Interesting QC Case Studies: An interactive session

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NRL, Melbourne, Australia

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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

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…
The capital city of Australia is...?

- Sydney
- Melbourne
- Canberra
- Gold Coast
- None of the above
<table>
<thead>
<tr>
<th>The capital city of Australia is...?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sydney</td>
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<td>Melbourne</td>
</tr>
<tr>
<td>Canberra</td>
</tr>
<tr>
<td>Gold Coast</td>
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</tbody>
</table>
Scenario 1
Scenario 1

NRL Limits

NRL Limits
Scenario 1

NRL Limits

NRL Limits
<table>
<thead>
<tr>
<th>What is the likely cause of the results in Scenario 1?</th>
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</thead>
<tbody>
<tr>
<td>There is no problem at all</td>
</tr>
<tr>
<td>This is reagent lot variation</td>
</tr>
<tr>
<td>The QC is failing and needs review</td>
</tr>
<tr>
<td>The operators are at fault and need retraining</td>
</tr>
<tr>
<td>The instrument is failing and needs attention</td>
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</table>
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
Scenario 1

**Answer:**

Classic Lot Variation...
Scenario 1

NRL Limits

NRL Limits
Scenario 1

Cut-off
Scenario

???

Cut-off

NRL
Science of Quality

Note: Custom Y Axis range used.
Scenario 2
Scenario 2

Lab data by reagent lot

Which set is the issue?
<table>
<thead>
<tr>
<th>What is the likely cause of the results in the red boxes?</th>
</tr>
</thead>
<tbody>
<tr>
<td>This is reagent lot variation</td>
</tr>
<tr>
<td>The QC is failing and needs review</td>
</tr>
<tr>
<td>The QConnect Limits are wrong and need review</td>
</tr>
<tr>
<td>There are two lots of the QC in use</td>
</tr>
<tr>
<td>Something else is going on...</td>
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</tbody>
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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 QC Connect Limits are wrong and need review

There are two lots of the QC in use

Something else is going on...
Scenario 2

Peer group data
Scenario 2

Answer:

Something else is going on…

Wrong QC data entered into EDCNet
Scenario 2

- Non-QConnect QC data entered into EDCNet
Scenario 2

Peer group data
Scenario 3
QConnect
Blue lot for Lab 43

New QC lot
Previous QC lot by reagent lot
Current QC lot by reagent lot
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!!!
Current QC lot by reagent lot
Current QC lot by instrument
Previous QC lot by instrument
What is the source of variation in Scenario 3?

<table>
<thead>
<tr>
<th>QC lot issue</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument issues</td>
<td>B</td>
</tr>
<tr>
<td>Reagent lot issues</td>
<td>C</td>
</tr>
<tr>
<td>All of the above</td>
<td>D</td>
</tr>
<tr>
<td>None of the above</td>
<td>E</td>
</tr>
</tbody>
</table>
Scenario 3

Instrument calibration issues?

Separation of the two instruments
Lab 361 by reagent lot
Lab 361 by instrument
Lab 361 positive control by reagent lot
Lab 361 positive control by instrument
Lab 365 by reagent lot
Lab 365 by instrument
Lab 365 positive control by reagent lot
Lab 365 positive control by instrument
So... back to Lab 43?
Lab 43 positive control by reagent lot
Lab 43 positive control by instrument
Look familiar?

QConnect Blue

Positive Ctrl
### What is your likely conclusion now?

<table>
<thead>
<tr>
<th>Choice</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instruments in different labs are showing variability?</td>
<td></td>
</tr>
<tr>
<td>Reagent lots are showing variability?</td>
<td></td>
</tr>
<tr>
<td>QC lots are performing variably in different labs?</td>
<td></td>
</tr>
<tr>
<td>Combination of the above?</td>
<td></td>
</tr>
<tr>
<td>None of the above</td>
<td></td>
</tr>
</tbody>
</table>
**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*
Scenario 4
Grifols Tigris by peer group for QConnect HCVRNA
QConnect HIVRNA data
<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the cause for the problem in Scenario 4?</td>
</tr>
</tbody>
</table>

- Reagent lot variation
- Assay Calibration
- QC stability issues
- QC viral load is not homogenous
- Something else...?
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...?
Assays often perform in a sigmoidal pattern

Increasing analyte conc.
Ultrio Elite and Plus assays do not!!!

Increasing analyte conc.

Increasing signal

Presence of NA

Absence of NA
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
Scenario 5
Lab 25

- All data submitted
  - HPV16NAT
Data by Reagent lot
Data by Instrument
Data by Operator
<table>
<thead>
<tr>
<th>What is the cause of the variation in Scenario 5?</th>
</tr>
</thead>
<tbody>
<tr>
<td>QC Lot variation</td>
</tr>
<tr>
<td>Reagent Lot variation</td>
</tr>
<tr>
<td>Instrument Lot Variation</td>
</tr>
<tr>
<td>Operator variation</td>
</tr>
<tr>
<td>Something else....!</td>
</tr>
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</table>
Variation Source

Operator Variation!

Different sample preparation techniques developed over time
Data by Operator
Lab manager monitored before/after retraining
New QC lot

‘Normalised’ practices continue
HPV18NAT

Data by Operator

Variation also present
HPV18NAT

Retraining date
Data by Operator

‘Normalised’ practices continue
Lab 1043

- Different user
- Similar experiences

‘Normalised’ practices after retraining
Lab 1043

- Consistency continues across three QC lots
Operator Variation

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