# Target Product Profile for a Multiplex Multi-Analyte Febrile Illness Test for use on the MAPDx platform

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scope of the Platform</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Intended Use</td>
<td>In the context of infectious diseases, intended for individual patient management for patients presenting with symptoms consistent with severe febrile illness without a known source(^1) to test for the presence of markers of current infection by target pathogens</td>
<td></td>
</tr>
<tr>
<td>2 Description of System</td>
<td>The system will consist of an instrument(^2) designed for use in combination with a self-contained, disposable assay cartridge(s)(^3) containing all required reagents to execute a test from sample to result</td>
<td></td>
</tr>
<tr>
<td>3 Target Use Setting</td>
<td>Level 2(^4) Healthcare Facility (District Hospital or above) defined as having a functioning laboratory with trained personnel, water, electricity with intermittent surges and/or outages, limited climate control, dust, and medical staff onsite; The target use setting does not include mobile testing facilities</td>
<td>Level 1(^4) Healthcare Facility with rudimentary staffed/equipped laboratory, inconsistent electricity, including frequent surges and/or outages, no climate control, dust, but trained medical staff on-site for result interpretation and patient management</td>
</tr>
<tr>
<td>4 Target User</td>
<td>Trained laboratory personnel (e.g., 1-2 year certificates)</td>
<td>Minimally skilled healthcare personnel (e.g. 3-6 months, able to operate an integrated test with minimal additional steps)</td>
</tr>
<tr>
<td>5 Target population</td>
<td>Adults to children &gt; 6 months of age</td>
<td>Same, plus neonates (including pre-matures) up to 6 months of age</td>
</tr>
<tr>
<td>Instrument</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Instrument Design</td>
<td>Single integrated instrument with universal port(s) capable of interfacing with one or more cartridge designs for simultaneous detection of multiple analytes to achieve the intended use</td>
<td></td>
</tr>
<tr>
<td>7 Size</td>
<td>Small, table-top instrument (50 cm x 75 cm by 50 cm, or smaller)</td>
<td></td>
</tr>
<tr>
<td>8 Weight</td>
<td>(\leq 25) kg</td>
<td>(\leq 10) kg</td>
</tr>
</tbody>
</table>

---

\(^1\) Severe febrile illness without a source is defined as “Febrile illness, independent of duration (acute and persistent), without evidence of localized infection by history, physical examination, and appropriate diagnostic tests and severity identified by danger signs.”  

\(^2\) Instrument is used throughout the document; however, any innovative design/embodiment that meets the described characteristics is acceptable  

\(^3\) Assay cartridge is used throughout the document; however, any innovative design/mechanism that meets the described characteristics is acceptable  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 Power Requirements</td>
<td>Local 110-220 AC mains power, plus UPS (to complete current cycle); UPS and circuit protector must be integrated within the system</td>
<td>Same, with rechargeable battery back-up (8-hour operation)</td>
</tr>
<tr>
<td>10 Throughput</td>
<td>Random access(^5) required(^6) with throughput up to 8 sample runs per instrument per 8-hour day</td>
<td>Random access required(^6) with throughput up to 40 sample runs per instrument per 8-hour day</td>
</tr>
<tr>
<td>11 Environmental Stability – Operating Range of Platform</td>
<td>Operation at 10-35°C and up to 90% non-condensing humidity at altitude up to 2,500 meters; Able to function in direct sunlight and low light; able to withstand dusty conditions</td>
<td>Operation at 5-45°C and up to 90% non-condensing humidity at altitude up to 3,000 meters; Able to function in direct sunlight and low light; able to withstand dusty conditions</td>
</tr>
<tr>
<td>12 Biosafety</td>
<td>Closed, self-contained system; easy decontamination of instrument surfaces</td>
<td></td>
</tr>
<tr>
<td>13 Training</td>
<td>&lt;2-days training for skilled laboratory staff</td>
<td>&lt;1-day training for minimally skilled staff</td>
</tr>
<tr>
<td>14 Service, Maintenance and Calibration</td>
<td>Daily preventive maintenance can be performed by laboratory staff in &lt;30 minutes (with hands on time &lt;10 minutes); Mean time between failures of at least 24 months or 10,000 tests, whichever occurs first; Self-check alerts operator to instrument errors or warnings; and need for instrument calibration onsite on a yearly basis by minimally trained technician</td>
<td>Routine preventive maintenance no more than 30 minutes 1x per week (with hands on time &lt;10 minutes); Mean time between failures of at least 36 months or 30,000 tests, whichever occurs first; Self-check alerts operator to instrument errors or warnings; and ability to be calibrated remotely, or no calibration needed</td>
</tr>
<tr>
<td>15 Patient Identification Capability</td>
<td>Manual entry of alphanumeric patient identifier keypad or touch screen compatible with protective gloves</td>
<td>Same, plus bar code, RFID or other reader</td>
</tr>
<tr>
<td>16 Result Readout</td>
<td>Quantitative based on the analytes of detection. Qualitative result available to user where that result is sufficient to inform clinical decision making; Ability to select which test results are reported to the user based on the intended use in the regional epidemiological context in which the test is applied</td>
<td></td>
</tr>
<tr>
<td>17 Data Display</td>
<td>On-instrument visual readout with ability to function in various lighting conditions ranging from direct sunlight to low ambient light conditions; able to add information (patient ID, operator ID, date, location, etc.)</td>
<td></td>
</tr>
</tbody>
</table>

\(^5\) Random access refers to the capability of the device to perform any test in any sequence at any time, with no interdependence on other test runs

\(^6\) Note – no random access is required if time to result is less than 30 minutes
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>18</strong> Connectivity</td>
<td>Integrated Local Area Network (LAN) port; Integrated WI-FI 802.11b/g/n; USB 3.0; Internally designatable static IP address; Support for DHCP issued IP addresses; Support for HTTPS and SFTP protocols; Ability to update connectivity software stack via USB or LAN</td>
<td>Integrated Local Area Network (LAN) port; Multi-band GSM chipset 2G, 3G, LTE; Integrated Bluetooth 5.0; Integrated WI-FI 802.11ac; USB 3.0; Internally designatable static IP address; Support for DHCP issued IP addresses; Bi-Directional communication – ability to update connectivity software stack</td>
</tr>
<tr>
<td><strong>19</strong> Data Export</td>
<td>Export of all instrument and test data over integrated hardware; Secured data export with end-to-end encryption; Data export in .CSV file format; Configurable destination IP and DNS address; User initiated data export; and Connectivity to external printer</td>
<td>Export of all instrument and test data over integrated hardware; Export of data via GSMA SMS; Secured data export with end-to-end encryption; Data export using interoperable standards Configurable destination IP and DNS address; User initiated data export; and Scheduled/automatic data export Connectivity to external printer</td>
</tr>
<tr>
<td><strong>20</strong> Manufacturing</td>
<td>ISO 13485:2016 compliant</td>
<td></td>
</tr>
<tr>
<td><strong>21</strong> List Price ≤ Instrument</td>
<td>≤ $15,000 USD</td>
<td>≤ $5,000 USD</td>
</tr>
<tr>
<td><strong>Assay Cartridge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>22</strong> Description of Assay Cartridge</td>
<td>Self-contained, disposable cartridge(s) compatible with the universal cartridge port(s) of the instrument, containing all required reagents to execute a test from sample input to result; The assay cartridge will meet universal, “semi-open” design specifications made available by the manufacturer of the multiplex diagnostic platform to selected assay developers worldwide for use on such platform</td>
<td></td>
</tr>
</tbody>
</table>

7 List Price— the price the manufacturer has arrived at for the product, taking into account the cost of goods and other factors (e.g., margin); the list price does not include any volume or other discounts or potential markup for distribution or other costs, including freight, taxes, etc.
8 The semi-open system will consist of three components:
   1. **Instrument Manufacturer**: will design, develop, and manufacture the multiplex diagnostic instrument and design an open cartridge for use on it.
   2. **OEM Cartridge Manufacturer**: will manufacture open cartridges to pre-designed specifications on behalf of the instrument manufacturer.
   3. **OEM Assay Manufacturers (Multiple)**: will develop assays for the cartridge based on an assay developer’s toolkit provided by the instrument manufacturer.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 Pathogen Targets</td>
<td>Detection of all the following to the limit of detection listed in Appendix 1:</td>
<td>Same, plus detection of any of the following to the limit of detection listed in</td>
</tr>
<tr>
<td></td>
<td>• Typhoidal salmonella</td>
<td>Appendix 1 in descending level of priority:</td>
</tr>
<tr>
<td></td>
<td>• Streptococcus pneumoniae</td>
<td>• Neisseria meningitidis</td>
</tr>
<tr>
<td></td>
<td>• Staphylococcus aureus</td>
<td>• Klebsiella spp</td>
</tr>
<tr>
<td></td>
<td>• Non-typhoidal salmonella</td>
<td>• Orientia tsutsugamushi</td>
</tr>
<tr>
<td></td>
<td>• Escherichia coli</td>
<td>• Haemophilus influenzae</td>
</tr>
<tr>
<td></td>
<td>• Rickettsial spp</td>
<td>• Dengue virus (all serotypes)</td>
</tr>
<tr>
<td></td>
<td>• Leptospira spp</td>
<td>• Lassa virus</td>
</tr>
<tr>
<td></td>
<td>• Brucella spp</td>
<td>• Histoplasma capsulatum</td>
</tr>
<tr>
<td></td>
<td>• Burkholderia pseudomallei</td>
<td>• Enterococcus faecalis</td>
</tr>
<tr>
<td></td>
<td>• Coxiella burnetii</td>
<td>• Borrelia recurrentis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chikungunya virus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pseudomonas spp</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acinetobacter baumannii</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Enterobacter spp</td>
</tr>
<tr>
<td>24 Analytes</td>
<td>Ability to simultaneously detect multiple analyte types (e.g. nucleic acids and</td>
<td>Ability to simultaneously detect multiple analyte types (e.g. nucleic acids and</td>
</tr>
<tr>
<td></td>
<td>serologic markers [antibodies, antigens and host biomarkers]) to achieve the</td>
<td>serologic markers [antibodies, antigens and host biomarkers]) to achieve the</td>
</tr>
<tr>
<td></td>
<td>intended use at the same time, from a single specimen, in one or more assay</td>
<td>intended use at the same time, from a single specimen, in a single assay</td>
</tr>
<tr>
<td></td>
<td>cartridges; Analytes per pathogen target are listed in Appendix 1</td>
<td>cartridge; additional analyte detection capabilities preferred (e.g. clinical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>chemistries, cell counts); Analytes per pathogen target are listed in Appendix 1</td>
</tr>
<tr>
<td>24 Clinical Sensitivity</td>
<td>≥ 90% (95% CI) per pathogen based upon optimal sample volume input</td>
<td>≥ 95% (95% CI) per pathogen based upon optimal sample volume input</td>
</tr>
<tr>
<td>25 Clinical Specificity</td>
<td>≥ 95% per pathogen based upon optimal sample volume input</td>
<td>≥ 98% per pathogen based upon optimal sample volume input</td>
</tr>
<tr>
<td>26 Multiplexing Capabilities</td>
<td>Ability to detect a minimum of 6 pathogens(^9) at the same time, from the same</td>
<td>Ability to detect a minimum of 15 pathogens at the same time, from the same sample,</td>
</tr>
<tr>
<td></td>
<td>sample, in one or more assay cartridges</td>
<td>in the same assay</td>
</tr>
<tr>
<td>27 Limit of Detection in</td>
<td>Equivalent or improved relative to reference assays for similar target analytes</td>
<td></td>
</tr>
<tr>
<td>Multiplex Format</td>
<td>(see Appendix 1 below)</td>
<td></td>
</tr>
<tr>
<td>28 Test Kit</td>
<td>All materials required for the test, including the assay cartridge, reagents,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>buffers or other consumables to test one patient, included in individually packed,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>self-contained kit</td>
<td></td>
</tr>
<tr>
<td>29 Additional Third-Party</td>
<td>None, except for sample collection and sample prep (e.g. volumetric pipettes)</td>
<td>None; cartridges contain all required reagents</td>
</tr>
<tr>
<td>Consumables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 Specimen Type</td>
<td>Whole blood</td>
<td></td>
</tr>
</tbody>
</table>

\(^9\) Assuming one or more analytes or assay targets per pathogen are required
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>31 Sample Volume</strong></td>
<td>The minimal sample volume required to reach clinically relevant sensitivities in a 24-hour period, which in some cases could require up to 10 mL depending on sample volume and limit of detection (See Appendix 2);&lt;sup&gt;10&lt;/sup&gt; For children 5 years to 6 months of age should require no more than 5 mLs of whole blood</td>
<td>Same as minimal requirements and for neonates (including premature) - or children &lt;2kg should require no more than 2 mL of whole blood</td>
</tr>
<tr>
<td><strong>32 Sample Preparation</strong></td>
<td>Minimal sample processing; no more than 3 steps (requiring operator intervention); no more than 1 precision step (e.g. volumetric pipetting); centrifugation or other off-cartridge sample processing steps acceptable</td>
<td>All sample processing steps are self-contained and performed within the assay cartridge; no precision steps required to be performed by the user</td>
</tr>
<tr>
<td><strong>31 Cross Reactivity</strong></td>
<td>No relevant cross reactivity with microorganisms outside of the scope of the pathogens of interest, i.e. targets should be designed to not cross-react with other species within a genus or species that could be considered contaminants within the laboratory environment (e.g., <em>Staphylococcus aureus</em> vs. <em>Staphylococcal epidermidis</em>)</td>
<td></td>
</tr>
<tr>
<td><strong>32 Interfering Substances</strong></td>
<td>No interference for an individual or mixtures of analytes due to interfering substances</td>
<td></td>
</tr>
<tr>
<td><strong>33 Test Result</strong></td>
<td>Qualitative based on the analytes of detection; Qualitative result available to user where that result is sufficient to inform clinical decision making</td>
<td></td>
</tr>
<tr>
<td><strong>34 Time to Result</strong></td>
<td>&lt;90 minutes</td>
<td>&lt;30 minutes</td>
</tr>
<tr>
<td><strong>35 Controls – Internal Process</strong></td>
<td>A full internal process control must be integrated into the assay cartridge and the instrument</td>
<td></td>
</tr>
<tr>
<td><strong>36 Controls – Positive/Negative</strong></td>
<td>External positive and negative controls are not required for each test and but are performed daily</td>
<td>External positive and negative controls are not required for each test and do not need to be run daily</td>
</tr>
<tr>
<td><strong>37 Environmental Stability - Transportation</strong></td>
<td>No cold chain requirements; Stable at 2 – 45°C for up to 7 days, can tolerate short term temperature fluctuations from 0 - 50°C; Up to 90% non-condensing humidity for up to 7 days</td>
<td>No cold chain requirements; Stable at 2 – 45°C for up to 15 days, can tolerate short term temperature fluctuations from 0 - 50°C; Up to 90% non-condensing humidity for up to 15 days</td>
</tr>
<tr>
<td><strong>38 Environmental Stability – Operating Range</strong></td>
<td>10 – 35°C</td>
<td>5 – 45°C</td>
</tr>
<tr>
<td><strong>39 Waste/Disposal Requirements</strong></td>
<td>Direct disposal or incineration of consumables</td>
<td>Same, and no use of cyanide-containing reagents</td>
</tr>
</tbody>
</table>

<sup>10</sup> Volume requirements could be circumvented by off-cartridge processing steps as defined in the sample preparation characteristic
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimum Requirement</th>
<th>Optimal Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Shelf Life and Storage Conditions</td>
<td>12 months, 70% humidity from date of manufacture (based upon real-time/accelerated</td>
<td>18 months, 95% humidity from date of manufacture (based upon real-time/accelerated</td>
</tr>
<tr>
<td></td>
<td>stability studies) at up to 30 °C</td>
<td>stability studies) at 40 °C</td>
</tr>
<tr>
<td>41 Manufacturing</td>
<td>ISO 13485:2016 compliant</td>
<td>ISO 13485:2016 compliant</td>
</tr>
<tr>
<td>42 List Price of Assay Cartridge</td>
<td>≤ $15 USD at volume production</td>
<td>≤ $5 USD at volume production</td>
</tr>
</tbody>
</table>

Appendix 1: List of Reference Testing and Limit of Detection for Priority Pathogens

<table>
<thead>
<tr>
<th>Rank</th>
<th>Pathogen</th>
<th>Sample type</th>
<th>Gold standard</th>
<th>Pathogen circulation/mL (Ref)</th>
<th>Analyte Type Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Typhoidal salmonella</td>
<td>WB</td>
<td>Blood culture</td>
<td>1 (Wain, 1998; S. typhi)</td>
<td>Molecular</td>
</tr>
<tr>
<td>2</td>
<td>Streptococcus pneumoniae</td>
<td>WB</td>
<td>Blood culture</td>
<td>1-30 (Lehman 2008)</td>
<td>Molecular</td>
</tr>
<tr>
<td>3</td>
<td>Staphylococcus aureus</td>
<td>WB</td>
<td>Blood culture</td>
<td>1-30 (Lehman 2008)</td>
<td>Molecular</td>
</tr>
<tr>
<td>4</td>
<td>Non-typhoidal salmonella</td>
<td>WB</td>
<td>Blood culture</td>
<td>1 (Wain, 1998; S. typhi)</td>
<td>Molecular</td>
</tr>
<tr>
<td>5</td>
<td>Escherichia coli</td>
<td>WB</td>
<td>Blood culture</td>
<td>200 (Yagupsky, 1990)</td>
<td>Molecular</td>
</tr>
<tr>
<td>6</td>
<td>Rickettsia ssp</td>
<td>Buffy coat/WB</td>
<td>IFA (4-fold rise)/qPCR</td>
<td>210 (Dittrich, 2014)</td>
<td>Molecular &amp; Serology</td>
</tr>
<tr>
<td>7</td>
<td>Leptospira</td>
<td>WB/serum</td>
<td>MAT (4-fold rise)/qPCR</td>
<td>10000 (Agampodi, 2012)</td>
<td>Molecular &amp; Serology</td>
</tr>
<tr>
<td>8</td>
<td>Brucella</td>
<td>WB/serum</td>
<td>Blood culture/serology</td>
<td>88 (Young, 1995)</td>
<td>Molecular &amp; Serology</td>
</tr>
<tr>
<td>9</td>
<td>Burkholderia pseudomallei</td>
<td>WB/pus</td>
<td>Blood culture</td>
<td>~10 (Supaprom et al. 2007)</td>
<td>Molecular</td>
</tr>
<tr>
<td>10</td>
<td>Coxiella burnetii</td>
<td>WB/serum</td>
<td>IFA (4-fold rise)/qPCR</td>
<td>10 (Wielders, 20103)</td>
<td>Molecular &amp; Serology</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Neisseria meningitidis</td>
<td>WB</td>
<td>Blood culture</td>
<td>1.6x10^6 (DNA copies/mL; children) (Hackett et al. 2004)</td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
<td>------------------------</td>
<td>----</td>
<td>---------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10⁴ CFU/mL (Zwahlen et al. 1984)</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Klebsiella</td>
<td>WB</td>
<td>Blood culture</td>
<td>10 (Yagupsky, 1990)</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>Orientia tsutsugamushi</td>
<td>Buffy coat / WB</td>
<td>IFA (4-fold rise)/qPCR</td>
<td>300-10⁵ (Singhsilarak et al. 2005; Dittrich et al. 2011)</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>Haemophilus influenzae</td>
<td>WB/CSF</td>
<td>Culture</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>Dengue virus (all serotypes)</td>
<td>WB/serum</td>
<td>IFA, ELISA (4-fold rise)/qPCR, NS1</td>
<td>100000 (Alm, 2014)</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>Histoplasma capsulatum</td>
<td>WB/urine</td>
<td>Blood culture/Antigen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>Lassa virus</td>
<td>WB/serum</td>
<td>qPCR</td>
<td>600 (Trombley, 2010)</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>Enterococcus faecalis</td>
<td>WB</td>
<td>Blood culture</td>
<td>1-30 (Lehman 2008)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>Borrelia recurrentis</td>
<td>WB</td>
<td>Microscopy</td>
<td>10⁵-10⁶ (Fotso and Drancourt, 2015)</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Chikungunya virus</td>
<td>WB</td>
<td>PCR</td>
<td>10⁴ (Reddy et al. 2014)</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>Pseudomonas</td>
<td>WB</td>
<td>Culture</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>Acinetobacter baumannii</td>
<td>WB</td>
<td>Blood culture</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>Enterobacter spp</td>
<td>WB</td>
<td>Blood culture</td>
<td>NA</td>
</tr>
</tbody>
</table>
**Appendix 2: Pathogen load per blood volume**

Required test blood volumes will be influenced by the lower limit of detection (LOD) of the test (e.g., and LOD would require 10 mL to detect Typhoidal salmonella)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Pathogen</th>
<th>Pathogen circulation/mL (Ref)</th>
<th>Number of pathogens per 1 mL</th>
<th>Number of pathogens per 5 mL</th>
<th>Number of pathogens per 10 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Typhoidal salmonella</td>
<td>1 (Wain, 1998; Wain et al. 2001; S. typhi)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>Streptococcus pneumonieae</td>
<td>1-30 (Lehman 2008)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Staphylococcus aureus</td>
<td>1-30 (Lehman 2008)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>Non-typhoidal salmonella</td>
<td>1 (Wain, 1998; S. typhi)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>Escherichia coli</td>
<td>200 (Yagupske, 1990)</td>
<td>200</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>6</td>
<td>Rickettsia ssp</td>
<td>210 DNA copies/mL (Dittrich, 2014)</td>
<td>210</td>
<td>1050</td>
<td>2100</td>
</tr>
<tr>
<td>7</td>
<td>Leptospira</td>
<td>100000 (Agampodi, 2012)</td>
<td>10000</td>
<td>50000</td>
<td>100000</td>
</tr>
<tr>
<td>8</td>
<td>Brucella</td>
<td>88 (Young, 1995)</td>
<td>88</td>
<td>440</td>
<td>880</td>
</tr>
<tr>
<td>9</td>
<td>Burkholderia pseudomallei</td>
<td>~10 (Supaprom et al. 2007)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>Coxiella burnetii</td>
<td>10 (Wielders, 20103)</td>
<td>10</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>11</td>
<td>Neisseria meningitidis</td>
<td>1.6x10^6 (DNA copies/mL; children) (Hackett et al. 2004)</td>
<td>10000</td>
<td>50000</td>
<td>100000</td>
</tr>
<tr>
<td></td>
<td>Pathogen</td>
<td>Reference</td>
<td>Lower Limit</td>
<td>Upper Limit</td>
<td>Count</td>
</tr>
<tr>
<td>---</td>
<td>--------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>--------</td>
</tr>
<tr>
<td>12</td>
<td>Klebsiella</td>
<td>10 (Yagupsky, 1990)</td>
<td>10</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>13</td>
<td>Orientia tsutsugamushi</td>
<td>300-10^6 (Singhsilarak et al. 2005; Dittrich et al. 2011)</td>
<td>106</td>
<td>5x10^6</td>
<td>10^7</td>
</tr>
<tr>
<td>14</td>
<td>Haemophilus influenzae</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>15</td>
<td>Dengue virus (all serotypes)</td>
<td>100000 (Alm, 2014)</td>
<td>10000</td>
<td>500000</td>
<td>100000</td>
</tr>
<tr>
<td>16</td>
<td>Histoplasma capsulatum</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>17</td>
<td>Lassa virus</td>
<td>600 (Trombley, 2010)</td>
<td>600</td>
<td>3000</td>
<td>6000</td>
</tr>
<tr>
<td>18</td>
<td>Enterococcus faecalis</td>
<td>1-30 (Lehman 2008)</td>
<td>1*</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>19</td>
<td>Borrelia recurrentis</td>
<td>10^3-10^5 (Fotso and Drancourt, 2015)</td>
<td>1000</td>
<td>5000</td>
<td>10000</td>
</tr>
<tr>
<td>20</td>
<td>Chikungunya virus</td>
<td>10^4 (Reddy et al. 2014)</td>
<td>10,000</td>
<td>50,000</td>
<td>100,000</td>
</tr>
<tr>
<td>21</td>
<td>Pseudomonas</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>22</td>
<td>Acinetobacter baumannii</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>23</td>
<td>Enterobacter spp</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Targets with 1 circulating pathogen per mL are statistically unlikely to be present in each 1mL, therefore > than 1mL would be required to ensure pathogens are present for detection; NA: not available*