Validation of Ifakara Ambient Chamber Test

PAMCA Annual Meeting 2023 Symposium 14 ID488

Dr Sarah J Moore
Outline

• What is the Ifakara Ambient Chamber Test (I-ACT)?
• Example from the Global Fund sponsored studies of PBO Insecticide treated nets (ITN)
  • Comparison against experimental hut data
  • Repeatability
• Conclusions & next steps
Why validate?

A laboratory is required to carry out validation when:

i. it has designed or developed a new method

ii. needs to demonstrate comparability between a new vs standard method

iii. A standard method has been modified

Matope et al Mal J *in press*
PRIMARY ENDPOINTS
1. Proportion of mosquitoes dead after 24 (+) hours
2. Proportion of mosquitoes blood-fed

SECONDARY ENDPOINTS
1. Deterrence
2. Induced exophily
3. Personal protection
ITN evaluation in I-ACT
Non inferiority trials were conducted of all PBO ITNs in Mbe and Ifakara

The study arms were as follows:

1. Untreated net (control)
2. Olyset Plus unwashed (reference LN)
3. Olyset Plus washed 20x (reference washed LN)
4. PermaNet 3.0 unwashed
5. PermaNet 3.0 washed 20x
6. VEERALIN LN unwashed
7. VEERALIN LN washed 20x
8. Tsara Boost unwashed
9. Tsara Boost washed 20x
10. Olyset Net LN (standard pyrethroid, positive control) unwashed
11. Olyset Net LN washed 20x

Courtesy of Dr Raphael N’Guessan
The same nets were evaluated in IACT

<table>
<thead>
<tr>
<th></th>
<th>I-ACT</th>
<th>Ifakara</th>
<th>Mbe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arms*</td>
<td>12</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Nights</td>
<td>54</td>
<td>36</td>
<td>132</td>
</tr>
<tr>
<td>Observations / arm</td>
<td>106</td>
<td>72</td>
<td>132</td>
</tr>
<tr>
<td>Power</td>
<td>&gt;90%</td>
<td>90%</td>
<td>89%</td>
</tr>
<tr>
<td>Mosquitoes entering</td>
<td>15</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Variation between huts</td>
<td>0.00</td>
<td>0.15</td>
<td>0.01</td>
</tr>
<tr>
<td>Variation between sleepers</td>
<td>0.03</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Variation between observations</td>
<td>0.45</td>
<td>1.0</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* 2 control arms were run

Data on variability courtesy of: 1) huts Joe Challenger  2) IACT Olukayode Odufuwa
Mortality point estimates vary by location and assay—patterns the same in Mbe, Ifakara and I-ACT
Blood feeding estimates vary by location and assay—patterns the same in Mbe, Ifakara and I-ACT.
Relative Mortality – similar at hut sites

Ifakara Non-Inferiority Assessment (Mortality - Combined)

Mosquito mortality

Veeralin
Tsara Boost
Permanet3.0

N.I.M.
Favours candidate

Odds Ratio

MBe Non-Inferiority Assessment (Mortality - Combined)

Mosquito mortality

Veeralin
Tsara Boost
Permanet3.0

N.I.M.
Favours candidate

Odds Ratio

Courtesy of Dr Joe Challenger
Relative mortality patterns from West African, Ifakara huts and I-ACT – same decision reached

Reference Olyset Plus

24 hour mortality

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Reference</th>
<th>%M24</th>
<th>%M24</th>
<th>OR (95% CI) estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PermaNet 3.0 HUT TZ</td>
<td>45.5</td>
<td>37.5</td>
<td>1.41 (1.11, 1.79)</td>
<td>8</td>
</tr>
<tr>
<td>PermaNet 3.0 HUT IC</td>
<td>15.2</td>
<td>13.6</td>
<td>1.10 (0.90, 1.35)</td>
<td>1.6</td>
</tr>
<tr>
<td>PermaNet 3.0 IACT TZ</td>
<td>97.3</td>
<td>89.75</td>
<td>1.99 (1.60, 2.47)</td>
<td>7.55</td>
</tr>
<tr>
<td>TsaraBoost HUT TZ</td>
<td>40.5</td>
<td>37.5</td>
<td>1.17 (0.92, 1.49)</td>
<td>3</td>
</tr>
<tr>
<td>TsaraBoost HUT IC</td>
<td>15.45</td>
<td>13.6</td>
<td>1.10 (0.80, 1.41)</td>
<td>1.85</td>
</tr>
<tr>
<td>TsaraBoost IACT TZ</td>
<td>98.15</td>
<td>89.75</td>
<td>2.21 (1.77, 2.78)</td>
<td>8.4</td>
</tr>
<tr>
<td>Veeralin HUT TZ</td>
<td>48.5</td>
<td>37.5</td>
<td>1.56 (1.23, 1.97)</td>
<td>11</td>
</tr>
<tr>
<td>Veeralin HUT IC</td>
<td>17.65</td>
<td>13.6</td>
<td>1.30 (1.10, 1.60)</td>
<td>4.06</td>
</tr>
<tr>
<td>Veeralin IACT TZ</td>
<td>97.4</td>
<td>89.75</td>
<td>2.03 (1.63, 2.52)</td>
<td>7.65</td>
</tr>
</tbody>
</table>
Repeatability: mortality point estimates vary slightly by year – patterns the same in Ifakara huts and I-ACT – same decision reached
Published IACT validations

• Agreement between WHO tunnel, experimental hut and I-ACT for Interceptor and Interceptor G2

• Agreement between WHO bioassay methods and I-ACT for field aged pyrethroid nets

Influence of testing modality on bioefficacy for the evaluation of Interceptor® G2 mosquito nets to combat malaria mosquitoes in Tanzania

Ummi Abdul Kibondo1, Olukayode G. Odufuwa2,3, Saphina H. Ngonyani1, Ahmadi B. Mpelepele1, Issaya Matanila1, Hassan Ngonyani1, Noel O. Makungwa1, Antony P. Mseka1, Kyeba Swai1,2, Watson Ntabaliba1, Susanne Stutz3, James W. Austin1 and Sarah Jane Moore1,4,7

Comparing the new Ifakara Ambient Chamber Test with WHO cone and tunnel tests for bioefficacy and non-inferiority testing of insecticide-treated nets

Dennis J. Massue1,2,3,*, Lena M. Lorenz2, Jason D. Moore1,2,*, Watson S. Ntabaliba3, Samuel Ackermann1, Zawadi M. Mbomma4, William N. Kitinza1, Emmanuel Mtwu5, Selemani Mtibaga1, John Bradley6, Hans J. Overgaard7 and Sarah J. Moore1,2,4

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Conclusion

I-ACT shows reproducibility from internal validation

I-ACT conclusions matched those from hut trials in two locations

Measures precisely

Lower heterogeneity than hut trials

Needs validation in other locations

Next validation will be in Papua New Guinea
Study team

- Sarah Moore (Study director) smoore@ihi.or.tz
- Amanda Ross (Statistician on ITN study)
- **Olukayode Odufuwa** (Study Investigator)
- **Ummi Kibondo** (Study Investigator)
- **Emma Mbuba** (GLP Coordinator/Study Investigator)
- **Kyeba Swai** (Study Investigator)
- Jason Moore (Test facility manager)
- Rose Philipo (Project manager)
- Alwisa Urassa (Quality assurance)
- Hassan Ngonyani (Field testing)
- Safina Ngonyani (Laboratory testing)

**Thanks to those providing data, figures and statistical advice**

John Bradley (LSHTM)
Raphael N’guessan (LSHTM)
Joe Challenger (Imperial College)
Tom Churcher (Imperial College)