A review of WHO guidelines and their application to a proposed new category, Durable Lining (DL)

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John H. Thomas, Ph.D., DART Managing Director
Durable Lining – Guideline development

Guidelines for Testing

- IRS
- LN

Durable Lining (DL)

- hybrid of IRS and LN
- unique features
- range of applications

DL fits many WHO-established guidelines but has unique characteristics
What Should Set the Base Lines for Testing Criteria:

Performance Criteria generally set Testing Criteria.

Durable Linings design and performance should logically respond to lessons learnt from malaria control experience today with LLINs and IRS; and provide an effective alternative where current limitations of IRS &/or LLINs may limit their long term suitability if we are to achieve millennium and RBM goals for malaria control.

- **Feasibility** (logistically feasible and suitable for end user/home )
- **Physical durability** (the product will last several years in a condition that continues to afford protection)
- **Insecticide residual durability** (will last at a lethal dose for an acceptable length of time)
- **Acceptability** (end users will want it, use it and maintain it),
- **Effectiveness** (does it work in application)
- **Affordability** (“value for money”, cost of obtaining consistent correct usage and protection / families/ year)
Performance challenges / lessons learnt from LLINs and IRS?

LLINs:
- Chemical durability is generally good and outlasts LLIN material durability.
- Challenges converting numbers “distributed” into nets “hung over sleeping areas” with “sustained and correct usage”.
- LLIN physical durability is proving very variable, but consistently lower than previously assumed = more costly to maintain effective coverage than expected.

IRS:
- Relatively fast to roll out but challenging for logistics, safety and the environment
- Challenging to obtain consistent application quality/coverage and insecticide dosage
- Acceptance / coverage rates are hard to sustain year on year
- Remains a vital tool for short term emergencies : expensive to sustain.
- Short residual life results in sub lethal dosing phases, unprotected periods for households, and its mode of action advances insecticide resistance
- Delays in spray round delivery can result in very serious consequences.
Late timing can result in dramatic increases in malaria cases.

Impact of 2-month delay in spraying on malaria incidence*

For every month of delay, there is a 15% increase in odds to contract malaria (Kleinschmidt, et al, 2007)

*WHO, 2005, Malaria Field Handbook
DL Design Feasibility and Material Durability Criteria
Durable Lining (DL) – Feasibility for traditional house design

Specifications of ZeroVector®
- woven shade cloth
- 100% polyethylene, 50% shading
- 55 gm/sqm
- 4.4 gm insecticide a.i./kg material
- 2.35m x 100m rolls
- Color options
- Plastic nail caps
- Nails

DL provides community protection and overcomes many IRS challenges
Durable Lining – Physical characteristics must suit application / durability targets

Selvedge on top + bottom (5cm high)

Horizontal: PE Treads (weft)

Vertical: PE yarns (warp)

Medium Rib

DART’s DL is an insecticide impregnated shade cloth
Durable Lining – operation issues: installation testing

### 1. Load test

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Simulate DL fixed on wall for 4 years or has a heavy item hanging on it</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect</td>
<td>Static load applied to a number of interventions, over a longer time</td>
</tr>
<tr>
<td>Sample</td>
<td>30cm wide shade cloth, fixed several places and applied a heavy load, increased by day</td>
</tr>
<tr>
<td>Evaluation</td>
<td>The DL should not fall down</td>
</tr>
</tbody>
</table>
Durable Lining – operation issues: installation testing

2. Pull test

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Child pulls on DL unattended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect</td>
<td>Increased downward load applied to a very limited area of fixing.</td>
</tr>
<tr>
<td>Sample</td>
<td>10cm wide shade cloth, fixed one place. Applied an increasing downward load until fixing failed</td>
</tr>
<tr>
<td>Evaluation</td>
<td>Quantified load measure of each fixing products ability to grip DL and wall</td>
</tr>
</tbody>
</table>

installation methods need to keep material up for years
3. Peel test

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Child pulls on DL unattended</th>
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</thead>
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<tr>
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</tbody>
</table>

installation methods need to keep material up for years
Insecticide Durability in Target Usage Areas

- Intrinsic insecticidal activity – a.i. deltamethrin, known from IRS and LN studies
- Diagnostic concentration – dosage as mg/sqm established
- Irritant or excito-repellent properties - deltamethrin
- Cross-resistance to other insecticides – same as for other pyrethroids
- Efficacy and residual activity on relevant substrates – no limitations noted

DL should be placed where pyrethroid resistance is not advanced
Related Published Studies:


Durable Lining – Phase I (laboratory studies)

Aim of WHO Guidelines for Phase I:

• Intrinsic insecticidal activity
• Diagnostic concentration
• Irritant or excito-repellent properties
• Cross-resistance to other insecticides
• Efficacy and residual activity on relevant substrates

IRS residual testing:
• 30 minute exposure, 24 hr mortality
• cutoff at 80% mortality
• evaluate @ 1 wk, monthly until below cutoff
• hold substrates @ 30°C between tests
• mud, concrete, plywood, bamboo, thatch

LN residual testing:
• 3 minute exposure, 1 hr KD, 24 hr mortality
• cutoff at 95%KD, 80% mortality
• wash 20X
• evaluate after each wash until below cutoff

Durable Lining residual characteristics:
• expected to be a replacement for IRS, so, 30 minute exposure?
• structure surfaces infrequently washed but do get covered with dust, washing?
• Covers variety of wall surfaces, should all be tested?
Durable Lining – field trials / study overview

<table>
<thead>
<tr>
<th>Country</th>
<th>Study objectives</th>
<th>Name of PI</th>
<th>Institution affiliation</th>
<th>Study title</th>
<th>Study outline</th>
<th>Scale (units with DL)</th>
<th>Results</th>
<th>Timing</th>
<th>Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso</td>
<td>Phase II hut study</td>
<td>Corbel</td>
<td>IRD</td>
<td>Evaluation in Phase II huts in resistance area</td>
<td>typical hut study in area with high DM resistance, entomological</td>
<td>6 huts</td>
<td>susceptible ok; resistant not</td>
<td>01-Nov-08</td>
<td>30-Mar-10</td>
</tr>
<tr>
<td>USA</td>
<td>mosquito behavior</td>
<td>Achee</td>
<td>Uniformed Services University</td>
<td>Evaluate mosquito behavior in presence of DL</td>
<td>lab study of behavior followed by hut eval</td>
<td>lab</td>
<td>excellent effects with partial cover</td>
<td>30-Jan-10</td>
<td>30-Dec-10</td>
</tr>
<tr>
<td>USA</td>
<td>nuisance insects</td>
<td>Miller</td>
<td>Virginia Tech</td>
<td>Test against pests such as cockroaches, ants, bedbugs, flies</td>
<td>lab screen</td>
<td>lab</td>
<td>not started</td>
<td>planned 7/15/10</td>
<td>30-Sep-10</td>
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Laboratory and hut studies validate efficacy
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<td>USA</td>
<td>mosquito behavior</td>
<td>Achee</td>
<td>Uniformed Services Univer</td>
<td>Evaluate mosquito behavior in presence of DL on walls</td>
<td>lab</td>
<td>excellent effects with partial cover</td>
<td>30-Jan-10 to 30-Dec-10</td>
</tr>
<tr>
<td>USA</td>
<td>behavior and hut study</td>
<td>Clark</td>
<td>USDA</td>
<td>lab and hut evaluations of DL</td>
<td>lab + 4 huts</td>
<td>not started</td>
<td>planned 6/15/2010 to 31-Dec-10</td>
</tr>
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<td>USA</td>
<td>nuisance insects</td>
<td>Miller</td>
<td>Va Tech</td>
<td>test against pco pests such as cockroaches, ants, bedbugs, flies</td>
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</tr>
<tr>
<td>Equatorial Guinea</td>
<td>acceptability, durability, efficacy</td>
<td>Abrahan + Rowland</td>
<td>MCDI + LSHTM</td>
<td>comparison of DL, IRS, and LN curtains, small scale</td>
<td>20 huts</td>
<td>excellent on all measures</td>
<td>15-Oct-08</td>
</tr>
<tr>
<td>Ghana</td>
<td>acceptability, durability, efficacy</td>
<td>Knowles + Rowland</td>
<td>AngloGold + LSHTM</td>
<td>STA&amp;D, small scale</td>
<td>30 huts</td>
<td>excellent on all measures</td>
<td>09-Oct-08</td>
</tr>
<tr>
<td>Mali</td>
<td>acceptability, durability, efficacy</td>
<td>Coulibaly + Rowland</td>
<td>MRTC + LSHTM</td>
<td>STA&amp;D, small scale</td>
<td>20 huts</td>
<td>excellent on all measures</td>
<td>05-Sep-08</td>
</tr>
<tr>
<td>Nigeria</td>
<td>user acceptability</td>
<td>Knox</td>
<td>VF</td>
<td>long-term evaluation of DL, demo type small scale</td>
<td>50 huts</td>
<td>excellent on all measures</td>
<td>07-Nov-06</td>
</tr>
<tr>
<td>South Africa</td>
<td>acceptability, durability, efficacy</td>
<td>Mulder + Rowland</td>
<td>Agricultura l Research Station + LSHTM</td>
<td>STA&amp;D, small scale</td>
<td>17 houses</td>
<td>excellent on all measures</td>
<td>09-Oct-08</td>
</tr>
<tr>
<td>Vietnam</td>
<td>acceptability, durability, efficacy</td>
<td>Hoan Le</td>
<td>VF</td>
<td>STA&amp;D</td>
<td>25 houses</td>
<td>excellent on all measures</td>
<td>15-Mar-09</td>
</tr>
</tbody>
</table>

Small-scale trials (<50 houses) to determine feasibility, acceptability, entomological + chemical durability
<table>
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<th>Results</th>
<th>Timing</th>
<th>Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>village trial, evidence of disease reduction</td>
<td>Carnevale</td>
<td>IRD, Sonamet</td>
<td>Comparison of vector control interventions</td>
<td>multiple villages with DL, IRS, PN, ZF</td>
<td>200 huts</td>
<td>excellent at interim</td>
<td>23-Dec-08</td>
<td>30-Sep-10</td>
</tr>
<tr>
<td>Kenya</td>
<td>village trial, evidence of disease reduction</td>
<td>Vulule</td>
<td>KEMRI</td>
<td>Evaluation of DL for community protection</td>
<td>multiple villages comparing DL with IRS for disease reduction</td>
<td>500 huts</td>
<td>excellent at 6 mo.</td>
<td>30-Sep-09</td>
<td>01-Oct-11</td>
</tr>
<tr>
<td>Kenya</td>
<td>village trial, evidence of disease reduction</td>
<td>Gimnig</td>
<td>CDC</td>
<td>Phase III type village trial comparing DL and nets for disease impact</td>
<td>large trial (2700 huts) to compare DL with nets over multiple years</td>
<td>2,700 huts</td>
<td>Data not collected</td>
<td>15-May-10</td>
<td>01-Apr-12</td>
</tr>
</tbody>
</table>

Village-scale trials (500 or more houses) to compare conventional tools and determine disease impact

Large-scale trials (501 - 3,000 houses)
Durable Lining – Feasibility: house installation testing

Delivers a reliable strength under a variety of situations.

The best solution, across all characteristics measured, was the use of a specific plastic nail cap (20mm diameter) with local nails approximately 3.5 cm in length having a head 3mm to lock the cap in place.
Acceptability

Significant community and family acceptance in every study to date
Durable Lining (DL) – resident acceptability

Residents have a very positive impression that DL improves the interior of the house and controls mosquitoes and nuisance insects.
15 months after installation
DL is still solid in houses in Ghana, Mali, Equatorial Guinea and South Africa. > 2.5 years in Nigeria

But DL material durability should be monitored over multiple years (4-5) to prove “real” life (learning from LLIN life assumptions).
Durable Lining (DL) – insecticide residual activity n should ideally be equivalent to the material durability

DM rate of loss slows over time leading to conclusion reservoir is sufficient for 5 yrs

Deltamethrin content in Nigerian field trial

Number of months in use:

1  3  5  7  9  11  13  15  17  19  21  23  25

DM content (mg/g):

0  0.5  1  1.5  2  2.5  3  3.5

100% mortality
In cone test
Aedes sp.
Durable Lining (DL) – Insecticidal activity should not vary with substrate (as IRS does)

Malaria Research & Training Centre, Bamako, Mali

% Mortality (An. gambiae; 2 cones/wall; 10 min exposure; 24 hr)

Durable Lining vs IRS on surfaces
AngloGold Ashanti, Obuasi, Ghana

% Mortality 6 mo post install

% Mortality 6 mo post install

Nine months
Durable Lining (DL) – performance vs IRS

Equatorial Guinea, MCDI trial on wooden houses

- DL efficacy remains considerably above WHO cutoff level at 12 months

Equatorial Guinea
- Installed Oct 2008
- IRS is FENDONA
- Cone bioassay
- Anopheles gambiae (sl)
- 5 houses, 3 cones ea.
- 30 min exposure
- 24 hr mortality evaluation
Durable Lining – Phase II (small-scale studies)

Aim of WHO Guidelines for Phase II:

- Efficacy and persistence under different ecological settings
- Dosage of application
- Handling and application
- Perceived side-effects

IRS hut testing:
- no rotation between huts
- cover walls, ceilings, doors
- test papers to evaluate spray coverage & dose
- no washing of sprayed surfaces
- use different surface types
- evaluate spray safety & operational issues
  - adverse effects, ease of application

LN hut testing:
- rotate nets between huts
- cut holes deliberately in nets
- use washed nets
- compare to negative control

Durable Lining characteristics:
- surface coverage, need for ceiling questionable
- coverage of open eaves?
- what pre-test handling needed?
- compare to IRS? LN?
- installation considerations

DL has characteristics similar to both IRS and LN, with some additional unique
DL large trial – malaria impacts in Angola

- Paired villages (large), multi-year study
- Designed to measure reduction in malaria impact.
- Two villages per treatment to be assessed for vector control and parasiteamia.

<table>
<thead>
<tr>
<th>Méthode de lutte</th>
<th>IP « moyens »</th>
<th>Population estimée</th>
<th>IP « élevés »</th>
<th>Population estimée</th>
</tr>
</thead>
<tbody>
<tr>
<td>villages</td>
<td>IP</td>
<td></td>
<td>villages</td>
<td>IP</td>
</tr>
<tr>
<td>LLIN</td>
<td>Caala</td>
<td>60%</td>
<td>Cahata</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1836</td>
<td></td>
<td>678</td>
</tr>
<tr>
<td>LLIN + ZF</td>
<td>Canjala</td>
<td>65%</td>
<td>Capango</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2166</td>
<td></td>
<td>413</td>
</tr>
<tr>
<td>IRS</td>
<td>Candieiro</td>
<td>63%</td>
<td>Libata</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2987</td>
<td></td>
<td>2856</td>
</tr>
<tr>
<td>WL</td>
<td>Barragem</td>
<td>70%</td>
<td>Chisséquélé</td>
<td>84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3251</td>
<td></td>
<td>2517</td>
</tr>
</tbody>
</table>
% Parasiteamia in children in 8 paired villages, Lobito Angola

15,006 blood slides examined; 4,828 parasite +ve. Children 2-9
Average No. Mosquitoes (anopheles + culex) trapped / home / night, Lobito Angola

1080 house trap nights; 2065 mosquitoes caught of which 754 were anophèles
Average No. Anopheles mosquitoes trapped / home / night, Lobito Angola

80% reduction from 2008 to 2009 (0.9 anopheles per house to just 0.2)
KENYA: Densities of *An. gambiae* female mosquitoes in KEMRI 12 paired village study
Densities of *An. funestus* female mosquitoes in KEMRI 12 paired village study

4565 mosquitoes: 61.8% *Culex quinquefasciatus* say; 28.1% *Anopheles gambiae* s.l.; 10.5% were *An. funestus*. 

**DL Installation + Start of rainy season**

Density (females/house/night)
*P. falciparum* parasite prevalence in control, intervention and IRS villagers, KEMRI Kenya
Durable Lining – Phase III (large-scale trials)

Aim of WHO Guidelines for Phase III:

- Efficacy and residual activity
- Operational issues
- Community acceptance

IRS village testing:
- human landing rates
- density reduction
- residual on different wall surfaces
- acceptability by operators & residents

LN village testing:
- user compliance
- mass killing effects
- impact on vector density

Durable Lining characteristics:
- surface coverage, need for ceiling questionable
- coverage of open eaves?
- what pre-test handling needed?
- compare to IRS? LN?
- installation considerations

Village scale tests combine all aims for IRS and LN
Design of a potential study: What to measure if 10,000 people were targeted for each intervention?

<table>
<thead>
<tr>
<th>IRS</th>
<th>DL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Spraying time</td>
<td>• Installation time</td>
</tr>
<tr>
<td>• Coverage rate</td>
<td>• Coverage rate</td>
</tr>
<tr>
<td>• Delay in spraying</td>
<td>• Delay in installation</td>
</tr>
<tr>
<td>• Acceptance rate (push back from the</td>
<td>• Acceptance rate (push back from the</td>
</tr>
<tr>
<td>households)</td>
<td>households)</td>
</tr>
<tr>
<td>• Insufficient cycles of spraying</td>
<td>• Program cost</td>
</tr>
<tr>
<td>• Program cost</td>
<td></td>
</tr>
</tbody>
</table>
Cost Effectiveness of Prevention Tools

- Global Fund TRP want prevention tools to use at national level that give “Value for Money”
- What are the indicators to consider for “value for money”? 
  - Basic tool costs alone?
  - Cost of ensuring families receive and correctly use and maintain an effective tool?
  - Cost of maintaining adequate community level coverage and usage.
  - Impact on lives and suffering (added treatment costs) caused by timeliness or delay in tool delivery
  - Impact on lives and suffering caused by lack of continuity of “protection” (resulting from limits of tool chemical and material durability or family usage duration)
  - Cost implications on resistance management from annual sub lethal dosing cycles with IRS or longer lasting insecticidal activity (with materials).
  - Suitability of the tool for long term malaria prevention at household level once malaria transmission control/eradication has been achieved, and the tools cost an usage implications
Durable Lining warrants a separate category for vector control

Durable Lining is an alternative prevention tool, a hybrid between IRS and LN:

- Coverage for surfaces, and mosquito entry points
- High acceptability within communities,
- Aesthetic qualities ensure maintenance and long term acceptance
- Long residual activity
- Physical durability for many years
- Breaks malaria transmission cycle and likely to be a good tool for maintaining malaria control gains with minimal need for external input.
Changing people's behavior to use these is a challenge!