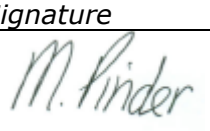
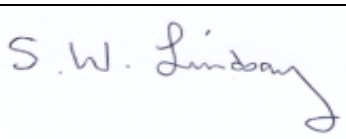
STANDARD OPERATING PROCEDURE FOR:

Internal clinical monitoring of AvecNet Trial

SOP Details:

Version: 1.0 Eng The English version will be definitive	**Date operational:**	
Author(s): Margaret Pinder **Title:** Dr	*Signature* 	*Date* 7th Dec 2013
Reviewed by: **Title:**	*Signature*	*Date*
Approved by: Steve Lindsay **Title:** Prof	*Signature* 	*Date* 8th Dec 2013
Date to be reviewed:	August 2014	
Current review changes: Non applicable – new version		
Location:	Original hard copy with: Steve Lindsay / Study File Hard copies with: Clinical monitor / Alfred Tiono / Sagnon N'Falé Electronic version: Steve Lindsay / Study File	
Confidential, unauthorised copying prohibited		

Review History:

First Operational:	August 2013			
Reviewed:				
Updated yes/no:				

Index of contents

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
AV	Adverse event
CNRFP	Centre Nationale de Recherches et Formation sur le Paludisme, Burkina Faso
CRF	Case report form (synonym: Case Record Form, also Data Collection Form)
CV	Curriculum vitae
DMC	Data Monitoring Committee
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
GCP	Good clinical practice
LLIN	Long-lasting Insecticidal bed Net
LSM	Local safety monitor
PI	Principal Investigator
PPF-LLIN	Long-lasting Insecticidal bed Net with pyriproxfen in addition to permethrin
SAE	Serious adverse event
SDV	Source data verification
SOP	Standard operating procedure; instructions or directions for performing certain operations or processes in a consistent way

2. BACKGROUND

2.1 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. To achieve this populations of the trial villages will be consented to join the study and in 2014 all will be provided with LLIN and then over the next two malaria seasons the LLIN will all be withdrawn and replaced by PPF-LLIN at times fixed by the study design. The major clinical monitoring issues concern enrolment and follow-up of the child cohort for the primary outcome and documentation of adverse events in the child cohort and also in asthmatic subjects and pregnant women who may have an increased risk of adverse events due to PPF-LLIN.
2.2 The conduct of this clinical research is a co-operative undertaking between the sponsor and the investigator. Each is responsible for ensuring that the conduct of the clinical trial conforms to the protocol and adheres to applicable laws, regulations and guidelines
2.3 The Sponsor ensures that the investigators and other study staff understand the protocol and related data collection needs. The sponsor also ensures that personnel, equipment and other protocol specific requirements are met.
2.4 In accordance with the principles of good clinical practice (GCP) and Guidelines for Good Clinical Practice in Clinical Trials there should be systems with procedures implemented that assure the quality of every aspect of a clinical investigation and monitoring is an integral part of the quality system.
2.5 It is essential that trials are monitored to the highest quality to verify that:
• the rights, safety and well being of all human participants are protected;
• the reported trial data are accurate, complete and verifiable from source documents; and
• the conduct of the trial is in compliance with the currently approved protocol including amendments, SOPs, GCP and all applicable regulatory requirements

3. SCOPE

This standard operating procedure (SOP) describes the monitoring of the AvecNet Trial by the sponsor's (University of Durham) clinical trial monitor(s). These procedures all CNRFP staff involved in the AvecNet project, this includes the Principle Investigator, the Local Principle Investigator, the clinician in-charge of the clinical AvecNet HERE CNRFP Field Site in Banfora, the clinician in-charge of the the data manager of the CNRFP Field Site in Banfora for the collection of data.

4. RESPONSIBILITIES

4.1 In this Durham University sponsored trial the University appoints appropriately trained and qualified individual(s) to monitor the clinical investigations.
4.2 The PI, Prof Steve Lindsay, with advice from the local PI, Dr Alfred Tiono, ensures that all staff is properly trained to perform their duties.
4.3 The monitor(s) follow this procedure.
4.4 The Principal Investigator (PI) designates the local PI, Dr Alfred Tiono to ensure that the monitor is given access to facilities and documents, that staff is available as requested by the monitor, that responses to visit reports is provided, where applicable, and that action is taken to correct any identified deficiencies.

5. HEALTH & SAFETY

5.1 Any severe adverse events will be recorded during the trial. Study staff taking finger-prick blood samples should wear latex gloves.

6. PROCEDURES

6.1 General requirements

6.1.1 The objectives of the monitoring visits are:

- To check that the study is being carried out in accordance with the final approved protocol, GCP and applicable regulations;
- To identify any problems and suggest solutions;

- To ensure adequate supplies of trial documents (e.g. Case Record Forms) and clinical trial materials (e.g. drug supplies) are available for the ongoing trial;
- To check CRFs entry, verify against source documents and clarify any queries;
- To check facilities and procedures; and
- To maintain good relations with the investigator and trial personnel.

6.1.2 The extent and nature of monitoring are documented in a monitoring plan to assure that each person involved in the monitoring process carries out his/her duties.
6.1.4 The local PI must allow access by the monitor to all facilities as needed and make available all the essential documents and in particular the CRFs, informed consent forms and source documents.
6.1.5 The monitor records any monitoring visit and other monitoring procedures in a monitoring visit log (attachment 1). The local PI maintains the log at the site as essential document.
6.1.6 The monitor notes any non-compliance and notifies the local PI and ensures that appropriate corrections and preventive actions are taken.
6.1.7 For practical help one can consult the Joint Project Workstream Documents developed by UK Medical Research Council and Department of Health: http://www.ct-toolkit.ac.uk.

6.2 On-site Monitoring

6.2.1 Monitoring visits will be
- prior to the initiation of a clinical investigation (Initiation Monitoring),
- periodically when the study is commenced, (Interim Monitoring),
- after the study is completed or early terminated, where appropriate (Close-out Monitoring).

6.2.2 The monitor gathers all relevant documents and material needed for the monitoring visit or to be distributed to the site.

6.2.3 The following key areas are considered in the context of an interim monitoring visit:

Trial status and eligibility

6.2.4 Review the current status and progress of the study.
6.2.5 Verify that only eligible participants are enrolled. Verify the subject logs and check the entries against the CRF. In studies recruiting large numbers from a more general population, check eligibility criteria for only a sample of the participants.
6.2.6 Report the actual recruitment rate and participant enrolment versus anticipated enrolment and withdrawals in detail.

Informed Consent

6.2.7 Ensure that the consent procedures result in freely given and appropriately informed consent.
6.2.8 Verify that consent was given for every participant before entering the study by checking the signed or thumb printed and dated consent forms. Randomly select 4 villages and check all consent forms from these villages.
6.2.9 Ensure that the correct information sheet was used during the consent process.

Review of case report forms and source documents

6.2.10 Check the accuracy and completeness of the entries including corrections of data into the forms. A source document designation log (see attachment 3) clarifies the sources for the original data. Verify that:
- participant identifiers are consistent;
- the randomisation procedure is adhered;
- the data required by the protocol are reported completely and accurately on the forms and are consistent with the source documents, if applicable (for primary efficacy and safety endpoints 100% of CRF data should be verified against source data);

- any modifications on treatment and/or type of measures are well documented for each of the study participant;
- adverse events, concomitant medication and inter current illnesses are recorded in accordance with the protocol on the forms;
- visits that the participants fail to make, tests that are not conducted, and examinations that are not performed are clearly reported on the forms;
- all withdrawals and dropouts of enrolled participants from the study are reported and explained on the forms;
- the source documents and other study related records are kept up-to-date and maintained appropriately.

6.2.11 **Note:** Do not make any corrections or entries on the CRFs or any source documents!
6.2.12 Provide the completed case report correction/clarification form (attachment 4) to the study team members for their corrective actions.

Adverse events

6.2.13 Determine whether adverse events (AEs) or other safety findings and especially all serious adverse events (SAEs) are appropriately reported within the time periods required by the protocol, SOPs, GCP, and the applicable regulatory requirement(s) to the sponsors representative, the PI, Prof Steve Lindsay, the local safety monitor (LSM), the relevant Ethics Committees, and to TSC, DMC/DSMB or corresponding bodies as appropriate.

Investigational products

6.2.14 Review that the investigator prepared or received all documents and all study supplies needed to conduct the investigation properly.
6.2.15 Ensure in case of investigational medicinal products that appropriate storage, dispensing, accountability and return or destruction arrangements are in place. Verify that:
- the investigator has the current Investigator's Brochure (IB) or current information on products (e.g. Summary of Product Characteristics, package insert, etc) for medicinal products being used;
- storage times and conditions are acceptable (including net storage), and that supplies are sufficient throughout the trial;
- the products are supplied in a way specified in the protocol;
- participants are provided with necessary instructions on properly using, handling, storing, and returning the products;
- the receipt, use, and return of the products at the sites are controlled and documented adequately; and
- the disposition of unused products at the sites complies with applicable regulatory requirement(s) and is in accordance with the protocol and/or sponsor requirements.

6.2.16 If investigational medicinal products are dispensed by others than the investigator, verify that the requirements of the study are understood by the study team member and that the correct supplies are being used.
6.2.17 If medicinal products are coming from routine stocks, confirm that what is being dispensed is the product specified in the protocol.

Essential documents

6.2.18 Determine whether the local PI maintains all essential documents up to date and that these documents are accurate, complete, timely, and legible, that they are dated and identify the study, and that they are filed appropriately.
6.2.19 Verify that the local PI and other investigators provide all the required reports, notifications, applications, and submissions.

Site performance

6.2.20 Verify that the qualifications of investigator(s), resources, the facilities including equipment and staff are adequate and will remain throughout the study period.

6.2.21 Ensure that all study team members are adequately informed about the study and trained.
6.2.22 Verify that all study team members are performing their specific trial functions, in accordance with the protocol and any other written agreements, and have not delegated these functions to unauthorised individuals.
6.2.23 Review organisational changes and verify how they will affect the conduct of the study.

Deviations

6.2.24 Verify that all study team members follow the approved protocol including all approved amendment(s), GCP, regulatory requirements and other protocol-specific requirements.
6.2.25 Communicate any deviations to the local PI and any major deviation to the PI manager.

6.3 Monitoring visit procedures

6.3.1 Prior to the monitoring visit, the monitor arranges in advance with the PI and the local PI a suitable date for the visit and informs the site about the expected duration and purpose of visit, planned visits of other departments involved and items for discussion, and confirms the arrangement in writing.
6.3.2 The monitor uses a monitoring checklist guiding him/her through the procedures (see attachment 2).
6.3.3 The study team members review the previous monitoring visit report, if any and monitoring contacts and ensure that outstanding actions are established.
6.3.4 The local PI reviews any changes to the conduct of the study including staff that may necessitate revision of any documents.
6.3.5 Nominated team members and other relevant staff as appropriate must be available on the days of the monitoring visit. The local PI and the study clinician must be in country and available for the visit.
6.3.6 The monitor normally requires time to go through the CRFs and associated documents alone. The study team provides an appropriate space for the study monitor to perform his/her duties.
6.3.7 At the end of the visit a meeting with the local PI and other appropriate staff members takes place to give update on findings and to discuss any issues, and to plan the date for the next monitoring visit. The local PI informs the PI is informed of the major findings by Skype on the last day of the monitoring visits.
6.3.8 After the monitoring visit the monitor writes a report by using the template (attachment 5 a-c). The local PI and reviews the report and the monitor and local PI sign and date it.
6.3.9 The monitor forwards the report to the PI, the other lead scientists (Prof Hilary Ranson and Dr Margaret Pinder), and the lead entomologist (Dr Sagnon Nfale) within two weeks. The local PI maintains the report as essential document (i.e. keeps a copy, files to Study File and electronic Study File); the monitor keeps a copy.
6.3.10 If any documents are taken by the monitor this must be recorded in the report. If source documents are taken the monitor must ensure that these be returned to the respective department.

7 Attachments

Number	Title
1	Monitoring visit log
2	Monitoring checklist
3	Source document designation log
4	Case report correction/clarification Form
5 a-c	Monitoring Visit Report Form for Initiation, Interim or Close-out visits

8 References

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Harmonised Tripartite Guideline for Good Clinical Practice E6 (R1). June 1996.
SOP-CTS-004. Preparation of Clinical Study Protocols.
SOP-CTS-006. Essential Documents for Clinical Research Projects.
SOP-CTS-009. Recording, Management and Reporting of Adverse Events

Appendix 1: Purposes of Types of Monitoring Visits

A. Initiation visit

- to ensure that the study protocol has been approved and to ensure sponsor and site commitment to the study;
- to ensure ethics committee (EC) approval before any study related procedures are conducted;
- to review the anticipated process for obtaining informed consent;
- to ensure that all essential documents are on file;
- to ensure the necessary staff is available and educated/trained about the study, case report form (CRF) completion, the protocol and study specific procedures, serious adverse events (SAE) reporting and review of source documentation requirements;
- to ensure adequate supplies of study documents and study material to conduct the study; and that adequate storage facilities are available;
- to ensure that the required resources are adequate;
- to ensure that the necessary logs e.g. temperature, responsibility, etc are in place;
- to review the monitoring plan;
- debriefing at the end of the visit which consists of discussion on visit findings and information on outstanding issues to be resolved before activation;
- submitting of monitoring report giving a summary of the visit and focusing on outstanding issues to be followed up; and
- to ensure that final site activation letter from sponsor was submitted informing the site that recruitment may begin..

B. Interim visit(s)

- to review the filing of essential documents
- to review investigational products storage and accountability records
- to check that the study is being carried out in accordance with the approved protocol, SOPs, GCP and regulatory requirements by reviewing such things as signed consent forms and patient eligibility
- to verify selected data items and/or adverse events recorded on the CRFs compared with data in the clinical records (Source Data Verification) to identify errors, omission or inaccuracies and clarify any queries
- to verify that SAEs or other safety concerns are reported as required
- debriefing at the end of visit by discussing findings and attempting to resolve issues and carry out necessary training or re-training
- submitting monitoring report summarising the findings and identifying significant facts, deficiencies/deviations detected and actions to be taken

C. Close out visit

- to ensure that the filing of essential documents is completed
- to ensure that all CRFs are completed and that all queries raised have been answered
- to ensure that supplies are returned to the sponsor, where applicable
- to ensure that adequate archiving/long term storage of essential documents are in place
- to reconcile the investigational products and ensure that unused products are returned or destroyed
- to ensure that the data base has been locked

MONITORING VISIT LOG

Principal Investigator		**Short title**	**AvecNet**
Site and address		**Protocol #/**	

Visit date	Name of monitor	Monitor's signature	Trial staff seen at visit	Signature of trial staff

SOURCE DOCUMENT DESIGNATION LOG

Principal Investigator		**Short title**	AvecNet
Site and address		**Protocol #/**	

S/N	Source documents	Related data	Comments	Initials
1.	Certified copy of Infant Welfare Card (IWC)			
2	Certified copy of Antenatal Clinic Card			
3.	Vital Signs/ Anthropometric measurement form			
4.	Sensitization notes			
5.	Clinical progress notes			
6.	Referral notes			
7.	Laboratory request forms			
8.	VCT forms			

S/N	Source documents	Related data	Comments	Initials
9.	Case report forms			
10.	Medical records			
11.	Other:			
12.	Other:			
13.	Other:			
14.	Other:			
15.	Other:			
16.	Other:			
17.	Other:			

Investigator Name _____ Investigator Signature _____ Date

CASE REPORT CORRECTION/CLARIFICATION FORM

Principal Investigator			**Short title**	AvecNet	
Site and address			**Protocol #/**		
Subject ID		**Subject initials**		**Date**	

CRF page	SD type	Discrepancy	Investigator initials	CRA initials

MONITORING CHECKLIST

1. Agenda
2. Correspondence with site – recent and relevant
3. Monitoring SOP
4. Previous monitoring report
5. Note book and sticky notes
6. Documents to pre-review and note
    a. Protocol
        i. Study objective
        ii. Eligibility criteria, e.g. fever temperature ≥37.5°C
        iii. Procedures, e.g. calculation of malaria parasites density
        iv. Safety reporting, e.g. timeline and who receives the report
        v. Sample handling, e.g. exportation, storage
    b. Key procedural SOPs
        i. Informed consent
        ii. Screening
        iii. Enrolment
        iv. Randomisation
        v. Safety reporting
        vi. IMP handling
        vii. Any other procedure related SOPs
    c. Previous monitoring report(s)
        i. General feel of the study quality
        ii. Outstanding issues, occurring over time
        iii. Areas of need – previous monitored ones or not
7. Case report correction/clarification forms
8. Monitoring visit report form
9. Any other relevant documents for study file

Visit Date **Short Title:** AvecNet Initiation Monitoring Visit

INITIATION MONITORING VISIT REPORT

PROJECT NAME	OTHER NUMBER(S)
TRIAL TITLE	
PRINCIPAL INVESTIGATOR(S) / CENTRE	**SPONSOR**
INVESTIGATIONAL PRODUCT(S)	**INDICATION**

Monitor	Visit date	Attendees (Name and Title)

SECTION 1: STUDY RECRUITMENT / STATUS SUMMARY		
Item No.	***Timelines & Recruitment***	***Date***
1	Previous visit	
2	Initial drug supply	
3	Projected enrolment	
4	Projected FSFV	
5	Projected LSLV	
		No. of Subjects
6	Projected enrolment	
Item No.	**COMMENTS**	

Abbreviations
FSFV = First subject first visit; LSLV = Last subject last visit; SAE = Serious Adverse Event; SD = Source Document; c/s =clinically significant; EOS = End of Study; OI=Outstanding Issue; CTSM = Clinical Trials Support Manager;

SECTION 2: OUTSTANDING ISSUES					
Section	Item No.		Yes	No	NA
		Were any action items identified for follow-up in the previous visit report			
		If yes, please list and indicate current status			

Visit Date **Short Title:** AvecNet Initiation Monitoring Visit

SECTION 3: GENERAL ITEMS				
Item No.	***The following items were reviewed/ discussed at the visit:***	Yes	No	NA
1	Final protocol			
Comment	(Version: Date:);			
2	Objective of study - Recruitment commencement and rate			
Comment				
3	Informed consent procedure			
Comment				
4	Randomisation (including retention & breaking of code)			
Comment				
5	Adequacy of staff and Training requirements			
Comment				
6	CRF and completion instructions			
Comment				
7	Data processing and management			
Comments				
8	GCP/ applicable regulations requirements			
Comments				
9	IEC/IRB communication and reporting			
Comments				
10	Handling, storage and recording of study drugs			
Comment				
11	Study drugs' dispensing and accountability			
Comment				
12	Adverse event and serious adverse event reporting			
Comment				
13	Study file and documentation			
Comment				
14	Monitoring procedures/ plan			
15	Access to subject records			
Comment				
16	Laboratory requirements and reference ranges			
Comment				
	GENERAL COMMENTS			

Visit Date **Short Title:** AvecNet Initiation Monitoring Visit

SECTION 4: Documents / Materials				
Item No.	***The following items were supplied / supply reviewed***	Yes	No	NA
1	Investigational product			
2	Other study supplies			
3	CRFs			
4	Randomisation codes			
5	Study file			
6	Investigator's brochure			
7	Other			
	If yes please list below			
Item No.	***The following items were received***	Yes	No	NA
8	Copy of approval letter from local Ethics Committee			
9	Copy of approval letter from local Regulatory Authority			
10	Copy of protocol signature page			
11	Other			
	If yes please list below			
Item No	**COMMENTS**			

Visit Date **Short Title:** AvecNet Initiation Monitoring Visit

SECTION 5: ITEMS IN STUDY FILE				
Item No.	***All deviations must be documented***	Yes	No	NA
1	Fully executed confidentiality agreement			
2	Fully executed investigator agreement			
3	Signed final protocol			
4	IEC approval letter for protocol			
5	IEC approved subject information			
6	IEC approved informed consent			
7	IEC approved advertisements			
8	IEC composition/member list			
9	Regulatory approval			
10	Import authorisation			
11	Sample CRF			
12	Sample of SAE report form			
13	Sample of labels			
14	Sample of source documentation			
15	Source documentation designation form			
16	Indemnity/ Insurance certificate			
17	Data management plan			
18	Signed & dated investigator CV			
19	Signed & dated staff CVs			
20	Signed authorised study staff log			
21	Lab certification/ quality control			
22	List of normal lab values			
23	Analytical plan			
24	Investigator's Brochure/Package insert/SmPC/Safety statement			
25	Shipping documentation			
26	Others			
Item No	**COMMENTS**			

Visit Date **Short Title:** AvecNet Initiation Monitoring Visit

SECTION 5: ITEMS IN STUDY FILE				
Item No.	***All deviations must be documented***	Yes	No	NA

SECTION 6: ACTION ITEMS FROM CURRENT VISIT		
Item No.		**Responsible person**

SECTION 7: NEXT STEPS		
Item No.		**Responsible person**

SECTION 8: NARRATIVES AND SUMMARY OF INITIATION VISIT	
Item No.	

PREPARED BY:		
PRINT NAME	SIGNATURE	DATE
REVIEWED BY:		
PRINT NAME	SIGNATURE	DATE

Visit Date: **Short Title:** AvecNet: Interim Monitoring Visit

INTERIM MONITORING VISIT REPORT

PROJECT CODE / SCC NUMBER	**OTHER NUMBER(S)**
TRIAL TITLE	
PRINCIPAL INVESTIGATOR(S) / CENTRE	**SPONSOR**
INVESTIGATIONAL PRODUCT(S)	**INDICATION**

Monitor(s)	**Visit date / #**	**Attendees (Name and Title)**

SECTION 1: STUDY RECRUITMENT / STATUS SUMMARY		
Item No.	***Timelines & Recruitment***	***Date***
1	Initiation visit	
2	Previous visit	
3	Initial drug supply	
4	Following drug supply	
5	Projected FSFV	
6	Actual FSFV	
7	Projected LSLV	
8	Actual LSLV	
		No. of Subjects
9	Projected enrolment	
10	Sensitized (if applicable)	
11	Screened	
12	Failed screening	
13	Enrolled	
14	Drop-outs	
15	CRF completed	
16	SAEs	
Item No.	**COMMENTS**	

Abbreviations
FSFV = First subject first visit; LSLV = Last subject last visit; SAE = Serious Adverse Event; SD = Source Document; c/s =clinically significant; EOS = End of Study; OI=Outstanding Issue; CTSM = Clinical Trials Support Manager;

Visit Date: **Short Title:** AvecNet: Interim Monitoring Visit

SECTION 2: OUTSTANDING ISSUES					
Section	Item No.		Yes	No	NA
		Were any action items identified for follow-up in the previous visit report			
		If yes, please list and indicate current status			

SECTION 3: GENERAL ITEMS				
Item No.	***The following items were reviewed/ discussed at the visit:***	Yes	No	NA
1	New information about study drug			
2	New safety information			
3	New protocol amendment			
4	Updates of Investigator's Brochure			
5	Changes to informed consent document			
6	Changes to investigator's responsibility			
7	Notification from regulatory authorities			
8	Continued adequacy of facilities			
9	Changes of site personnel & evidence of suitability of new personnel collected			
10	Personnel signature pages updated			
12	Named investigator personally supervising the study			
Item No.	**COMMENTS**			

SECTION 4: ETHICS COMMITTEE (IRB) REQUIREMENTS				
Item No.	***Obtain copies of all new information indicated below***	Yes	No	NA
1	New information from EC			
2	New information to EC			
3	Notification to EC made and approval obtained for changes to study protocol and informed consent, if required			
Item No	**COMMENTS**			

SECTION 5: PROTOCOL COMPLIANCE				
Item No.	***All deviations must be documented***	Yes	No	NA
1	Compliance with protocol and amendments procedures			
2	Protocol amendments signed, if applicable			
3	Compliance with informed consent procedures			

Visit Date: **Short Title:** AvecNet: Interim Monitoring Visit

SECTION 5: PROTOCOL COMPLIANCE				
Item No.	***All deviations must be documented***	Yes	No	NA
4	Source of study participants remains unchanged			
5	Compliance with inclusion/ exclusion criteria			
6	Procedure for entering study participants followed			
7	Specified replacement procedure followed, if applicable			
8	Compliance with concomitant drugs			
9	Follow up of subjects withdrawals undertaken, if applicable			
10	All protocol deviations reported to investigator			
Item No	**COMMENTS**			

SECTION 6: ICF and CRF REVIEW AND SOURCE DATA VERIFICATION		
Subject #	**List Visit Reviewed**	**List verified source document by visit day & form**
Subject #	**COMMENTS**	

SECTION 7: SERIOUS ADVERSE EVENTS					
Did a Serious Adverse Event occur?				**Yes**	**No**
If yes complete below					
Subject ID #	**Brief Summary of SAE**	**Reported to**			
		Sponsor		**EC**	
		Yes	**No**	**Yes**	**No**

SECTION 8: CLINICAL LABORATORY REQUIREMENTS				
Item No.	***All changes require documentation and all deviations must be documented***	Yes	No	NA
1	Reference ranges unchanged			
2	QA (e.g. certification, proficiency testing, etc) of laboratory up to date			
3	Methods of analysis remain consistent			
4	All required samples collected			
5	Samples collected according to protocol			
6	Samples stored properly			
7	Samples transported properly			

Visit Date: **Short Title:** AvecNet: Interim Monitoring Visit

SECTION 8: CLINICAL LABORATORY REQUIREMENTS				
Item No.	***All changes require documentation and all deviations must be documented***	Yes	No	NA
8	Lab sample (specimen) kit quantity adequate			
9	Sample kit expiry dates and storage conditions acceptable			
10	Equipment maintained and calibrated			
11	Clinical laboratory reports received (by site) promptly			
12	Clinical laboratory requisitions completed properly by site			
13	Clinical laboratory reports completed properly (i.e., dates and times of sample collection, receipt, analysis, and reporting to site specified)			
14	Clinical laboratory reports have correct identifiers			
15	Clinical laboratory reports reviewed (by site) promptly			
16	Clinical laboratory reports documented for significance (signed and dated by Investigator within time)			
17	Clinically significant values reported as AEs			
18	Laboratory data correctly transcribed to CRF's if applicable			
Item No	**COMMENTS**			

SECTION 9: DRUG MANAGEMENT and ACCOUNTABILITY				
Item No.	***All deviations must be documented***	Yes	No	NA
1	Randomisation procedures followed			
2	Blinding maintained, if applicable			
3	Emergency treatment unblinding code securely stored			
4	Emergency treatment unblinding code intact			
5	Treatment allocation in correct sequence, if applicable			
6	Dosing instructions followed			
7	Receipt, use & return of study drug controlled & documented			
8	Storage requirements of study drug adequate*			
9	Accountability of study drug reviewed			
10	Expiry dates of study drug acceptable			
11	Quantity of study drug remains adequate			
	* If there is any concern that the study drug has not been stored properly (e.g., inappropriate exposure to temperature, light, etc.) since the last visit or there is no evidence of adequate storage since the last visit, the PI and Clinical Trial Monitor must be notified immediately.			
Item No	**COMMENTS**			

SECTION 10: MAINTENANCE OF STUDY FILE

Visit Date: **Short Title:** AvecNet: Interim Monitoring Visit

Item No.	***All deviations must be documented***	Yes	No	NA
1	Investigator file reviewed			
2	Indexing/organisation of file acceptable			
3	Security of file acceptable			
4	Documents missing (if yes, provide list)			
5	New documents retrieved (other than CRF's)			
Item No	**COMMENTS**			

SECTION 11: ACTION ITEMS FROM CURRENT VISIT		
Item No.		**Responsible person**

SECTION 12: NEXT STEPS		
Item No.		**Responsible person**

SECTION 13: NARRATIVES AND SUMMARY OF INTERIM MONITORING VISIT	
Item No.	

PREPARED BY:		
PRINT NAME	SIGNATURE	DATE
REVIEWED BY:		
PRINT NAME	SIGNATURE	DATE

Visit Date: **Short Title:** AvecNet: Close-out Monitoring Visit

CLOSE-OUT MONITORING VISIT REPORT

PROJECT CODE / SCC NUMBER	**OTHER NUMBER(S)**
TRIAL TITLE	
PRINCIPAL INVESTIGATOR(S) / CENTRE	**SPONSOR**
INVESTIGATIONAL PRODUCT(S)	**INDICATION**

Monitor	**Visit date / #**	**Attendees (Name and Title)**

SECTION 1: STUDY RECRUITMENT / STATUS SUMMARY		
Item No.	***Timelines & Recruitment***	***Date***
1	Previous visit	
2	Last drug supply	
3	Projected enrolment	
4	Actual enrolment	
5	Projected LSLV	
6	Actual LSLV	
7	Database locked	
		No. of Subjects
8	Projected enrolment	
9	Actual enrolment	
Item No.	**COMMENTS**	

Abbreviations
LSLV = Last subject last visit; SAE = Serious Adverse Event; SD = Source Document; c/s =clinically significant; EOS = End of Study; OI=Outstanding Issue; CTSM = Clinical Trials Support Manager;

SECTION 2: OUTSTANDING ISSUES					
Section	Item No.		Yes	No	NA
		Were any action items identified for follow-up in the previous visit report			
		If yes, please list and indicate current status			

Visit Date: **Short Title:** AvecNet: Close-out Monitoring Visit

SECTION 3: GENERAL ITEMS				
Item No.	***The following items were reviewed / discussed at the visit:***	Yes	No	NA
1	All original CRFs including reactogenicity/diary cards in-house			
Comment				
2	All applicable source data are filed			
Comments				
3	All participants have given Informed consent prior to study participation			
Comments				
4	All data queries resolved			
Comment				
5	Any protocol deviations or waivers generated			
Comment				
6	Investigational product accountability complete			
Comment				
7	Instructions given on disposal of returning of investigational products and other supplies			
Comment				
8	Study file is complete and current			
Comment				
9	All lab samples archived / shipped according to protocol			
Comments				
10	Record retention requirements reviewed and arrangements made			
Comment	Name and location of storage facility:			
	GENERAL COMMENTS			

SECTION 4: Documents / Materials				
Item No.	***The following items were retrieved / retrieval reviewed***	Yes	No	NA
1	Copy of the authorised study staff log			
2	Copy of the investigational products accountability and dispensing logs			
3	Copy of the subjects screening log			
4	Original and signed CRFs			
5	Other			
	If yes please list below			
Item No	**COMMENTS**			

Visit Date: **Short Title:** AvecNet: Close-out Monitoring Visit

SECTION 5: ACTION ITEMS FROM CURRENT VISIT		
Item No.		**Responsible person**

SECTION 6: NARRATIVES AND SUMMARY OF CLOSE-OUT VISIT	
Item No.	

PREPARED BY:		
PRINT NAME	SIGNATURE	DATE
REVIEWED BY:		
PRINT NAME	SIGNATURE	DATE