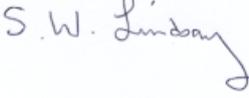


STANDARD OPERATING PROCEDURE:

Selection of study children for the longitudinal cohort and additional children at cross sectional surveys (AvecNet specific)

SOP Details:

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Author(s): Margaret Pinder Title: Dr	<i>Signature</i>	<i>Date</i>
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Reviewed by: Alfred Tiono Title: Dr	<i>Signature</i>	<i>Date</i>
		2/12/2013
Approved by: Steve Lindsay Title: Prof	<i>Signature</i>	<i>Date</i>
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1. DEFINITIONS AND ABBREVIATIONS

AvecNet	AvecNet is a consortium of African and European researchers committed to ensuring the sustainability of malaria vector control in Africa and is an EU funded project lead by Prof Hilary Ranson, Liverpool School Tropical Medicine
AvecNet	AvecNet is also used as the short name for the trial "To assess whether addition of pyriproxyfen, an insect juvenile hormone mimic, to long-lasting insecticidal mosquito nets provides additional protection against clinical malaria over current best practice. Protocol for a two-armed cluster randomized wedge-shaped trial in Burkina Faso", which is funded by AvecNet as part of WP6
CNRFP	Centre Nationale de Recherches et Formation sur le Paludisme, Burkina Faso
LLIN	Long-lasting Insecticidal bed Net
PPF-LLIN	Long-lasting Insecticidal bed Net with pyriproxyfen in addition to permethrin
SOP	Standard Operating Procedure

2. BACKGROUND

Reductions in malaria are currently being recorded in many countries in sub-Saharan Africa¹ largely due a massive scale-up of long-lasting insecticidal nets (LLINs) and indoor residual spray campaigns^{2,3}. Future success, however, is threatened by the development of insecticide resistance in the vectors and currently bed nets can only be treated with pyrethroids⁴. To increase the effectiveness of LLINs, alternative types of bednets are being developed where another active ingredient is added to the pyrethroid. The AvecNet trial investigates the effectiveness of pyriproxyfen added to permethrin on LLIN⁵. Pyriproxyfen is an insect juvenile hormone mimic, recommended for vector control by the World Health Organization since it is effective at extremely low concentrations and is safe to people, and there is no cross resistance with other classes of insecticide used for vector control⁶.

The primary objective of the AvecNet trial is to assess whether PPF-LLINS provide added protection against clinical malaria in children compared with LLIN over two malaria transmission seasons of follow up. The secondary objectives are to assess whether PPF-LLINS provide added protection compared to LLINs against anaemia and/or parasite prevalence in children and to assess and compare the prevalence of microscopy confirmed gametocyte carriers (GC) in LLINs group versus PPF-LLINS group. To meet these objectives the trial needs to enrol an unbiased cohort of children balanced for age that is representative across the study site. These will be followed by passive case detection for malaria. Children in a cohort that are provided with transport fares and free medication, however, are less likely to be infected with *P. falciparum* at the end of the transmission season. To access this bias, for the cross-sectional surveys, non-cohort children of a similar age will be enrolled and sampled in addition to children in the cohort. The cohort of children will also be followed for malaria before the interventions are put in place to estimate baseline variations in malaria across the study area.

3. SCOPE

These procedures involve the statisticians (Mrs Mariabeth Silkey and Dr Brian Faragher), the epidemiologist (Dr Margaret Pinder), the local principal investigator (Dr Alfred Tiono) and the principal investigator (Prof Steve Lindsay)

4. RESPONSIBILITIES

Mrs Mariabeth Silkey and Dr Margaret Pinder are responsible for production of the random lists by cluster for each enrolment; i.e. baseline, start of year1 and start of year 2 and the cross-sectional surveys. Dr Alfred Tiono is responsible for ensuring these lists are in a format suitable for field application. Prof Steve Lindsay and Dr Brain Faragher oversee the process.

5. HEALTH & SAFETY

There are no health and safety issues for this SOP.

6. PROCEDURES

6.1 Overview

A cohort of children aged 6 months to 5 years will be enrolled at the start of the study and followed for malaria by passive case detection before the interventions are put in place (baseline) and each transmission season during and after the interventions are put in place (year 1 and year 2). This cohort of children is also surveyed at the start and end of the transmission seasons in year 1 and year 2. At the start of the transmission season in year 1 and year 2 children over 5 years of age leave the cohort and are replaced by younger children aged 6-18 months. In addition, during the start and end of the transmission season surveys, where possible, an average of 50 additional non-cohort children aged 6 months to 5 years resident in the cluster will be enrolled into each survey

6.2 Listings for the selection of children for the longitudinal cohort

At the start of the trial the child cohort will be selected from the baseline Demographic Surveillance System (DSS) database, data collected in July 2013. The final DSS dataset of village clusters that consent to participate in the trial will be interrogated electronically to provide random listings for each cluster of all children aged between 6 months and 5 years of age on the 1st November 2013. When a cluster consists of more than one village the sample will be taken from the combined number of children in the cluster. In each cluster children will be enrolled with equal numbers aged 6-35 months and 36-60 months on 1st November 2013.

An average of 50 children will be enrolled in each cluster with a range of 30-100 to allow for the variation in cluster sizes. The total population per cluster is indicative as the SOP was finalized before the actual cluster populations were known and the actual ranges of cluster populations need to be used once they are known:

Total cluster population under 5y	Total children to enrol
50-99	30
100-159	40
150-199	50
200-249	60
250-299	70
300-359	80
350-399	90
>400	100

The primary list for selection thus has the total children indicated for the cluster size with half of these aged 6-35 months and half aged 36-60 months.

In addition a secondary selection list of children will be generated for each cluster. Children can only be enrolled from this list if one or more child on the primary list fails to meet the inclusion criteria (detailed below). The child should be replaced by one of the same age group (i.e. aged 6-35 months or 36-60 months) from the secondary list.

The primary and secondary lists thus form the screening log and document the study number given to each child. An example from a previous study is provided in the Annex. Records will be kept of the numbers of children selected from the primary list and the reason for non-enrolment will be recorded on the primary screening list.

In July 2014 all children over 5years on 1st July 2014 will be excluded from the cohort and replaced by an equal number of children aged 6-18 months. At the same time, other children who have left the cohort will also be replaced by children of the same age group, where possible. The same procedure will be repeated in 2015.

Inclusion Criteria

The subject must meet all the following criteria to be considered eligible for inclusion in the study:

- They are on the randomization list.
- They can be of either sex but must be in the correct age range. Check the birth date on the health card of the child or registration of birth certificate.
- They must be resident in the study village. Check that they are not short-term visitors
- Informed consent by caregiver for the child to participate in the study must be provided

Exclusion Criteria

- Children born outside the age range
- Those who are expected to be non-resident during several months of the transmission season will be excluded.
- Current active participation in any trial involving administration of an investigational malaria vaccine or malaria drug
- Children under routine chemoprevention treatment

6.4 Listings for the selection of additional non-cohort children for the cross-sectional survey

During the surveys all children of the cohort who are present will be sampled and in addition an equal number of children in the village, who meet the inclusion and exclusion criteria above but are not in the cohort will be sampled if possible. Parental consent must be provided and the child must be present on the DSS listings. Before the surveys listings, by cluster, village and residential compound, of all children in the cohort and all additional children will be prepared by from the most recent DSS data. To ensure that the additional children are of the same age range as the cohort, in the July surveys the additional children should be aged 6 months to 5 years and in the December they should be aged 1 year to 5 years and 6 months.

References

- 1.WHO. World Malaria Report 2011. Geneva: World Health Organization; 2011.
- 2.Lengeler C. Insecticide-treated bed nets and curtains for preventing malaria. The Cochrane Database of Systematic Reviews. 2004; (2): CD000363 pub2. DOI: 10.1002/146.

3. Pluess B, Tanser FC, Lengeler C, Sharp BL. Indoor residual spraying for preventing malaria. *Cochrane Database Syst Rev.* 2010; **4**: CD006657.
4. Ranson H, N'Guessan R, Lines J, Moiroux N, Nkuni Z, Corbel V. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol.* 2011; **27**: 91-8.
5. Ohashi K, Nakada K, Ishiwatari T, Miyaguchi J, Shono Y, Lucas JR, et al. Efficacy of pyriproxyfen-treated nets in sterilizing and shortening the longevity of *Anopheles gambiae* (Diptera: Culicidae). *J Med Entomol.* 2012; **49**: 1052-8.
6. WHO. Pesticides and their application for the control of vectors and pest of public health importance. 6th edition ed. Geneva: WHO; 2006.

ANNEXE

Example of first and second selection listings for children enrolled into a cohort.

random listing

village	vill_c	cluster_	house	child_id	fname	lname	sex	DOB	mum	dad	agegrp	sele	Age	Consent	ID	Notes
name	ode	code	hold									ct	OK?	provided	number	
village name	01	07	2	10-02-0113	Isata	name	Female	20-Sep-02	mum name	dad name	5 to 10	1				
village name	01	07	2	10-02-0131	Dawda	name	Male	19-Sep-06	mum name	dad name	<5	1				
village name	01	07	2	10-02-0128	Tijan	name	Male	02-Feb-07	mum name	dad name	<5	1				
village name	01	07	2	10-02-0106	Aminata	name	Female	2002	mum name	dad name	5 to 10	1				
village name	01	07	2	10-02-0107	Yaya Jammeh	name	Male	2006	mum name	dad name	<5	1				
village name	01	07	2	10-02-0117	Mariama	name	Female	15-Nov-05	mum name	dad name	5 to 10	1				
village name	01	07	2	10-02-0126	Maladou	name	Female	30-Nov-98	mum name	dad name	>10	1				
village name	01	07	2	10-02-0114	Yaya Jammeh	name	Male	24-Aug-06	mum name	dad name	<5	1				
village name	01	07	2	10-02-0127	Mariama Yebe	name	Female	16-Feb-02	mum name	dad name	5 to 10	1				
village name	01	07	2	10-02-0105	Husanatou	name	Female	1998	mum name	dad name	>10	1				
village name	01	07	2	10-02-0132	Jameh	name	Female	15-Dec-09	mum name	dad name	<5	1				
village name	01	07	2	10-02-0129	Mahamadou Koreka	name	Male	17-Nov-09	mum name	dad name	<5	1				
village name	01	07	2	10-19-0129	Bubacarr	name	Male	2002	mum name	dad name	5 to 10	1				
village name	01	07	3	10-03-0115	Mariama	name	Female	02-Dec-03	mum name	dad name	5 to 10	1				
village name	01	07	3	10-03-0134	Fatoumata	name	Female	Jan-05	mum name	dad name	5 to 10	1				
village name	01	07	3	10-03-0117	Ansu	name	Male	Jun-00	mum name	dad name	>10	1				
village name	01	07	3	10-03-0110	Ebrima	name	Male	24-Aug-07	mum name	dad name	<5	1				

random listing

village	vill_c	cluster_	house	child_id	fname	lname	sex	DOB	mum	dad	agegrp	select	Age	Consent	ID	Notes
name	ode	code	hold									ct	OK?	provided	number	
village name	01	07	1	10-01-0105	Amadou	name	Male	2000	mum name	dad name	>10	2				
village name	01	07	1	10-01-0104	Alpha Omar	name	Male	1998	mum name	dad name	>10	2				
village name	01	07	2	10-02-0112	Fatoumata	name	Female	1999	mum name	dad name	>10	2				
village name	01	07	3	10-03-0125	Sulay	name	Male	Dec-98	mum name	dad name	>10	2				
village name	01	07	3	10-03-0119	Sainey	name	Female	16-Oct-06	mum name	dad name	<5	2				
village name	01	07	3	10-03-0131	Isatou	name	Female	05-Jul-09	mum name	dad name	<5	2				
village name	01	07	3	10-03-0137	Mamadou	name	Male	Aug-07	mum name	dad name	<5	2				
village name	01	07	3	10-03-0109	Jariatou	name	Female	07-Dec-03	mum name	dad name	5 to 10	2				
village name	01	07	3	10-03-0114	Gillajo	name	Male	Sep-99	mum name	dad name	>10	2				
village name	01	07	4	10-04-0125	Morro	name	Male	1998	mum name	dad name	>10	2				
village name	01	07	4	10-04-0126	Mabintou	name	Female	2003	mum name	dad name	5 to 10	2				
village name	01	07	4	10-04-0114	Julla	name	Female	07-Jul-04	mum name	dad name	5 to 10	2				
village name	01	07	4	10-04-0111	Jainaba	name	Female	1998	mum name	dad name	>10	2				
village name	01	07	4	10-04-0115	Ebrima	name	Male	28-May-06	mum name	dad name	<5	2				
village name	01	07	5	10-05-0115	Fatoumata	name	Female	2006	mum name	dad name	<5	2				
village name	01	07	5	10-05-0116	Mamakoi	name	Female	2000	mum name	dad name	>10	2				
village name	01	07	5	10-05-0112	Sanna	name	Male	1998	mum name	dad name	>10	2				