Finding the “Bugs” through EQA

UK NEQAS for Microbiology

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The Traditional Benefits

- Provides insight into laboratory performance
- Checks efficacy of internal quality activities
- Improves standards (national/international)
- Educational impetus for improvement
  - Only true if you use EQA failure as an improvement opportunity
- Demonstrates a commitment to quality

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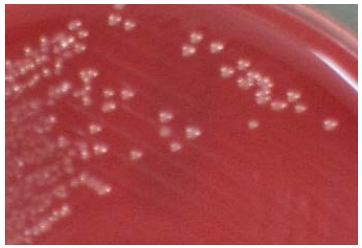
Case studies

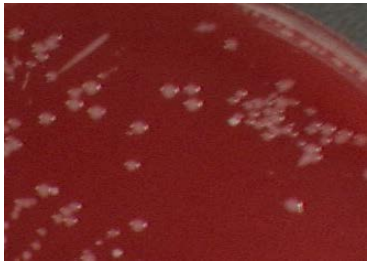
- Examine the outcomes of the investigation of EQA failures
  - Proving how this invaluable activity improves practice (if done)
  - Shows that dependence or reliance on equipment for diagnosis without the foundation knowledge can lead to incorrect results and therefore poor clinical outcome

Case study 1

- General bacteriology:
  - EQA specimen contained an organism grown from ‘sterile site’
  - 80 participants reported the incorrect organism
  - Identified that a large proportion (59/80) who obtained the wrong result reported the same organism – *Pasteurella sp.* using the Vitek system
  - Contacted the manufacturer (some participants also did this)



Kingella kingae
Target organisms



Pasteurella sp.
(impostor)

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Case study 1 - contd.

- *Kingella kingae* - gram-negative ((?? Facultative anaerobe) aerobic coccobacilli – relatively inactive biochemically
- *Pastereulla* – gram-negative facultative anaerobic coccobacilli
- Selecting the VITEK before doing some basic identification analysis (Gram, catalase, urease) and moving straight to a biochemical analysis

Case study 1 - contd.

- What should have been done technically?
  - Catalase (*Kingella* – negative; *Pasteurella* – positive)
- This would have resulted in the selection of the correct ID panel

LESSON LEARNED

This demonstrates that conventional tests are still helpful and should be used as an adjunct to testing in commercial kits/instruments for groups of organisms where it is recognised that discrimination may not be optimal for these methods

Case study 1 – contd.

- Actions
  - Manufacturers. Nothing to be done. The science is still sound as long as the basic bacteriology decision-making is sound. Increase validation against more isolates.
  - Laboratories. Adjust algorithms to ensure the decision-making on which biochemical profile is selected is sound.

Case study 2

General bacteriology scheme

- Specimen containing *B. parapertussis* and participants were asked specifically to confirm whooping cough
- 24/424 reported *B. bronchiseptica*, mostly using the same platform

Case study 2 – contd.

- Initial query raised by a participant laboratory requesting the method used by other laboratories
- All information was passed to the manufacturer (specimens were made available for investigation)
- Investigations:
  - Manufacturer established that the particular strain was not included in their database
  - Participants elected to go straight to the equipment without using basic bacteriological techniques first (Standards for Microbiology Investigations (SMIs) recommend growth on charcoal selective agar followed by further analysis using antisera and the common ID tests)
    - Reason given was to get EQA right - this was not how a clinical sample would have been treated

Case study – 2 contd.

Lessons learned

- Always treat EQA specimens as you would clinical samples
- Manufacturers do ‘lag’ behind with updating regarding strains

Case study – 2 contd.

Actions

- Manufacturer stated the strain would be incorporated into future panels (Currently they do give guidance on supplementary testing for the ID obtained)

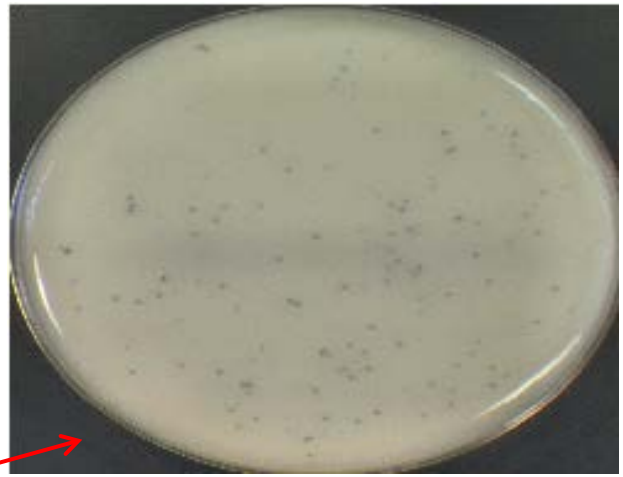
Case study 3

MRSA screening scheme

- A particular strain with an MIC very close to the breakpoint for the proprietary agent in the selective media - unknown fact to UK NEQAS
- Participants were requested to confirm the presence of MRSA
- 45 participants reported a negative result on culture
  - 35 participants were using Brilliance agar

Case study 3 – contd.

- The negative result was not observed during quality control of the specimen which included growth on the Brilliance agar



Case study 3 contd.

- Antibiotic breakpoints
  - Regularly updated by the various anti-susceptibility protocols, e.g. EUCAST, BSAC
  - Manufacturers do not regularly re-assess the media against the current circulating strains

- This is detected through EQA failures on specific organisms
- This could also have highlighted batch issues with the media

Case study 3 – contd.

Lessons learned

- Review of EQA/PT results must be done with vigour
- Dialogue and communications between EQA providers, participating laboratories, reference laboratories and manufacturer and potentially the competent authorities are essential for continuous improvement

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Case study 3 – contd.

Actions

- Manufacturer contacted and communications were started
  - Specimen sent for analysis
  - Strain is not currently in the panel used to validate the media by the manufacturer
    - Did not explain why some growth was obtained by UK NEQAS and some participants.

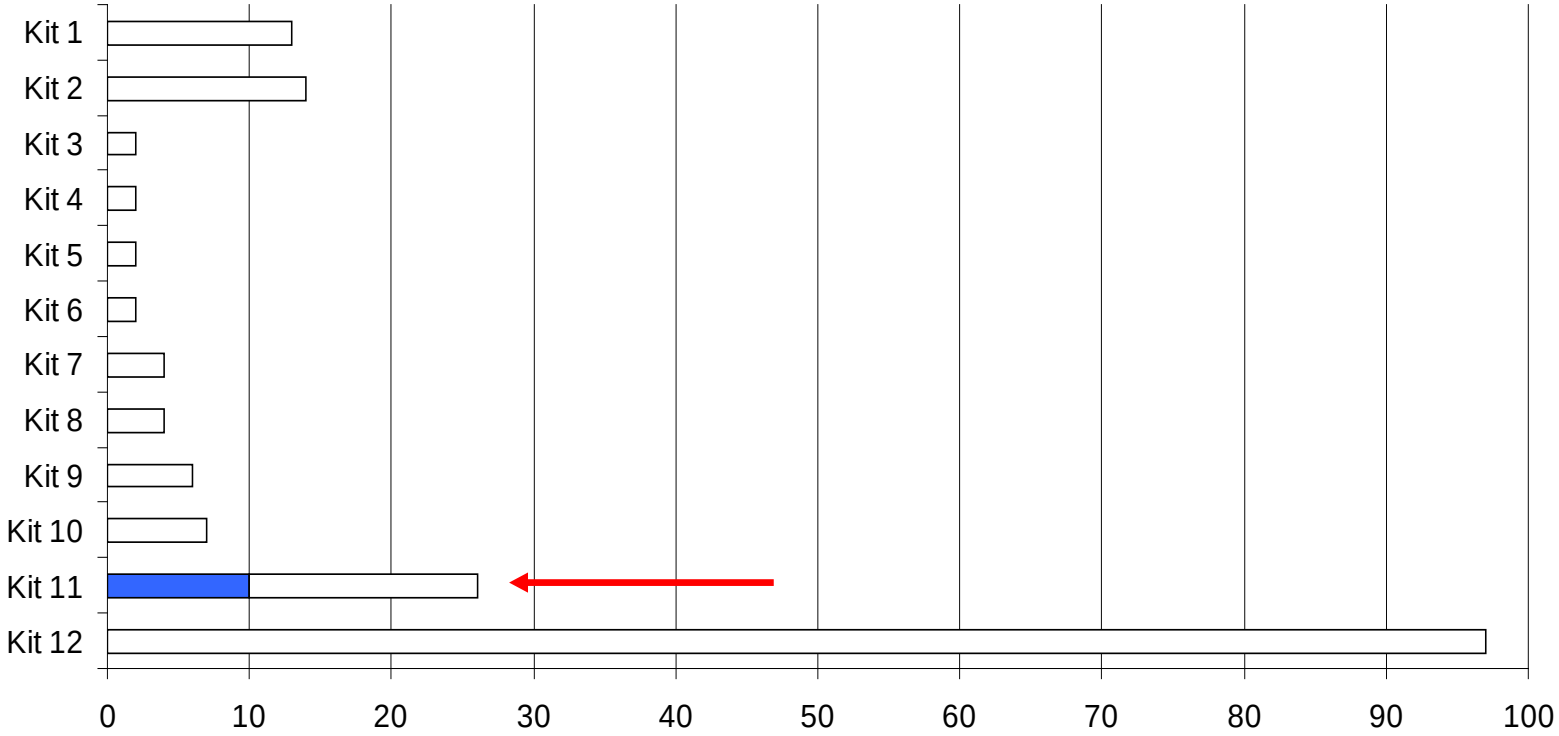
Case study 4

- Measles IgG serology
  - 4% participants reported equivocal or negative result all using one particular manufacturer's kit for a specimen identified as positive with other manufacturers' kits
  - Reported to manufacturer with full pre- and post distribution testing
  - Repeat samples were made available

Case study 4 – contd.

- ‘Histogram’ showing how the problem is readily identified through the use of graphics

Key?????



Case study 4 - contd.

- Manufacturer investigated the issue
- Adjusted kit to increase sensitivity

"…….developed in order to improve the sensitivity of the kit ; it is based on the use of a new sera panel to be introduced during the manufacturing and batch release processes."

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Case study 5

- Rubella IgG screening
  - Participants using one particular assay reported results of rubella IgG levels lower than participants using other assays with almost a third reporting a result below 10IU/mL (considered the cut-off for determining susceptibility)

Case study 5

- Analysis of the results lead to the following actions:
  - Manufacturer contacted with offer of specimens
    - This resulted in good discussions and scientific debate
  - Retrospective analysis of similar samples

Case study 5 – contd.

- Statistically significant differences between methods used for detecting and quantifying rubella IgG antibodies.
  - A study in 2006 looking at rubella IgG positive samples with 'low' levels of antibodies (median 10 to 21 IU/mL) showed assays from three manufacturers produced the lowest quantitative values.

- Analysis of data in 2010 (after the introduction of the specific assay in this distribution) showed a significant difference in the quantitative values between the new assay compared with another platform from the same manufacturer.
  - In this analysis three EQA samples with low levels of rubella IgG (median 16 to 20 IU/mL) were assessed using normal linear regression with the specific assay as the comparator assay. There were significantly higher and lower values against the comparator assay.

Case study 5 – contd.

- Further EQA samples classed as rubella IgG negative (<10 IU/mL) distributed over the past two years also showed variable results

- The data suggested that sera that are truly negative for rubella IgG antibodies (indicative of susceptibility to rubella virus) will result in quantitative values of 5 IU/mL or lower for all assays

Case study 5 - contd.

- Benefits:
  - This specimen highlighted the ongoing issues with accurate quantification of antibodies and the arbitrary cut off value delineating ‘protective’ levels
  - Contributed to the general scientific debate

Lessons to highlight to participants

- Carry out good basic laboratory investigations even if you have automated equipment
- Know your equipment – how it works, what are the limitations
- Never vary from the instruction: “Treat EQA samples as you would clinical samples”
- Don’t be driven by scores
  - Follow-up on failures: that’s where the real lessons are
- Staffing levels v qualifications: which is more important

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Conclusion

- The case studies show that EQA is much more than an accreditation tool
- The hidden benefits include:
  - Encouraging scientific debate (Rubella IgG)
  - Improved manufactured kits (MRSA, Measles IgG)
  - Improved good scientific practice (Kingella/Bordetella)
  - Staff training and/or qualifications:
    - Just because you have a machine doesn't mean you can have less qualified staff

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Thank you

Our normal tea-time – the cake icing reads: “Microbiologists do it with culture and sensitivity”

Cakes for the visiting haematologists

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