The Value of Rapid Microbiological Methods
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Background

• First job was in the development of microtiter plate bacterial rapid identification systems (35 years ago!!)
• Worked at MHRA for 14 years
  • Led for the inspectorate with regards to the introduction for RMM
  • Worked with a number of companies on the introduction of RMM
  • Co chaired a training event for PIC/S inspectors on RMM
  • Chair Annex 1 working group until December 2018
• Joined AbbVie in 2019, one of my roles is working with colleagues to assess the potential use of RMMS
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Agenda

• Speakers background
• Where are we now?
• RMM pros and cons
• Summary
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Where are we now?

1. Starting to see the use of raw material and finished product rapid methods:
   a) ATP
   b) DNA
   c) Fluorescence

2. Some uptake for environmental monitoring
   a) Swabbing
   b) Florescent light scattering techniques

3. Starting to see the use in water systems
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RMM pros and cons

• What are the classical tools:
  • Agar (settle plates, swab streak, air samples)
  • Broth (swabs)
  • Mainly Tryptone Soya Broth or agar/Casein digest, usually with inhibitors
• Raw materials using specialist growth medium
  • R2A
  • MacConkey etc.
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RMM pros and cons

The classical methods are all very reliable so why would we want to move away from them?!

But can you keep a secret, they are not really!!!
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RMM pros and cons

• Interpretive issues
  • Deliberate or accidental difference in reading
  • Second person verification requirements becoming more stringent
    • Independent read?
    • Photos?
<table>
<thead>
<tr>
<th>BACTERIUM</th>
<th>Nose</th>
<th>Pharynx</th>
<th>Mouth</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus mitis</em></td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td><em>Streptococcus salivarius</em></td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em></td>
<td>+</td>
<td>+</td>
<td>++</td>
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<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Neisseria sp.</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>+</td>
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</tr>
<tr>
<td>Proteus sp.</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Haemophilus influenzae*</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Lactobacillus sp.</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Corynebacteria</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Actinomycetes</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Spirochetes</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Mycoplasmas</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- **Will grow on TSA/TSB**
- **Will NOT* grow on TSA/TSB**
- **May grow on TSA/TSB**

* Under typical incubation conditions
Important

Absence of evidence is not evidence of absence
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Cons:

- May need new authorisation/Filing (in multiple different regions)
- Therefore may be expensive to implement
- What about the validation
- What do I do with the new information from my new “more sensitive” methodology where the traditional methods used to recover zero contaminants from my product or environment, now have constant low level recovery. What does that mean?
- Frequently breaking paradigms e.g. Florescent events
Cons:

• False Positives?
  • What does this mean?
  • Does it compare to CFU?
  • How do we set baselines?
  • How do I convince myself?
  • How do I convince a regulator?
• What about real false positives?
• Regulators are very conservative!?
• Industry is conservative!?
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RMM pros and cons

Pros:
• Learn more about our processes
• Financially (cheaper longer term)
  • Less inventory held (5 days (or less) rather than 14 days for sterility test)
  • Less inventory at risk
• May be more effective/sensitive
• React quicker so that we can investigate/assess the process and therefore the impact quicker, also more likely to find the root cause
• May be better positioned to support other new technology such as WFI by RO?
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RMM pros and cons

Pros:
• Data integrity/Governance controls
• More consistent interpretation of data
• Number of regulators are keen to support new methodology (innovations and guidance meetings)/ Industry working together
• Current GMPs!!!!!!!
• Improved patient safety
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Summary

• Current uptake of methods is improving
• It's not necessarily easy
• May be short term costs
• Need to talk with the regulators and suppliers (needs to be a tripartite conversation)
• But may be improved savings further down the line
• Better knowledge of our process
• Improved compliance (DI etc.)
• The lake may not be empty but at least we will know
• Improved patient safety
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Why wouldn’t we?
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Thank you for your time
Any questions?