STANDARD OPERATING PROCEDURE FOR:

Selection and randomization of the clusters (AvecNet specific)

SOP Details:

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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 pyriproxfen in addition to permethrin
SOP	Standard Operating Procedure
GIS	Geographical Information Systems
GPS	Geographical Positioning Device

2. BACKGROUND

The primary aim of the Avecnet trial is to assess whether pyriproxyfen and pyrethroid treated LLINs (PPF-LLIN) provide added protection against clinical malaria in children compared with pyrethroid-only LLINs (LLIN) over two malaria transmission seasons of follow up. The trial uses a cluster-randomized controlled design since: (1) LLINs are a community-level intervention, and (2) the village, or cluster of villages, is a suitable unit for randomization. The populations of the trial villages will be consented to join the study, enumerated and geo-positioning co-ordinates will be determined for each compound, ("concession" in French) which usually consist of one or more related households each with their own houses. Trial clusters will consist of one or more villages ("village/ hameau de culture" in French) depending on their spatial distribution and population.

The primary outcome the trial is the incidence of clinical malaria in a cohort of resident children aged 6 months -5 years old. Trial clusters should have at least 50 children aged 6 months -5 years old and it is planned to enroll an average of 50 children per cluster (range 30-100, depending on cluster size). The enrolment will be stratified by age at above and below 24 months. Malaria cases will be followed passively by parent / carers taking their sick child to the nearest health facility. Cases of malaria will be recorded by study nurses in close collaboration with government health workers at five health facilities surrounding the study site (Tiefora, Koflandé, Boussara Brousse, Madiasso and Kangounadeni).

The PPF-LLIN are expected to impact on the breeding capacity of the malaria vector (*An gambiae* s.l.) in stagnant water bodies located in and around villages. The trial, therefore, uses a step-wedge design in which the intervention is rolled-out gradually over time to cover the entire trial area. Thus the impact of the intervention can be measured over time and space. This SOP describes the procedure to ascribe villages to clusters and to roll-out the intervention (PPF-LLIN) to these clusters over the two malaria transmission seasons of the trial.

3. SCOPE

These procedures involve the epidemiologist (Dr Margaret Pinder), the statisticians (Mrs Mariabeth Silkey and Dr Brian Faragher), the principle investigator (Prof Steve Lindsay), the local principle investigator (Dr Alfred Tiono) and the entomologist (Dr Sagnon Nfale) to group the study villages into clusters and assign the order in which clusters will be provided with the intervention (PPF-LLIN).

4. RESPONSIBILITIES

Dr Tiono collaborates with the demographic surveillance team to obtain the population and geo-location data of the trial villages and provides this to Dr Pinder. Dr Pinder will collaborate with Mrs Silkey, overseen by Dr Faragher, to use the latest demographic surveillance and geo-location data from the Banfora study site to group the study villages into clusters and generate a series of possible random lists for the order in which clusters will be provided with the intervention. Prof Lindsay will have one of the possible selected. Dr Tiono and N'fale will check the final selection for feasibility on the ground.

5. HEALTH & SAFETY

5.1 There are no health and safety issues for this SOP

6. PROCEDURES

6.1 Data on the population in all consenting households in the research area will be collected by standard demographic surveillance methods (SOP) with the geo-position of all households measured by handheld GPS devices.

6.2 The GPS data will be used to group the villages into 40 approximately equal clusters.

6.3 Each village-cluster will then be listed with its health centre, total population, total children aged 6-35months, total children aged 36-60 months and the expected number of children to be enrolled.

6.4 Balanced randomization lists of village-clusters for PPF-LLIN distribution at the eight time points will then be generated. At each time point, which constitutes one wedge, five village-clusters will be randomly selected.

6.5 At each step of the wedge village-clusters will be selected, as far as is possible, to maintain an even balance of children in the two arms of the trial. This will also maintain a balance of the total population per cluster as the number of children enrolled varies with village-cluster size.

6.6 The randomization will also be balanced, as far as possible, to ensure that within each health centre catchment area half of village clusters will have PPF-LLINs and half will have LLINs by end-December 2014.

6.7 It is anticipated that there will be several possible balanced randomizations and these will be numbered from one upwards.

6.8 A member of the study DSMB will then be asked by Prof Lindsay by email to select a number in the series.

6.9 This randomization will be checked by Dr Tiono and Dr N'Fale for feasibility on the ground for the clinical and entomological studies.

6.10 This will then be the randomization used for the trial and it will be sent to the PI and local PI and filed in the Study File.

7. APPENDIX

Estimated children to enrol with varying cluster size

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