AN UPDATE

Neil F. Lobo / Nicole L. Achee / John Greico
University of Notre Dame
Department of Biological Sciences
Eck Institute for Global Health
What are Spatial Repellents?
Product Description and Paradigm Claim

• Spatial repellents are products designed to release volatile chemicals into the air and prevent human-vector contact within the treated space.

Deployment of spatial repellent products in enclosed and semi-enclosed spaces will reduce pathogen transmission.

PROTOTYPES
How Spatial Repellents are Expected to Function
Mechanism of Action

Spatial repellents elicit ‘spatial repellency’ which refers to a range of insect behaviors induced by airborne chemicals.

CONTINUAL RELEASE

Chemical Exploitation

Graphic by Kristina Davis
Role of Spatial Repellents in Vector Control
Filling Gaps

• Addresses vector behavior variability
  – day-time, early evening and/or outdoor biting

• Facilitate coverage and reduce delivery challenges
  – adding a consumer product distribution model (uptake enhancement)
  – top-down delivery during epidemics (dengue) and/or routinely (malaria)
  – less bulky than LLINs, IRS and/or space-spraying

• Tools for insecticide resistance mitigation
  – additional target sites, mode of action & functional doses beyond toxicity

• New paradigm to drive R&D for novel chemical actives/products
Evidence –

*Entomology and Epidemiology*
Evidence of Spatial Repellents to Prevent Disease

A household randomized, controlled trial of the efficacy of 0.03% transfluthrin coils alone and in combination with long-lasting insecticidal nets on the incidence of *Plasmodium falciparum* and *Plasmodium vivax* malaria in Western Yunnan Province, China

Nigel Hill1, Hong Ning Zhou2, Fuyu Wang2, Xiaofang Guo2, Ilona Carneiro1 and Sarah J Moore1,4

Coils alone: 77% PE
LLINs alone: 91% PE
Coils + LLIN: 94% PE

Impact of a Spatial Repellent on Malaria Incidence in Two Villages in Sumba, Indonesia

Din Syafruddin,* Michael J. Bangs, Dian Sidik, Iqbal Elyarzar, Puji BS Aih, Krisin Chan, Siti Nurleila, Christian Nixon, Joko Hendarto, Irsa Wahid, Hasnamdin Ishak, Claus Baagh, John P. Grieco, Nicole L. Achhe, and J. Kevin Baird
Eijkman Institute for Molecular Biology, Jakarta, Indonesia; Department of Parasitology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; Public Health and Malaria Control, International SOS, Kuala Kencana, Papua Indonesia; Department of Entomology, Faculty of Agriculture, Kasetsart University, Bangkok 10600, Thailand; Department of Epidemiology, Faculty of Public Health, Hasanuddin University, Makassar, Indonesia; Eijkman-Oxford Clinical Research Unit, Jakarta, Indonesia; The Sumba Foundation, Bali, Indonesia; Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Department of Biological Sciences, Eck Institute for Global Health, University of Notre Dame, Notre Dame, Indiana; Centre for Tropical Medicine, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom

Coils alone: 52% PE
32% lower outdoor landing in houses with SR
Guidance on Operational Implementation
Primary VCAG Questions

• What is the product coverage required for protection?

• **How does efficacy vary** with geography or vector bionomics?

• Do repellents have either a diversion or a community-wide protection effect?

• Are current pyrethroid-based repellents effective against resistant vector populations?
Newly Funded Research Program (2014-2019)
Generating an Evidence Base

• **GOAL:**
  • Evaluate the public health impact of one spatial repellent product to reduce and prevent transmission of *Plasmodium* spp. and dengue viruses.

• **OBJECTIVES:**
  o Provide a quantitative estimate of protective efficacy (PE)
  o Provide inputs into program-relevant questions of optimization/application
  o Confirm and measure the entomological correlates of reduced infection
  o Drive efforts to acquire full recommendation of spatial repellent products

*Scale-back of Study from Africa sites (Indonesia and Peru only)*
Present status of Primary VCAG Questions

• What is the product **coverage required** for protection?
  • Indonesia (malaria) and Peru (Dengue) only

• **How does efficacy vary** with geography or vector bionomics?
  • Indonesia (malaria) and Peru (Dengue) only. **Not possible in Africa**

• Do repellents have either a **diversion or a community-wide protection effect?**
  • **Not possible** (was planned as part of the Kenya study)

• Are current pyrethroid-based repellents **effective against resistant vector populations?**
  • **Not possible** at present (possible if insecticide resistance appears)
Program updates

• Malaria (Indonesia)
  – Follow-up of
    • ~1240 subjects
    • from ~2,719 enrolled households
    • began April 18, 2016 (to Jan 29, 2018).
  – 28,816 Bloodspots collected
    • 47x active + passive collections
    • since December, 2016 (Intervention placed)
  – 46x HLC collections
    • 4 sentinel sites in 12 clusters have occurred following intervention.
  – SHEILDS replaced at 2 week intervals since deployment.
  – Ends in March, 2018

– Also,
  • Puskesmas (HIS) versus active data collection
  • Effect of SR on non-vector species
Program updates

- **Peru (Dengue)**
  - Weekly febrile surveillance in 16,204 persons for active virus infection has occurred as of Oct 2016.
  - Baseline samples from 2,017 subjects for longitudinal sero-conversion have been collected as of Oct 2016.
  - Annual longitudinal follow up samples initiated in November 2017, ~800 samples obtained so far.
  - SHEILDS replaced at 2 week intervals since deployment.
  - Adult mosquito monitoring carried out at 2 week intervals since deployment.
  - Application of 980 self-administered cell phone questionnaires determine participant perceptions and acceptability.
## Acknowledgements

<table>
<thead>
<tr>
<th>Grantee</th>
<th>Kenya</th>
<th>Peru</th>
<th>Zambia</th>
<th>Tanzania</th>
<th>Indonesia</th>
<th>External Advisors</th>
</tr>
</thead>
<tbody>
<tr>
<td>U. Notre Dame</td>
<td>CDC</td>
<td>KEMRI</td>
<td>UCDavis</td>
<td>NAMRU-6</td>
<td>Johns Hopkins University</td>
<td>NMCC</td>
</tr>
<tr>
<td>Nicole Achee (coPI)</td>
<td>John Gimnig (PI)</td>
<td>Eric Ochomo (PI)</td>
<td>Thomas Scott (PI)</td>
<td>LTC Robert Hontz (Dept. Dir. Virology)</td>
<td>Jennifer Stevenson (PI)</td>
<td>Chadwick Sikaala (PI)</td>
</tr>
<tr>
<td>Neil Lobo (coPI)</td>
<td>Mary Hamel (PI)</td>
<td>Amy Morrison (Proj Coord)</td>
<td>Busiku Hamainza (PI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caleb Reinking (Data Manager)</td>
<td>Monica Shah (Epidem)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jared Olsen (Data Programmer)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>David Pettifor (Data Programmer)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fang Liu (Statistician)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marianne Raybaud (Coordinator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>John P. Grieco (Advisor)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Funding provided by:

**Bill & Melinda Gates Foundation**
Grant OPP1081737: "Spatial Repellent Products for Control of Vector-borne Diseases"
Sr. Program Officer: Mike Reddy

**Products (and some funds) donated by:**

**SC Johnson**
Collaborator: Maude C. Meier, Curtis Conklin, David Eland, Tom Putzer

**FHI 360**
Collaborator: Maude C. Meier, Curtis Conklin, David Eland, Tom Putzer

**SC Johnson**
Collaborator: Maude C. Meier, Curtis Conklin, David Eland, Tom Putzer

**FHI 360**
Collaborator: Maude C. Meier, Curtis Conklin, David Eland, Tom Putzer

**FHI 360**
Collaborator: Maude C. Meier, Curtis Conklin, David Eland, Tom Putzer
Thank you

nachee@nd.edu  (Nicole Achee)
nlobo@nd.edu  (Neil Lobo)
jgrieco@nd.edu  (John Grieco)
Progress on Public Health Value

1950’s – 2007
varied Phase 1, Phase2 entomological studies

2007
Hill et al. Yunnan Province, China 77% PE - P. falciparum 0.03% transfluthrin coils

2007
Syafrudin et al. Sumba Island, Indonesia 52% PE - Pl. spp 0.00975% metofluthrin coils

2009
Syafrudin et al. Sumba Island, Indonesia PE TED - Pl. spp Transfluthrin emitter

2013
Achee et al. Second Meeting, VCAG Paradigm claim and historical data review

2013
1,240 >6-59mo

ca. Aug 2016
Scott, Morrison et al. Iquitos, Peru PE TED - DENV1-4/Zika Transfluthrin emitter

ca. May 2016
Achee et al. Geneva, VCAG Paradigm claim and new trial data review

ca. May 2019
2,400 >2-15yr 9,000 febrile surveillance

Currently funded trial

2019 - ?
MPAC Endorsement

Next steps (TBD):
Pilot implementation trial
Expansion of malaria trial
Expansion of dengue trial

Spatial Repellents