

NATIONAL DRUG AUTHORITY

GUIDELINES FOR THE CONDUCT OF ECTOPARASITICIDES FIELD TRIALS IN UGANDA



THE REPUBLIC OF UGANDA

GUIDELINES
FOR THE CONDUCT OF ECTOPARASITICIDE FIELD TRIALS
IN UGANDA

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ABBREVIATIONS

NDA	National Drug Authority
FTA	Field Trial Application
PI	Principal Investigator
UNCST	Uganda National Council for Science and Technology
IRC	Institutional Review Committee
CLHE	Commissioner Livestock Health and Entomology
MAAIF	Ministry of Agriculture Animal Industry and Fisheries
SAEs	Suspected Adverse Events
GMP	Good Manufacturing Practice
RO	Research Organisation
ARO	Agricultural Research Organisation
FAO	Food and Agricultural Organisation
OIE	Office International des - Epizootices
GLP	Good Laboratory Practice
GCP	Good Clinical Practice
CoA	Certificate of Analysis
BP	British Pharmacopoeia
USP	United States Pharmacopoeia

GLOSSARY

Adverse drug reaction (abbreviated **ADR**) or **Adverse Drug Event** (abbreviated **ADE**) is an expression that describes the unwanted, negative consequences associated with the use of given ectoparasiticide.

Adverse event (AE) is any untoward change in health or "side-effect" that occurs in an animal used in a field trial while receiving the treatment (field trial ectoparasiticide, application device, etc.) or within a pre-specified period of time after the treatment has been completed.

Ectoparasiticide: An agent that is applied directly to the host to kill ectoparasites i.e. ticks, mites, lice, fleas, tsetse flies, biting and nuisance flies.

Efficacy: is used to express the extent to which a drug works under ideal circumstances i.e. in field trials and a laboratory study

Field Trial Protocol: is a document that describes the objective(s), design, methodology, statistical considerations, and organization of a field trial.

Guideline: is any document that aims to streamline particular processes according to a set routine.

Principal investigator (PI): is an individual who is qualified by training and has experience as an appropriate expert who conducts a research study, and where appropriate, under whose immediate direction the investigational agent is administered or dispensed. When a team of individuals conducts an investigation, the responsible leader of the team will be the Principal Investigator.

Sponsor: derived from the Latin sponsor (pl. sponsores), word meaning guarantor.

INTRODUCTION

NDA regulates issues related to safety, quality, efficacy, handling and use of pharmaceutical and other medical products in Uganda. It is required that all medicines used in Uganda are registered with the National Drug Authority (NDA) sec 35, and any field study using registered or unregistered medicine must receive written approval from NDA for that purpose.

Guidelines outlined in this document are drawn in accordance with the legal requirements of the National Drug Policy and Authority Act Cap. 206. Part IV, section 40.

National Drug Policy and Authority Act 2000 Edition, Chapter 206 states that with respect to clinical trials:

- (1) The authority may issue a certificate to any person for the purpose of carrying out clinical trials in respect of a drug (in this case ectoparasiticides) that may be specified in the certificate.
- (2) No person may carry out any field trial in respect of any drug (in this case ectoparasiticides) unless he / she is in possession of a certificate issued under Sec 40 Subsection (1).

The guidelines set out the procedures that should be followed by applicants who wish to conduct field trials (in this case ectoparasiticides field trials) in Uganda and the steps that NDA will take to review, evaluate and permit the conduct of such studies.

This guideline gives minimum requirements on how to conduct ectoparasiticides field trials, to establish the efficacy and safety of products used in animals against ectoparasites of veterinary importance. This includes ectoparasites that may or not need animals' involvement to complete their life cycle and these include ticks, tsetse flies, mites, lice, nuisance and biting flies.

This document gives guidance on the nature and extent of the efficacy data required to gain commercial / pre - registration approval of Ectoparasiticides in Uganda.

All field trials shall be conducted using the final formulation intended for marketing in Uganda.

All ectoparasiticides registered for use in Uganda shall be retested under field conditions for efficacy and safety every after 5years

NDA reserves the right to amend any part of the guidelines whenever it deems fit

CHAPTER ONE

1. PROCEDURE FOR SUBMISSION OF APPLICATIONS

1.1 Where to Apply

The application to conduct a field trial in Uganda should be submitted to:

The Executive Secretary/Registrar
National Drug Authority
P.O. BOX 23096
KAMPALA, UGANDA
Secretariat Office, Plot 46 – 48 Lumumba Avenue
Telephone: (+256) 41-255665/347391/347392
Fax: (+256) 41-255758/343921
E-mail: ndaug@nda.or.ug

1.2 Who can apply?

Any individual, company / institution or their representative with a permanent address in Uganda will be legible to apply. The names, physical address, telephone number, fax number, and e – mail address of the applicant shall be given.

1.3 Application Fee

Every application for conducting a field trial shall be accompanied with a non-refundable application fee. The fee shall be paid in the form of cheques, bank draft, or electronic transfer in favor of National Drug Authority in US\$ or the equivalent in Uganda currency.

NB. The Board shall from time to time determine the fee for approval for the conduct of a field trial in Uganda

1.4 The Field Trials Application Form (FTA)

- Application for authorization of the conduct of a field trial shall be made on prescribed forms which are available at the NDA Secretariat Head Office or on the NDA website (www.nda.or.ug)
- Only one copy of completed form shall be submitted for each application.
- The application should be submitted in writing, in the format and numbering set out in the field Trial Application Form [Attachment 4]. The text and diagrams must be clear and legible (12 pt Times New Roman font).
- The information requested in the application form should be submitted, but in full, to enable quick review of studies. However each

section should be cross-referenced to the detail in the Trial Protocol, Investigators Brochure, and other appended documentation.

1.5 Presentation of the Application

The application should be bound in a single volume (or series of volumes) and the pages of the FTA numbered sequentially. The appended documents should be bound together with the application, with tabbed sections identifying each appended document.

1.6 Supporting documentations

Complete, legible copies of key (peer reviewed) publications supporting the information in the application should be attached. They should be cross-referenced from within the FTA text. Additional data will be requested as and when necessary.

1.7 Electronic format

The Protocol, Investigators Brochure, and Reference Publications should also be supplied on appropriate data storage device. Microsoft -word version 7 is an acceptable format, as well as Acrobat PDF files.

1.8 Language

Application for Field Trial Licence must be in English. All other data, particulars supporting documentations, labels and package inserts must also be in English.

When supporting documentation is not originally in English, a copy of the document in its original language, accompanied by authenticated translation in English shall be submitted.

1.9 Confidentiality

NDA commits to maintain the confidentiality of any information submitted as part of a field trial application, supporting documents or associated correspondence. A separate, trial-specific, confidentiality agreement with the applicant may be entered into prior to an application, if the applicant desires this.

2. PROCEDURES FOR REVIEW AND APPROVAL OF APPLICATIONS

2.1 Completeness of application

On receipt, NDA will vet the application for completeness. The application shall be complete if it includes; field trial fees, all necessary documentations,(appendices, attachments, one copy of a complete checklist etc).

NB. Data from any source will be considered provided they are valid and relevant to the application. This data should represent nationally / internationally acceptable standards.

Receiving here means acknowledging that the said documents are complete and NDA reference number has been allocated to the document.

2.2 Application Reference Number

When an application is received, an acknowledgement of receipt will be issued with a reference number for each application. This reference number must be stated in all correspondence concerning the application.

2.3 Supplementary Information and Updates

Any new information available for the product such as adverse effects, changes in formulation or manufacturer for the active ingredients or finished products must be reported to NDA. If changes such as, animal owner consent form, updates and additional trial sites are made, NDA must be immediately informed. NDA may request for further supplementary data or documentation when appropriate.

In case additional quantity of study investigation product(s), additional trial site(s), additional new product, additional manufacturing site/re-packer, additional port of entry, and change of applicant, extension of product's shelf life or a new protocol is required. A new FTA must be made where the Sponsor/PI will need to fill in the relevant section where changes applied.

2.4 Expert review

2.4.1 The application will be reviewed by experts appointed by NDA. There is a confidentiality agreement with the reviewers to ensure that the content of the application remains confidential.

2.4.2 The initial review may result in queries that need to be answered by the applicant. The reviewers will not have direct contact with the applicant and all correspondence should be directed through NDA.

2.4.3 The reviewers will generate a report that will be discussed by the Veterinary Medicines Committee of NDA for recommendation to the Clinical Trials Committee (CTC) of NDA for adoption.

2.5 Approval

2.5.1 NDA will consider the recommendation(s) of Veterinary Medicines committee (VMC), Clinical Trials Committee (CTC), and decisions of the Institutional Review Committee (IRC).

2.5.2 For NDA to approve any field trial application, approval from IRC and registration with UNCST are a pre-requisite.

NDA reserves the right to offer final approval for drug related field trials. It is acceptable to NDA that parallel submissions are made to NDA and UNCST by the applicant. It is important that queries and amendments required by either body are conveyed to each body for information

2.5.3 NDA may approve the trial application or may reject the application and specify the reasons for rejection.

2.5.4 The decision made shall be communicated to the applicant in writing.

In case of rejection, the applicant may appeal and provide additional information where applicable.

2.6 Post-trial review

The final Report from each field trial conducted in Uganda shall be submitted to NDA. The format of the report shall be as per the protocol used in the trial.

3. The Institutional Review Committee (IRC)

This shall be an independent body, constituted by the Commissioner Livestock Health and Entomology (CLHE) of Ministry of Agriculture Animal Industry and Fisheries (MAAIF) in consultation with Uganda National Council for Science and Technology (UNCST) whose responsibility shall be to verify that, the safety, integrity, rights and welfare of animals used in a particular trial are protected. The IRC should be constituted and operated so that the suitability of the investigators, facilities, protocols, and the eligibility of trial animal groups shall be objectively and impartially reviewed independently of the investigator, sponsor, and relevant authorities.

4. MONITORING OF FIELD TRIALS BY NATIONAL DRUG AUTHORITY

Inspection of Field trial site shall be conducted by NDA. The responsible officer of the regulatory authority may contact the PI or Sponsor for the date of inspection when required

- Such inspections shall be before commencement of the trial, or at predetermined intervals, or shall be at the request of the Veterinary Medicines Committee, responsible for Field trial review.
- However, in the case of complaints or reports of unexpected adverse reactions, inspections shall take place at short notice and may be unannounced.

The monitoring will include - but not be limited to:

- Inspection of facilities used in the trial
- Monitoring of staff conducting the trial
- Compliance with the approved Protocol
- Verifying that accurate, complete and current records according to the Protocol are kept at the field trial sites at all times.
- Verifying that Suspected Adverse Events are reported as required by the Protocol
- Verifying that external inspections intended to monitor and audit the trial are conducted as required by the Protocol and that reports are available.

5. REPORTS AND FINAL REVIEW

5.1 Reports of Suspected Adverse Events

The Principal Investigator (PI) shall report to the IRC, Sponsor and NDA all Suspected Adverse Events (SAEs), both expected or unexpected, as soon as possible but not later than seven (7) calendar days upon receiving notice of such events.

Additional follow up information shall be made available to NDA as soon as possible, but in any case not later than fifteen (15) calendar days.

5.2 Progress and Final Trial Reports

In the case of trials lasting for more than 6 months, an interim report (refer to Attachment 6) shall be submitted at 6 months' intervals or as shall be requested by NDA. The interim report shall include the number of animals so far treated, number and type of suspected Adverse Events (SAEs) reported, number of discontinued animals and the reason for discontinuation.

The PI or Sponsor shall submit an end of Study Summary Report pertaining to all the sites conducting the trial to NDA, within 3 months from the completion of the trial.

SAEs occurring in other countries under the same study shall be reported to NDA promptly.

5.3 Product Accountability and Disposal

Product Accountability/Disposal report shall be submitted to NDA within 3 months from completion of the trial. The report shall include:

- Date the trial started and ended
- Field trial license number
- Field Trial Certificate for the relevant site.
- Date(s) and quantity received for each trial product
- Balance of the trial product
- Product Destruction Certificate, and/or written evidence of re-export of the unused product supplies to the country of origin (whichever will be applicable).

5.4 Archiving

It is the responsibility of the Investigator and the Sponsor to archive and ensure the safety of all the documents related to the trial. The licence holder/applicant shall inform NDA in writing prior to destroying the documents. Documents shall be retained for a minimum period of 10 years.

6. RETRIAL OF ECTOPARASITICIDES ON MARKET

NDA recommends that all Ectoparasiticides on Uganda market be retied every after five years to ascertain their efficacy.

CHAPTER TWO

2. GUIDELINES FOR APPLICATION FOR THE FIELD TRIAL OF ECTOPARASITICIDE LICENSE

The approval for importation or manufacture of field trial related investigational products is dependent on the approval of the field trial.

2.1 PRODUCTS THAT REQUIRE FIELD TRIAL LICENCE

Prior to importation/manufacturing of ectoparasiticide product, the Principal Investigator or Sponsor is required to apply for Field Trial License from NDA.

2.1.1 Imports

Products including placebo, which are not registered with NDA and are intended to be imported for purpose of field trial must have a Field Trial Licence.

A product with a marketing authorization (registered product) when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use in a field trial also requires a Field Trial License.

2.1.2 Manufacture

An ectoparasiticide manufactured for a purpose of a field trial requires a Field Trial Licence.

2.2 PROCEDURES FOR APPLICATION FOR FIELD TRIAL LICENSE

2.2.1 Who can apply for Field Trial Licence?

Application for Field Trial License for a particular product shall be made by any Principal Investigator (PI) or an authorized person from a locally incorporated pharmaceutical company (Sponsor), Institution with a permanent address in Uganda who intends to import/manufacture the product for the purpose of a field trial.

The holder of a Field Trial Licence for a particular product need not necessarily conduct the field trial himself or herself.

2.2.2 Responsibilities of the Applicant

- a) The applicant shall be responsible for the product and all information supplied in support of his/her application for Field Trial Licence of his/her product. He/she shall be responsible for updating any information relevant to the product/application.
- b) In cases where the applicant is not the manufacturer and where secrecy considerations prevent disclosure of certain information to the applicant, such information may be furnished to NDA through the applicant in a sealed envelope marked CONFIDENTIAL.
- c) The Sponsor should not supply an investigational product until all the required documentation has been obtained (e.g. approval from the appropriate IRC and regulatory authority (ies)).
- d) The Sponsor should ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s), is manufactured in accordance with any applicable GMP and is coded and labeled in a manner that protects blinding, if applicable.
- e) The Sponsor should state the investigational product(s) acceptable storage conditions (e.g. temperature, protection from light), shelf life, indications and contra indications, reconstitution fluids and procedures, and devices for product application.
- f) The Sponsor should:
 - Ensure timely delivery of investigational product(s) to the investigator(s),
 - Maintain records that document shipment, receipt, disposition, return and destruction of the investigational product(s),
 - Maintain a system for retrieving investigational product(s) and documenting this retrieval (e.g. for deficient product recall, reclaim after trial completion, expired product reclaim),
 - Maintain a system for the disposal of unused investigational product(s) and document the process,
 - Ensure that investigational product(s) are stable over the period of use. This stability data should be available on request and for monitoring purposes. If non-compliance with the specifications becomes evident in the stability studies during the period of use in the field trial, the Sponsor shall notify the Investigators and arrange to take appropriate steps;
 - Maintain sufficient quantities of the investigational product(s) used in the trial to reconfirm specifications, should this become necessary, and maintain records of batch sample analyses and

characteristics. To the extent stability permits, samples should be retained either until the analyses of the trial data are complete or as required by the applicable regulatory requirement(s), whichever represents the longer retention period.

- g) If a Sponsor or a PI decides to use a service of a Research Organisation (RO) for the conduct of a field trial, a letter of agreement should be submitted to NDA.
- h) Any person who knowingly supplies any false or misleading information in connection with his application for Field Trial License commits an offence under section 60 of the National Drug Policy and Authority Act.

2.3 CONDITIONS FOR THE FIELD TRIAL LICENCE

2.3.1 Endorsement of Field Trial License

- The License holder shall submit to NDA a copy of endorsed Field Trial License and/or evidence of delivery to the approved investigator(s)/trial sites on importation and supply of each consignment of the product.
- The product shall only be supplied to the investigator(s) at the trial sites named in the application for the Field Trial License for the purpose and use as stated in the said application. No change in investigator(s), trial sites or trial protocol shall be made without notification to NDA.
- The license holder shall ensure that adequate precautions are taken for all product(s), such as storage in a securely locked cabinet, access to which is limited, to prevent theft or illegal distribution.
- The license holder shall ensure that all the trial products(s) are applied only to animals involved in the said trial.

2.3.2 Notification of Change of Information to NDA

The license holder shall inform NDA of any change in information, or any information received by him/her that casts doubt on the continued validity of the data, which was submitted with, or in connection with the application for the Field Trial License.

2.3.3 Discontinuation of Trial

The license holder shall inform NDA of any decision to discontinue the trial to which the license relates and shall state the reason for the

decision. The licence holder should return the Field Trial License to NDA as soon as possible.

2.4 IMPORTATION AND RELEASE OF INVESTIGATIONAL PRODUCT

Shipping of investigational products shall be conducted according to instructions given by or on behalf of the Sponsor in the shipping order.

A pre-clearance inspection shall be carried out at the port of entry by NDA. This shall include the shipping documentation and overall physical condition of the consignment.

If specific storage conditions are essential to ensure the quality of the product, a device that will confirm that storage temperatures are not exceeded during transport should be included with the shipment.

2.5 DOCUMENTATION FOR INVESTIGATIONAL PRODUCT RELEASE

Documentation that should accompany each consignment of Investigational product should enable the NDA inspector at the port of entry to release the product to the investigator(s) responsible for conducting the field trial in the country.

This documentation should include at least:

- The Certificate of Analysis of each batch of the investigational product(s) as well as comparator(s), if relevant.
- A copy of the letter of approval of field trial.
- A copy of a valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin where applicable.

The Cover Sheet should be completed by the Sponsor and should accompany each consignment of investigational products. **See Annex 1**
The Check-list may be used by the Sponsor to ensure that the required documents are attached and correct. **See Annex 2**

NOTES ON THE APPENDICES

- This section comprises recommended formats for some of the Appendices.
- Failure to enclose necessary details and supporting documents may result in delay in the processing, or rejection of an application.
- Headings set out for each Appendix are minimum general requirements. These may not be applicable in all circumstances, neither are they exhaustive.
- Interpretation of these guidelines should be flexible and related to the proposed use of the product.
- Where a heading is not applicable or information is not available, indicate clearly in the appropriate section.
- Data in addition to those specified in the guidelines may be submitted to support the application for the field trial import licence. Such data must be presented in a well compiled manner as additional appendices, with a summary of the particulars.
- These guidelines do not preclude any other information required by NDA. Such additional information should be supplied to NDA on request.

ATTACHMENT 1: FORMAT FOR FIELD TRIAL PROTOCOL

When designing study protocols, the mode of action exhibited by the active substances e.g. killing, repellent, anti-feeding, as well as the life cycle of the parasite e.g. length, seasonality; parasitic stages should be taken into account,

N.B: The protocol should contain the following particulars, where applicable:

1. Name and Particulars of the Product

- State the name or code number under which the product will be imported and known during the trial. A separate application is required for each trial
- State clearly also the Proprietary name, Approved / INN / generic name, Strength / dosage form, Pharmaceutical form, Description, Labeling, include also information leaflet of the product.

2. Details of the manufacturer

2.1 Name of the manufacturer

2.2 Physical address

2.3 Postal address, telephone, Fax, email and website

2.4 Country of origin

3. Identification of the Trial

- a) Title of the Trial
- b) Version

4. Aim of the Trial

- a) State the objective(s)
- b) Rationale of trial.

5. Trial sites

- 5.1 At least two sites in two different geographical zones should be considered.

6. Tentative trial dates

NB: The trial should be conducted for a continuous period of six months to cater for the two seasons i.e. wet and dry seasons in Uganda.

6.1 Trial initiation

6.2 Trial completion

7. Investigator(s)

- 7.1 Name(s)
- 7.2 Curriculum Vitae and attached testimonials
- 7.3 Address
- 7.4 Telephone number(s)
- 7.5 Email(s)/Fax

8. Sponsor

- 8.1 Name(s)
- 8.2 Address
- 8.3 Telephone numbers, email, Fax

9. Trial animals

- 9.1 Species
- 9.2 Identification number of animal
- 9.3 Number of animals involved in the trial
- 9.4 Sex
- 9.5 Age
- 9.6 Weight

10. Husbandry

Complete description of management systems

11. Description of the trial

Animals should be infested with suitable numbers of parasites. The adequacy of infestation should be addressed in the statistical, parasitological and clinical relevance of the level of infestation. For a trial to be considered valid, parasites should be recovered from at least 80% of the negative control animals at each post-treatment observation.

Untreated control groups should be used provided there are no serious welfare implications of the disease.

- a) Trial design (e.g. randomised controlled trial, open- label parallel group, cross-over technique)
- b) Criteria for inclusion of potential trial animals and exclusion of some
- c) Group allocation
- d) Treatment procedure including other treatments these animals will receive during the study irrespective whether there is interaction with the product under investigation.
- e) Sample size: Statistically adequate numbers of treated and control animals should be included in each trial in order to achieve the trial objective(s) based on statistical consideration (sufficient to allow dropout, variability of effect etc).

- f) The applicant is required to justify the group size and it is recommended to seek the advice of a statistician.
- g) Ectoparasite count according to stages of engorgement and species should be indicated.

NB. An appropriate method should be described to fit this purpose. Ticks should be removed from test animals after each counting.

12. Efficacy testing

Methods used for the assessment of efficacy should be relevant for the parasite species involved and for the level of efficacy to be demonstrated. Although methods assume equal distribution and availability of active substance over the entire body, concentrations of active substance on different body sites can vary considerably, e.g. due to formulation used or the way treatment was performed. This should be taken into account.

Products with repellent or acaricidal products may demonstrate short term {up to 4 weeks} or long term {more than 4 weeks} persistent effects. Efficacy should be established at intervals throughout the period of effect claimed. The applicant should justify the methods used for the assessment of efficacy.

13. Efficacy calculations

A description of the method used to calculate efficacy of the product shall be provided.

14. Test facilities, equipment, and materials

There should be;

- a) In case of large animals, there should be adequate pasture for continued exposure to re-infestation.
- b) Suitable handling facilities for handling the animals during ectoparasiticide counts.
- c) Suitable equipment and measuring containers for accurate measurements and application of the trial formulation as well as that of the positive control formulation.
- d) Protective clothing, appropriate to the type of formulation under test.

15. Suspected Adverse events

- a) Methods of recording and reporting suspected adverse events/reactions should be in place.
- b) Provisions for dealing with complications for example anti dots.

16. Evaluation of results

- a. A description of data management procedures should be provided.
- b. Statistical methods and considerations. Any statistical significant difference between the treated and the control group should always be interpreted in terms of biological and clinical significance.

c. Participants withdrawn from the trial should be indicated and the reasons for withdrawal should be indicated.

17. Compensation of owner

A statement about compensation of animal owner should be included in case of death and injury of trial animals as a result of the trial. For parasitic infestations that create skin lesions, it is also useful to record the site and size of the lesions at the beginning and end of the trial.

18. Environment Impact Assessment (EIA)

Proof of an EIA study should be submitted at the end of the study.

ATTACHMENT 2: GUIDE FOR LABELLING FIELD TRIAL PRODUCT*Outer/carton labels & Unit Pack*

The following information should be presented on the labelling of the product for field trial:

<i>Parameters</i>	<i>Outer/carton labels</i>	<i>Unit Pack</i>
Study No./Protocol	√	√
Group code	√	√
Product Name/Code	√	√
Dosage Form	√**	√**
Name of Active Substance(s)	√**	√**
Strength of Active Substance(s)	√**	√**
Dilution for different species	√	√
Batch Number	√**	√**
Manufacturing date/retest Date	√	√
Expiry Date	√	√
For Field Trial Use Only	√	√
Name and address of manufacturer/final release/Product Owner(corporate address)/sponsor	√***	√***
Route of administration	√	√
Storage Conditions	√	√
Pack Sizes (unit/Vol)	√	√

** Where applicable

*** With letter of authorization

If the product is supplied without an outer carton, the information that is required on the outer carton should be stated on the inner carton

ATTACHMENT 3: LETTER OF AUTHORIZATION FROM MANUFACTURER

Date:
(Company's Name)

A company operating under the laws of, located in,
Local company name and address

Tel No:
Fax No:.....
E-mail:

To represent us in Uganda for the application of the Field Trial Licence
for:
Protocol No :
Release Date:

.....(The local company's
name and address) is authorized to be the Field Trial Licence Holder and
will be responsible for all matters pertaining to the Field Trial Licence
application for the above mentioned study protocol.

Yours faithfully.

.....
Authorized name & signature

ATTACHMENT 4: THE FIELD TRIAL APPLICATION FORM (FTA)

FTA Section 1. Identification of the Field Trial

- 1.1 Title of the Study
- 1.2 Protocol number, date, version:
- 1.3 Contact Person and contact details
- 1.4 [Space for NDA Reference Number]
- 1.5 Declaration of Intent signed by the Principal Investigator

We, the undersigned have submitted all the required documentation and have disclosed all the information required for approval of this application.
 We have read the Protocol and the Investigators brochure, appended.
 We have the authority and responsibility to oversee this field trial, and agree to ensure that the trial will be conducted according to the Protocol and all legal, ethical and regulatory requirements in Uganda.
 Applicant (Local Contact): NAME Date:
 Signature:
 Designation
 Principal Investigator: NAME Date:
 Signature:
 Designation

FTA Section 2. Basic Administrative Data on the Application

- 2.1 Name and address of the registered office of the Applicant

Particulars	Sponsor	Manufacturer	Applicant
Name			
Physical Address			
Postal Address			
Telephone Number/s			
Email			
Fax			

FTA Section 3. Products to be used in the Field Trial

- 3.1 Investigational products
 - 3.1.1 Identifier or name of investigational products (code if applicable)
 - 3.1.2 Registration number
 - 3.1.3 Manufacturer/s (Include all sites)
 - 3.1.4 Active ingredient, complete composition, potency and presentation
 - 3.1.5 Evidence of manufacture under conditions compliant with current codes of Good Manufacturing Practice

See Attachment 3 for details of the required information.

3.1.6 Release Specifications and tests. Include Certificate of Analysis.

3.1.7 Current approved Package Insert if available.

3.2 Comparator, Concomitant and Rescue medications (antidotes) and Placebo

3.2.1 Proprietary name and INN

3.2.2 Active ingredient/s, composition, and presentation

3.2.3 Registration number/s (country)

3.2.4 Approved Package inserts to be appended to application.

3.2.5 Evidence that Placebo is manufactured under GMP.

3.3 Details of handling field Trial products.

3.3.1 Shipping, delivery and distribution of field trial products.

3.3.2 Details of storage requirements and arrangements where necessary and monitoring during distribution.

3.3.3 Details of dispensing field trial products and waste disposal procedures.

3.3.4 Packaging and Labeling of the trial products

3.4 Estimates of quantities of each product to be used for the field trial, and for which an import permit is needed.

FTA Section 4. Sites & Investigators

4.1 National Principal Investigator or coordinator (Responsible person)

Name	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests	

4.2 For each Site list the following:

4.2.1 Site Identifier (Name)

Physical Address: (include GPS coordinates)

Telephone & Fax numbers

E-mail address

4.2.2 Description of the site facilities & Staff

- Infrastructures on the farm
- Facilities for special examinations (if required)
- Capacity to collect, prepare, store and transport field samples
- Storage and handling facilities for the field trial products.
- Name and qualifications of person with responsibility for dispensing field trial products.

4.3 Site Principal Investigator

Name	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests	

4.4 Site Sub-investigators and trial-specific support staff

Name:	
Qualifications	
Contact Details	
Physical address	
Declaration of Capacity & Interests	

4.5 For Animal farm Sites

- Responsible Administrator / Farmer
- Contact Details
- Append Signed Letter of Agreement for field Trial to take place.

4.6 Append Signed Agreement/s between the Investigators and the Sponsor/s and/or Field Research Organization. (Appendix 13)

FTA Section 5. Trial Animals

5.1 Numbers of animals as stipulated in the table below

Number of field trial sites	
Total number of animals to be enrolled in all sites	
Intended numbers of animals at each site – evidence of availability	

5.2 Duration

5.2.1 Estimated trial duration: Date initiated to End

5.3 What is the intended compensation incase of loss or injury to the animals in the trial?

NB. This will be after confirmation that the loss or injury of was due to the field trial product.

FTA Section 6. History of Previous and in-progress trials

6.1 List the titles of previous trials with this (or similar) field trial product in Uganda

6.2 List the titles of previous trials with this (or similar) field trial product in other countries

- 6.3 Append Interim or Final report-summaries of these trials to this application. (This may be in the Investigators Brochure.
- 6.4 Include a letter or certificate from the regulatory authorities in countries where previous trials have been undertaken (including those in-progress) that these trials have been GCP compliant.

FTA Section 7. Institutional Review Committee

- 7.1 Provide the local IRC approval of the Protocol for each site.
- 7.2 Will GCP training be provided for local staff and investigators?

FTA Section 8. Field Trial monitoring and reports

- 8.1 Describe the Safety and Monitoring Plan for each site.
- 8.2 Describe the system to be used to detect, record, assign causality and the actions for adverse events.
- 8.3 Describe the actions to be taken following reports of Suspected Adverse Events.
Cross-reference to detail in the Investigator's Brochure.
- 8.4 When will Interim Reports be submitted?
- 8.5 Final Report - Estimated due-date?

FTA Section 9. Insurance

- 9.1 Provide a copy of the current insurance certificate.
- 9.2 Provide evidence that each member of the Investigator team is covered by relevant Malpractice insurance for this trial

FTA Section 10. Description of the Trial

- 10.1 Is the Title of the Trial fully descriptive?
- 10.2 Summarized Rationale for this Field Trial, including relevance to Uganda
- 10.3 Brief Background information should include:
 - The problem statement and the justification of the field trial
 - Properties of the field trial product- hypothesis for action
 - Description of risks of the protocol and the potential harms of the field trial product.
 - Pre-field animal toxicology test results in-animals and in-vitro that establishes probable safety and efficacy in animals.
 - Prior Field trial report summaries that establishes probable safety and efficacy in animals.
 - Include evidence that the formulations used in the pre-field and previous trials are identical to that in this application. Any variations should be highlighted and justified. *
 - Published reviews or reports relevant to indicated ectoparasites and this type of product

- 10.4 Objectives of this trial (List as Primary and Secondary objectives and provide justification)
- 10.5 Trial Design: Describe and justify each component.

Randomization and blinding

Other details –

- 10.5.1 Animals involved in the Trial
 - Eligibility
 - Inclusion criteria - list and justify each
 - Exclusion criteria - list and justify each
- 10.5.2 Treatment regimens for each group.
- 10.5.3 Follow-up, sampling collection and monitoring plans; immediate monitoring - intermediate monitoring - long term monitoring.
 - Telephone access to investigators

10.6 Outcomes Measurements and Analysis

- 10.6.1 Describe each outcome/variable (including safety) and explain or justify
- 10.6.2 Describe the samples that will be collected and the analyses to be conducted on each sample
- 10.6.3 Provide evidence that the Laboratories that will conduct the Safety screening, and the End-point assays are accredited and competent to do the assays. (where applicable)
- 10.6.4 Describe the intended statistical analysis to be conducted. Provide evidence that the study is powered to provide the intended outcome.
- 10.7 Are any Sub-studies intended? Provide full details.
- 10.8 Will field samples be stored for any period beyond the duration of this trial?
 - 10.8.1 What is the purpose of such archiving?
 - 10.8.2 What controls are to be placed on their confidentiality and possible future use?
- 10.9 Informed Consent from animal owners (ICON)
 - 10.9.1 Append a copy of ICON.
 - 10.9.2 Are there separate ICON for sub-studies.

11 Publication Policy

Provide details of the Investigators and Sponsors intentions and freedom to publish the outcomes of this field trial

ATTACHMENT 5: FORMAT FOR DECLARATION BY INVESTIGATORS

Trial Protocol Number.
NAME:
Role in Trial
Trial Title:
Site: A current Curriculum Vitae is attached.

- 1 I am aware of the responsibilities of my role as in field trial number as required by the legal, ethical and regulatory requirements of Uganda.
- 2 I have read and understand the attached Protocol, Investigators Brochure and supporting documentation and I will comply with the procedures and requirements included in them.
- 3 I have read the attached Field Trial Application form as submitted to the National Drug Authority in Uganda and confirm that the information is complete, true and accurate, and conform to the Protocol and supporting documentation.
- 4 I will not commence with this trial before written authorization has been received from the Uganda National Drug Authority and the relevant Committee/s. I will provide the to NDA and other relevant bodies with reports as required.
- 5 I will obtain Informed consent from all animal owners participating in the field trial. I will ensure that every animal in the trial will be treated ethically
- 6 I DECLARE: I have no conflict of interest in terms of financial interests or personal relationships that may inappropriately influence my responsibilities and conduct of this field trial.
Initials:
- 7 I DECLARE: I have not previously been associated with any field study that has been terminated, or study-site that was closed, due to failure to comply with Good Field Practice.
Initials:.....

SIGNEDDATE

WITNESS:.....NAMEDATE

**ATTACHMENT 6: FORMAT FOR FIELD STUDY REPORTS
ICH TOPIC E3, STRUCTURE & CONTENT OF FIELD STUDY REPORTS
(CPMP/ICH/137/95)**

1. Title Page
2. Synopsis
3. Table of contents For the Individual Field Study Report
4. List of Abbreviations and Definition of Terms
5. Ethics
6. Investigators and Study Administrative Structure
7. Introduction
8. Study Objectives
9. Investigation Plans
10. Trial animals
11. Efficacy Evaluation
12. Safety Evaluation
13. Discussion and Overall Conclusion
14. Tables, Figures and Graphs referred to but not included in the text
15. Reference List
16. Appendices

**SAMPLE INTERIM/END OF STUDY SUMMARY REPORT
< Date>**

The Executive Secretary

National Drug Authority

Attention: Head, Drug Information Department

Dear < Insert Name>

INTERIM/END OF STUDY SUMMARY REPORT <Whichever applicable>

< Field Trial Protocol Title and Protocol Number>

<NDA Reference Number>

The following is a summary of the <Study title> trial conducted in <insert institution name>:

Number of animals screened: < **insert number**>

Number of animals Randomized: <**insert number**>

Number of animals discontinued: < **insert number**>

Reasons for discontinued: <**insert number**>

Reason for discontinuation: <**List of individual discontinued patient**>

Number of animals completed study: < **insert number**>

Number of Suspected Adverse Events SAE's: < **insert number**>

Number of Endpoints: <insert number if applicable, if not, to be removed>

Last batch of drug supplies collected back from site: < insert date>

Last batch of drug supplies sent back to < originating site> for destruction: <insert date>; if local destruction, attach copy of NDA destruction certificate.

List of any changes in trial personnel – including full CV and Declaration
List of Monitor and Audit reports to date.

ATTACHMENT 7: APPLICATION FOR FIELD TRIAL LICENCE

PRODUCT: REF:

Note: This is the recommended format for Appendix 2 for an individual drug.

Spacing should be adjusted by applicant as and when necessary.

Extension sheets for details and supporting documents should be appropriately numbered and referenced.

1. FINISHED PRODUCT

1.1 Description (physical characteristics):

1.2 Composition (Complete Formula)

1.2.1 Active Ingredient

Active Ingredient(s):	
Content	

1.2.2. Other Ingredients (adjuncts, excipients, preservative, colour, flavour, etc):

Name of Other Ingredient(s)	
Content	

1.3. Packing/Pack Size (brief):

2. MANUFACTURE OF PRODUCT

(Enclose in sealed envelope marked ‘**CONFIDENTIAL**’,

If desired.

If so indicate here, with appropriate reference).

2.1 Complete Batch Manufacturing Master Formula:

Name of Ingredients (Active and Otherwise)	
Quantities used per batch	

2.2 Manufacturing Process:

Brief Description and Principles.

3. QUALITY CONTROL

3.1 State whether quality control is done in part or solely by the manufacture’s own quality control department or an external laboratory.

- 3.2 If quality control tests are done by an external laboratory, state:
- i) name and address of the laboratory (where applicable)
 - ii) tests done by the external laboratory (where applicable)
 - iii) reasons why the tests are not done by the manufacturer;

3.3 Specifications for Ingredients, Active and Otherwise

Name of Ingredient	
Specifications	
Source (State Manufacturer's / packaging etc).	
Manufacturer & Country of Origin	

3.4 In- Process Quality Control:

Tests performed during manufacturing process and sampling protocols:

Tests	
Stage at which tests done	
Frequency of sampling	
Quality of sample taken each time	

3.5 Finished Product Quality Control:

Tests and Specification Limits (check and Release Specifications)

Test	
Acceptance Limits	
Release for test method and Limits(Manufacturers, etc)	

The Certificate of Analysis to be certified by Quality Assurance Manager.
 Certificate of Analysis of recent batch of product (**minimum 1 batch**) enclosed: []

4. STABILITY OF PRODUCT:

4.1 Storage condition must be included on the label.

4.2 Proposed shelf life of product:

N.B In the event that the extension of shelf life for field trial material is required, industry will provide supportive data to support the extension.

ANNEX 1: COVER SHEET (to be completed by the sponsor)

Fees (if applicable)
Trial Title
Protocol Number
Ectoparasiticide
Unique code number
NDA approval number of field trial
NDA reference number(s) of comparator drug(s) (if applicable)
NDA reference number(s) of concomitant drug(s) (if applicable)
Sponsor
Applicant
Trial sites
Sponsor Contact Person: Address Telephone number Fax number Cell number E-mail address
Batch number(s) and expiry date: Ectoparasiticide Comparator drug(s)
Quantities
Blinding done or not
Recommended storage temperature

ANNEX 2: CHECK-LIST of required documentation

To be supplied by the sponsor for use by the NDA inspector at the port of entry to authorize the importation of the investigational product.

IMPORTATION AND RELEASE OF INVESTIGATIONAL PRODUCTS			
CHECK-LIST of required documentation			
Are the following documents attached and correct, as indicated		YES	NO
1	Copy of NDA letter of approval of field trial		
2	Ectoparasiticide		
	Comparator (if applicable)		
3	Does the CoA reflect at least the following information:		
	Product name or code		
	Name of company / Sponsor		
	Batch number		
	Expiry date		
	Date of issue		
	Signature, qualification and title of responsible person		
	Results of physical and analytical tests		
4	Copy of valid Certificate of Manufacture issued by the competent Regulatory Authority in the country of origin		
5	Application Device (if applicable)		
6	Does the label clearly indicate Labeling: <i>outer packaging, immediate container</i>		
6.1	That the product is field trial material, e.g. "For use field in trial only"		
6.2	Product name or unique code (if blinded) <i>Does this concur with the information on the Cover Sheet</i>		
6.3	Storage temperature <i>Does this concur with the information on the Cover Sheet</i>		
6.4	Storage conditions (e.g. protection from light)		
6.5	Batch number <i>Does this concur with the information on the Cover Sheet</i>		
6.6	Date of Manufacture		
6.7	Expiry date		
	<i>Does this concur with the information on the Cover Sheet</i>		
6.8	Sponsor contact details		
	<i>Does this concur with the information on the Cover Sheet</i>		
7.0	Is the physical condition of the consignment acceptable		

ANNEX 3. CHECKLIST OF REQUIRED DOCUMENTS

Item	Requirement
Fees	Proof of payment
Materials transfer:	Applications for import and/or export of materials (if required)
FTA	Field Trial Application Form
APPENDIX 1:	Trial Protocol
APPENDIX 2:	Investigators Brochure
APPENDIX 3:	Animal owner Information Leaflet and Informed Consent Form
APPENDIX 4:	Certificate of GMP manufacture of the trial product or other evidence of manufacture quality, safety and consistency
APPENDIX 5:	Package Insert/s for other trial products.
APPENDIX 6:	Certificate of GMP manufacture of the placebo where applicable.
APPENDIX 7:	Evidence of accreditation of the designated Laboratories or other evidence of GLP and assay validation.
APPENDIX 8:	Insurance Certificate specific for the trial in consultation with NDA.
APPENDIX 9:	Signed and completed Declarations by all Investigators.
APPENDIX 10:	Approval of the Committees for the Protocol.
APPENDIX 11:	Full, legible copies of key, peer-reviewed published articles supporting the application.
APPENDIX 12:	Sample of the label for the imported products
APPENDIX 13:	Letter of authorization from the manufacturer/product owner
APPENDIX 14:	Pharmaceutical Data on dosage form and any other relevant information
APPENDIX 15:	Other supporting documents.

² Note:

Certificate of Good Manufacturing Practice (GMP) for the investigational product or statement on GMP from the manufacturer/re-packer (whichever is more relevant).

- *The GMP certificates or other documents must be issued by an authority recognised by NDA i.e. the authorities listed in the FAO/OIE certification Scheme On The Quality Of Pesticide Moving In International Commerce,*
- *Or the statement on GMP can be issued by the Quality Assurance Department where the product is manufactured.*
- *For local product, the manufacturing licence is required.*
- *For a comparator product, the following is required:*
 - i) *A GMP certificate*
 - ii) *If not available one of the following can be submitted:*
 - *Approval letter from the regulatory authority*
 - *Annual Registration of product Establishment*
 - *Package insert*
 - iii) *For a repacked product, a statement of GMP must be submitted by the re-packer.*

³*IRC approvals of study protocols should be submitted along with the FTA to NDA and should include: 3=Committee constituted by the CLHE of MAAIF*

- *Details of IRC membership*
- *A relevant minute of the meeting that approved the study protocol*
- *Any amendments to the trial protocol required by the IRC*
- *Any conditions included in the approval*
- *The final decision*