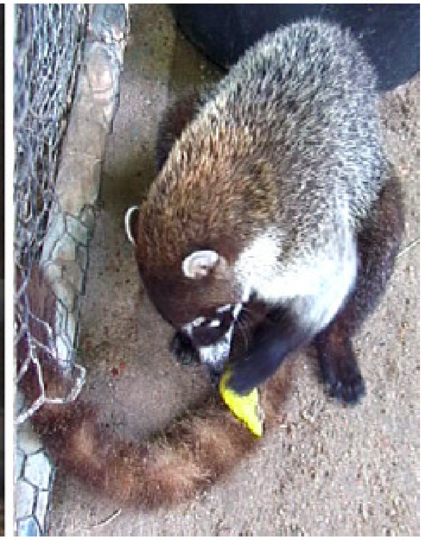
Spatial and individual repellents

5th Optimizing Evidence for Vector Control Interventions Work Stream Meeting
Tuesday 29th January 2013 9:00-12:00

Sarah J Moore, LSHTM and Ifakara Health Institute

New Paradigm - applying *personal* *protection* for *public* *health*



Animals anoint with repellent compounds from fruit and arthropods

Weldon PJ *et al* 2011 J Chem Ecol 37(4):348-59

Left “A smudge where our horses were soon at peace in the choking smoke” Mary Schäffer Fonds, **Whyte Museum of the Canadian Rockies (V527 / PS1 - 48)**

Right Men stand beside a smoke house used for protection against mosquitoes.
Photographer:G. C. BALDWIN AND T. RIGGS JR./National Geographic Stock

Lesson Learned

THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
Vol. 21, No. 5

THE INFLUENCE OF VECTOR BEHAVIOR ON MALARIA TRANSMISSION

R. ELLIOTT
Scientist, Pan American Health Organization, Guatemala, Guatemala

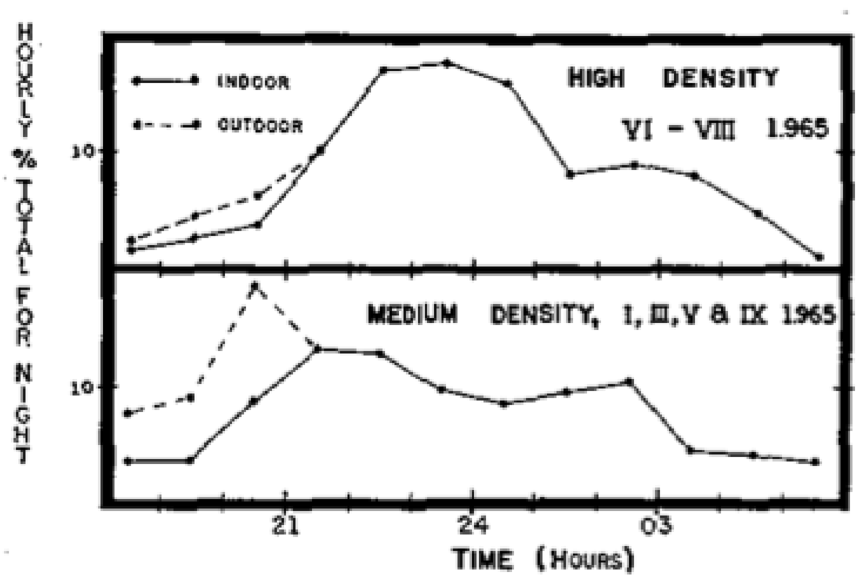


FIGURE 3. Man-vector contact in *A. darlingi*, El Pescado, Colombia.

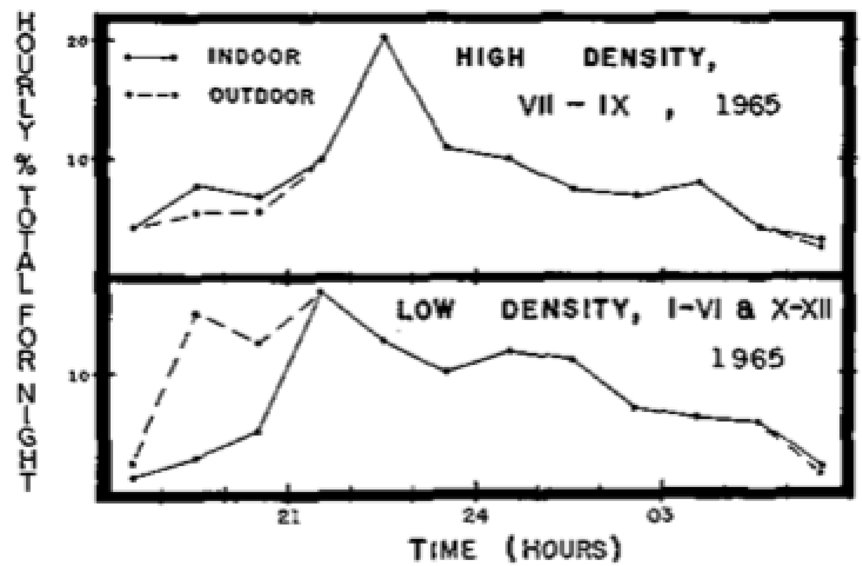


FIGURE 4. Man-vector contact in *A. nuneztovari*, Pto. Reyes, Colombia.

Key Evidence Generation 1. Identifying the problem

Time ✔

Place ✔

End user ✔

Individual ✔

Community ?

Elimination?

IVM ?

Key Evidence Generation 2. Identifying the process

Table 2 Key areas for strategic investment in spatial repellent research

	Key Areas for Strategic Investment in Spatial Repellent Research
1	Proof-of-Concept: demonstrating a spatial repellent will impact disease at the community level
2	Correlating entomological endpoints with reduction in infection incidence rates using repellent tools
3	Measuring the impact of diversion of repelled vectors to untreated sources under varying transmission dynamics
4	Defining the limitations of spatial repellency in both susceptible and insecticide resistant vector populations
5	Developing standardized protocols and measures for the evaluation of vector behavior modification as it relates to host-feeding following exposure to spatial repellents (i.e., host-seeking, feeding, resting, and oviposition) to identify long-term effects of spatial repellents
6	Engagement and recruitment of industry and academic partners to adopt standardized protocols and measures for the screening of chemical AIs to include spatial repellency
7	Identifying the underlying genetic/neurobiological basis of vector behaviors to provide insight into the rationale design of new repellents

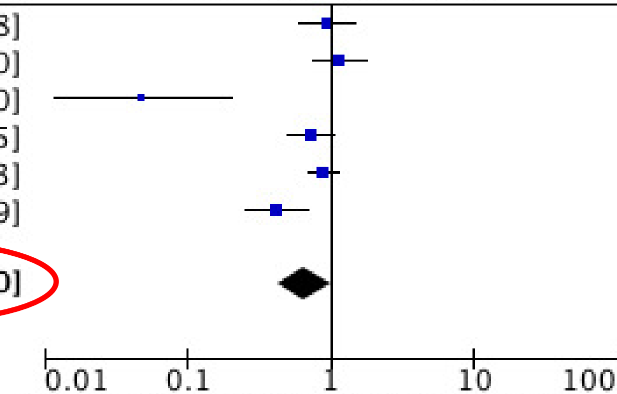
Achee *at al* (2012). Spatial repellents: from discovery and development to evidence-based validation. Malar J.11(1):164.

ROLL BACK MALARIA

Key Evidence Generation 3. Epidemiological Evidence that there is individual protection against malaria

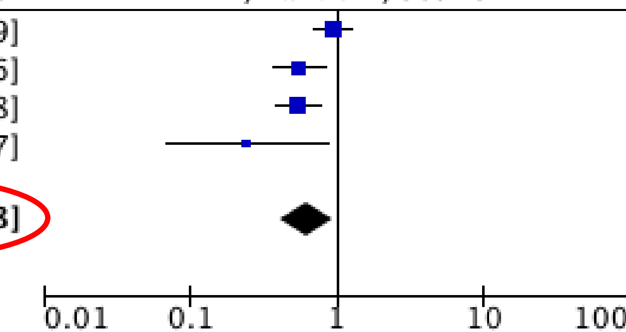
Study or Subgroup	Repellent Events	Repellent Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Chen-Hussey 2012	36	88508	38	87516	17.9%	0.94 [0.59, 1.48]
Deressa 2010	44	19192	36	18180	18.2%	1.16 [0.75, 1.80]
Hill 2007a	2	30824	40	29872	6.3%	0.05 [0.01, 0.20]
McGready 2001	48	8082	66	8064	19.3%	0.72 [0.50, 1.05]
Onyango 2013	122	101504	138	101660	21.2%	0.89 [0.69, 1.13]
Rowland 2004	23	14832	47	12720	17.2%	0.42 [0.25, 0.69]
Total (95% CI)		**262942**		**258012**	**100.0%**	**0.66 [0.44, 1.00]**
Total events	275		365			

Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 26.44$, df = 5 ($P < 0.0001$); $I^2 = 81\%$
Test for overall effect: Z = 1.94 (P = 0.05)



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Eamsila 1994	68	5976	118	9936	33.1%	0.96 [0.71, 1.29]
Kimani 2006	34	1080	60	1092	27.8%	0.56 [0.36, 0.86]
Rowland 1999	51	7008	82	6192	31.0%	0.55 [0.38, 0.78]
Soto 1995	3	344	12	344	8.1%	0.24 [0.07, 0.87]
Total (95% CI)		**14408**		**17564**	**100.0%**	**0.62 [0.41, 0.93]**
Total events	156		272			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 9.78$, df = 3 ($P = 0.02$); $I^2 = 69\%$
Test for overall effect: Z = 2.31 (P = 0.02)



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Key Evidence Generation 2. Identifying the process

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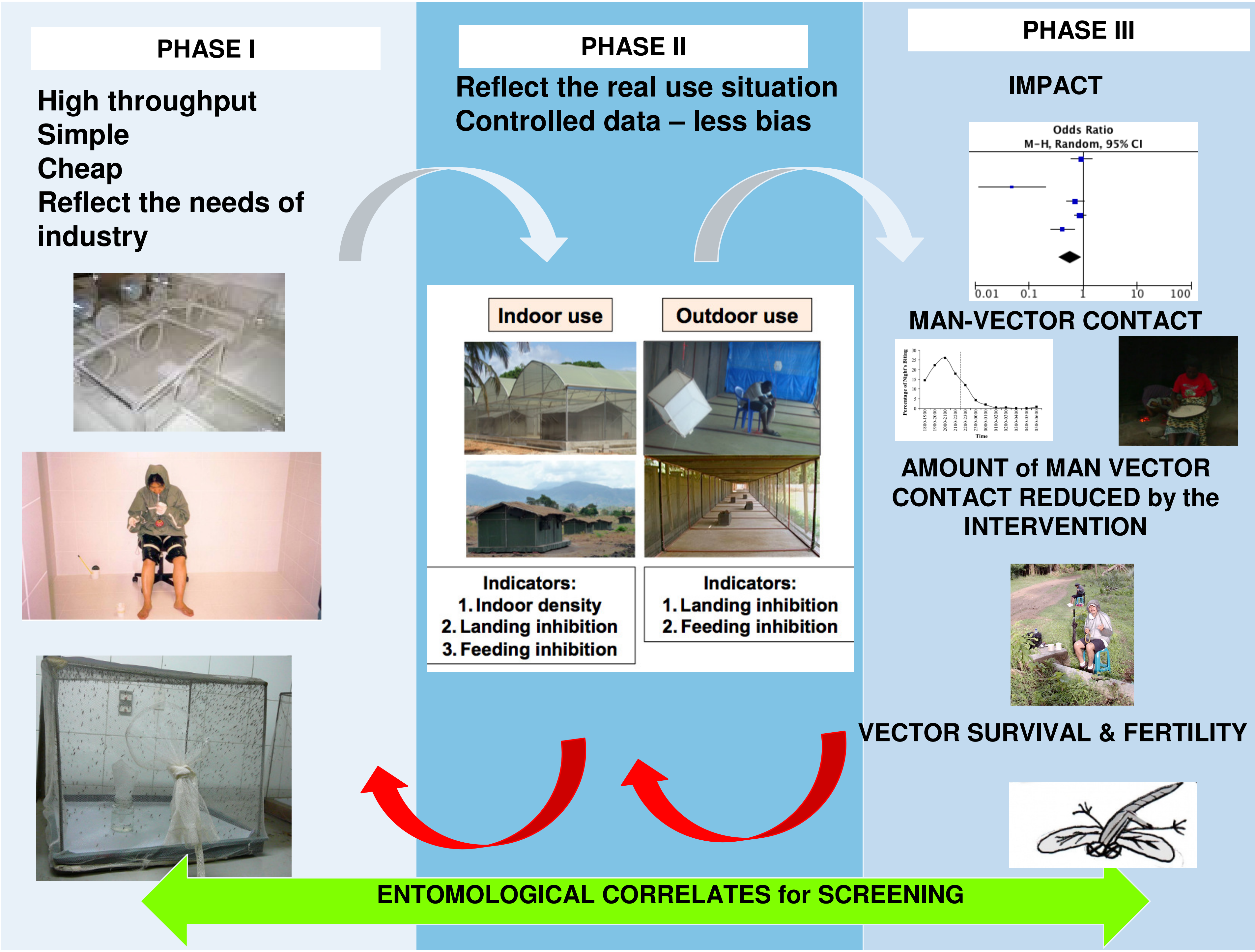
PHASE I
High throughput
Simple
Cheap
Reflect the needs of industry
PHASE II
Reflect the real use situation
Controlled data – less bias
Indoor use
Outdoor use
Indicators:
1. Indoor density
2. Landing inhibition
3. Feeding inhibition
Indicators:
1. Landing inhibition
2. Feeding inhibition
PHASE III
IMPACT
Odds Ratio
M-H, Random, 95% CI
0.01
0.1
1
10
100
MAN-VECTOR CONTACT
AMOUNT of MAN VECTOR CONTACT REDUCED by the INTERVENTION
VECTOR SURVIVAL & FERTILITY
ENTOMOLOGICAL CORRELATES for SCREENING

Key Evidence Generation 2. Identifying the process

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Key Evidence Generation 4. Vector endpoints – “Phase III”

- Agree upon specific **end points** for measuring repellency in intervention studies
- Develop **standardized protocols** to correlate repellent vector behavior endpoints with disease incidence during intervention
- Demonstrate an **individual** *(AND)* **community** level reduction in disease incidence
- Ensure **equity** of the intervention: determine if there is diversion of vectors from users to non-users
- Test these correlates in a **range of transmission scenarios**

Key Evidence Generation 4a. Vector correlates – “Phase II”

- What is the primary mode of action of currently registered active ingredients against key vector species (insecticide resistant and insecticide susceptible)
- what is the optimum dose of molecule needed?
- Over what distance does that protection extend?
- Where should the molecule be placed and in what format to maximise efficacy?

Key Evidence Generation 4. Data Quality

Guidelines for Efficacy Testing of Spatial Repellents

WHOPES document to be published in 2013

1. INTRODUCTION

The purpose of these guidelines is to provide specific and standardized procedures and criteria for efficacy testing and evaluation of spatial repellent active ingredients (AI) and formulated products intended to treat a volume of air (i.e., treated space) to create a vector free environment that is protective for all those inhabiting that space. The description of 'treated spaces' includes both indoor and outdoor spaces.

The aim of these guidelines is to harmonize the testing procedures carried out in different laboratories and institutions in order to maximize data quality and reporting to generate comparable data that may be used for meta-analysis if required.

Untreated bednets are a method of personal protection

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (2001) 95, 457–462

Do untreated bednets protect against malaria?

Siân E. Clarke[1]*, Claus Bøgh[1], Richard C. Brown[1], Margaret Pinder[2], Gijs E. L. Walraven[2] and Steve W. Lindsay[1,3] *[1]Danish Bilharziasis Laboratory, Jægersborg Allé 1D, DK-2920 Charlottenlund, Denmark; [2]Medical Research Council Laboratories, P.O. Box 273, Banjul, The Gambia; [3]School of Biological and Biomedical Sciences, University of Durham, South Road, Durham DH1 3LE, UK*

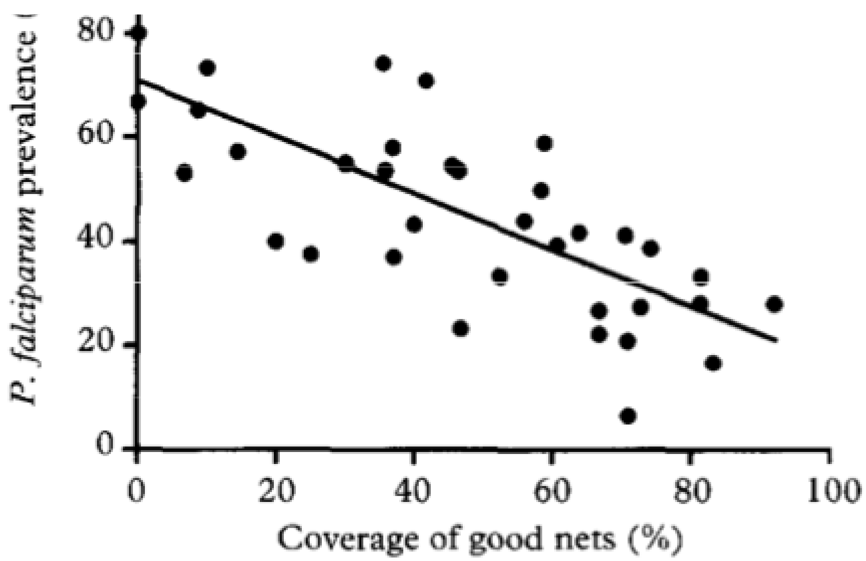

Fig. 2. Effect of coverage of untreated nets in good condition on the prevalence of *P. falciparum* in Gambian villages with ⩾15 infective bites per person per transmission season ($n = 36$). Villages for which the estimates of transmission may be inaccurate, owing to low mosquito numbers, are excluded.

There is economic benefit to encourage investment

45 to 50 billion mosquito coils are used annually by approximately 2 billion people worldwide*

Market share of mosquito coils is > $ 2 Billion**

Repellents reduce the clinical incidence of malaria

Source: Zhang, L. et al. Using charcoal as base material reduces mosquito coil emissions of toxins. *Indoor Air. 20 (2): 176-84 (2010).

***** source* Market Assessment for Public Health Pesticide Products. Bill & Melinda Gates Foundation, Boston Consulting Group, 2007.**

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	Product	Target market	Active ingredients	Disease applicability	Unit Price ($)	Price / night ($)
	Treated nets	Public Health	Pyrethroids	Malaria, filariasis, leishmaniasis	2.50 ITN 5.00 LLIN	<0.01
	Indoor residual spraying	Public Health	Pyrethroids carbamates OC, OP	Malaria, leishmaniasis	9.00 to 75.00	0.03 - 0.45
	Coils	Consumer	Pyrethroids	Nuisance?	2.50 To 3.00	0.02-0.05
	Emanator	Consumer	Pyrethroids	Nuisance	3.50 dispenser 0.02 per mat	0.03

Market Assessment for Public Health Pesticide Products.
Bill & Melinda Gates Foundation, Boston Consulting Group, 2007.

ISOMATE-CM FLEX IS FAST AND EASY TO APPLY

Insert CM FLEX dispenser until it stops at notch in the middle of coupling. Spread dispenser the length of the cut in the coupling. Flip dispenser back over coupling to lock in position.

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They have done it in agriculture – why not health?

- Twin-tube design for easy, quick application.
- Sustainable, flexible, affordable and effective mating disruption!
- **No batteries, no programming, no disposal and maintenance free.**
- High pheromone load rate provides season-long mating disruption.
- Superior dispensing technology delivers consistent, uniform release rate.
- Extensively tested by leading universities, public and private institutions.
- Real-time dispenser analyses available at www.pacificbiocontrol.com.
- Highly trained and experienced staff in mating disruption technology and IPM.
- Isomate is the most widely used mating disruption technology in the world.
- Compatible with other control methods.
- Long-term use can successfully reduce CM populations to low levels.
- Not toxic to bees or beneficial insects and mites.
- Residue free.
- No worker re-entry period or pre-harvest interval.
- Provides greater flexibility to schedule other orchard activities.
- No groundwater contamination when used as directed.
- Not affected by rainfall or overhead cooling.
- No phytotoxicity. No sticky residue on trees and fruit.
- WORRY FREE MATING DISRUPTION!