Diagnostics Inspection Update

Stephanie Croft, WHO PQT Inspections Group
Agenda

01 Key statistics from 2018 to 2019
02 Recurring deficiencies
03 Recommendations & Conclusion
04 Q&A
Statistics for 2019

January to December 2019

• 23 inspections completed in total. This included:
  • 20 onsite inspections (19 IVD sites + 1 Male circumcision device (MCD))
  • 3 desk assessments (new procedure adopted in 2019!)
  • 38 products covered in total during onsite inspections

<table>
<thead>
<tr>
<th>HIV</th>
<th>Malaria</th>
<th>Hep C</th>
<th>Hep B</th>
<th>Syphilis</th>
<th>Medical Device*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AgAb, 1/2, 2, CD4</td>
<td></td>
<td></td>
<td>HBsAg</td>
<td>HIV/Syphilis combo</td>
<td>Male Circumcision</td>
</tr>
<tr>
<td>Rapid</td>
<td>Pf/Pv,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self</td>
<td>Pf HRP2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total: 18</strong></td>
<td><strong>12</strong></td>
<td><strong>3</strong></td>
<td><strong>2</strong></td>
<td><strong>2</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>
Statistics for 2018

January to December 2018

- 20 onsite inspections completed in total. This includes:
  - 20 IVDs (no desk assessments)
  - 61 Products covered in total during onsite inspections

<table>
<thead>
<tr>
<th>HIV</th>
<th>Malaria</th>
<th>Hep C</th>
<th>Hep B</th>
<th>Syphilis</th>
<th>G6PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 self-test</td>
<td>Pf/PAN RDTs</td>
<td></td>
<td></td>
<td>HbsAg</td>
<td></td>
</tr>
<tr>
<td>HIV 1/2</td>
<td>Pf/Pv/Po/Pm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4</td>
<td>Pf, RDTs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total: 30</strong></td>
<td><strong>25</strong></td>
<td><strong>4</strong></td>
<td><strong>1</strong></td>
<td><strong>0</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>
Inspections by Country 2019

Total: 20 sites

- US: 15%
- Korea: 15%
- China: 15%
- Belgium: 15%
- India: 15%
- Thailand: 10%
- Malaysia: 10%
- UK: 15%

Copenhagen, Denmark  2 – 5 December 2018
Inspections by Country 2018

Total: 20 sites

- Korea: 20%
- Japan: 10%
- France: 15%
- China: 10%
- Ireland: 5%
- Malaysia: 5%
- India: 10%
- Italy: 5%
- US: 5%
- Germany: 10%
- South Africa: 5%
- Total: 20 sites
Inspections by type 2019

- Initial: 30%
- Routine: 26%
- Routine reinspection: 13%
- Desk review: 13%
- Follow-up: 31%

Total: 24 inspections
Inspections by type 2018

- Initial: 54%
- Follow-up: 21%
- Reinspection: 25%
- Desk review: 0%

Total: 20 inspections
Inspections by Outcome in 2019

- Compliant (action plan acceptable with follow up actions): 30%
- Compliant (action plan acceptable with no follow up actions): 40%
- CAPAs pending: 15%
- Follow-up required: 5%
- Non-compliant: 10%
Inspections by Outcome in 2018

- Compliant (action plan acceptable with follow up actions): 55%
- Compliant (action plan acceptable with no follow up actions): 15%
- Non-compliant: 10%
- Follow-up accepted: 5%
- Follow-up required: 15%
Level 4 and 5 deficiencies noted in 2018-2019

- Nbre of sites (Level 4s) in 2018
- Nbre of sites (Level 4s) in 2019
- Nbre of sites (Level 5s) in 2018
- Nbre of sites (Level 5s) in 2019

Copenhagen, Denmark 2 – 5 December 2018
Recurring Deficiencies

The level 5s observed in 2018-2019 were related to DATA INTEGRITY

- Falsification of batch manufacturing records (BMR)
- Falsification of QC testing results
Examples of recurring deficiencies

Clause 7.5.1.1 - Control of production and service provision – General requirements were not fully met, in that:
Numerous batch records were found of products that progressed through manufacturing without any of the previous stages in manufacturing being confirmed as compliant by either supervisors or QC. Product was release tested, and batches released and packed for delivery were observed in the warehouse. This level of **loss of control over production activities** including all in process controls, as well as the **lack of traceability** are considered critical.
Examples of recurring deficiencies

The requirements of Clause 7.5.3.2 - Traceability – General were not fully met, in that:

The batch records were not completed contemporaneously. The data was written on loose pieces of paper and transcribed into the batch records. (uncut sheets sorting, QC, packing) The discards were written on loose pieces of paper and these were destroyed.
Examples of recurring deficiencies

Clause 8.3 - Control of nonconforming product - repeat nonconformities noted with regard to the management of out of specification test results:

- Root cause of OOS identified as Possible error in sample preparation, but there was no further explanation provided on how this was identified as the root cause and no documented evidence that this was indeed the problem. The results were invalidated, tests were repeated with the original sample and failed results were replaced with acceptable results.
Examples of recurring deficiencies

Clause 8.3 - Control of nonconforming product (cont’d)

-OOS for stability tests were not trended. A review of all stability test results, including initial testing results, should be performed to identify any potential issues with the product.
Recommendations & Conclusion

• Number of inspections performed by WHO PQT remained consistent
• Number and type of deficiencies consistent from one year to next
• Manufacturers should learn from mistakes – Good documentation practices should be improved in general!
Questions and Answers

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