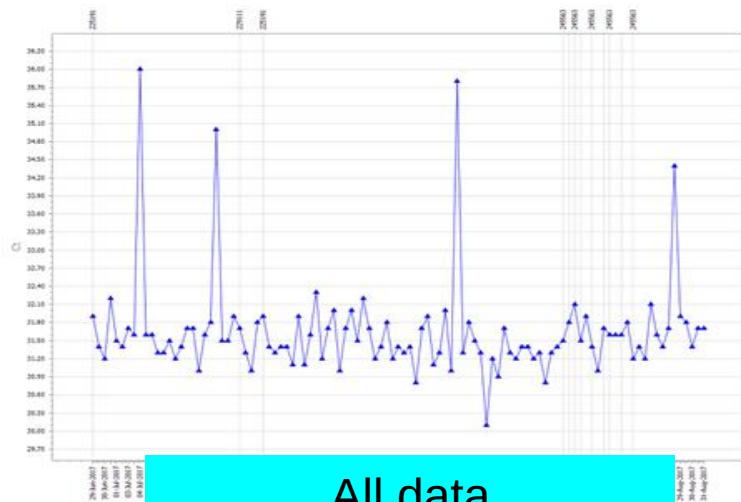
Results

- Generally, HCV RNA MPX v2.0 testing demonstrated greater imprecision
- No detectable differences in imprecision between participants testing HCV RNA on cMPX on the c6800/c8800 systems (past participants)
- QC was sensitive enough to see different protocols were being used for routine and cadaveric testing

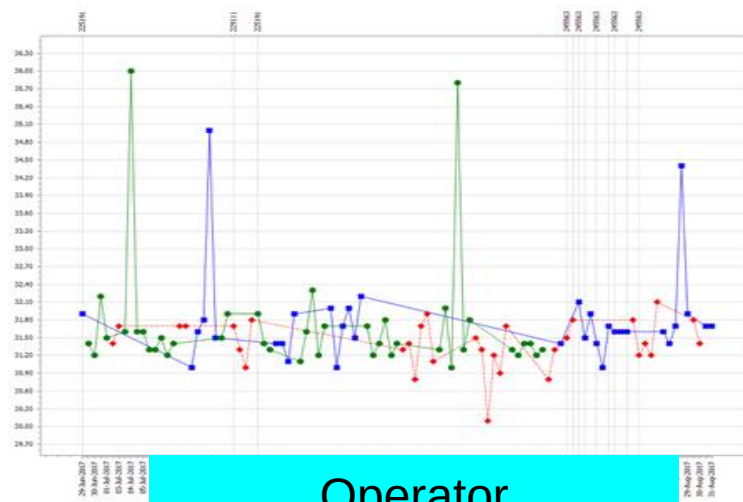
Results –

Investigation into unexpected results

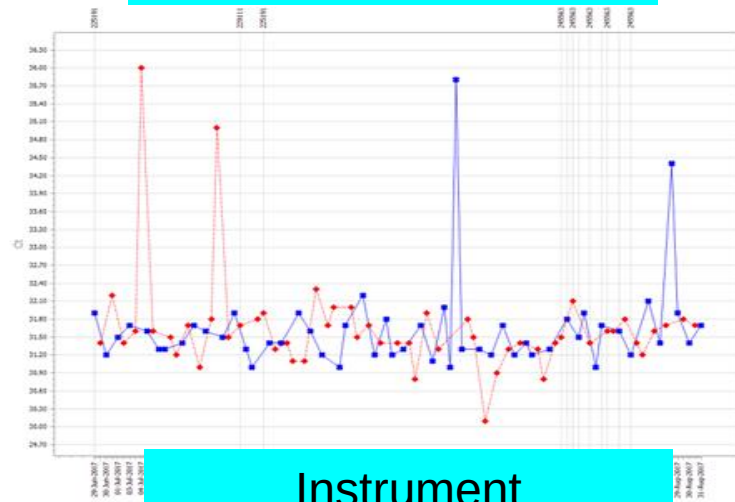




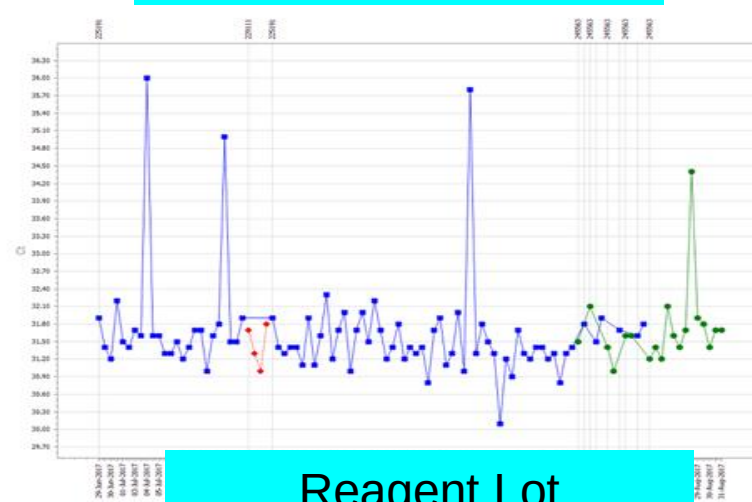
All data



Operator



Instrument



Reagent Lot

Mini-Pool and QC Testing

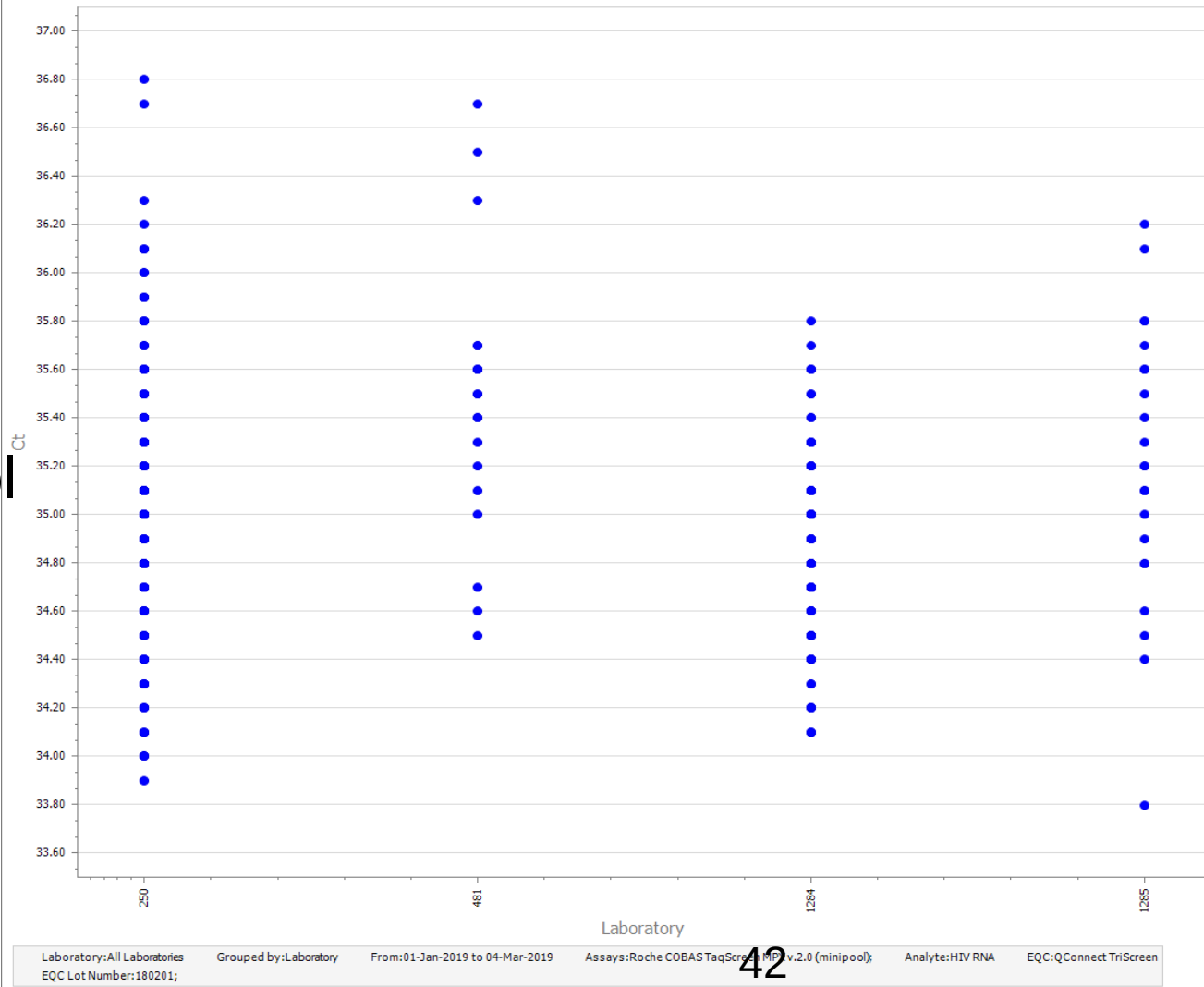
- Use of QC for cadaveric protocol demonstrated dilution possible
- Many donor centres using Roche cobas MPX v2.0 test in mini-pools of 6

Question -

Can NRL QConnect QCs be used in mini-pool format?

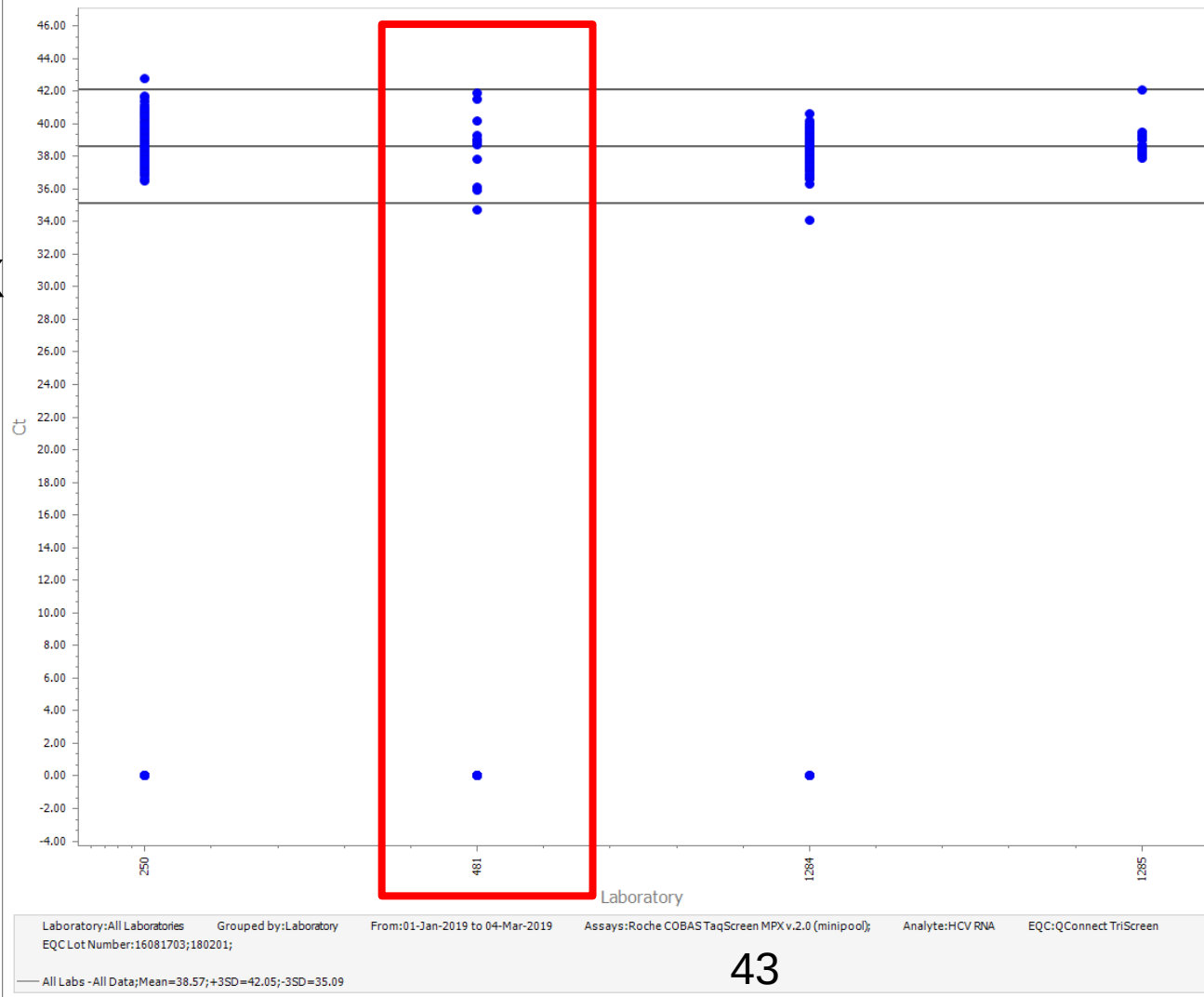
HIV RNA

- Roche cobas MPX v2.0 using minipool protocol



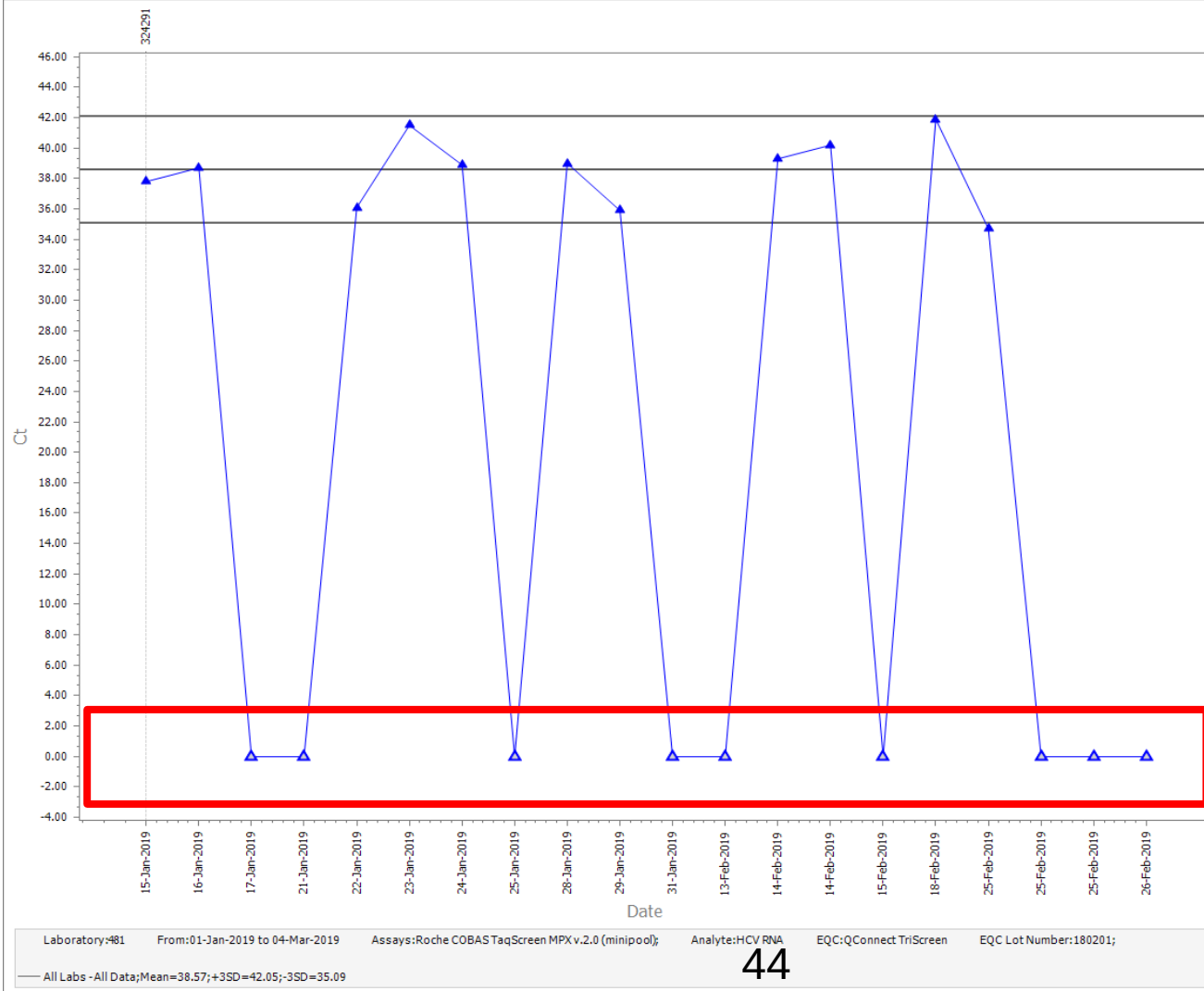
HCV RNA

- Roche cobas MPX v2.0
- HCV RNA “0” Ct values
- Few for two labs
- More for lab in red box



Lab 481

- Roche cobas MPX v2.0
- HCV RNA “0” Ct values
- Samples stored incorrectly on receipt



Conclusion

- Dilution possible but needs more work
- Limit of detection differences between MPX on 6800 and MPX v2.0 on s201 may play a role
- Use of QC for mini-pool testing highlighted variation was detectable even at high Ct values

General conclusions

- NAT screening – the ‘Big Two’
 - Grifols and Roche
 - Some ‘local’ manufacturers successful
- Serology
 - Diverse technologies and manufacturers
 - Assay selection driven by cost, availability and practicality
 - Higher error rates seen in manual testing

Where to From Here?

- Assay evaluation and selection
- Assay procurement
- Validated testing algorithms
- Quality management systems
- Quality assurance / quality control
- Training and competency

Thank-you!

Acknowledgements

- NRL EQAS team
- NRL QC team
- All the program participants

Think different

