MEETING REPORT

A review of the status and future

of durable wall linings (DL)

Hold under the work stream "Optimal choice of vector control methods"

of the RBM Vector Control Working Group (VCGW)

23 June 2010, Geneva, Switzerland

Convenors: **Christian Lengeler, Swiss TPH**
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1. Introduction

A new vector control technology: Durable Wall Lining (DL)
IRS was developed over 60 years ago, following the invention of DDT, the first insecticide with a sufficient residual activity to be used for this purpose. Since then, hardly anything has changed in the way IRS is implemented. The only major change has been that there is now a greater range of insecticides (12 different products in 4 chemical classes) with some of the newer products being longer lasting formulations (up to 12 months residual effect).

On the same model of how conventional ITNs with an insecticidal effect of maximum 12 months moved on to become LLINs that do not need to be re-treated for 3-5 years, there is a great rationale for making IRS also much longer lasting. This is especially important in areas that are difficult to reach, or where the weakness of the health system is such that repeated applications are difficult.

A solution to this problem has been found with Durable (Wall) Lining (DL). So far, the most advanced product is a woven shade cloth made of polyethylene with 50% shading and treated with 4.4 gm deltamethrin a.i./kg material. The type of treatment is similar to Type 2 LLINs (the insecticide being included in the fibre itself). This product is developed and manufactured by Durable Activated Residual Textiles S.A. (DART), a consortium of three partners: Vestergaard Frandsen®, Acumen Fund and Richard Allan. Other products are currently in the pipeline of a number of manufacturers.

On the 23rd of June 2010, a half-day meeting was called under the auspices of the "Optimal choice of vector control methods" workstream of the RBM Vector Control Working Group (VCGW) to discuss the current state of the DL technology, in support to the development pipeline of this technology.

2. Meeting objectives

1. To outline a testing programme leading to epidemiological and entomological proof-of-principle of DL as large-scale vector control tool, through full-scale comparative field trials.

2. To prepare and submit to WHOPES a recommendation with regard to the testing of DL (Phases 1-3).

3. To outline how a potential investment of CDC and USAID in DL research could be most effective.

4. To discuss and draft plans for the future development of DL with alternative (non-pyrethroid) insecticides.

3. Meeting format

Three invited presentations (see agenda below) were followed by a managed discussion on key areas related to the development plan of DL.

For reasons elaborated on below, the original agenda including the generation of a proposal for WHOPES testing of DL (objective 2) could not be followed. Objective 4 could only be dealt with partially.

Representatives from the vector control community as well as from all major vector control companies were invited (see list of participants as Appendix 1).

4. Revised agenda

Time	Topic	Presenter
Wednesday 23rd June 2010		
14.00-14.45	DL: an introduction	R. Allan - DART Chair: C. Lengeler – Swiss TPH
14.45-15.30	The potential place of DL in large-scale VC and the management of insecticide resistance	J. Lines – WHO/GMP
15.30-16.00	WHOPES testing rules for LLIN (that could provide a basis for testing DL) and IRS	J. Gimnig - CDC
16.00-16.45	Development plan and the generation of epidemiological information for DL (Managed general discussion)	All
17.00-17.15	**Tea**	
17.15-18.00	General discussion continued along two lines: 1. Target Product Profile 2. Proof-of-principle testing	
18.00-18.15	Finalization of outline recommendations	Chair C. Lengeler

5. Minutes

Part 1: 4 invited presentations

The meeting was opened at 14.00 with a short presentation on expected meeting outputs and meeting objectives (**Presentation 1 - Lengeler**). The main point of the introduction was to stress the need for new vector control (VC) interventions such as DL to follow a *triple development / registration path*: (1) The normal registration process with regulatory authorities in the country of production (Europe, North America, etc.); (2) the WHOPES process; and (3) the compilation of enough high-quality epidemiological evidence to convince major public heath donors to invest in the VC tool. In the case of DL, the purpose of the meeting was mainly to clarify issues related to (2) and (3).

The following presentation by the DART Technical Director (**Presentation 2 – Allan**) outlined the specific features of the only product to have reached currently production level. That presentation highlighted the fact that the DART product was an IRS-ITN hybrid, and reviewed key issues for product testing. It also defined product characteristics, including the expected operational duration of 5+ years, and key issues of installation.

The DART product bears resemblance with polyethylene plastic sheeting, for which operational experience exists in emergency situations. A considerable amount of field testing has taken place (17 field trials so far – see presentation). Hence a good body of knowledge is already available from laboratory and experimental hut studies to suggest that the performance of that product is at least on par with ITNs and IRS. So far, two medium-scale field trials are ongoing in Angola (Carnevale *et al*.) and Western Kenya (Vulule *et al*.). One additional large-scale trial is about to start in Western Kenya as well (Gimnig et al.) and plans are being finalized for a trial in Malawi (Gimnig *et al*.). While durability has not been assessed fully as yet, there is already good evidence that the product remains fully effective for at least 2 years. If it remained effective for 4-5 years at the same level of efficacy, the DART DL would certainly represent an attractive option for large-scale VC in Africa. Confirmed cost for the DART product are not available at present.

The next presentation (**Presentation 3 – Lines**) outlined the potential role of DL within malaria control more generally, and among VC tools specifically. The presentation also outlined the role of WHO/GMP, WHOPES and the RBM VCWG in setting standards for new VC products such as DL. Unfortunately, there is no clear definition of the kind of evidence that is required before conclusions can be drawn as to their usefulness. The presentation then focused on the important issue of insecticide resistance and the best tools/strategies we have currently to deal with that problem. Possibly, some of the current WHOPES testing criteria such as knock-down effect will have to be amended in order to allow for other insecticide classes that do not display a strong KD effect but give good mortality, to be considered. This is an obvious area for urgent consideration by WHO/GMP and the RBM board and needs to be increasingly considered in the frame of the GMAP. Obviously, this element needs also be taken into account for DL, and non-pyrethroids should be incorporated as much as possible in new products, possibly as mixtures of products.

The fourth and last presentation focused on current testing procedures required by WHOPES for the most commonly used VC products (**Presentation 4 – Gimnig**). It reviewed the three phases of testing, up to cluster randomized trials with entomological outcomes and considered both testing methods and measured outcomes. The presentation also stressed the need for the monitoring of VC interventions in operational settings and discussed important parameters of durability with LLINs – which would have some applicability for DL as well.

Part 2: General discussion

With the four initial presentations a good factual basis was laid for a general discussion. Because of time constraints, the planned group work could not be carried out. The general discussion focused on the following *two key areas*:

1. Definition of a *Target Product Profile* (TPP) for DL products, in terms of product characteristic, duration of action and class of insecticide.

2. Suggested testing procedures for both (WHOPES) testing and epidemiological and entomological proof-of-principle assessment.

The key discussion points are summarized below. Key conclusions and recommendations are presented at the end.

a) We should be free to look at a range of new concepts for DL, including alternative modes of action - for example repellency. Many materials / technological solutions could/should also be considered. As a result, it is not possible at this point in time to define uniquely the nature of DL. This means that the meeting was not in a position to define a Target Product Profile (TPP). As a result, it was also obviously not possible to recommend a specific WHOPES testing procedure and objective 2 (recommended testing procedure for WHOPES) was abandoned early.

b) Certainly, DL offer a new opportunity to "mosquito proof" houses regardless of their structure, and this should be kept in mind when working on the best application of the tool. More practical operational experience is urgently required for a range of endemic settings. Realistic costing assessments for this technology are also required, both for the cost of the product and for the installation and life-cycle costs.

c) Defining WHOPES testing procedures remains crucial in order for industry to be able to plan appropriately from early on. More work is urgently required on this. At this point testing procedures will have to be at least in part product-specific rather than class-specific. For a particular product, defining the TPP would be an obvious first step towards large-scale testing. IVCC will assist with that process. Obviously, developing a new TPP for each product complicates things but it represents the only pragmatic approach at this point.

d) There was a consensus that when producing testing guidelines for DL the opportunity could also be seized to revise the current testing guidelines for LLINs.

e) According to IVCC, testing guidelines should aim at assessing how a given product could fail to fulfil its defined TPP – for example by not lasting as long as expected, by not being acceptable to the population, etc.

f) One inquiry from an industry representative suggested that while waiting for the full proof-of principle from large-scale epidemiological testing (which could take 5 years), some sort of "interim recommendation" should potentially be considered for DL, so that the product could already be sold/used on the basis of more limited testing. This represents a rather new situation and no conclusion was reached by the group on that point. It is questionable, however, whether the big donors such as GFATM would accept that approach.

g) There was, however, consensus that the first DL to reach production level should be considered as a "first-in-class" and supported by public investments with regard to epidemiological proof-of-principle testing. Such testing will be costly and difficult; solid proof-of-principle testing for ITNs amounted to over USD 10 millions. Where the support for such testing would come from was not elaborated on, but the meeting gave support to the concept.

h) At least two large-scale studies are already planned with the DART product, one in Western Kenya and one in Malawi (both by CDC). In addition, some data will come from the current KEMRI work in Western Kenya and in Angola (see presentation 2). One more (unfunded) trial is planned in the Democratic Republic of Congo. The testing guidelines worked out for the LLIN-IRS combination trials (back –to-back meeting – see separate meeting) represent a good starting point for high-quality testing protocols for DL.

i) DL is similar to IRS in that it relies mainly on a mass effect, and hence on a very high coverage in the community to be effective. This should be born in mind when testing the product. The concept of "coverage" needs to be elaborated on, as much at the level of a given structure (what percentage of the walls need to be covered, do ceilings need to be covered?) that at the level of the community (which level of structure coverage is required to achieve an optimal mass effect).

j) Ideally, at least four large-scale cluster randomized controlled trial in different settings in Africa should be conducted (for ITNs the number was five). One site at least should be in an area with substantial pyrethroid resistance. It would be optimal if one arm could be IRS only, so that a direct comparison with that technology would be possible. If that was not possible, an LLIN arm would be adequate. Ideally, of course, the trial would have three arms, so that the effect of DL could be compared to both LLINs and IRS. Even better, a fourth arm would include the combination of IRS and LLIN in order to assess the value of the combination versus each intervention separately. Given the limited number of trials that will be possible to carry out over the next few years, such an approach would represent an optimal use of resources. However, these trials would be very large and require sites with a substantial level of residual malaria transmission.

k) There was agreement that alternative insecticides to pyrethroids should be used as soon as possible for integration into DL products. Even better, combinations of insecticides with different modes of action should be considered. However, for the first-in-class product deltamethrin was considered a suitable insecticide in order to demonstrate proof-of-principle. This would allow to avoid the myriad of regulatory and efficacy issues that are associated with a new class of insecticide, and allow to focus the testing on the potential of the technology itself.

l) In view of resistance development, DL might represent a new challenge because of the long duration the product (target: > 5 years). Hence, there is no way insecticides can be rotated every 1-2 years with this technology. Using mixtures is the best that could be done to mitigate resistance development. Resistance management should rate extremely high in the product definition

Part 3: Summary and recommendations

1. DL represents a new and distinct vector control intervention, with characteristics of both IRS and LLINs.

2. At present it is impossible to define a class-specific Target Product Profile (TPP) because different concepts are being worked on. Hence, only product-specific Target Product Profile can be developed.

3. WHOPES testing guidelines will need to be developed for each product at this stage, since it is not possible to have a class-specific Target Product Profile. More work on defining appropriate testing procedures is urgently required.

4. DL represents a new vector control tool and solid epidemiological evidence needs to be generated before it can be recommended for large-scale implementation. This should include at least four large-scale cluster randomized controlled trials in different settings, one at least with substantial pyrethroid resistance. Support from public sources should be used for that testing, while product-specific developments should be born by the manufacturers.

5. As much as possible, the application of DL should be used to “mosquito proof” the house. Operational experience including costing is urgently required.

6. For the first-in-class product the use of a pyrethroid insecticide is adequate because of the practical advantages for the required large-scale testing. For subsequent products, however, non-pyrethroids or mixtures of insecticides should be considered from the start.

Appendix 1: List of participants

		DL development meeting	
		Name	**Institution**
1		Mike Macdonald	USAID
2		Christian Lengeler	Swiss TPH
3		Jo Lines	WHO/GMP
5		Immo Kleinschmidt	LSHTM
6		Mark Rowland	LSHTM
7		Kalifa Bojang	MRC Gambia
8		Antoinette Tshefu	ESP Kinshasa
9		Tom McLean	IVCC
10		Robert Sloss	IVCC
11		Bob Wirtz	CDC
12		John Gimnig	CDC
13		Vincent Corbel	IRD
14		Kate Aultman	BMGF
15		Gary Clark	USDA
16		Richard Allan	DART
17		John Thomas	DART
18		Helen Jamet Pates	VF
19		John Invest	Sumitomo
20		Karin Horn	Bayer
22		Egon Weinmueller	BASF
23		Andy Bywater	Syngenta
24		Anuj Shah	A to Z
25		Bill Jany, Rod Flinn	Clark
26		Ole Skovmand	Intelligent Insect Control
27		Rajpal Yadav	WHO/WHOPES

Secretariat: Konstantina Boutsika, Swiss TPH