Interesting QC Case Studies: An interactive session

Vincini GA
NRL, Melbourne, Australia

February 2019

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QC Case Studies

- Series of cases to demonstrate -
  - What to look for
  - Common variation seen with QC use
  - How to troubleshoot scenarios
  - Step-wise investigations!
  - **Don't need to have right answer first time**

NRL has a troubleshooting checklist

www.nrlquality.org.au/qconnect/QC-Limits

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Before we get started on the Case Studies……

- How the Polling works
- On any electronic device, key the following into your browser:

  PollEv.com/nrl2019

- Let’s practice…

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The capital city of Australia is…?

- Sydney
- Melbourne
- Canberra
- Gold Coast
- None of the above

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The capital city of Australia is…?

Sydney

Melbourne

Canberra

Gold Coast

None of the above

Scenario 1

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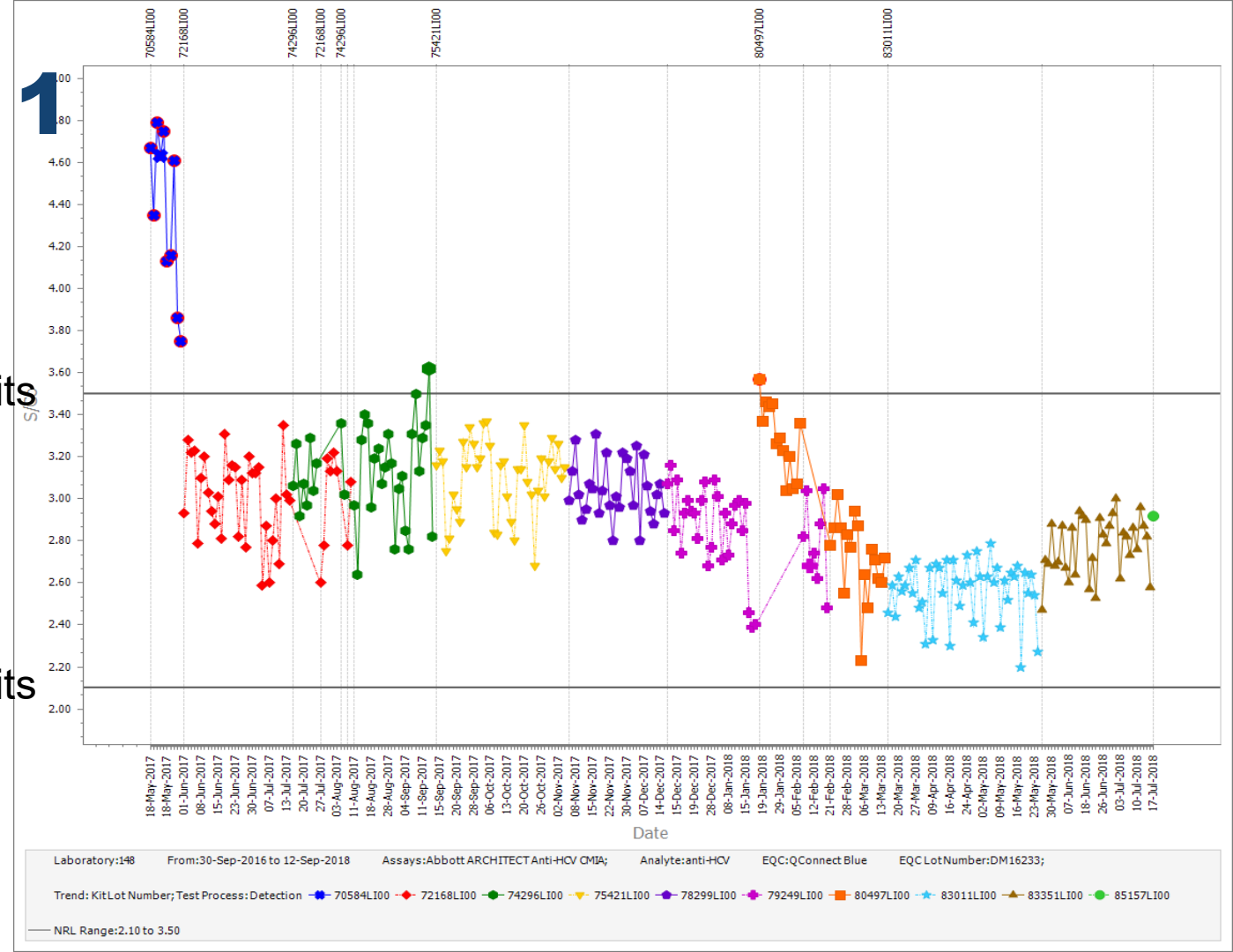
Scenario 1

NRL Limits

NRL Limits



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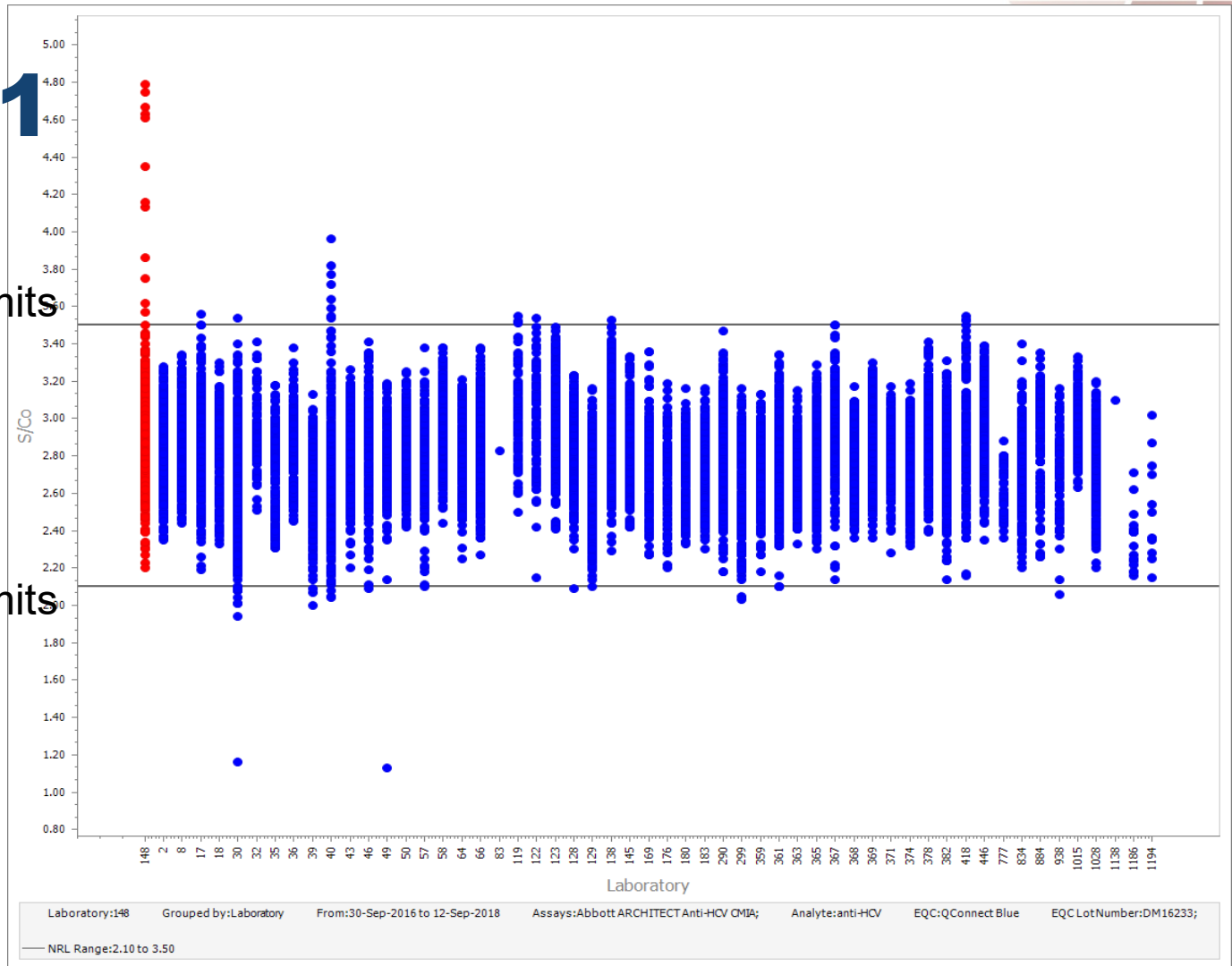
Scenario 1

NRL Limits

NRL Limits



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What is the likely cause of the results in Scenario 1?

There is no problem at all

This is reagent lot variation

The QC is failing and needs review

The operators are at fault and need retraining

The instrument is failing and needs attention

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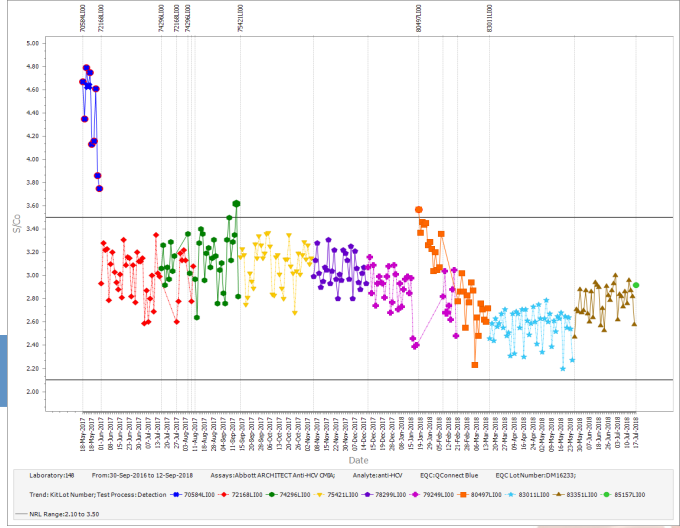

Scenario 1

Answer:

Classic Lot Variation…

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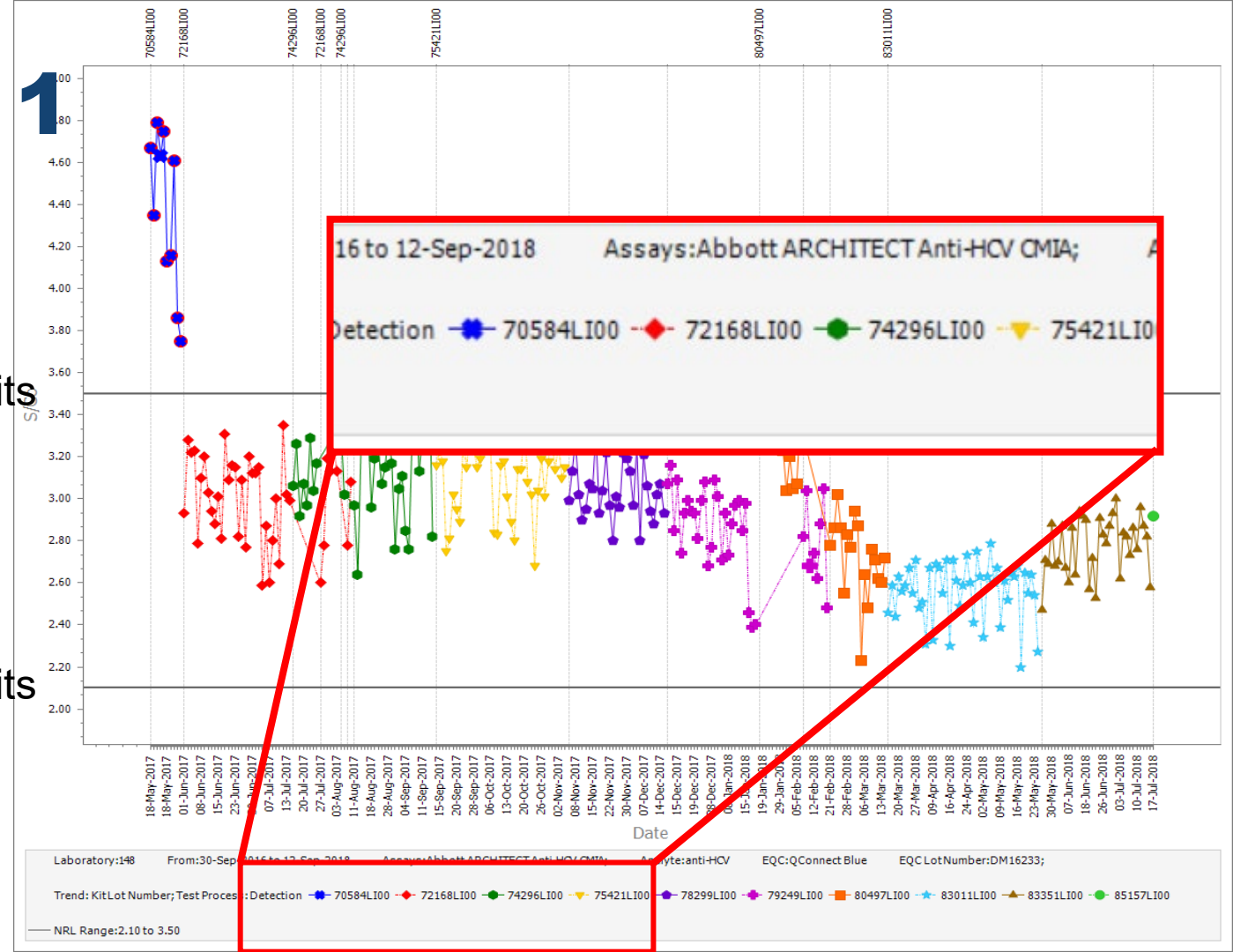
Scenario 1

NRL Limits

NRL Limits



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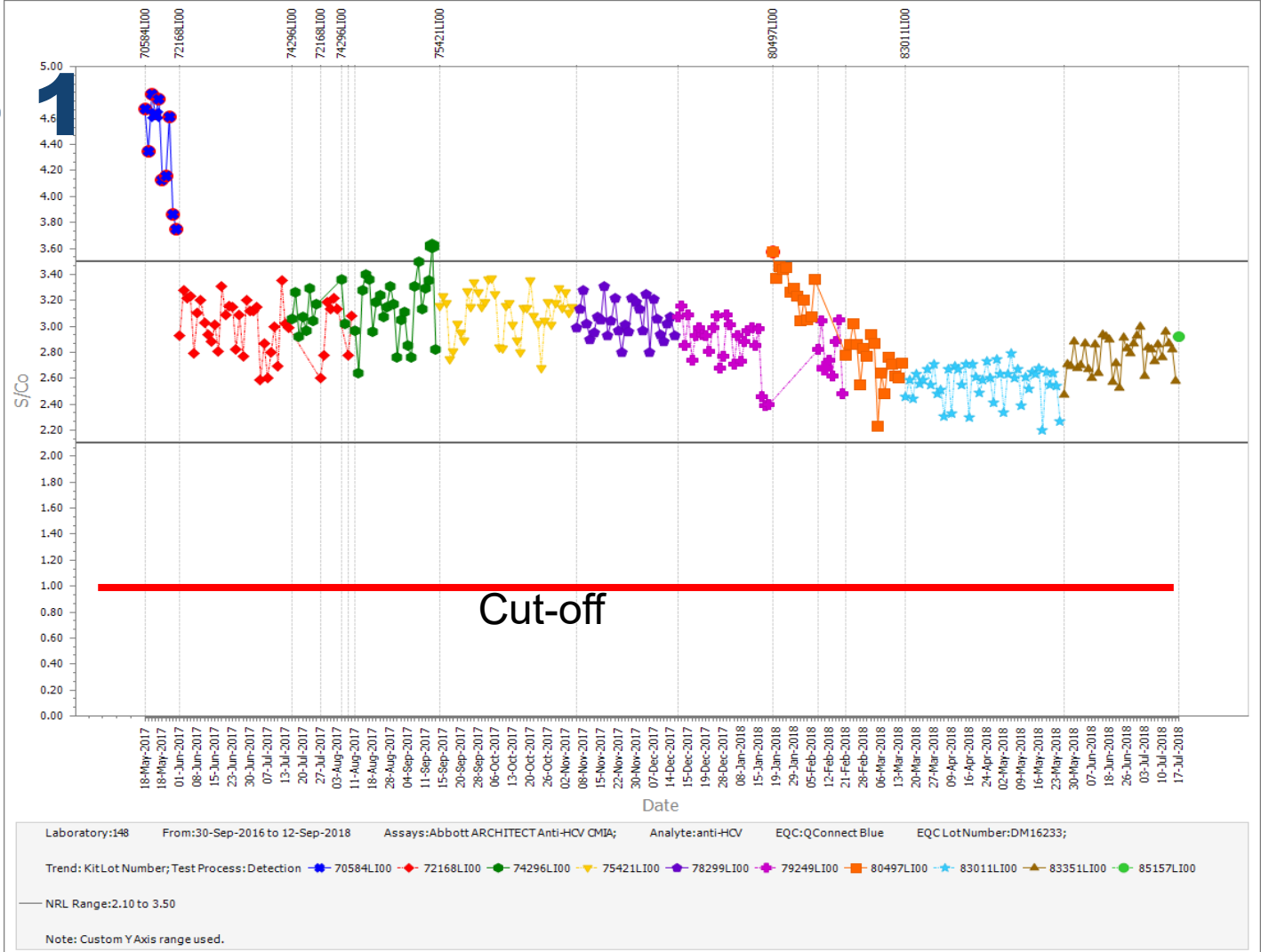
Scenario 1



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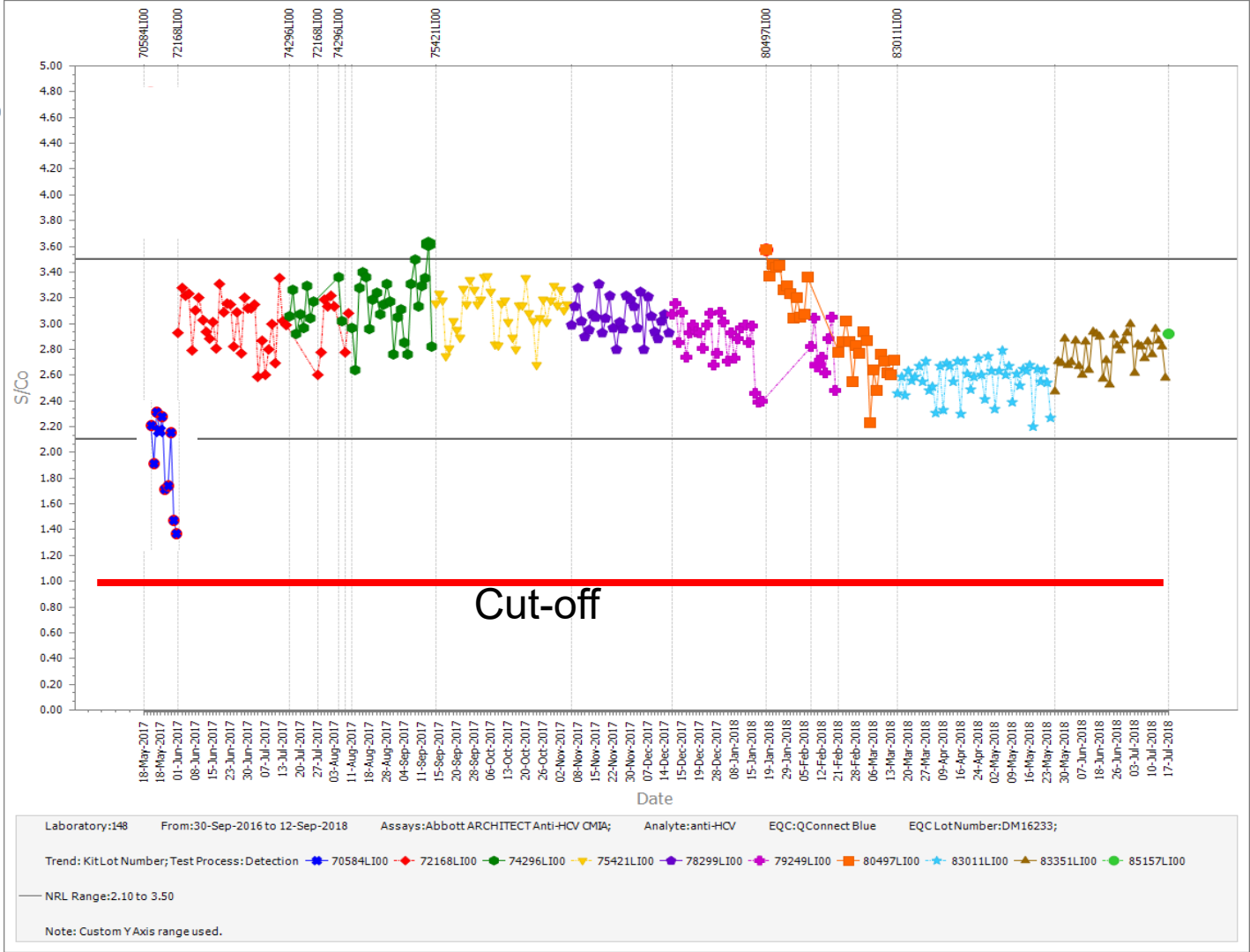
Scenario

- ???



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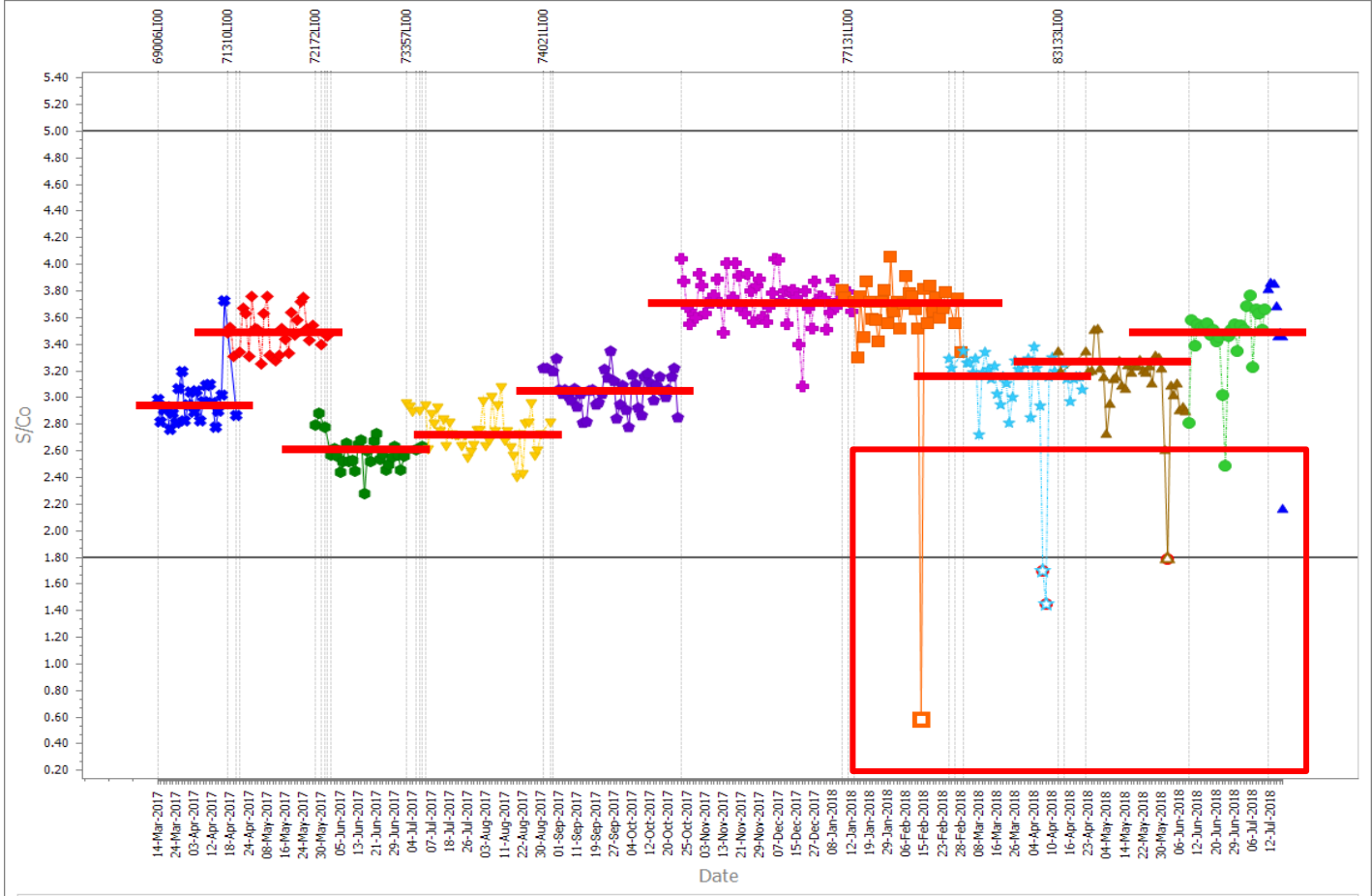

Laboratory:446 From:30-Sep-2016 to 12-Sep-2018 Assays:Abbott ARCHITECT HIV Ag/Ab Combo CMIA; Analyte:HIV p24 Ag/Anti-HIV EQC:QConnect Blue EQC Lot Number:DM16233;

Trend: Kit Lot Number; Test Process: Detection 69006LI00 71310LI00 72172LI00 73357LI00 74021LI00 77131LI00 78482LI00 79207LI00 83133LI00 84025LI00

NRL Range:1.80 to 5.00

WARNING: Maximum numbers of Trends (10) achived. Please reduce the Trends selection.

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Scenario 2

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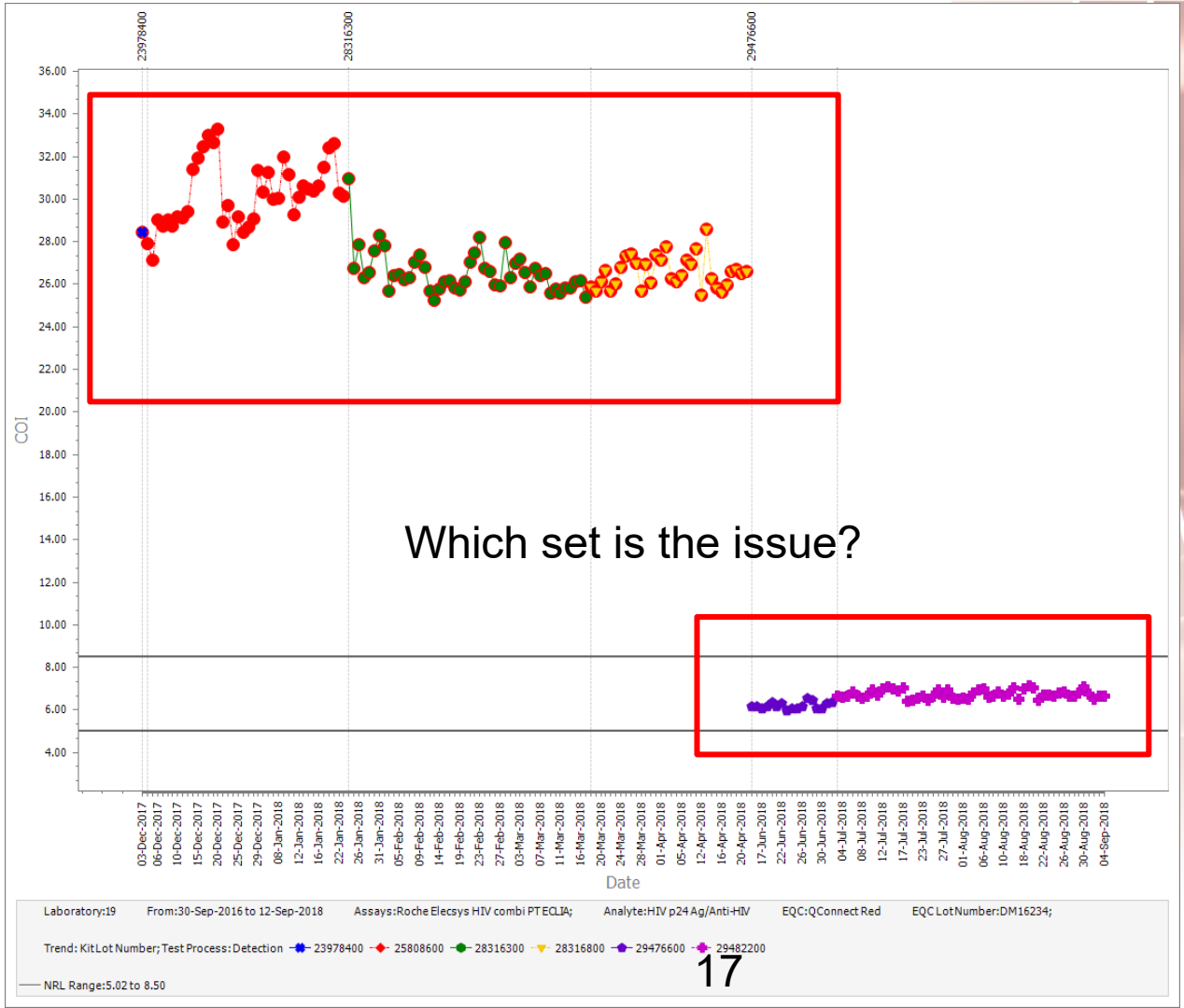
Scenario 2

- Lab data by reagent lot



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What is the likely cause of the results in the red boxes?

This is reagent lot variation

The QC is failing and needs review

The QConnect Limits are wrong and need review

There are two lots of the QC in use

Something else is going on...

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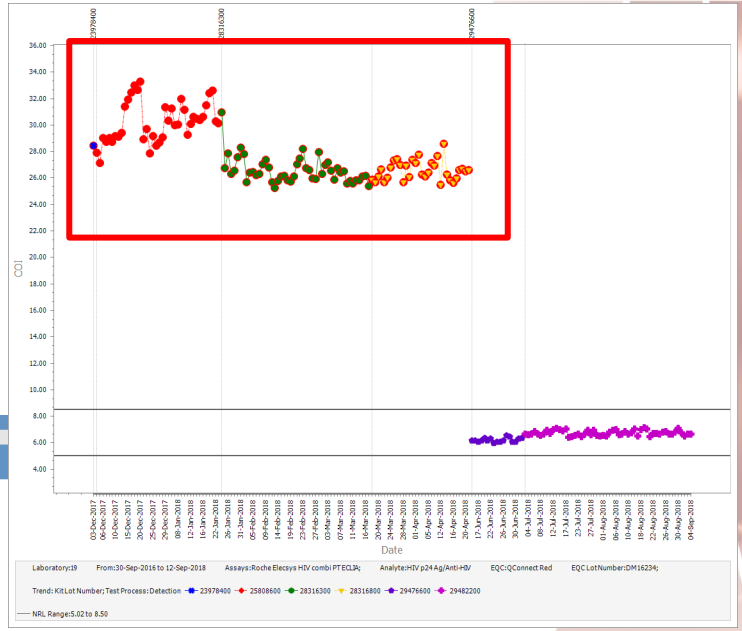
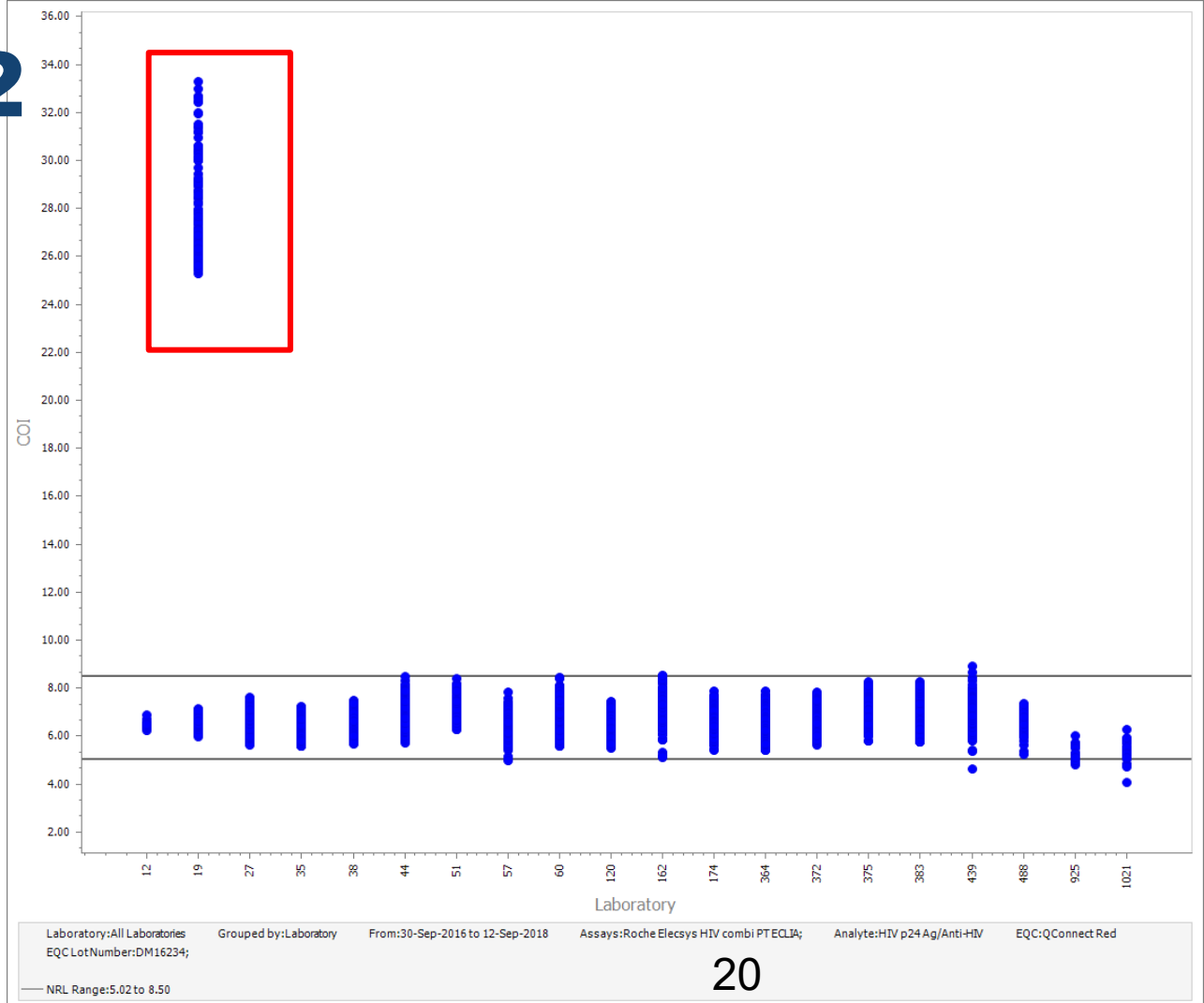


Scenario 2

- Peer group data



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Scenario 2

Answer:

Something else is going on…

Wrong QC data entered into EDCNet

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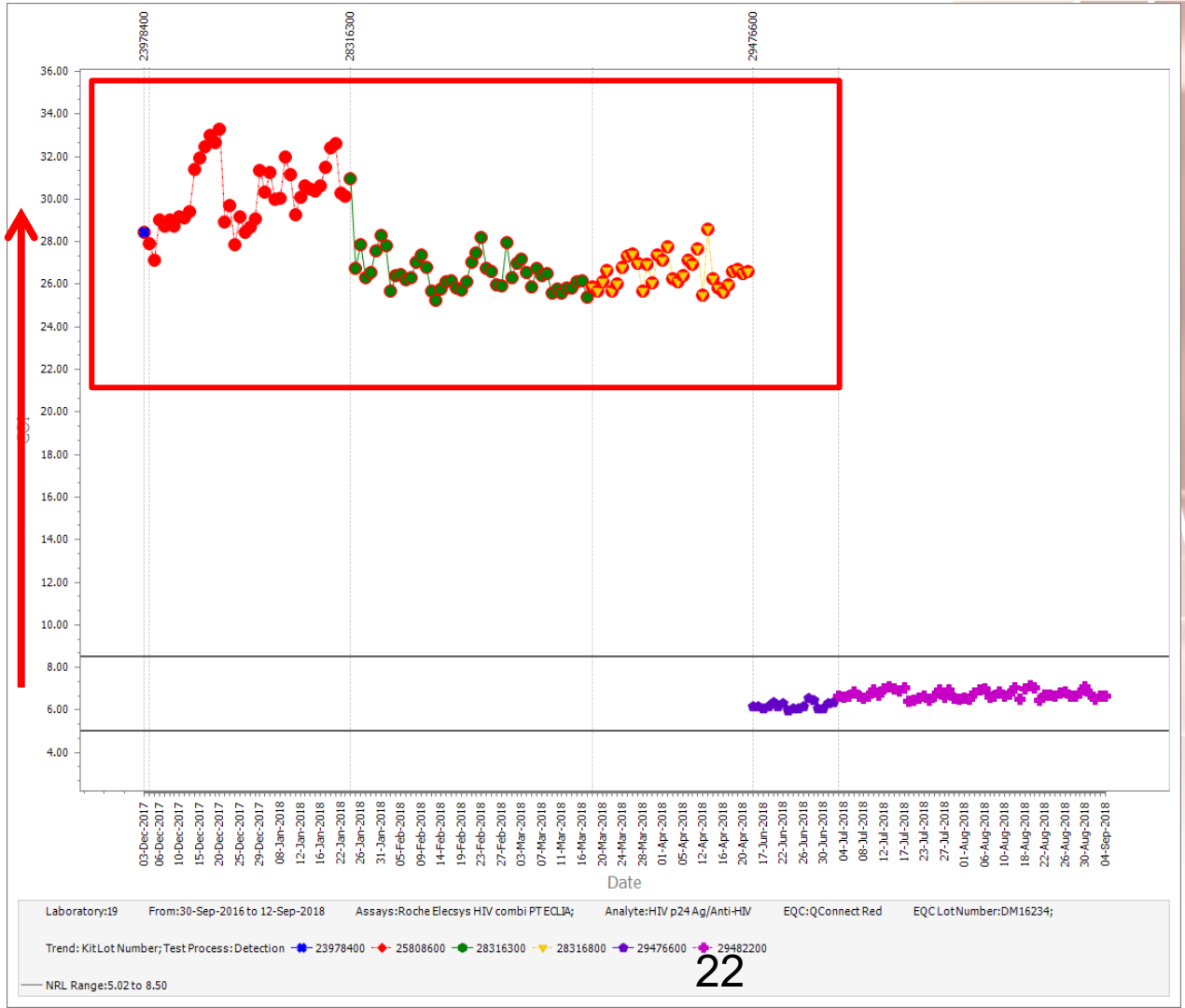
Scenario 2

- Non-QConnect QC data entered into EDCNet



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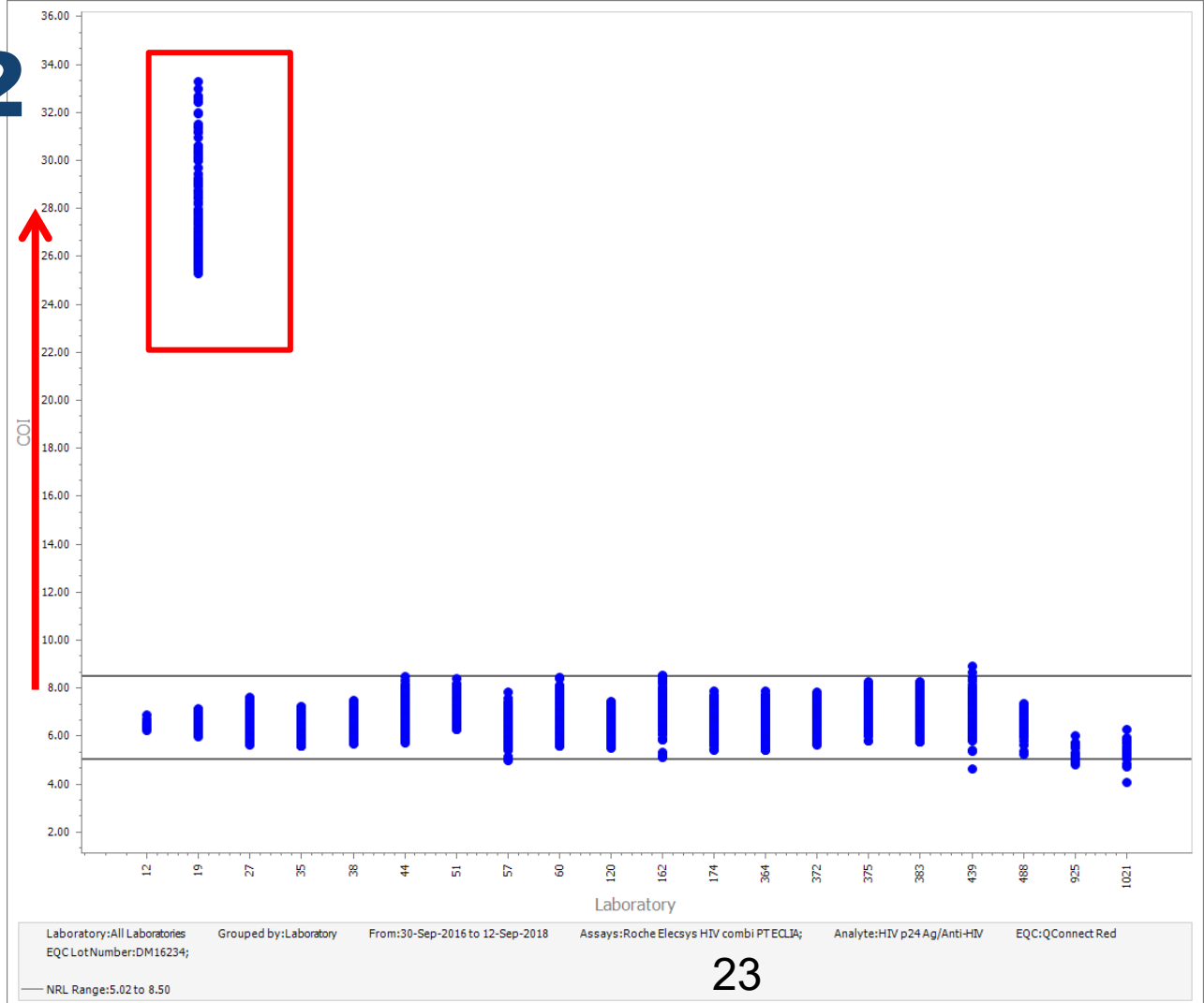
Scenario 2

- Peer group data



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Scenario 3

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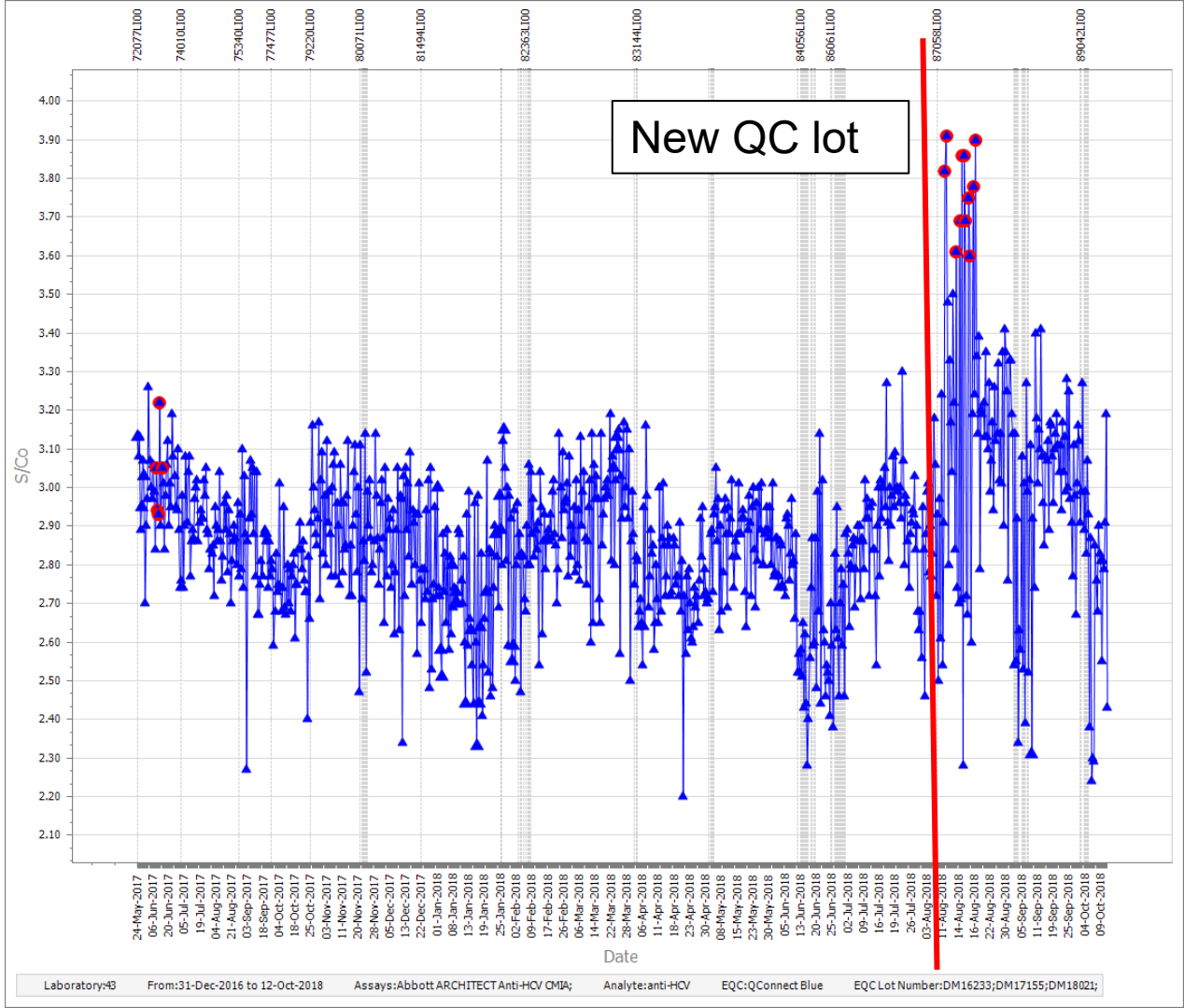
- QConnect Blue lot for Lab 43



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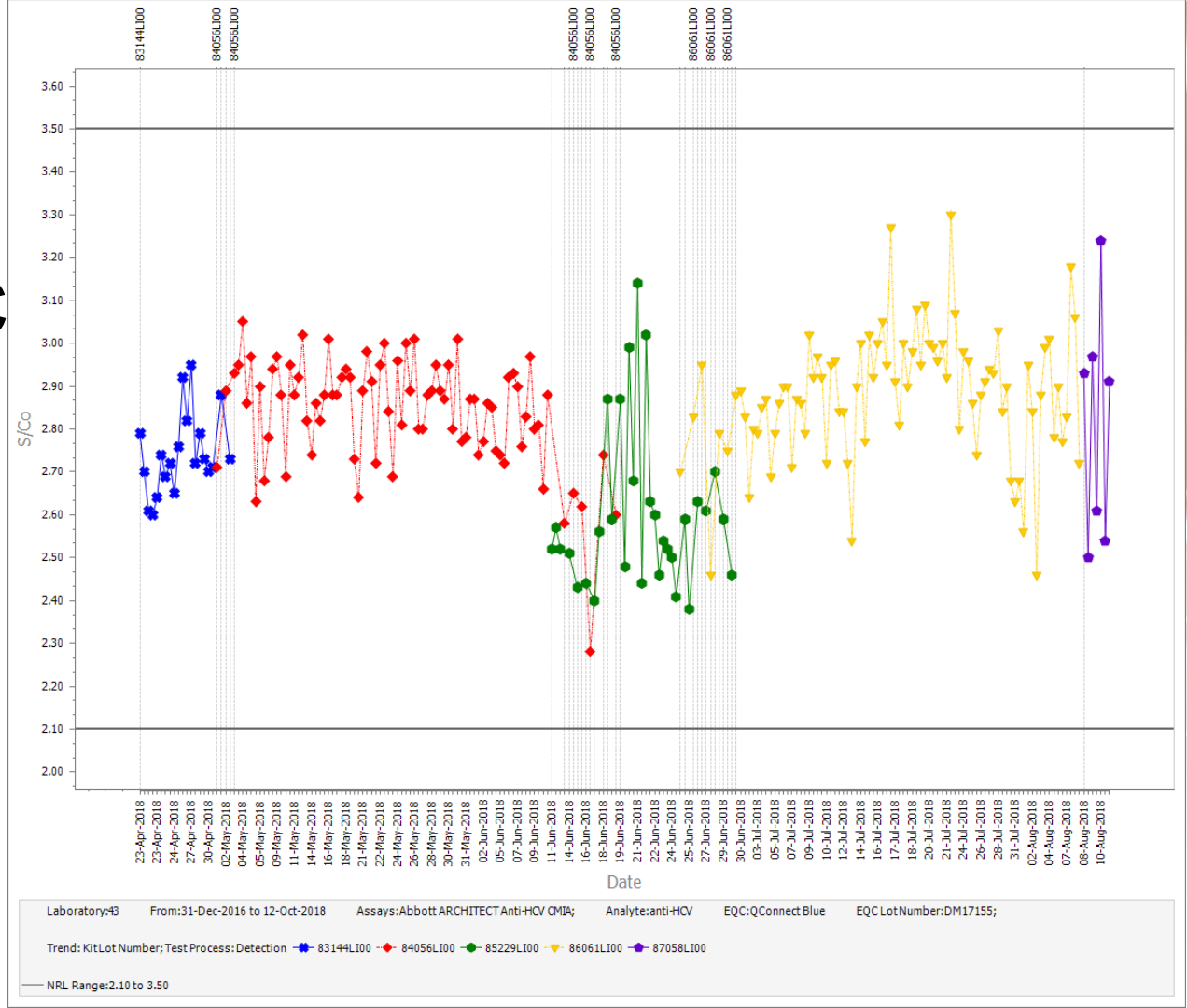
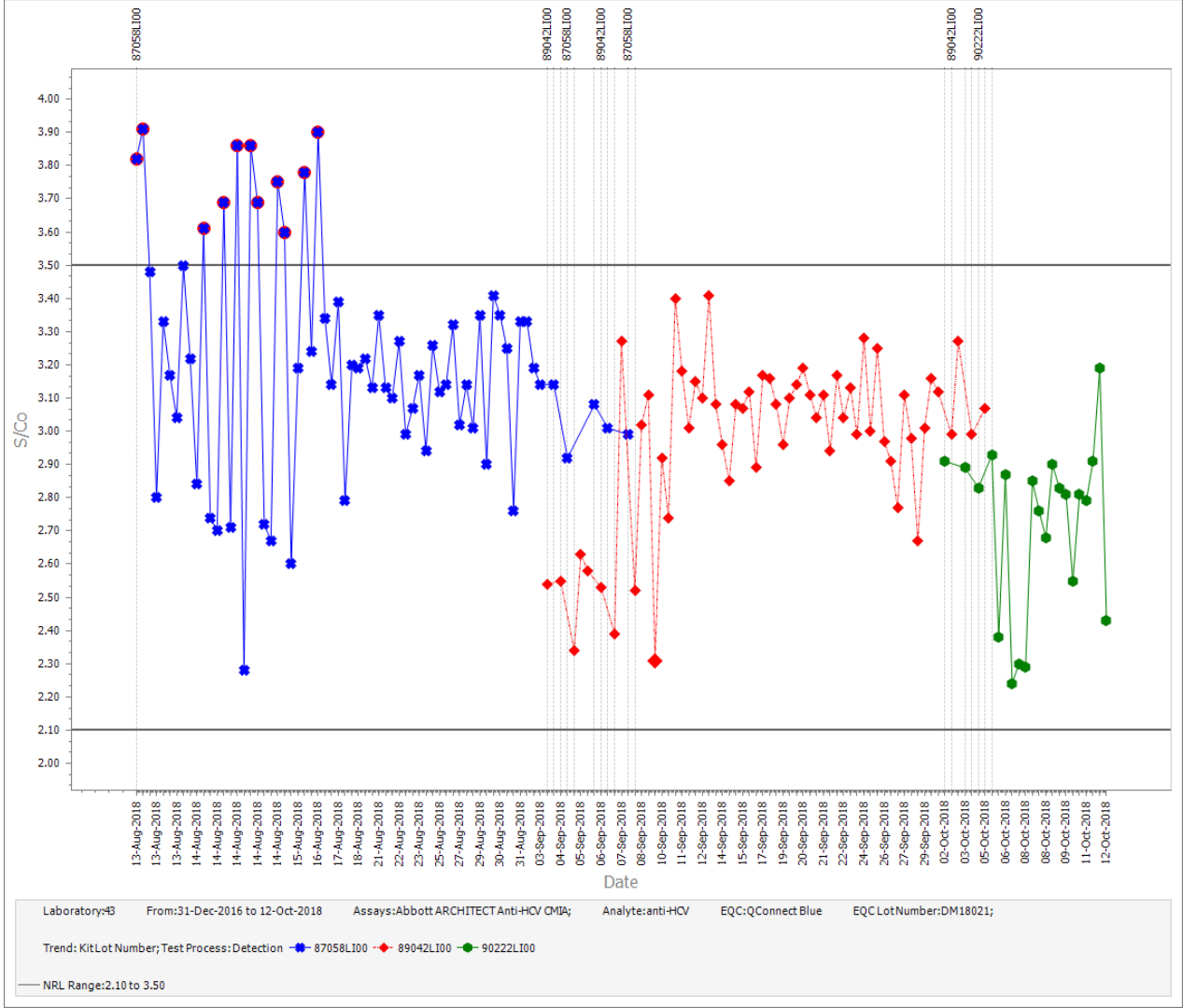
- Previous QC lot by reagent lot



NRL Science of Quality

- Current QC lot by reagent lot



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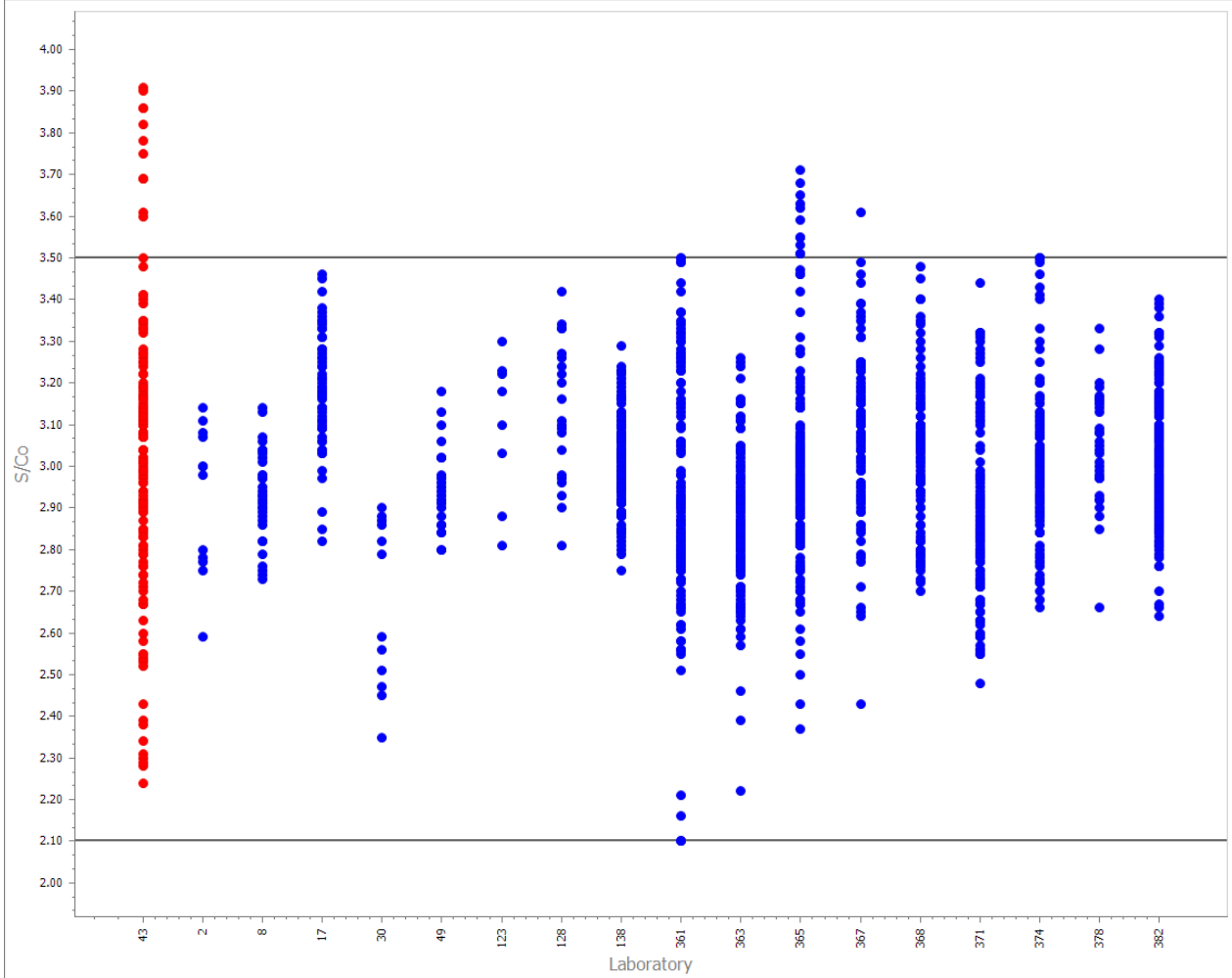

Laboratory:43 Grouped by:Laboratory From:31-Dec-2016 to 12-Oct-2018 Assays:Abbott ARCHITECT Anti-HCV CMIA; Analyte:anti-HCV EQC:QConnect Blue EQC Lot Number:DM18021;

NRL Range:2.10 to 3.50

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What is the likely cause of the results in Scenario 3?

There is no problem at all

This is reagent lot variation

The new QC is showing greater variation

The instruments in the lab are showing variation

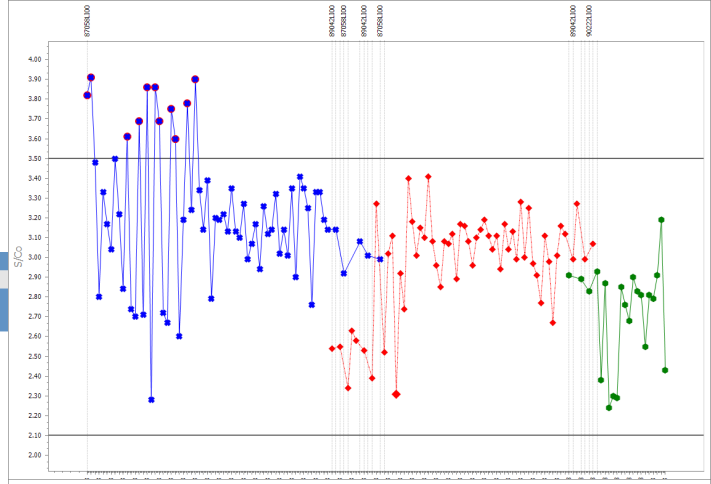
What is the likely cause of the results in Scenario 3?

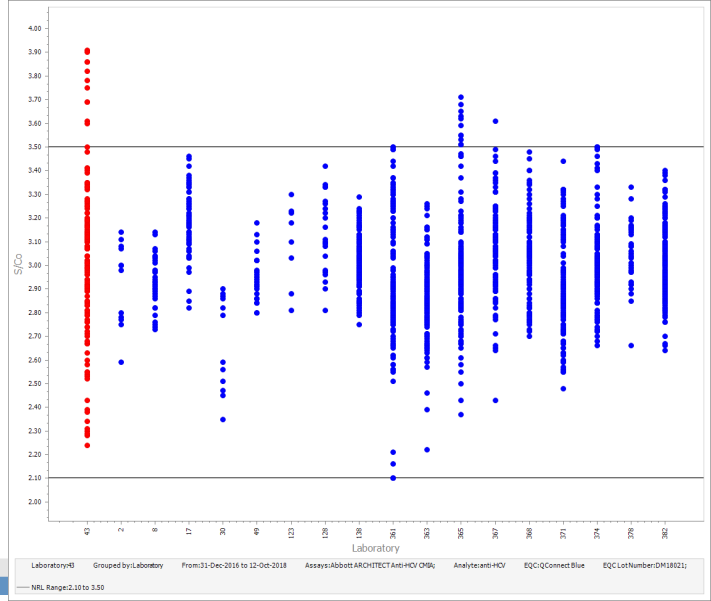
There is no problem at all

This is reagent lot variation

The new QC is showing greater variation

The instruments in the lab are showing variation





Scenario 3

- QConnect Blue QC lot issues?
- Introduction of a new QC lot!!!

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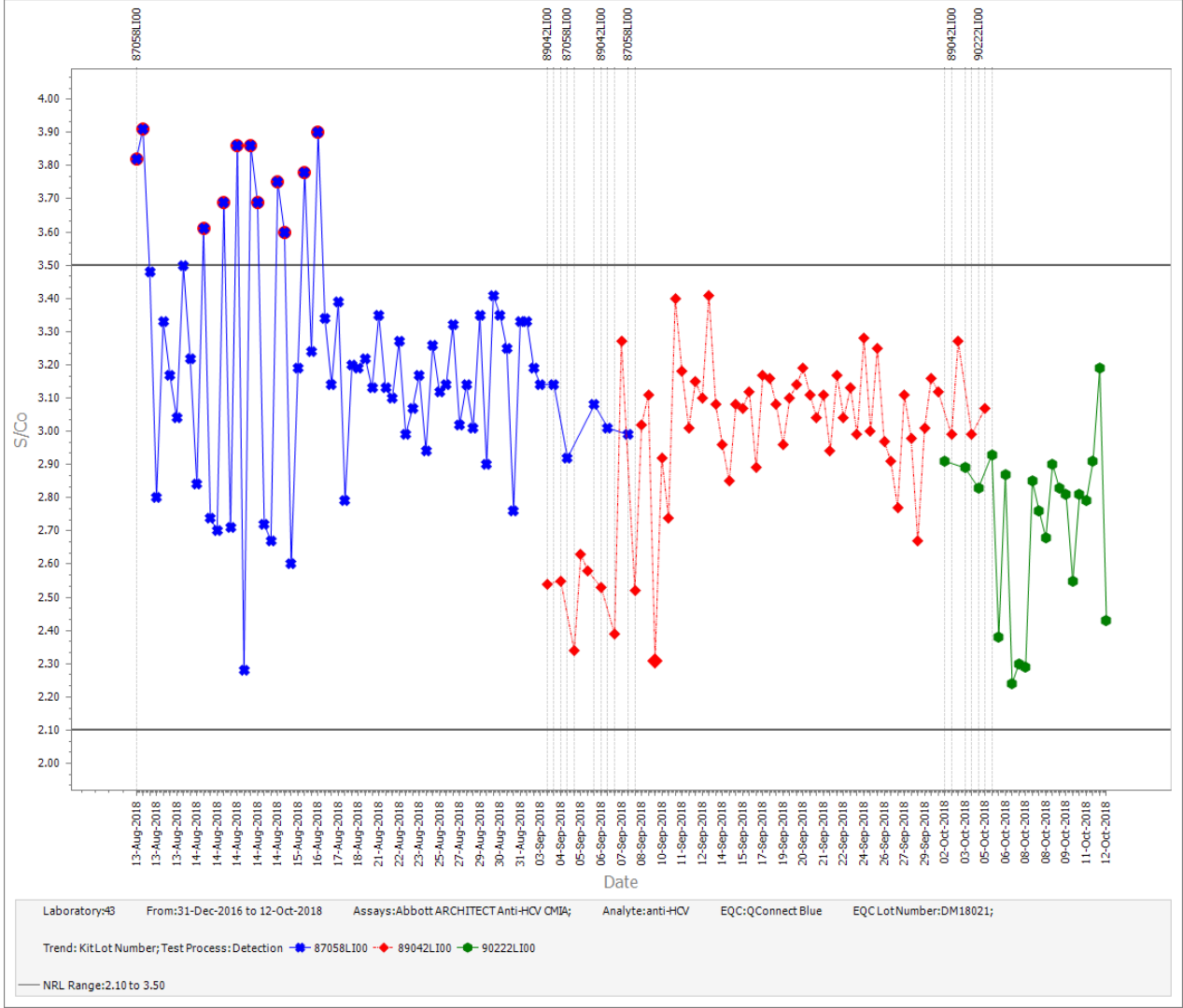
- Current QC lot by reagent lot



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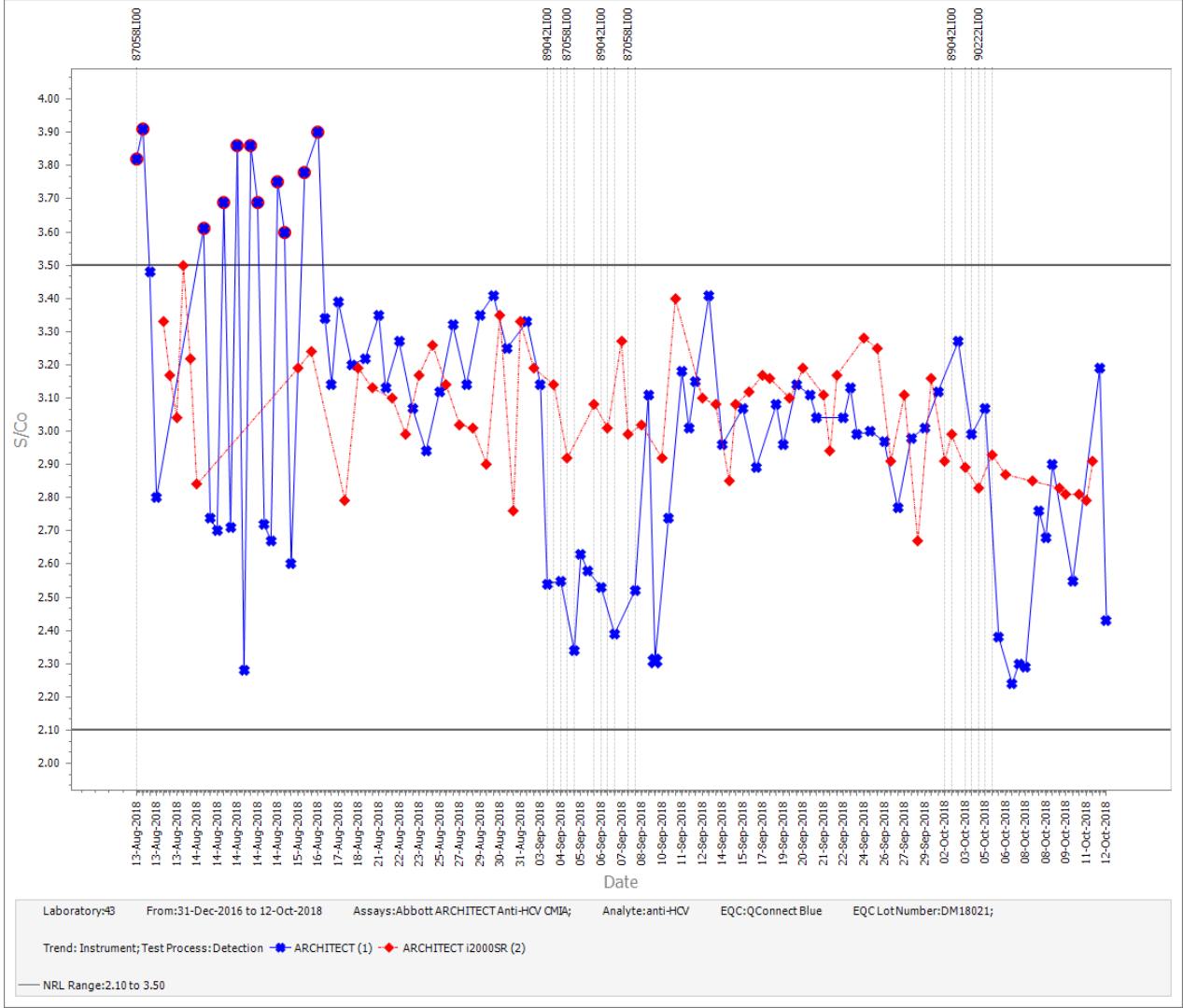
- Current QC lot by instrument



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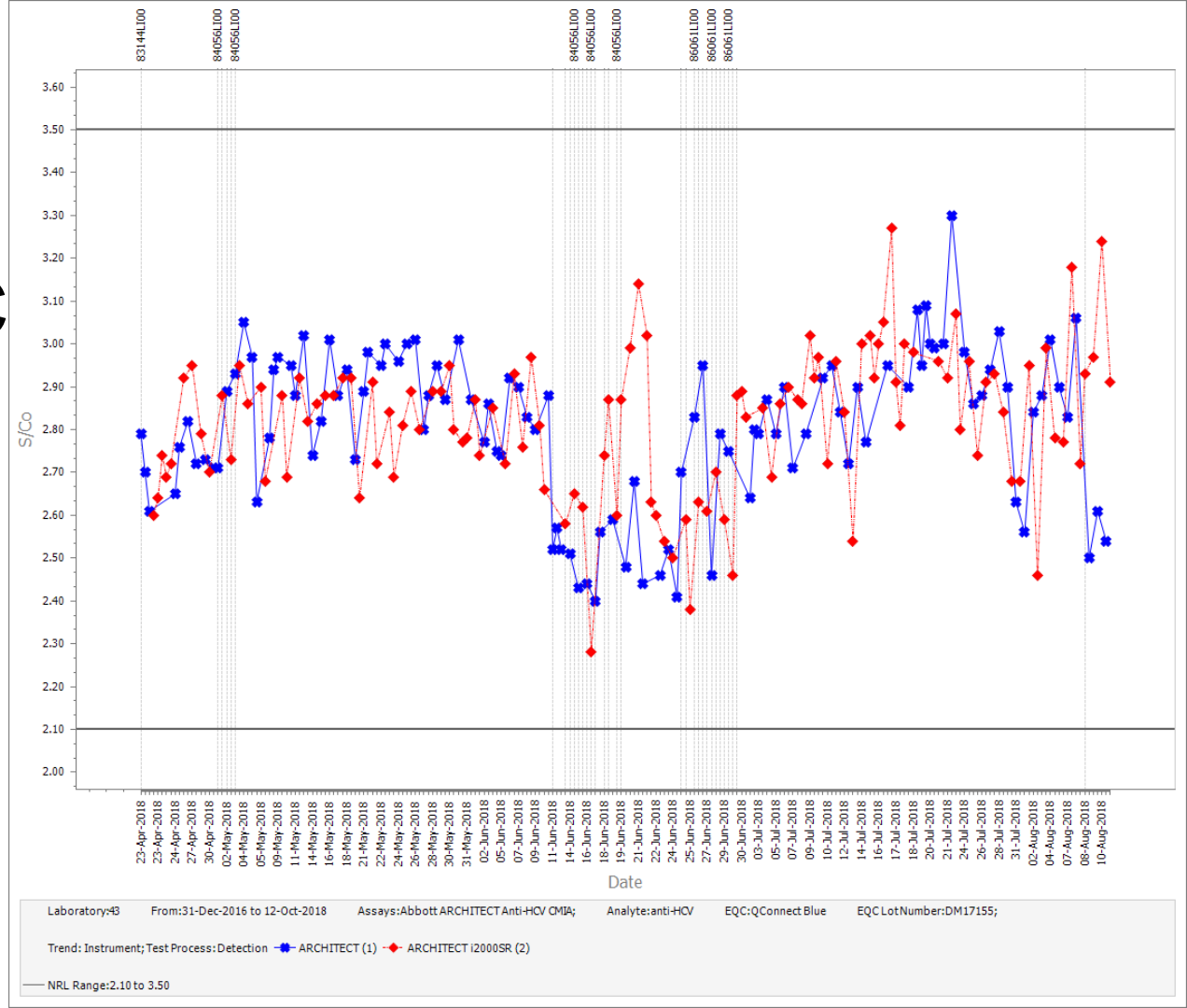
- Previous QC lot by instrument



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What is the source of variation in Scenario 3?

QC lot issue	A
Instrument issues	B
Reagent lot issues	C
All of the above	D
None of the above	E

Scenario 3

- Instrument calibration issues?
- Separation of the two instruments

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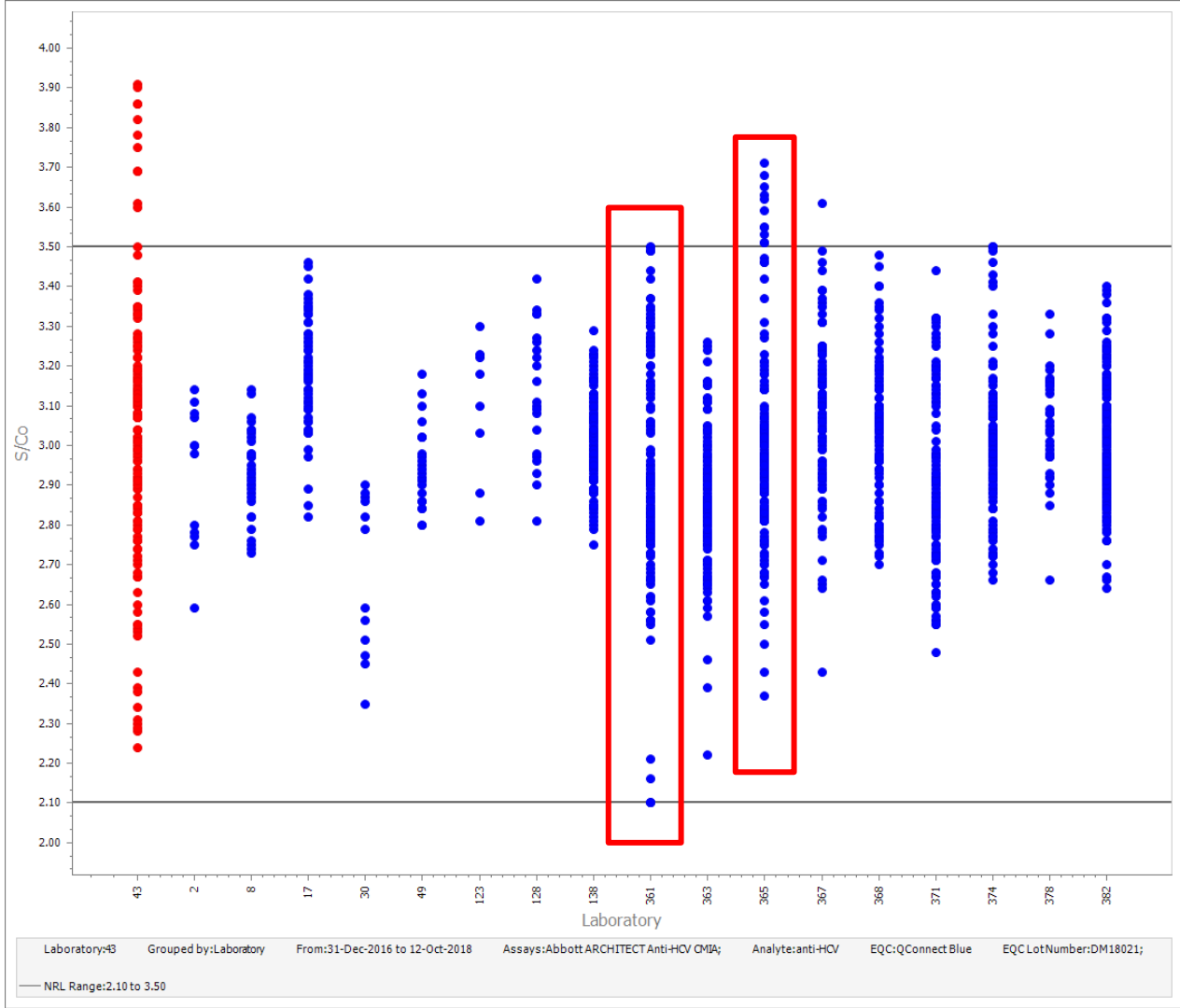

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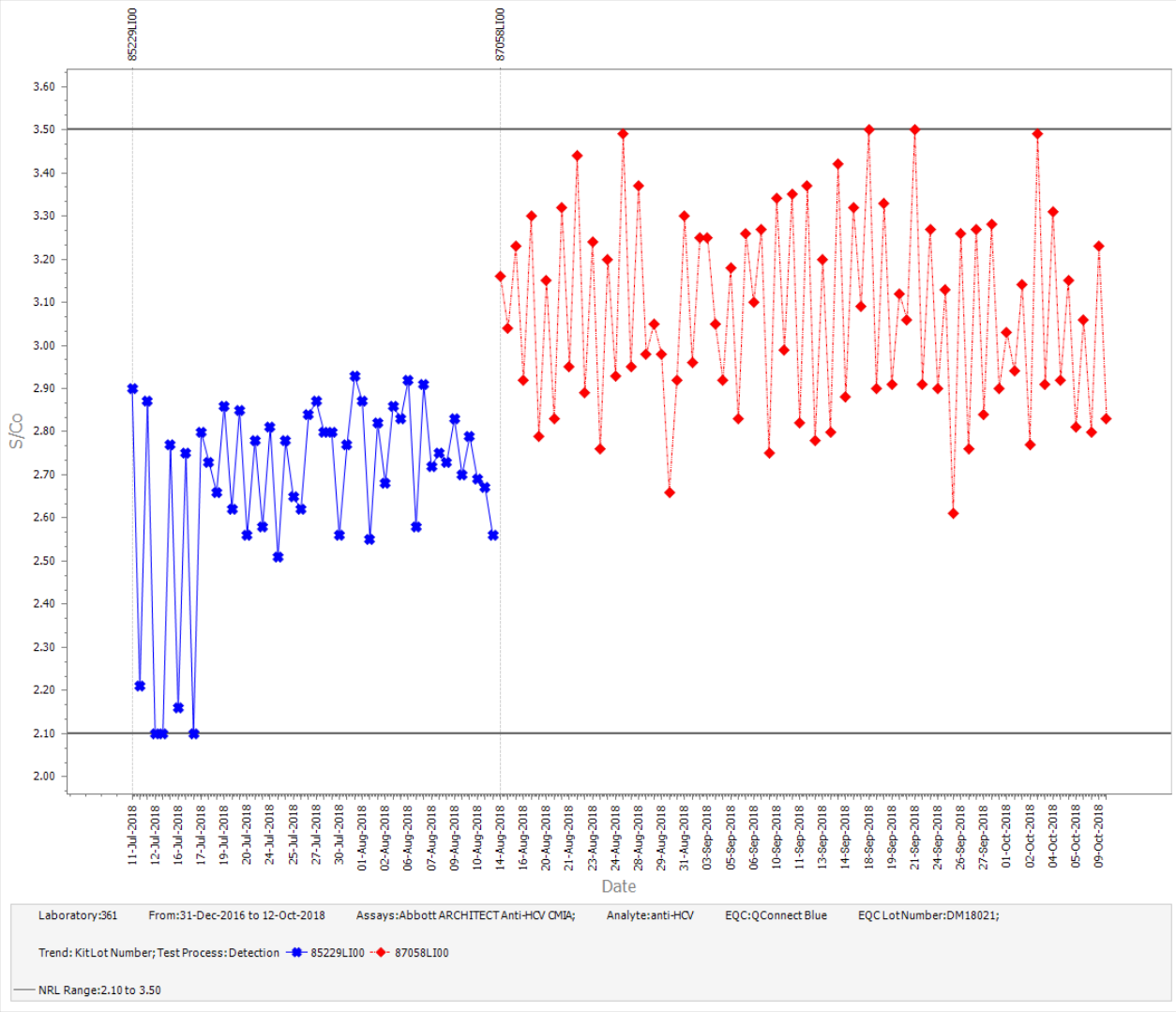
- Lab 361 by reagent lot



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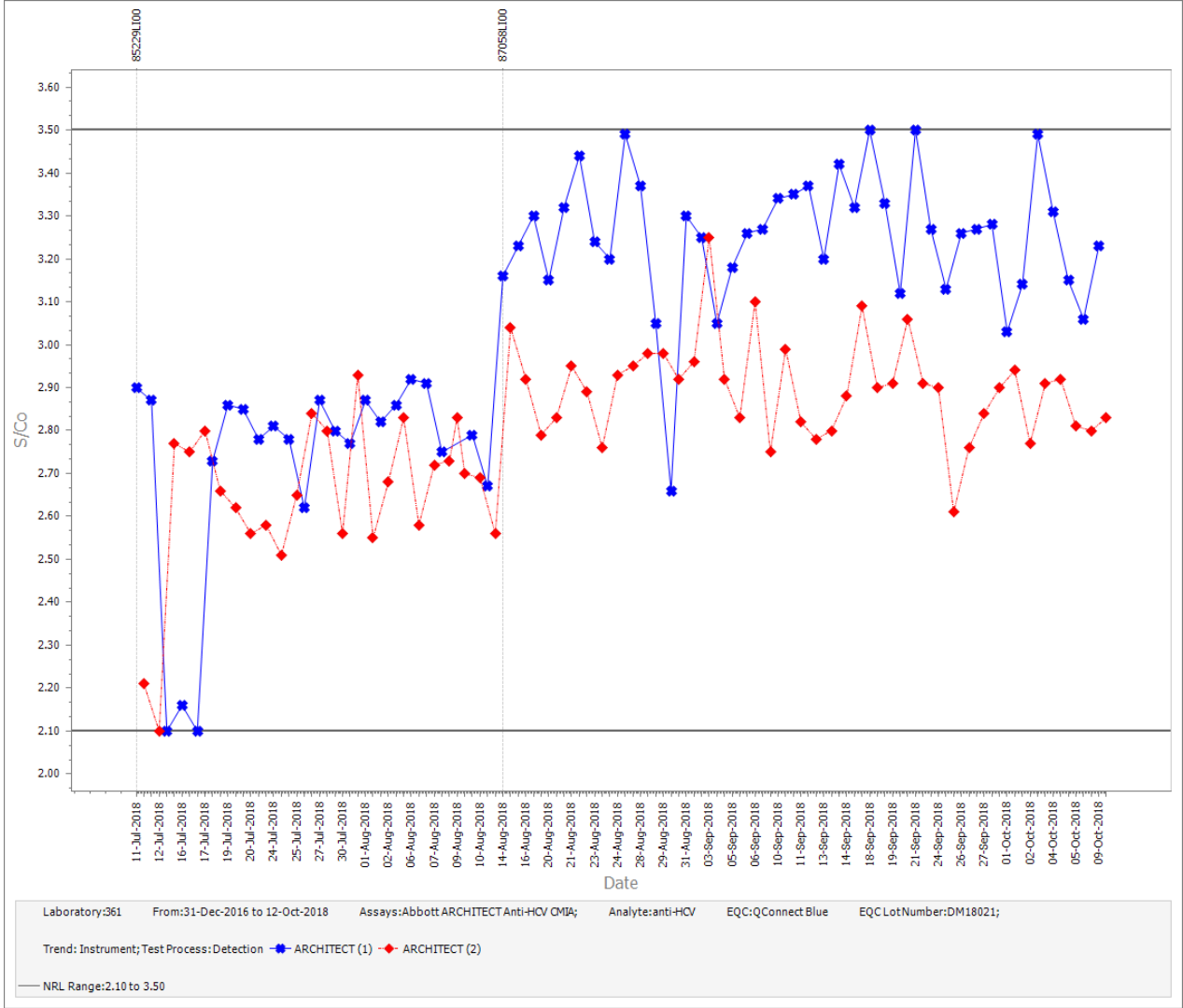
- Lab 361 by instrument



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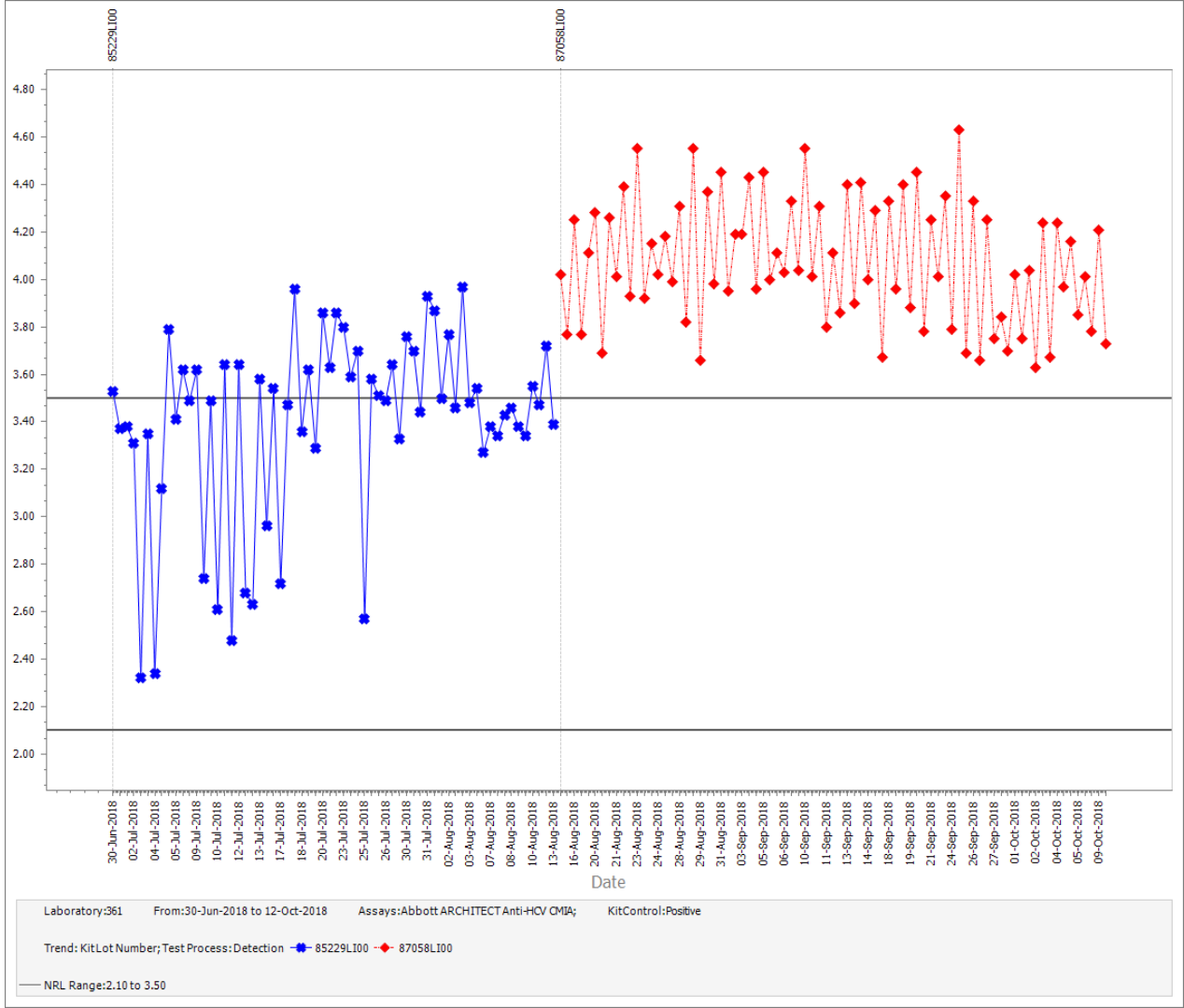
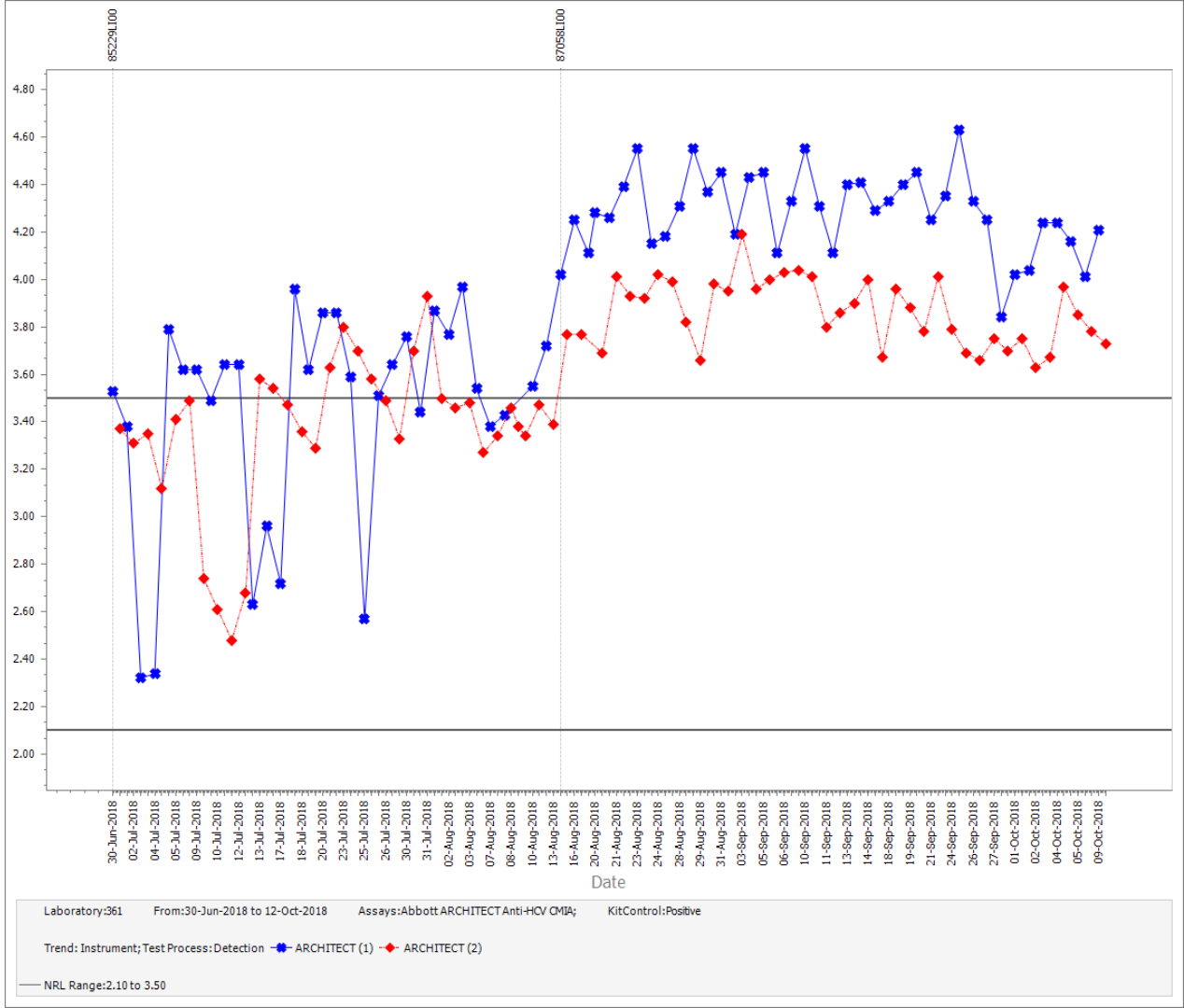
- Lab 361 positive control by reagent lot



NRL Science of Quality

- Lab 361 positive control by instrument



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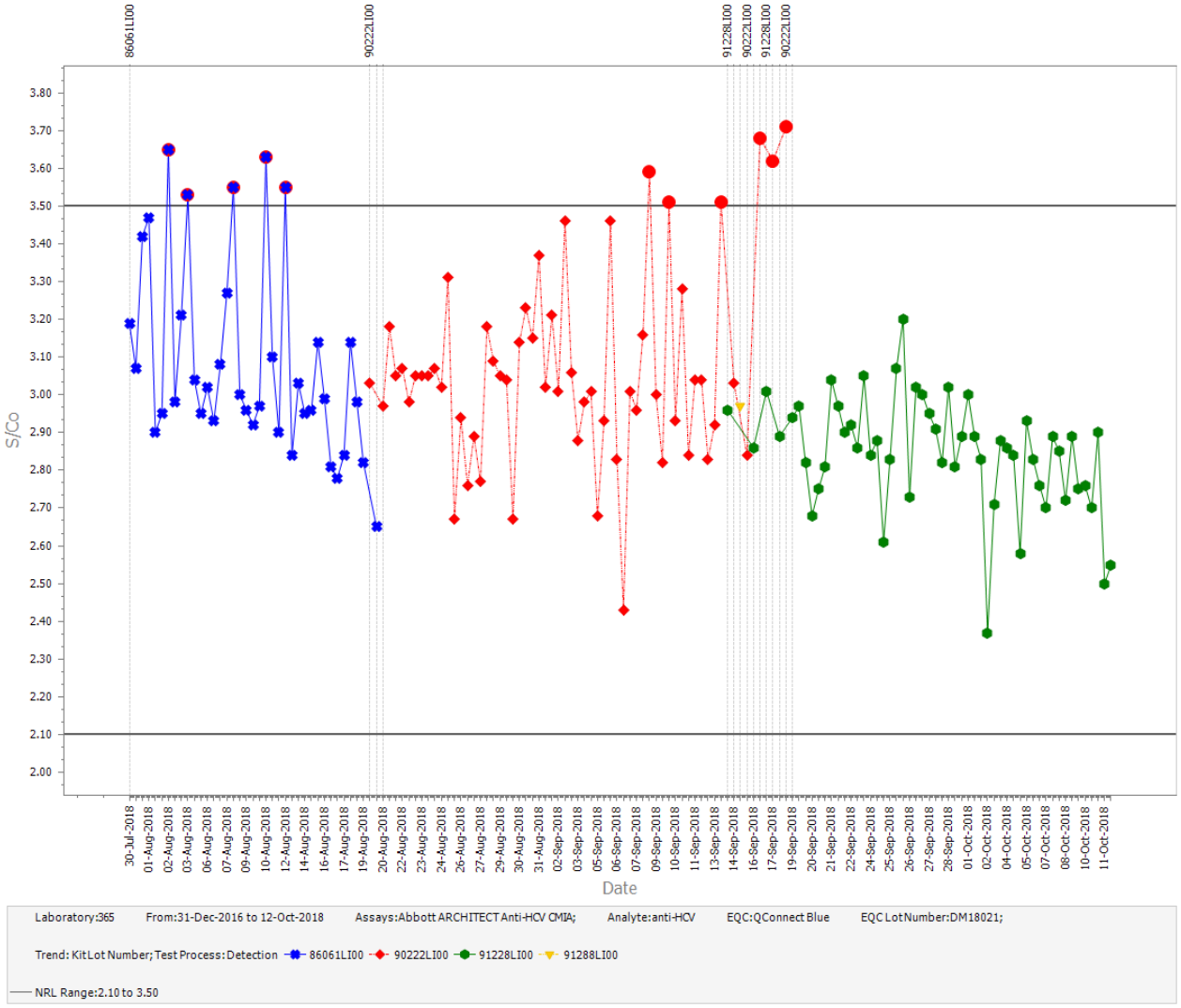
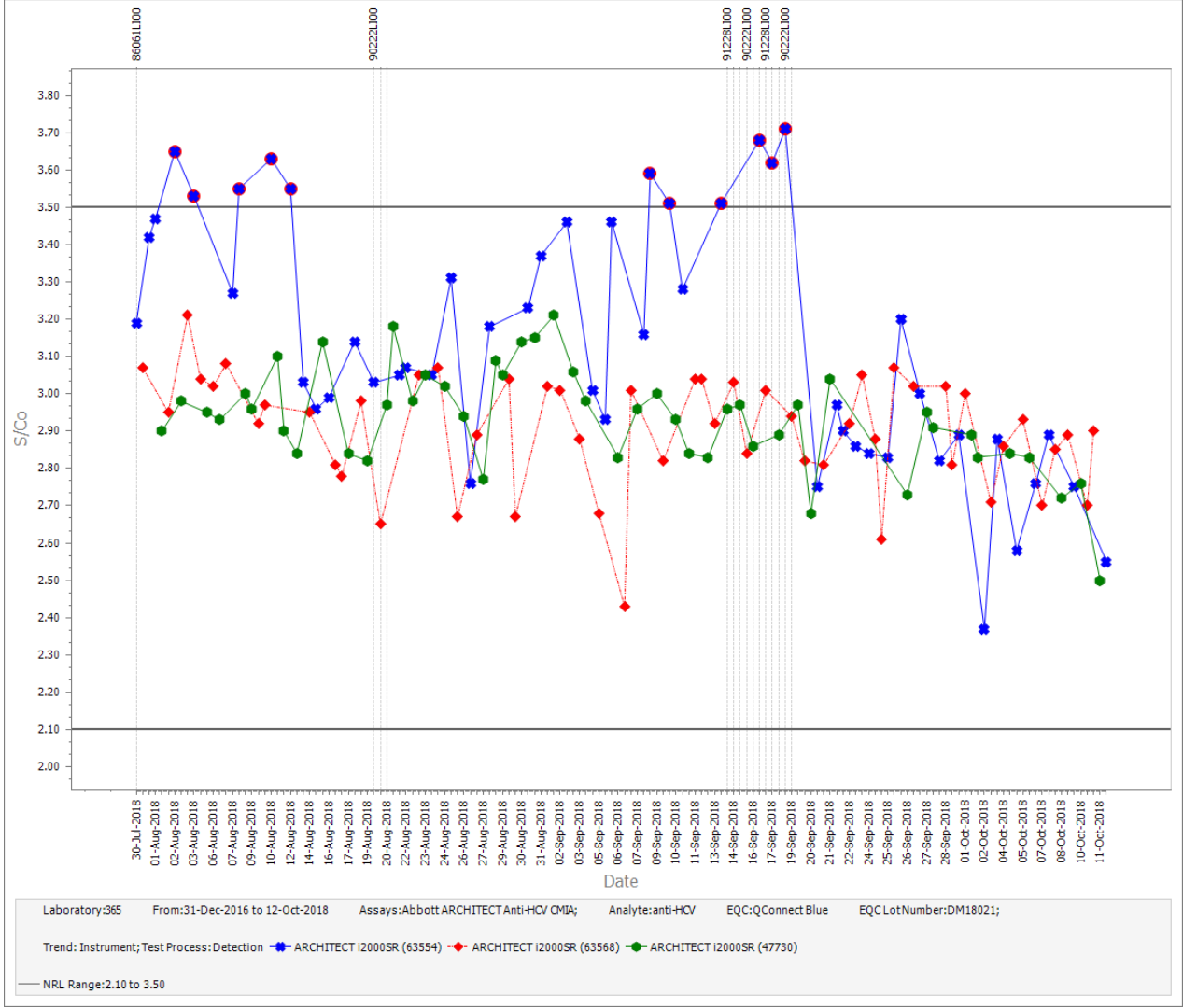
- Lab 365 by reagent lot



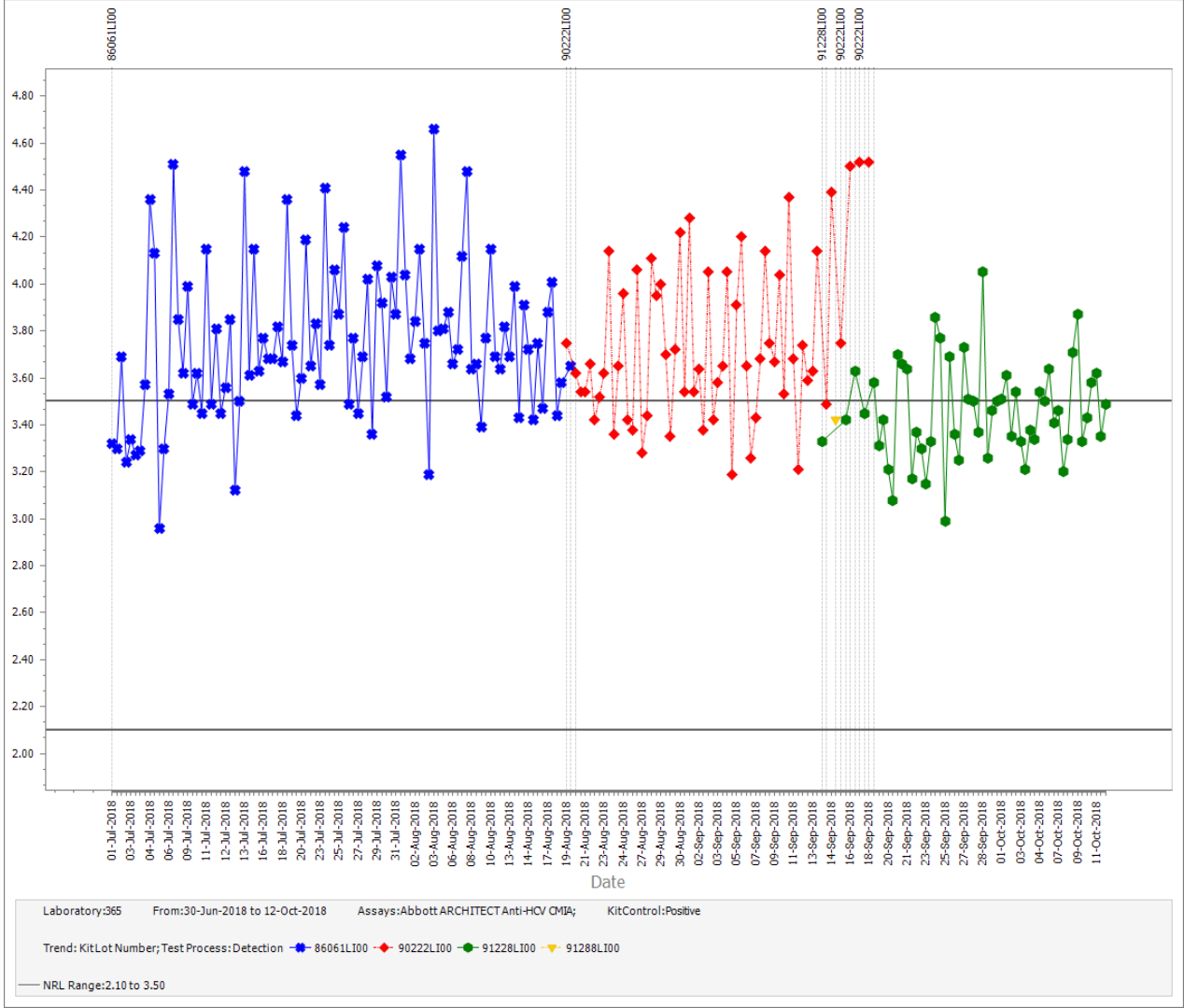
NRL Science of Quality

- Lab 365 by instrument



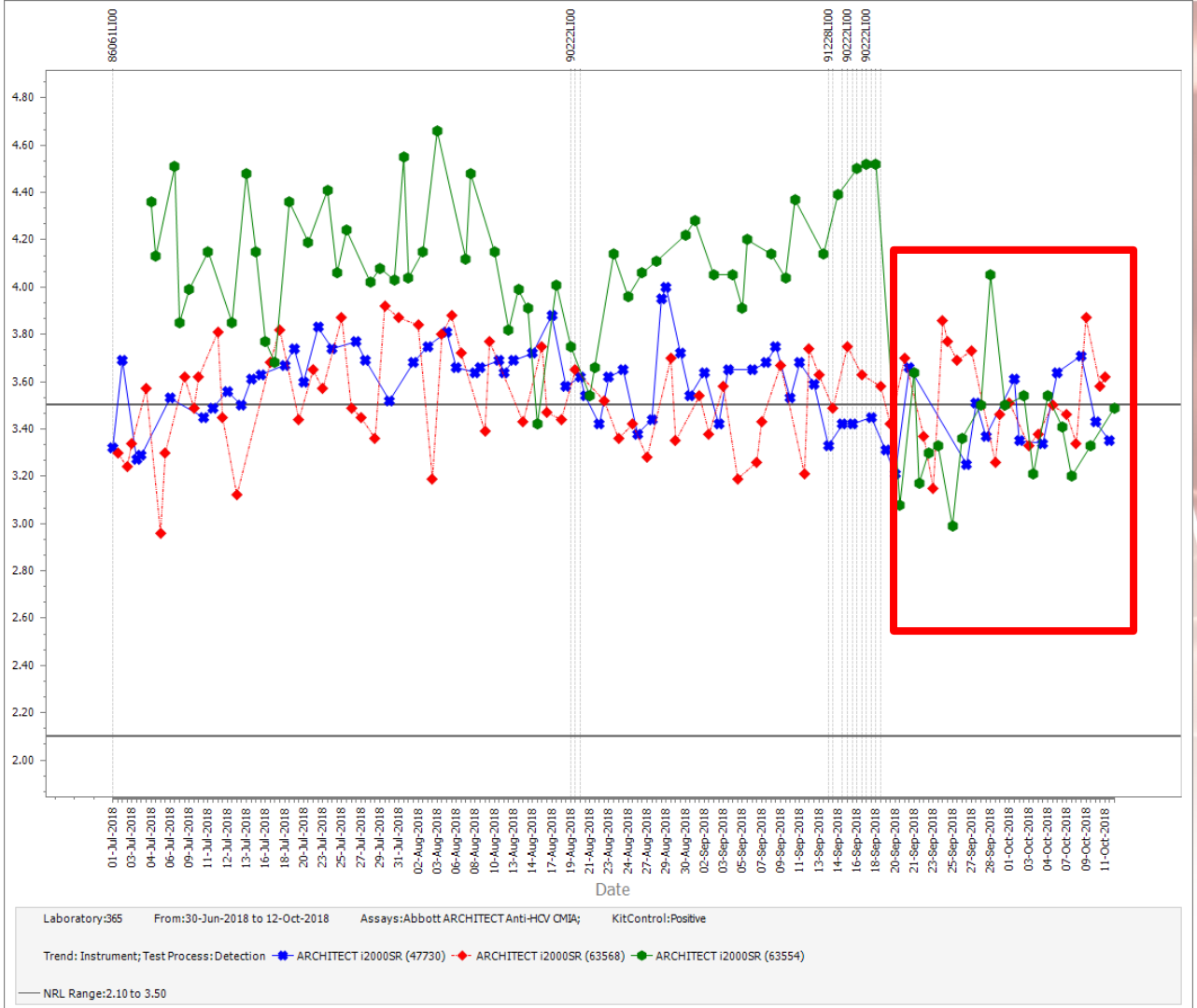
NRL Science of Quality

- Lab 365 positive control by reagent lot



NRL Science of Quality

- Lab 365 positive control by instrument



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- So… back to Lab 43?

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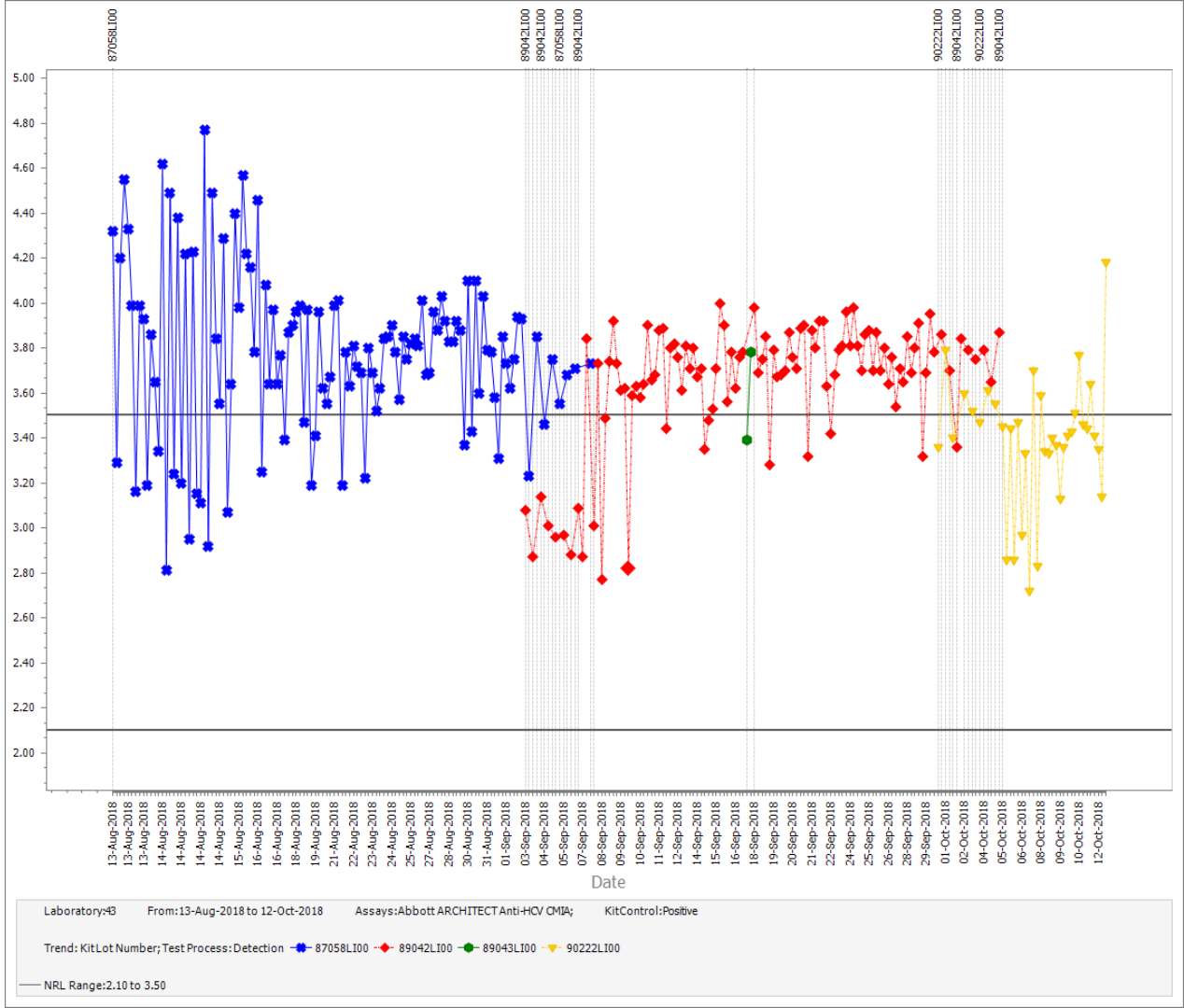
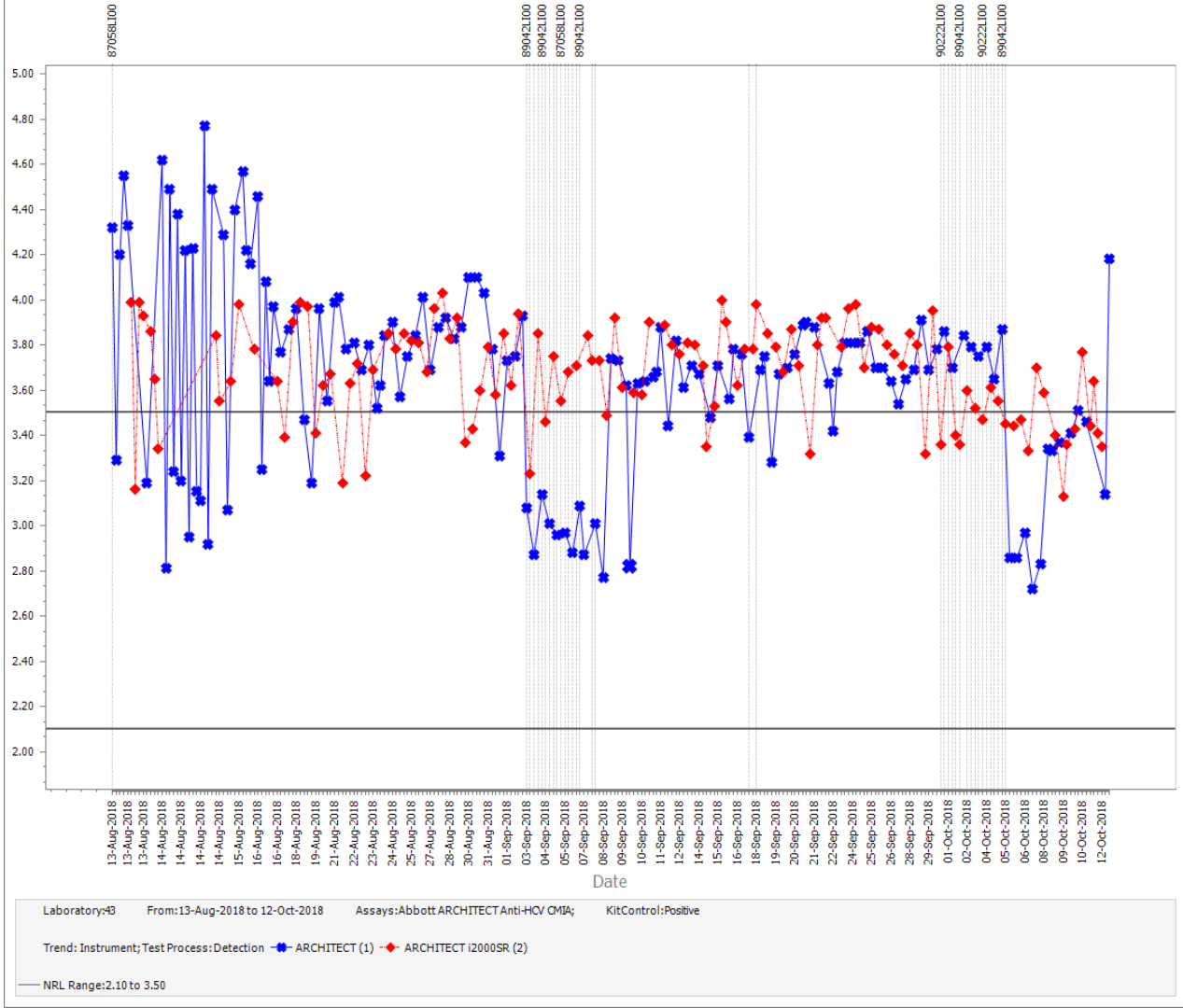
- Lab 43 positive control by reagent lot



NRL Science of Quality

- Lab 43 positive control by instrument



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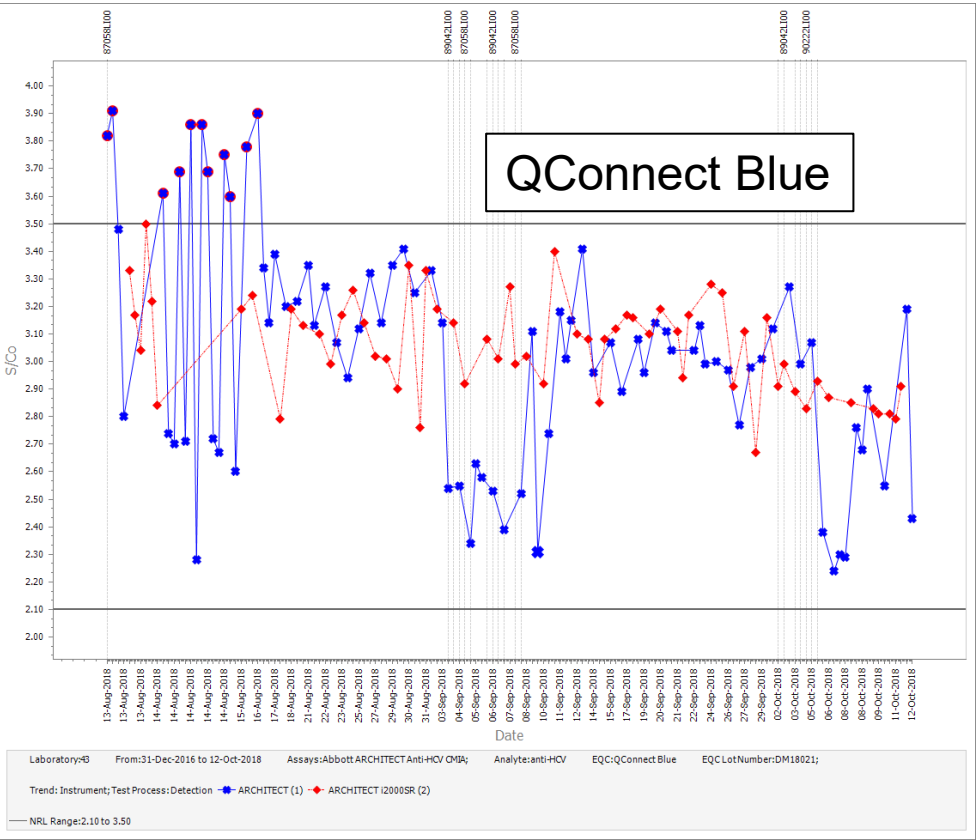
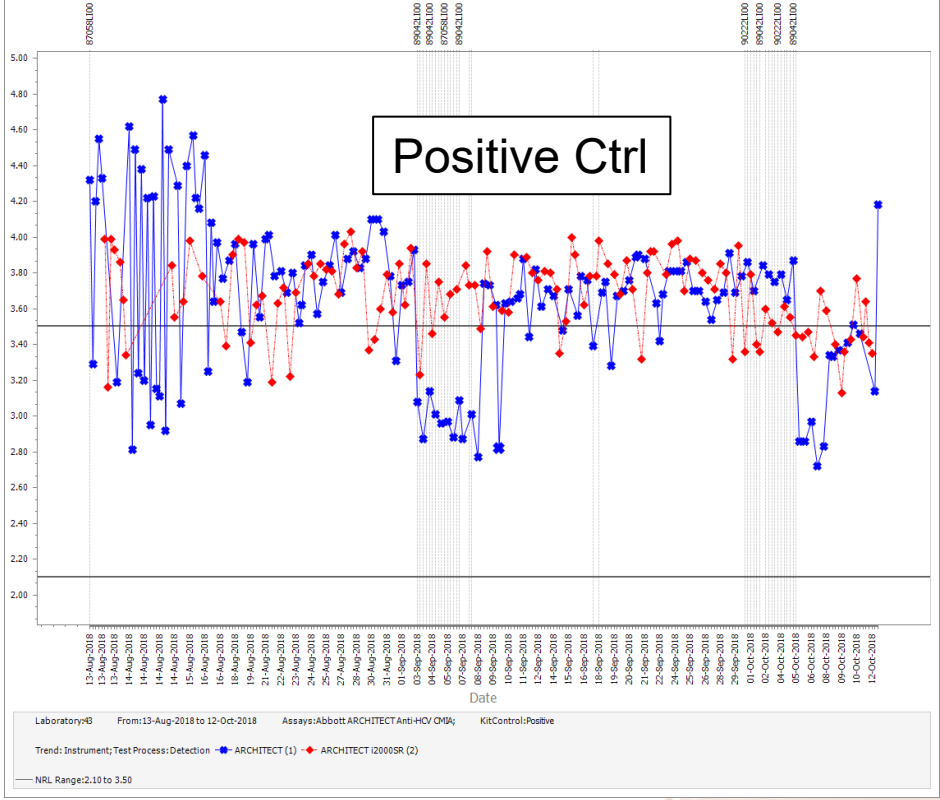
Look familiar?





What is your likely conclusion now?

Instruments in different labs are showing variability?

Reagent lots are showing variability?

QC lots are performing variably in different labs?

Combination of the above?

None of the above

- ***Answer***: Combination is most probable
- Assay calibration? Instruments behave differently
  - Review calibration dates and always compare performance of QC and kit controls
  - What is different with the two instruments in the first lab?
    - Architect i1000 vs i2000?
- Is clinical sensitivity affected? Not sure…
- Importance of monitoring instruments together!!!

*When you dig deeper, there is **always** something different*

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Scenario 4

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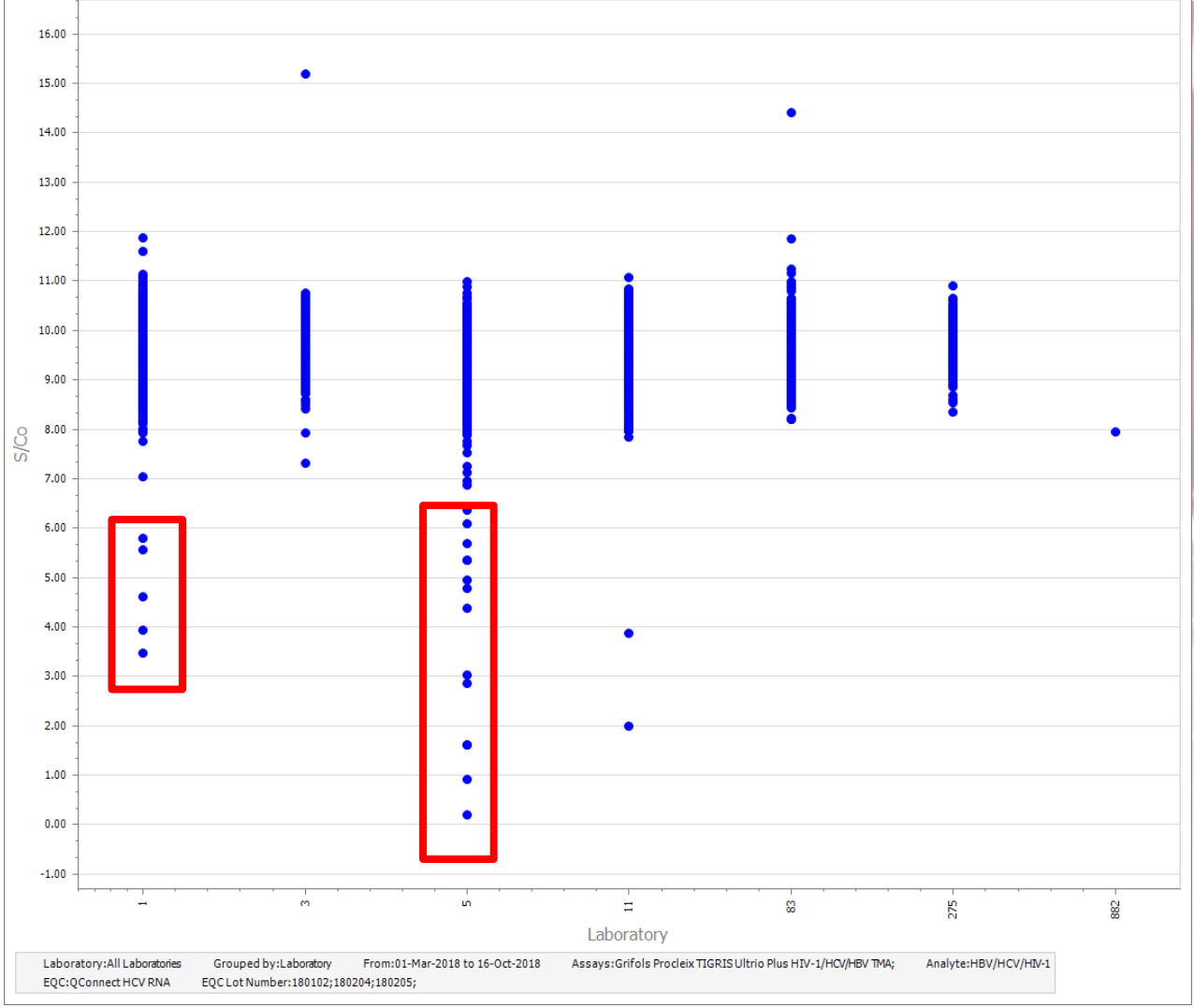
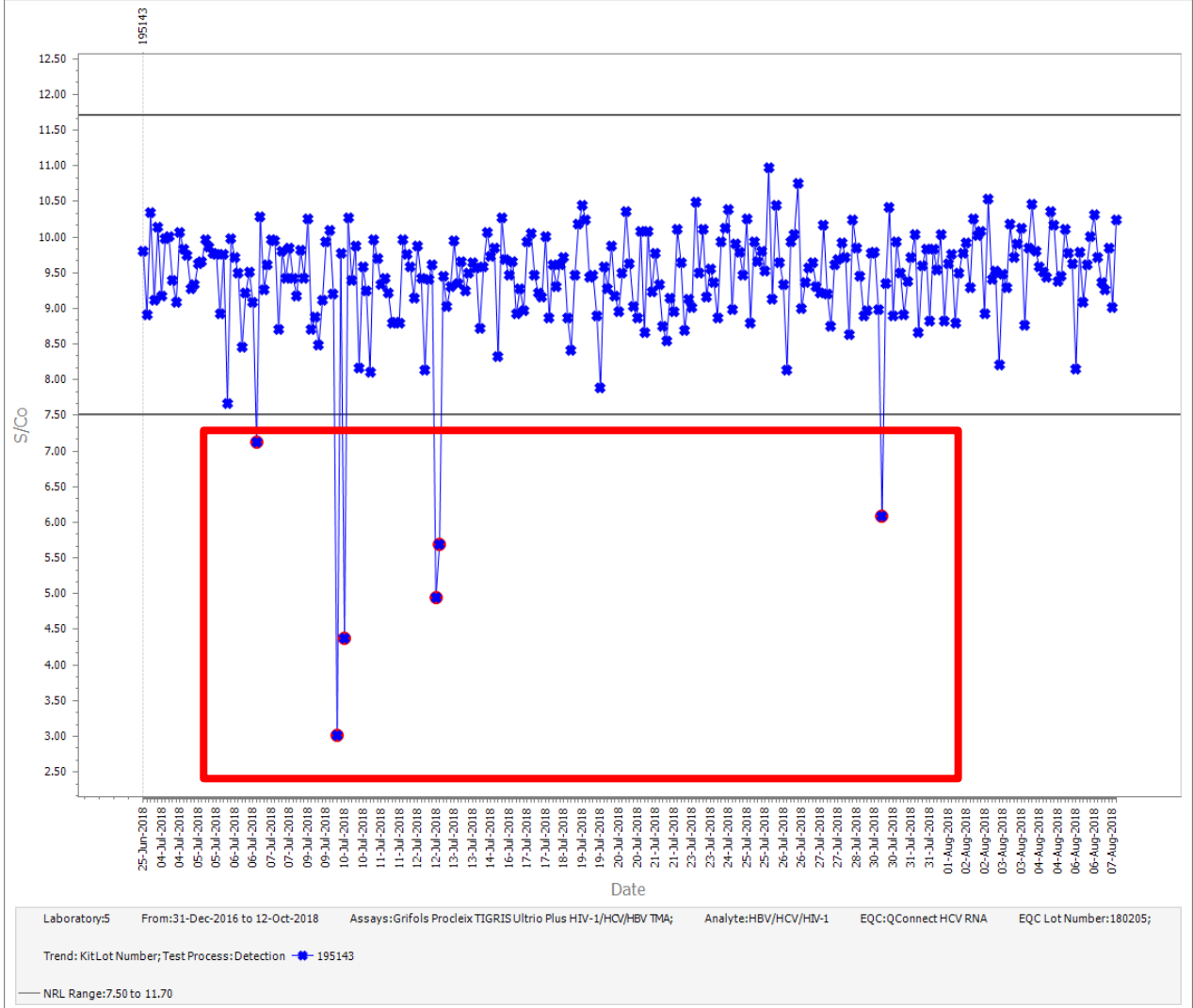
- Grifols Tigris by peer group for QConnect HCVRNA



NRL Science of Quality



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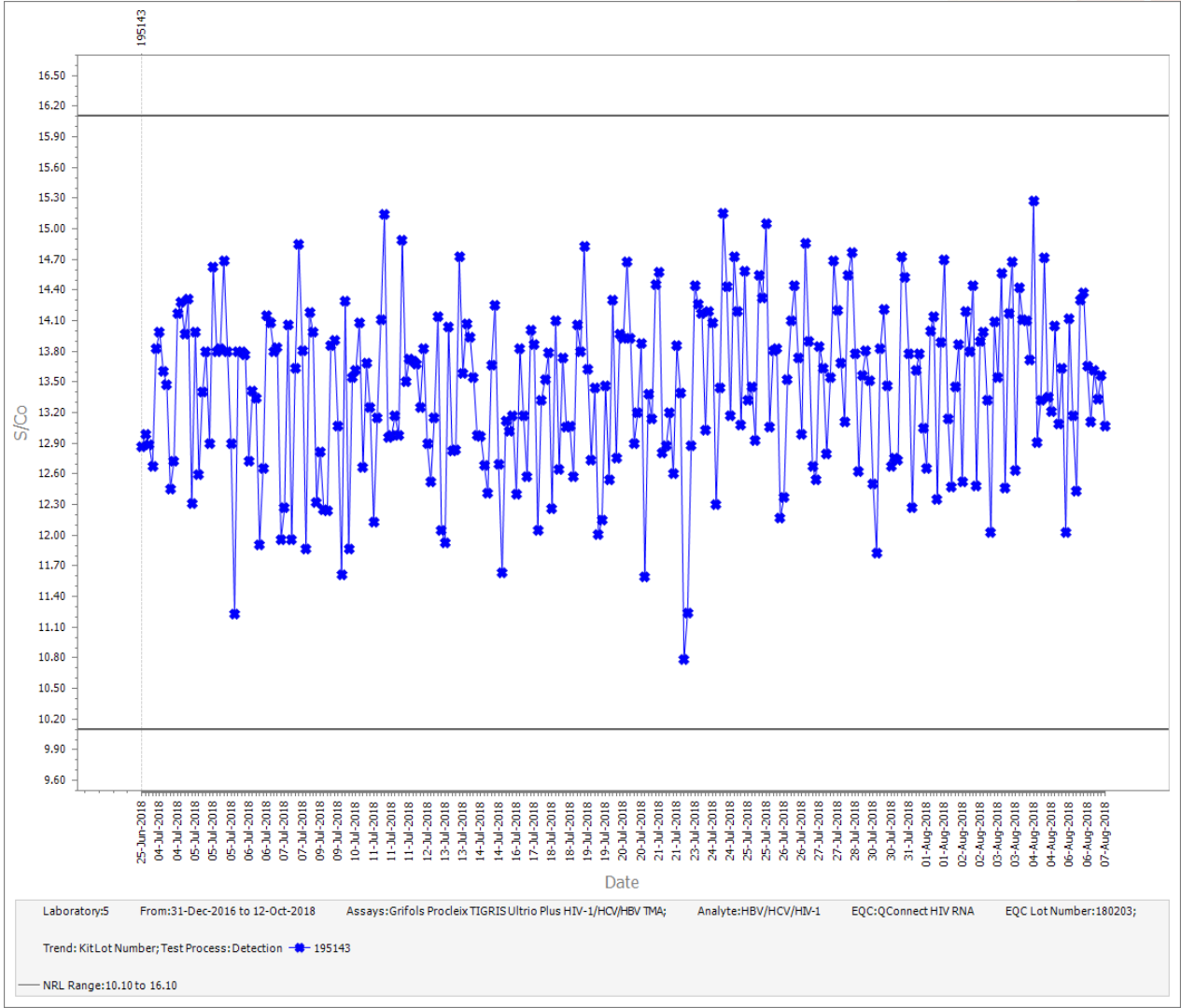
- QConnect HIVRNA data



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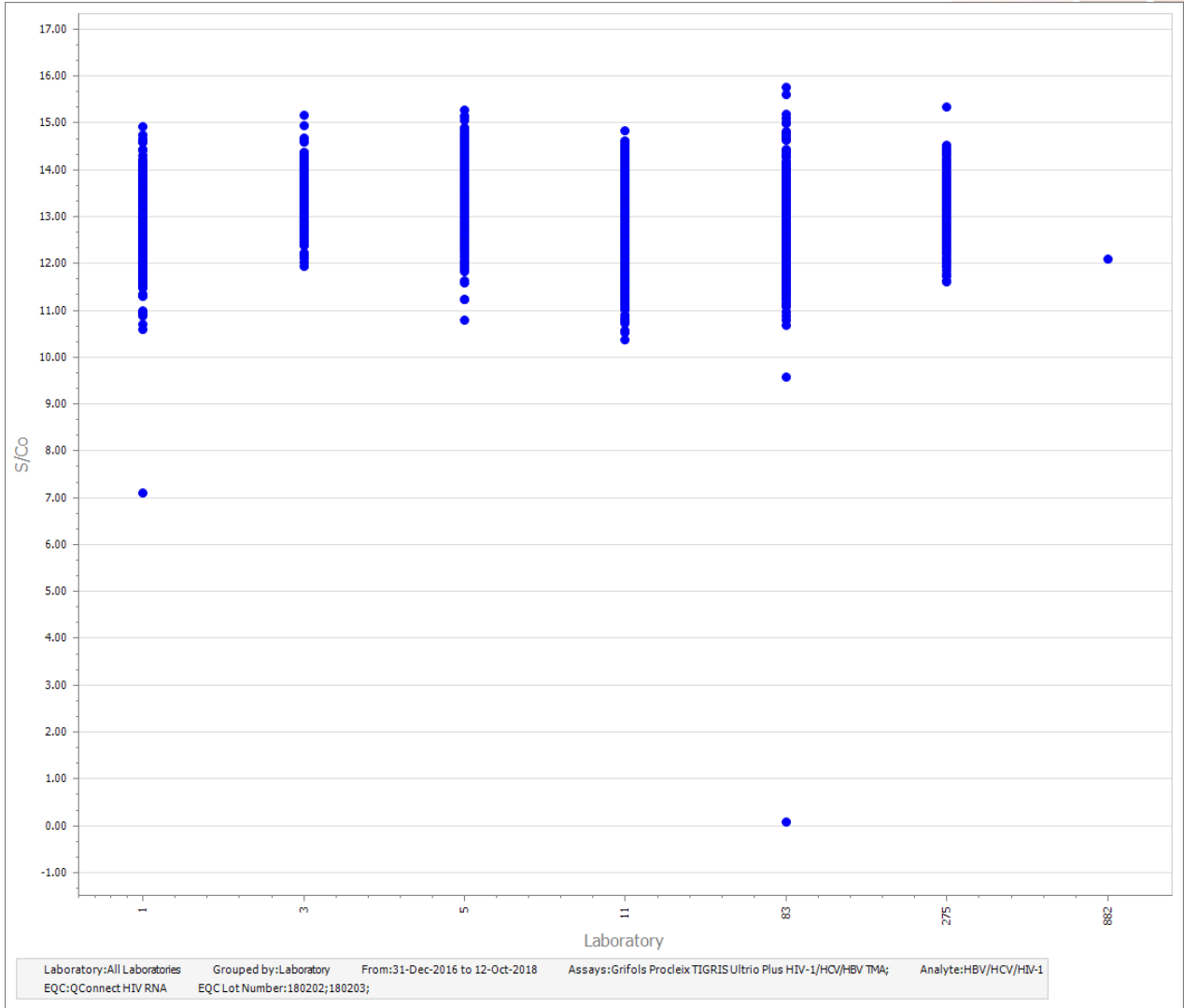
- QConnect HIVRNA peergroup data



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What is the cause for the problem in Scenario 4?

Reagent lot variation

Assay Calibration

QC stability issues

QC viral load is not homogenous

Something else...?

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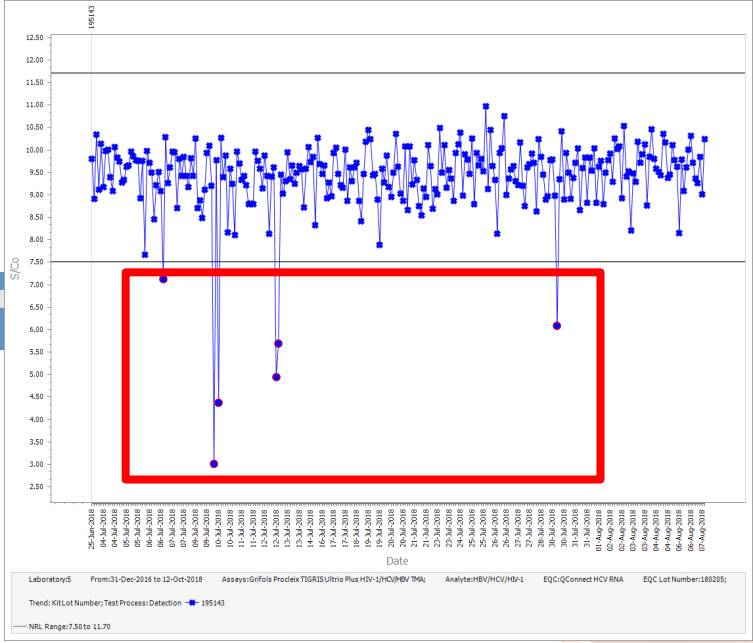
Reagent lot variation

Assay Calibration

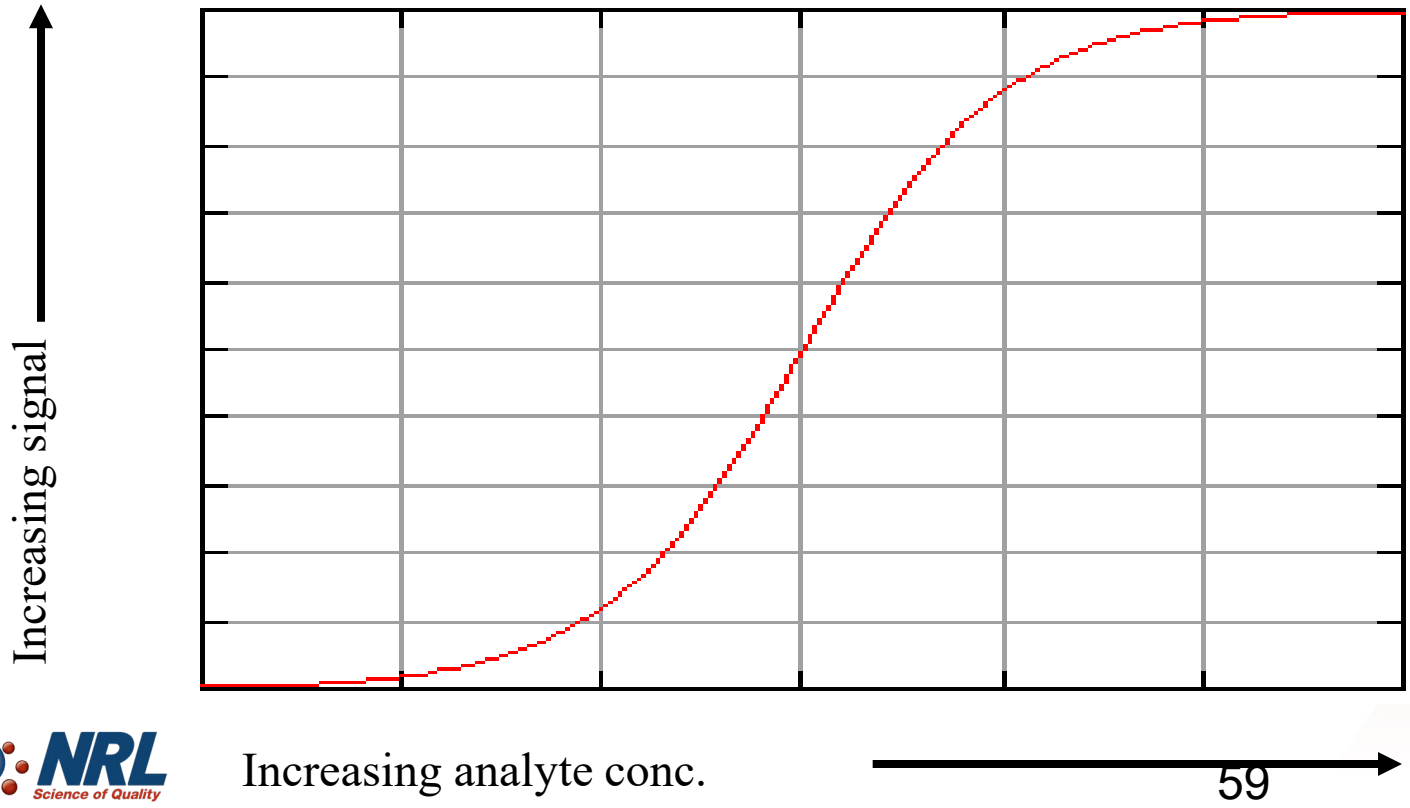
QC stability issues

QC viral load is not homogenous

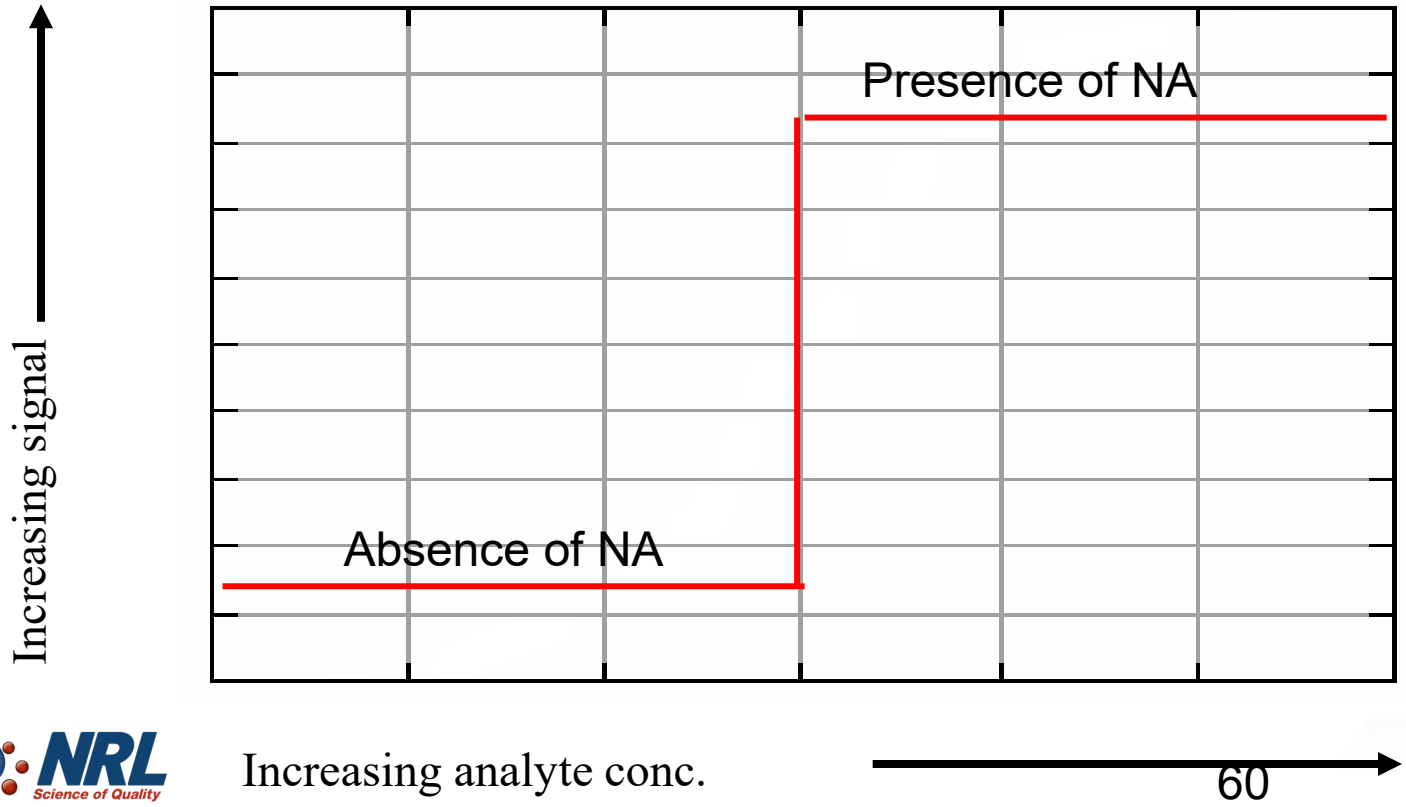
Something else...?

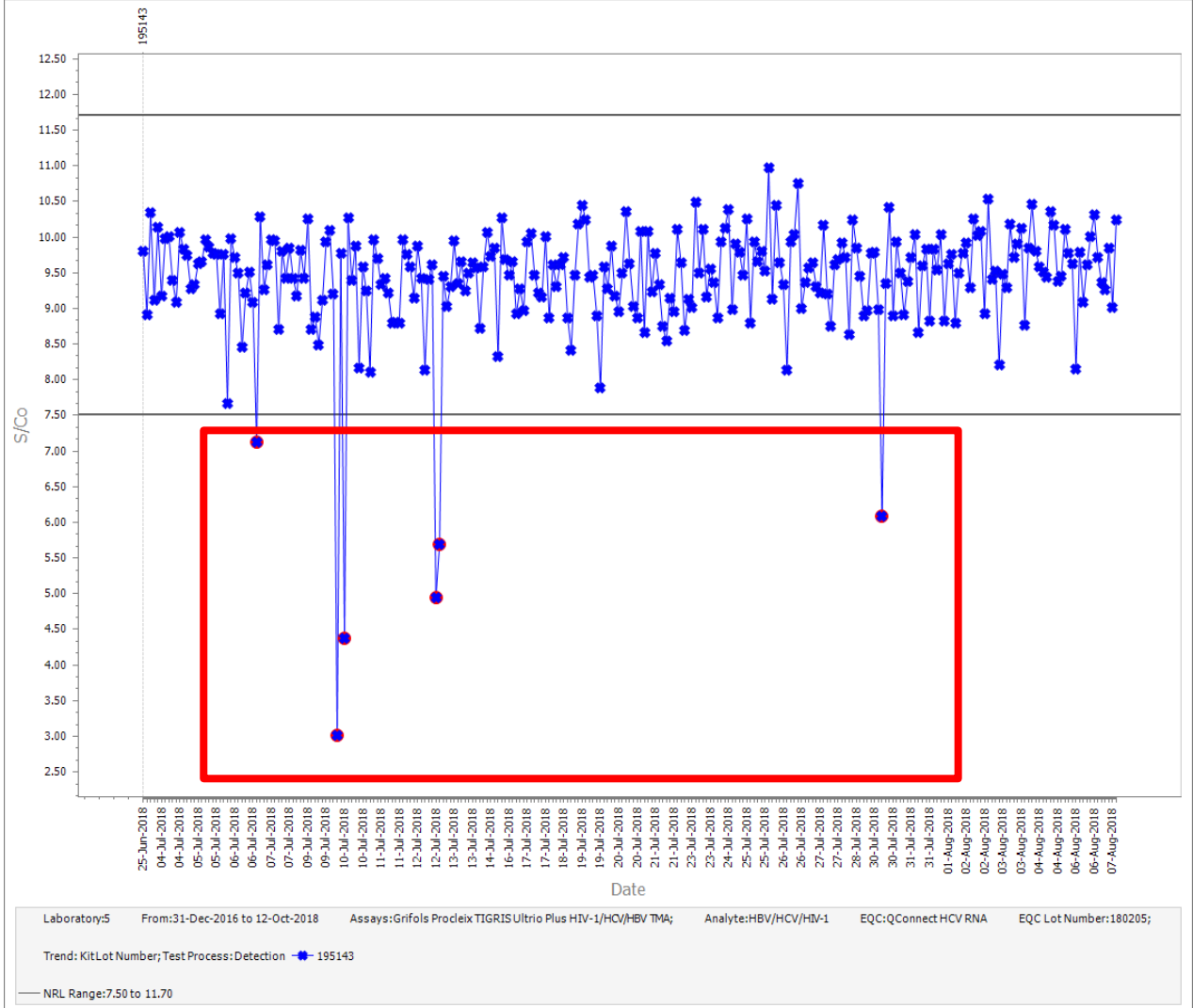


Assays often perform in a sigmoidal pattern



Ultrio Elite and Plus assays do not!!!





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Scenario 4

- ***Answer***: Something else… Unknown
- Instrument issue?
  - Likely an optics issue
  - Results are still positive by Manufacturer's IFU
  - Investigation ongoing
- Also look at other possible causes!!
  - Viral load for samples confirms reactivity
  - These assays perform better at LLOD than viral load assays

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Scenario 5

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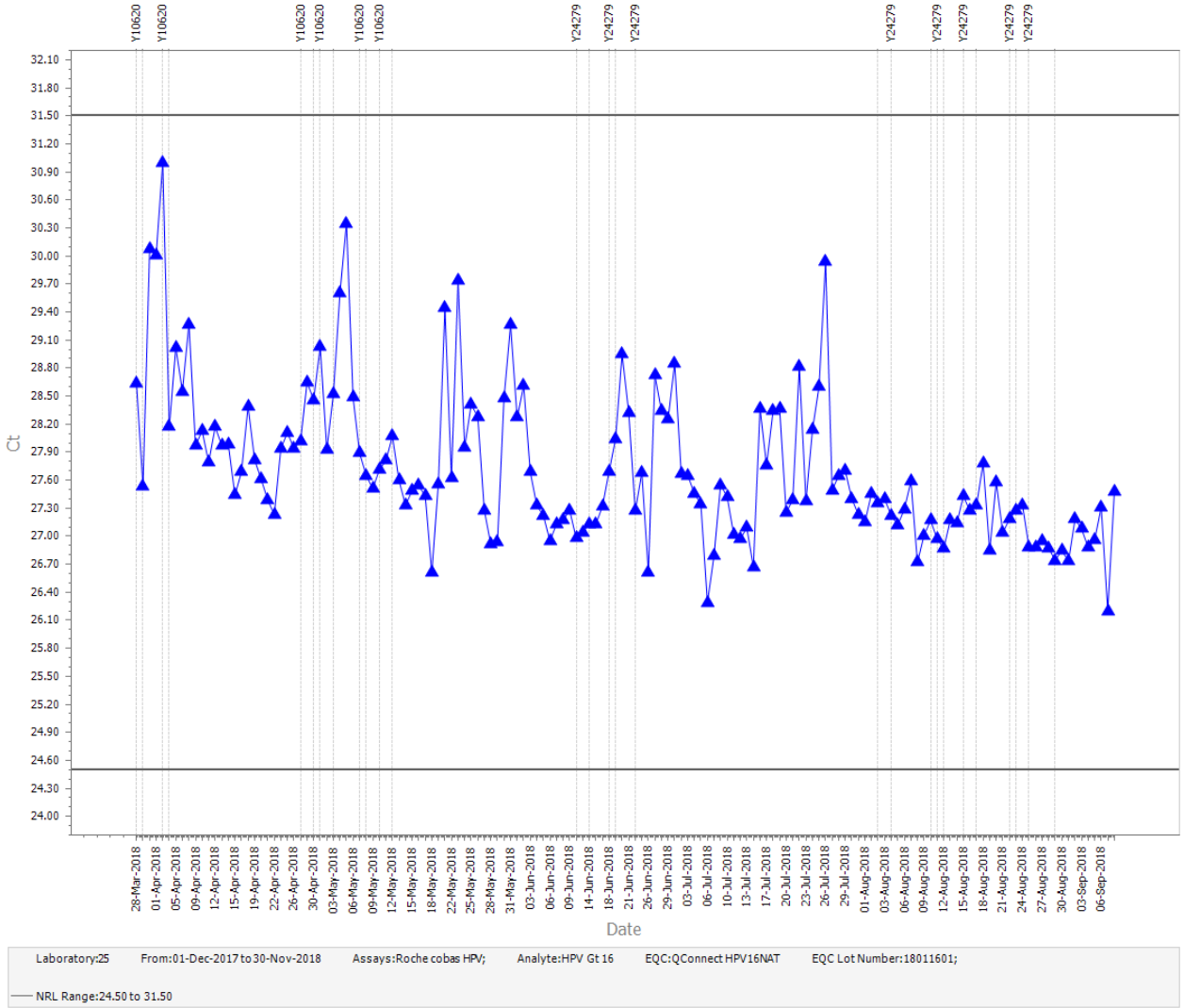
Lab 25

- All data submitted - HPV16NAT



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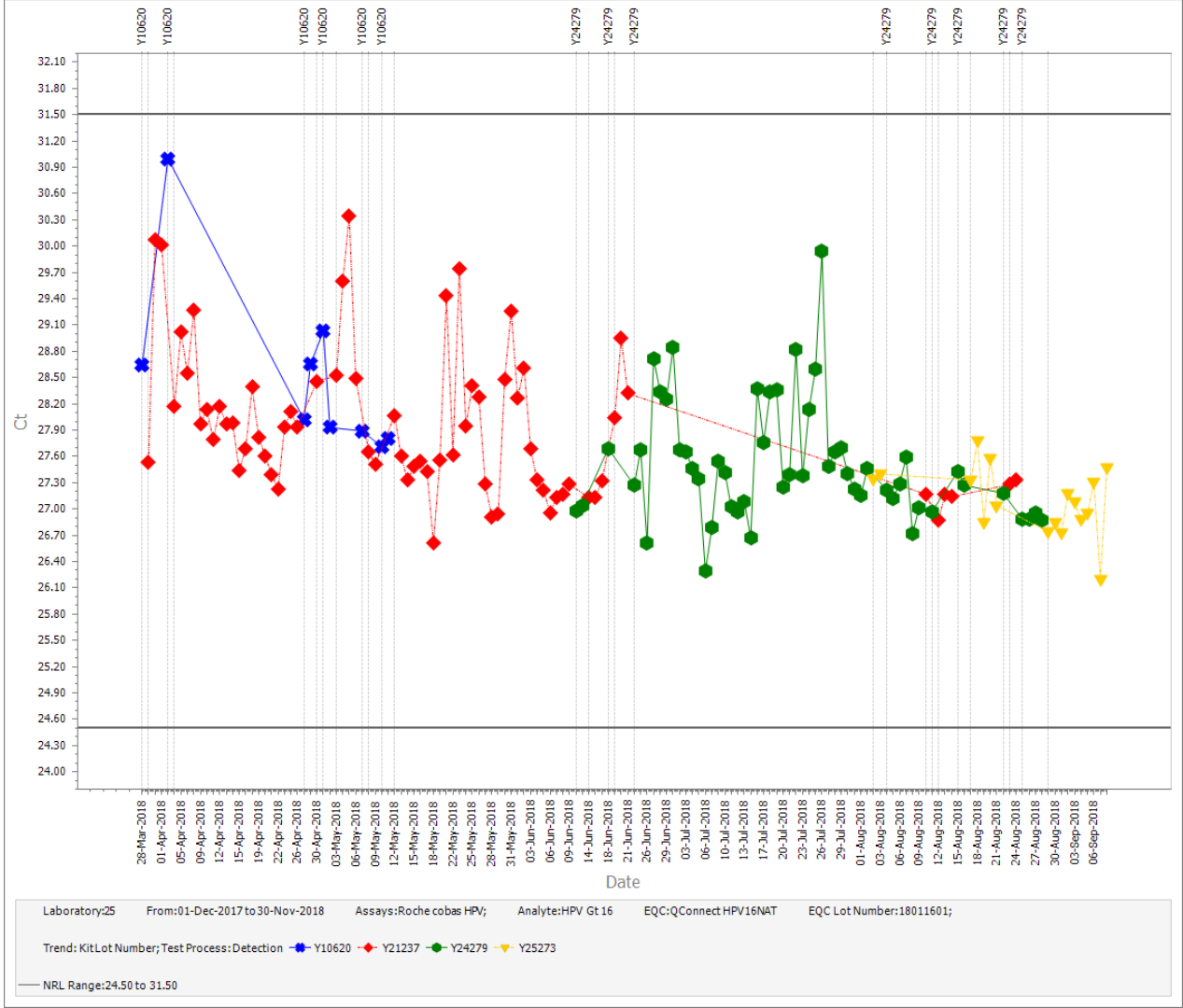
- Data by Reagent lot



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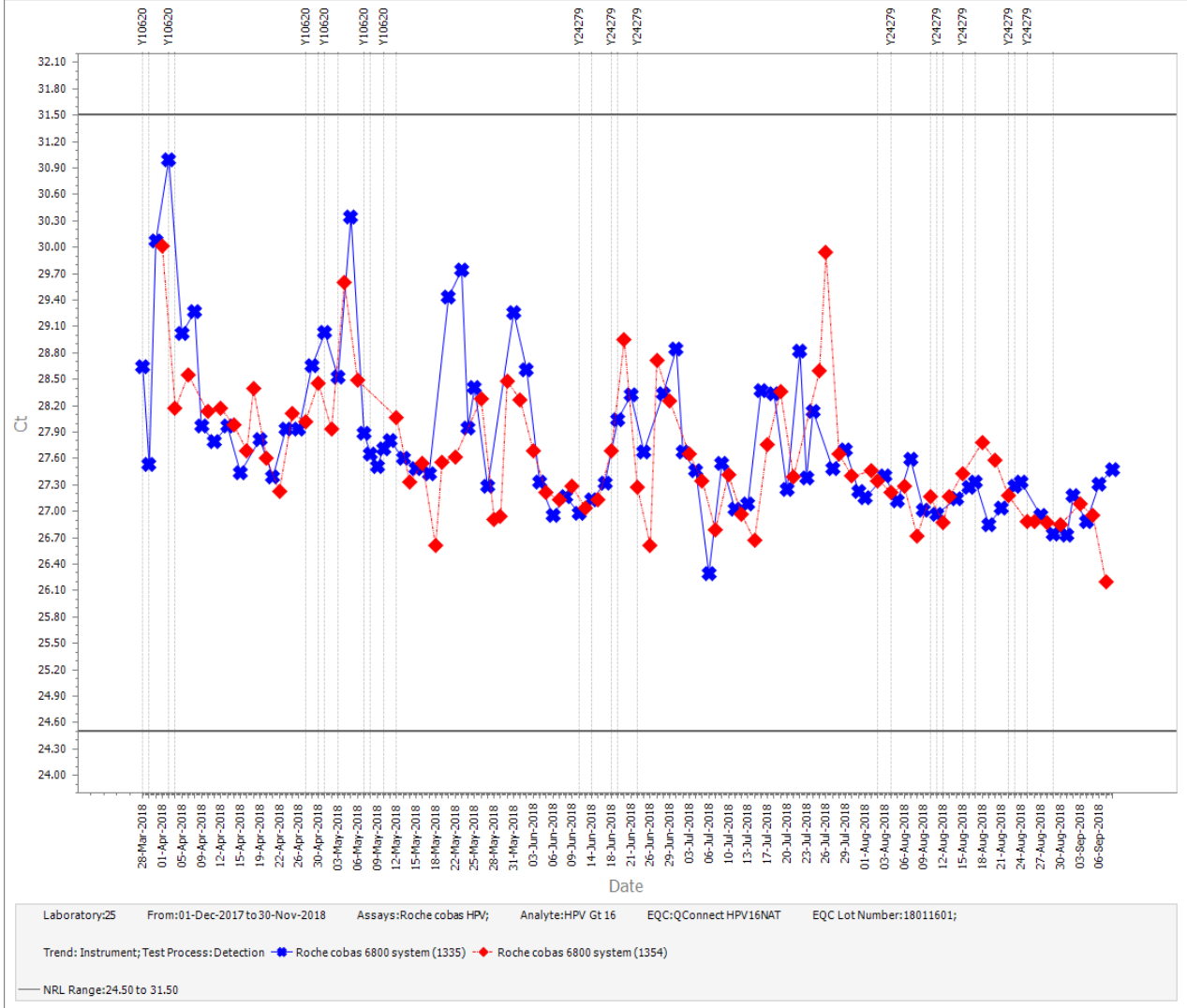
- Data by Instrument



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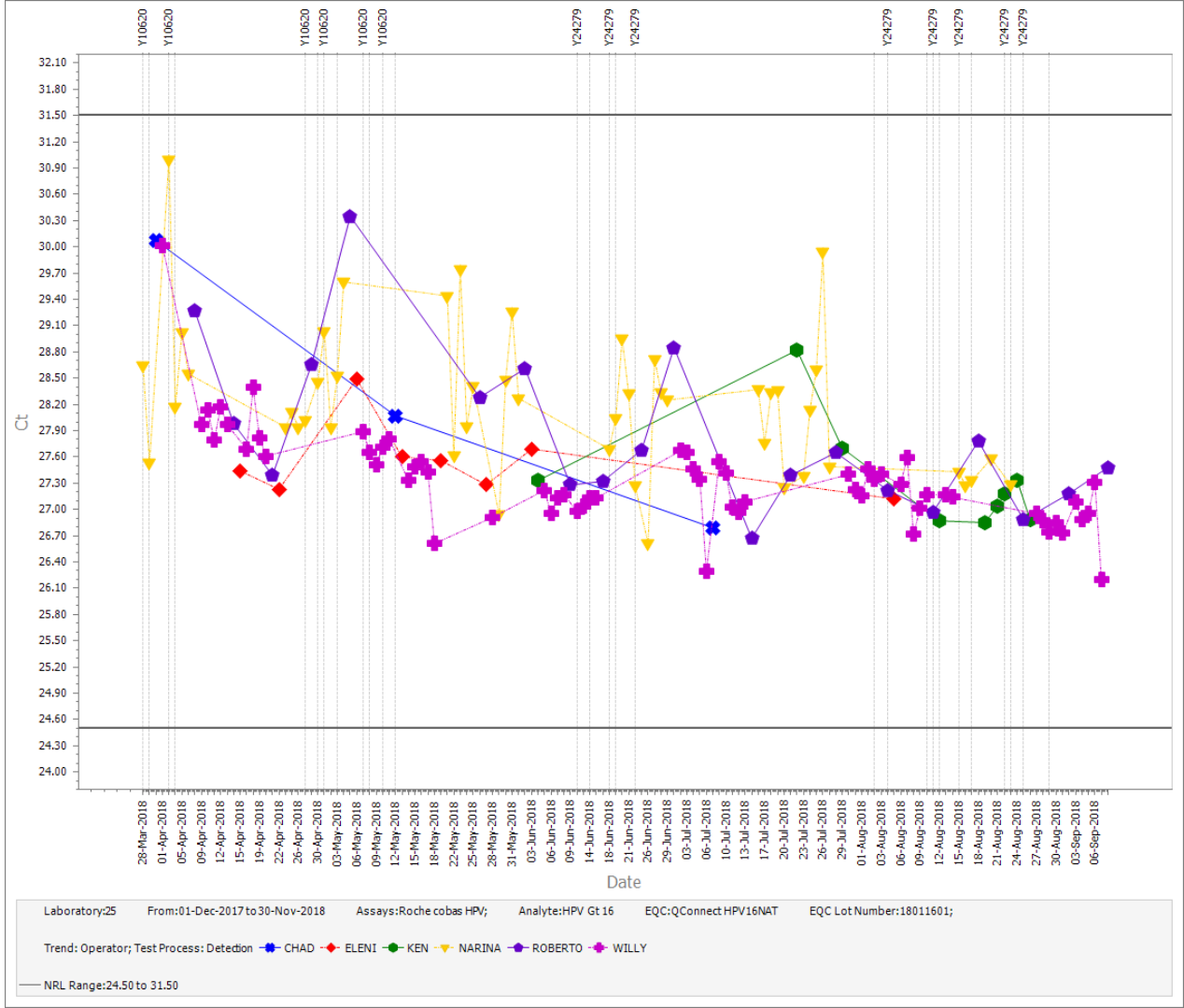
- Data by Operator



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What is the cause of the variation in Scenario 5?

QC Lot variation

Reagent Lot variation

Instrument Lot Variation

Operator variation

Something else....!

Variation Source

- *Operator Variation!*
- Different sample preparation techniques developed over time

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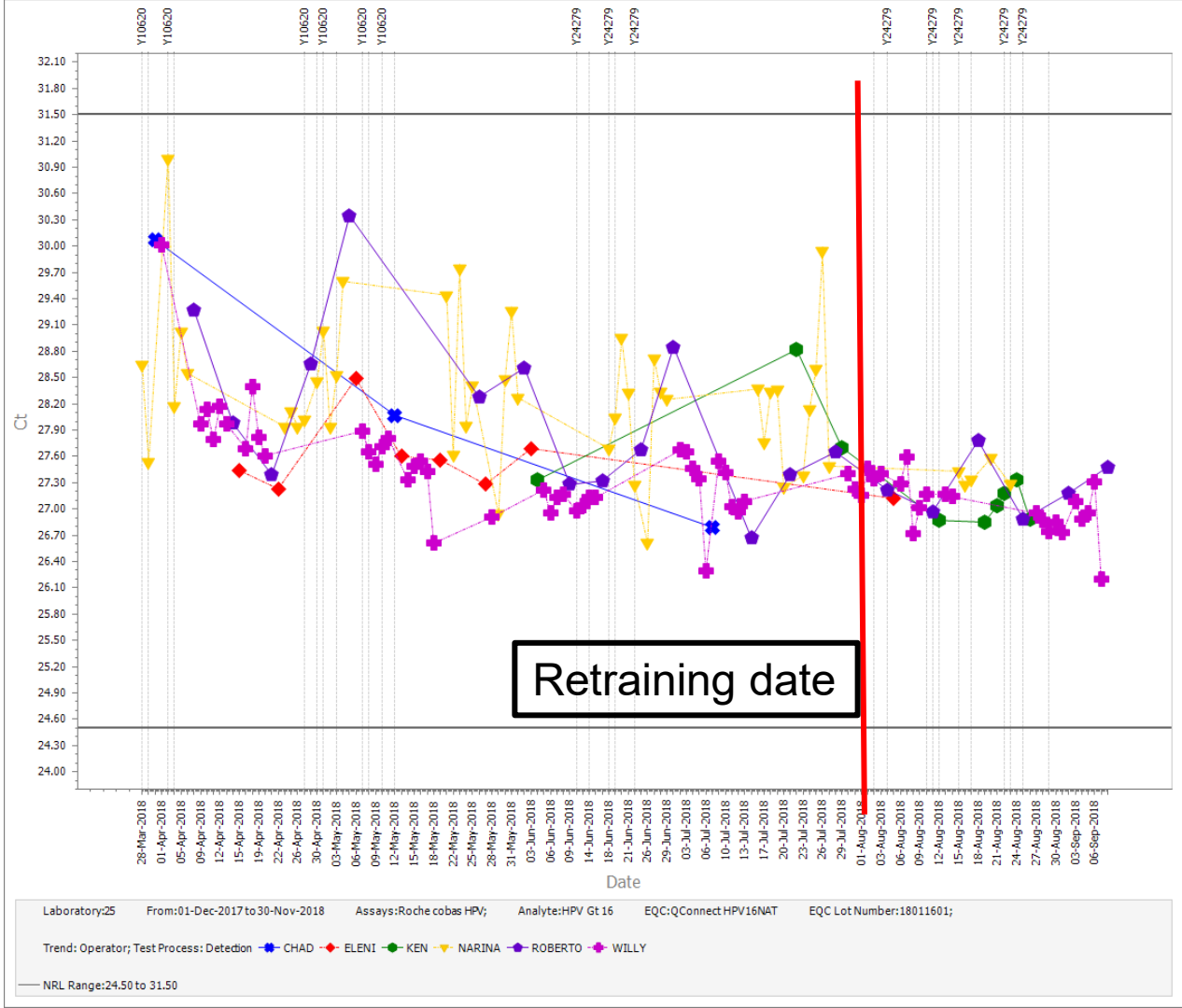
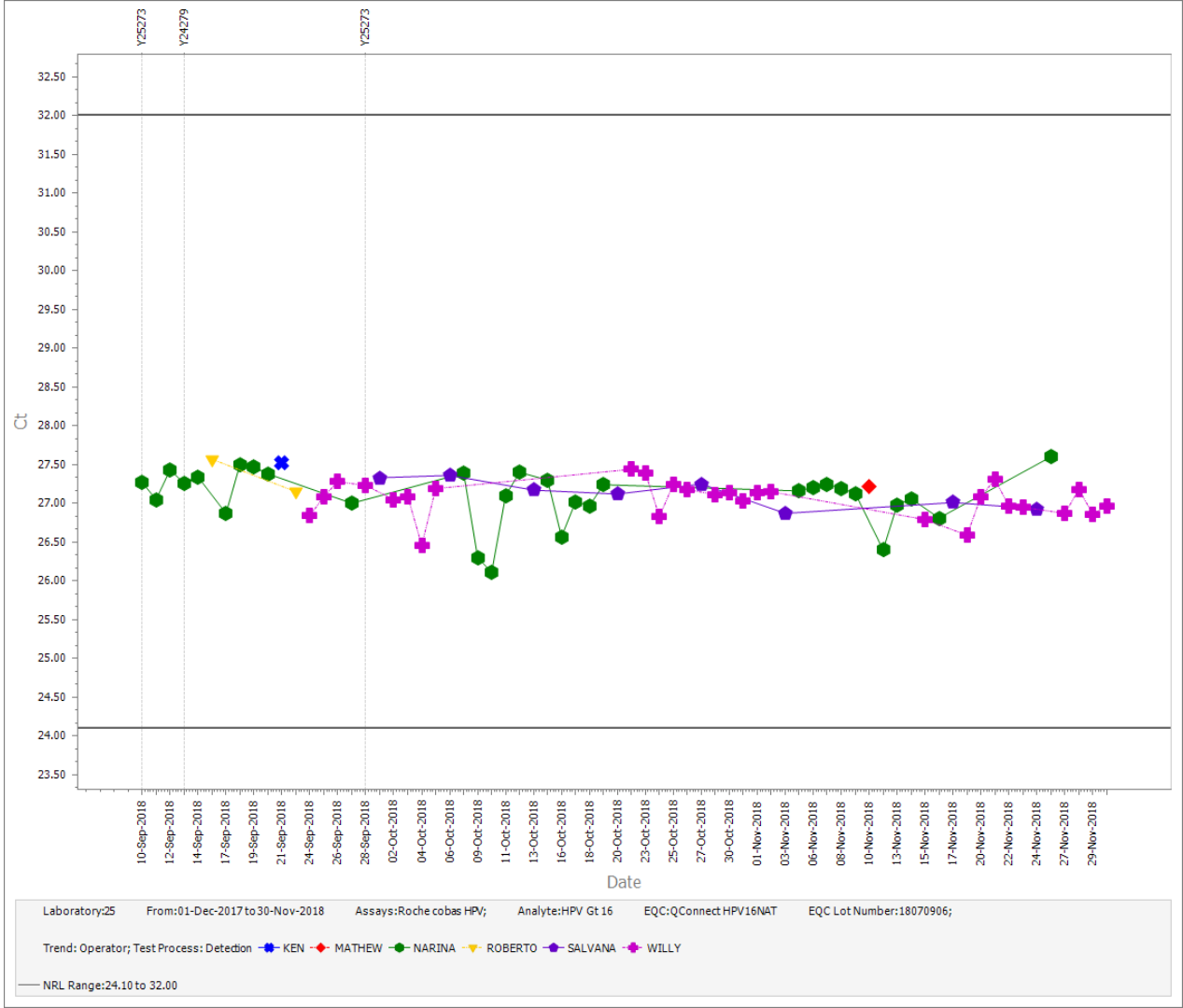
- Data by Operator
- Lab manager monitored before/after retraining



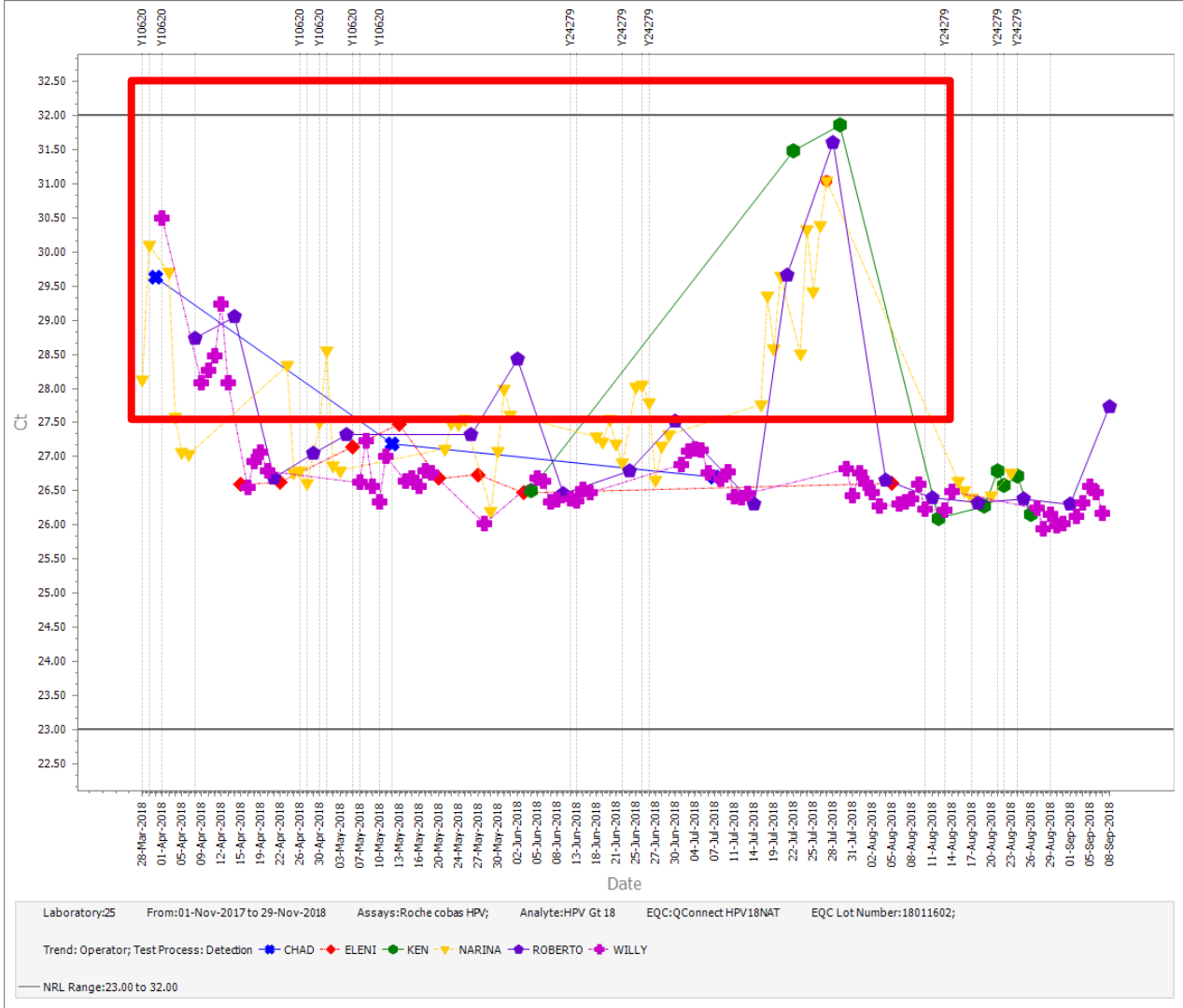
NRL Science of Quality

- New QC lot
- ‘Normalised’ practices continue



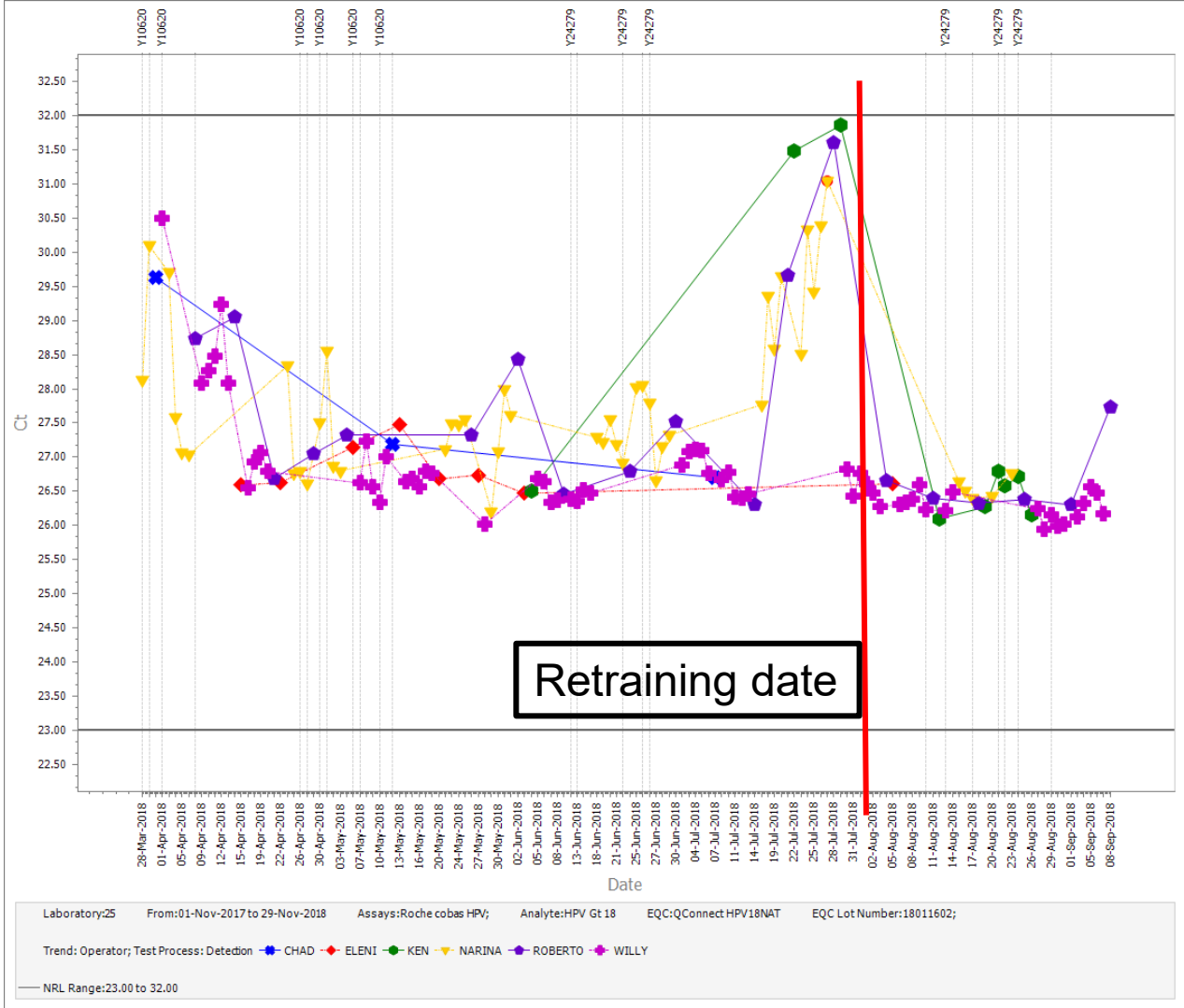
NRL Science of Quality

- HPV18NAT
- Data by Operator
- Variation also present



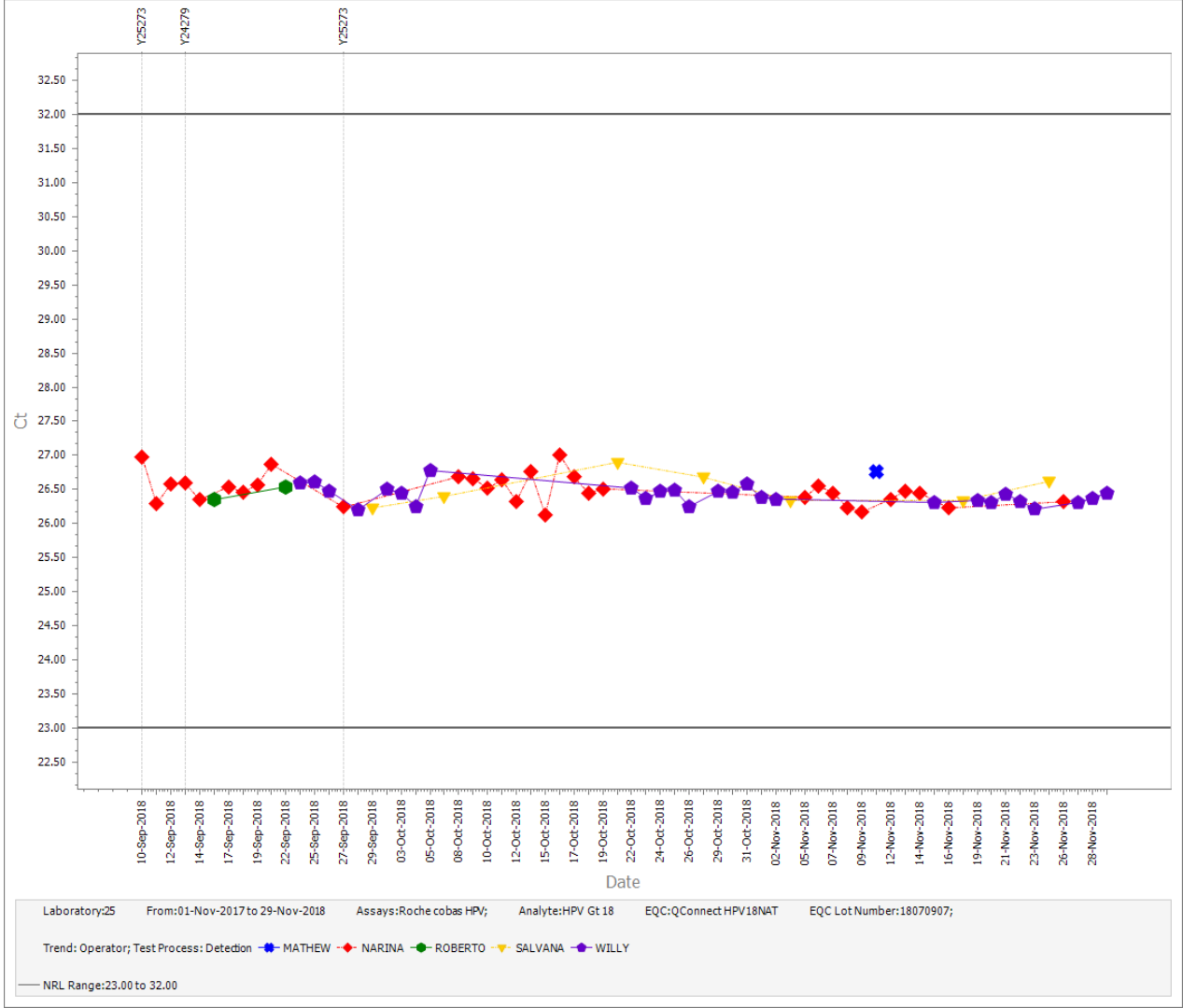
NRL Science of Quality

HPV18NAT



NRL Science of Quality

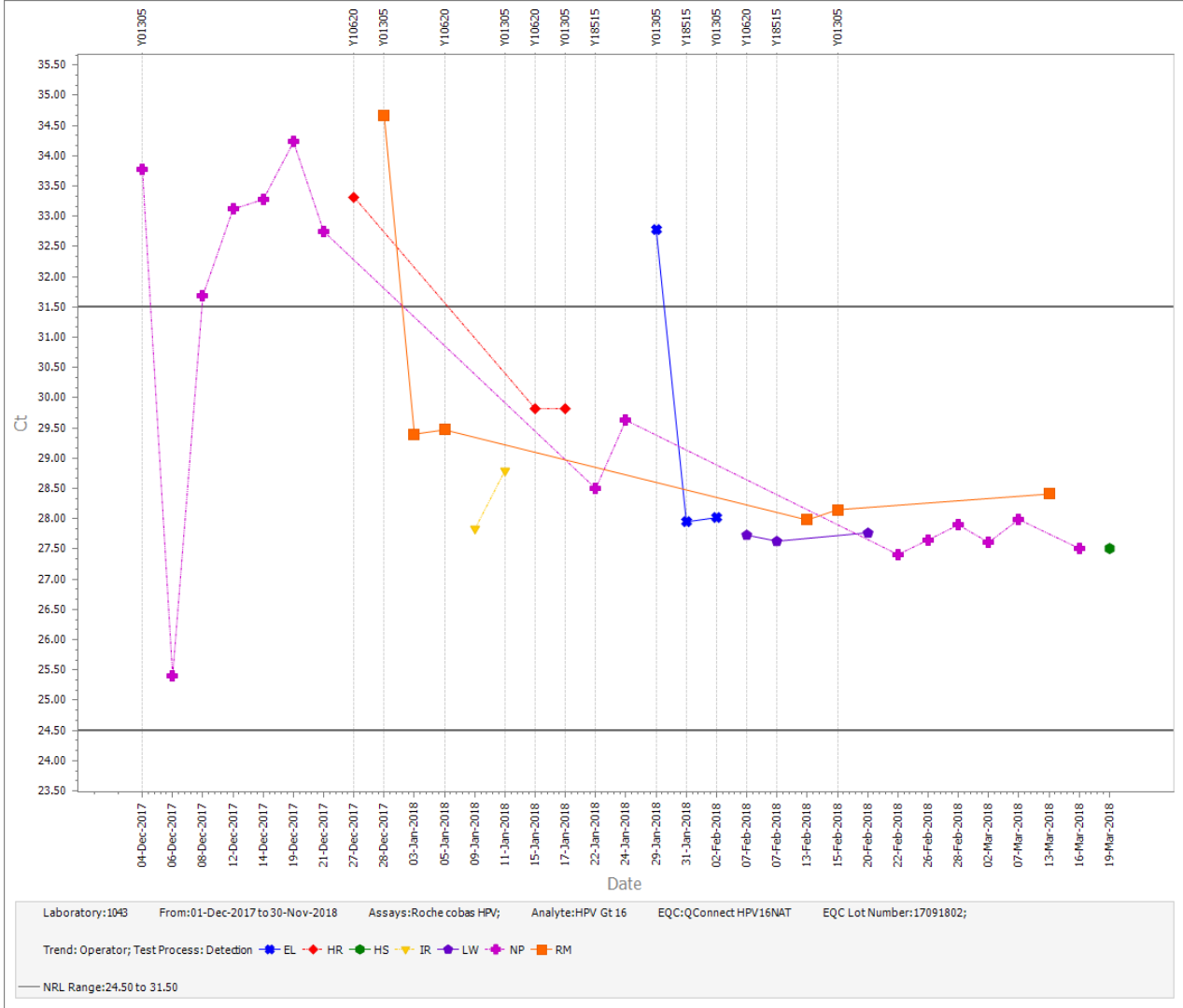
- Data by Operator
- ‘Normalised’ practices continue



NRL Science of Quality

Lab 1043

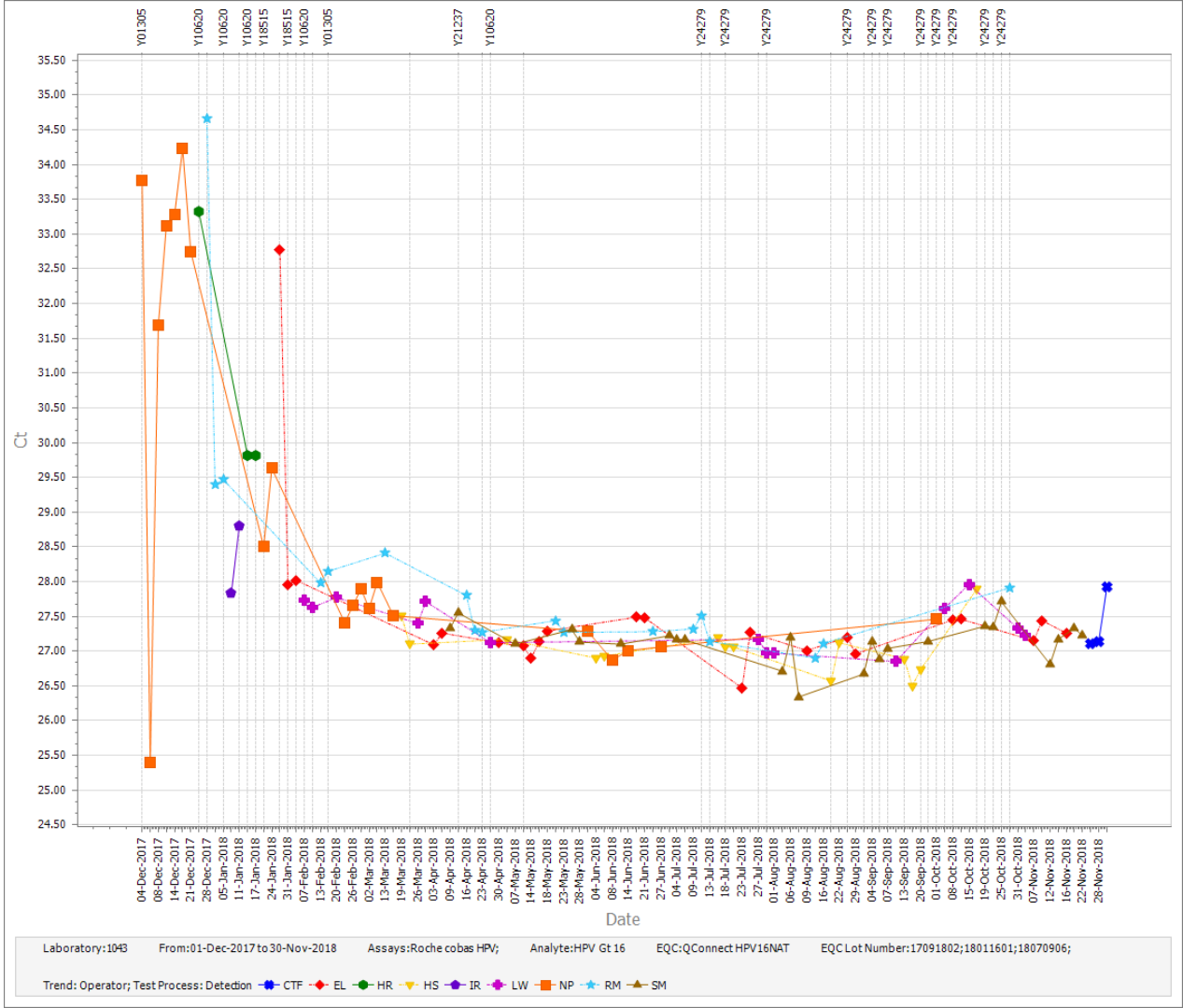
- Different user
- Similar experiences
- ‘Normalised’ practices after retraining



NRL Science of Quality

Lab 1043

- Consistency continues across three QC lots



NRL Science of Quality

Operator Variation

- Training and competency – critical
- Same preparation technique used for QC
- Understand importance of…
  - Recording data regularly
  - Actioning any suspicious trends

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Comments???

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