GUIDELINES FOR CONDUCTING EFFICACY FIELD TRIALS FOR ECTOPARASITICIDES IN DOMESTIC RUMINANTS IN THE EAST AFRICAN COMMUNITY

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Abbreviations

CoA	Certificate of Analysis
CP	Control Product
CRO	Contract Research Organization
CSG	Critical Study Group
EAC	East African Community
EFT	Efficacy Field Trial
ETAF	Ectoparasiticides Trial Format/Form
FAO	Food and Agriculture Organization
FSR	Final Study Report
GCLP	Good clinical and Laboratory Practices
GCP	Good Clinical Practices
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practices
IACUC	Institutional Animal Care and Use Committee
ICVP	Investigational and Control Veterinary Product
IVP	Investigational Veterinary Product
LTR	Local Technical Representative
MLs	Macrocyclic lactones
MRP	Mutual Recognition Procedure
PI	Principal Investigator
TWG	Technical Working Group
VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
WAAVP	World Association for the Advancement of Veterinary Parasitology
WHO	World Health Organization
WOAH	Word Organization for Animal Health

Definitions

1. Interpretation

In these guidelines, unless the context otherwise requires:

Act: means the applicable National laws that govern the use of ectoparasiticides in the EAC Partner State;

Adverse Reaction: means the unwanted, negative consequences associated with the use of given ectoparasiticides at manufacturer's recommended doses;

Adverse Event: means any untoward change in health or "side-effect" that occurs in an animal used in a trial while receiving the treatment (trial ectoparasiticides, application device, etc.) or within a pre-specified period of time after the treatment has been completed;

Applicant: means a sponsor or Contracted Research Organization (CRO) or authorized company with a permanent address in EAC Partner State and recognized by law.

Competent Authority: any organization that has the legally delegated or invested authority, capacity, or power to perform a designated function.

Regulatory Authority: means the institution responsible for ectoparasiticide registration/regulation;

Veterinary Ectoparasiticide: refers to 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: The extent to which an ectoparasiticide works in comparison to a comparator under field trial and laboratory setting, when used according to the manufacturer recommendations;

Efficacy Field Trial Protocol: A document that describes conduct of an ectoparasiticide efficacy field trial in accordance to the GCP guidelines;

Efficacy Field Trial: means a study conducted to establish the efficacy, safety and stability of an ectoparasiticides under field environment;

Guideline: means a document that aims to streamline processes according to a set routine for EFT by the competent authority

Informed Consent: a process by which a study participant voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the study participant's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

Inspection: the act of conducting an official review of documents, facilities, records, and any other resources that are deemed by the Competent Authority to be related to the clinical trial and that may be located at the site of the trial,

at the sponsor's and/or CRO"s facilities or at other establishments deemed appropriate by the Authority.

Investigator: A qualified veterinarian who is registered by a competent authority to practice veterinary medicine in the EAC member states, (or another qualified person as determined by a veterinary body/council) responsible for all aspects of the conduct of a field trial

Investigator Brochure: Is a comprehensive compilation of clinical and nonclinical data on the investigational product (ectoparasiticide, drug, supplement, device or other product) maintained by a drug developer or investigator that contains the body of information about the investigational product obtained before and during a clinical trial.

License: refers to a legal trial document issued by the competent Authority under laws of the country where the trials is to be conducted;

Multi-Centre Trial: a clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

Principal Investigator: refers to 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 product is administered or dispensed;

Sponsor: an individual or entity that is responsible for initiation, management and financing of an efficacy field trial (Ref. GCP/GLP guidelines 2004) **Trial Product**: means an ectoparasiticide

Trial: means ectoparasiticides efficacy study;

Trial Site: the location(s) where trial-related activities are conducted.

1.0 Introduction

This guideline gives guidance on how to study the efficacy of ectoparasiticides in domestic ruminants against all arthropod species that need animal involvement for completing their life cycle, i.e., where at least one parasitic stage occurs on the animal or feeds on the animal. Guidance is aimed at the principal ectoparasites found on domestic ruminants (mosquitoes (Aedes, Culex spp), flies, mites, lice, and ticks) but could be adapted to study the efficacy of products against less common (regional) ectoparasites and arthropod-related disorders, providing that any adjustments to the methods are justified.

The guideline is written principally for the treatment (application) methods currently available, but the same principles could be employed for testing novel formulations and active substance. This guideline gives some ectoparasite species-specific information to help in the practical implementation of the general principles of EFT conduct outlined herein. However alternative approaches may be used where scientifically justified by the applicant.

Applications to request for conduct of ectoparasiticide efficacy field trial using the EAC MRP guidelines should be submitted to the competent authority in any of the EAC Partner States for approval using the addresses below:

Country	Address
Burundi:	Ministry of the Environment, Agriculture and Livestock BP 161 Gitega, Burundi. BP 161 Gitega, Burundi. Website: www.minagrie.gov.bu
Democratic Republic of Congo	18-20, Av.Liberation(ex 24Novembre), Commune de la Gombe/ Kinshasa/RDC Ref. Immeuble SNDE
Kenya	Veterinary Medicines Directorate P. O. Box 66171-00800 NAIROBI, KENYA. Email: info@vmd.go.ke
Rwanda	Rwanda Food and Drugs Authority P.O. Box 1948 Kigali, Rwanda Nyarutarama Plaza Rwanda KG 9 Avenue, Kigali Email: info@rwandafda.gov.rw Website: https://rwandafda.gov.rw/
South Sudan	Ministry of Livestock and Fisheries P.O. Box 293 Juba. South Sudan http://mar.gov.sd/.
Uganda	The Secretary to the Authority, National Drug Authority, Plot 46 – 48 Lumumba Avenue P.O. Box, 23096, Kampala, UGANDA Website: www.nda.or.ug And The National Council of Science and Technology-, Plot 6, Kimera Road, Ntinda P.O.Box 6884, Kampala Uganda Email: info@uncst.go.ug Website: www.uncst.go.ug
United Republic of Tanzania; Tanzania Mainland	Tanzania Veterinary Laboratory Agency Veterinary Complex 131 Nelson Mandela Road P.O. Box 9254 Dar Es Salam Tanzania Email: info@tvla.go.tz Website: https://www.tvla.go.tz/
Zanzibar	Zanzibar Food and Drug Agency P.O.BOX 3595 Changu Road Mombasa Area, Zanzibar, Tanzania Email: info@zfda.go.tz

This guideline should be read together with the Laws and Regulations governing ectoparasiticide Efficacy Field Trial studies in the different EAC Partner States.

2.0 Objective

This document is intended to provide guidance on the general requirements for conducting and assessment of efficacy field trials for an ectoparasiticide

formulation, containing novel or established active substance(s) in the East African Region.

3.0 Scope

The guidelines relate to application of ectoparasiticides, including macrocyclic lactones (MLs) to domestic ruminants for control of ectoparasites in the East African Region. It provides guidance for conducting preregistration efficacy, safety, and stability field trials.

4.0 Legal Provision

Article 108 (e) of the EAC `Treaty provides for adoption of a common mechanism to ensure safety, efficacy and potency of agricultural inputs including chemicals, drugs, and vaccines in the region.

5.0 General Requirements

The aim of applying the ectoparasiticides on the animal is to eliminate or to reduce arthropod ectoparasites or to protect animals from them, to maintain animal health and to prevent losses in production. For those ectoparasite species that are permanently attached to the host throughout its life cycle, this requires an overall efficacy of approximately 100%, depending on the ectoparasite species. For ectoparasites that only complete part of their life cycle on the animal, treatment should be directed towards achieving ≥ 90% efficacy. For burrowing ectoparasites, treatment should at least result in resolution of clinical signs or the significant reduction of nuisance. This can be achieved by reducing ectoparasite burdens on the animal to clinically irrelevant levels, by preventing active stages from settling on the host by repelling or by environmental control.

Regarding the life cycle and the impact on animal health, the overall efficacy of treatment, expressed as relative reductions, should be approximately 100% for all lice species and Sarcoptes scabiei. For Psoroptes (b)ovis, Chorioptes bovis and ticks an efficacy of ≥ 90% should be achieved. For Demodex, treatment should result in elimination of clinical signs. For Haematobia, Stomoxys and larval arthropods (Hypoderma spp.) reductions should preferably be about 100%, but always ≥90%. For Musca and Hydrotea spp reductions should be 80%-100%, but preferably ≥ 90% and a significant reduction in Glossina spp population. The efficacy threshold for ticks is recommended to be ≥90%. According to World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines eradication/elimination claims should attain 100% while control claim should be at 95%. For single-host and multi-host ticks at least 95% efficacy is required for both therapeutic (control) and persistent efficacy claims.

6.0 Procedure

6.1 When designing EFT protocols, the effects/outcomes exhibited by the active substance (e.g. killing, repelling, anti-feeding) as well as the life cycle of the ectoparasite (e.g. length, seasonality, parasitic stages) should be considered.

6.2 Statistically adequate numbers of animals treated with the ectoparasiticide and the comparator should be included in each treatment group. The investigator is required to justify the group sizes and could seek the advice of a statistician where necessary.

6.3 Two types of studies should be performed: efficacy studies under controlled conditions to establish immediate and persistent efficacy of a product, depending on the claim, and field studies to confirm the results of the studies under controlled conditions. It is acknowledged that for some species e.g., Culicoides and warble fly, it is not possible, yet, to conduct laboratory studies. In these cases, controlled efficacy studies could be conducted on a farm in a region with a history of infestation.

6.4 Animals should be infested with a suitable number of ectoparasites (i.e., infestation rates which are production limiting (economic thresholds) and which depend on the type of an ectoparasite). The adequacy of infestation should be addressed in terms of the statistical, parasitological and clinical relevance of the level of infestation. For a study to be considered valid, the product used in the positive control animals should perform within the recommended cut off points against the specific ectoparasite

6.5 All studies should be conducted using the final formulation intended for marketing.

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

6.7 It should also be noted that most arthropods show marked seasonal activity. Depending on the mode of action of the active substance and the target ectoparasite stage, field studies should be carried out in the season in which activity is maximal, unless out of season treatment is more effective, e.g. due to specific ectoparasite stage-active substance interaction. Considerations should be given to environmental conditions [including management systems, seasonality, agro-ecological zones etc.] that affect the integrity of the active substance of the ectoparasiticides as well as ectoparasite diversity.

6.8 Appropriate analytical method should be used depending on the specific study design and objectives of the study. Percentage efficacy of treatment on parasitic stages based on tick survival can be calculated for each day post-treatment according to the WAAVP guidelines.

7.0 Assessment of Efficacy, Safety, and Stability

7.1 Primary Safety Variable

The post ectoparasiticides application mortality and other adverse events profile in the trial animals should be used as the primary variable to assess the safety of ectoparasiticides. The mortalities or other adverse events ascribable to the known side effects of the ectoparasiticides listed by treatment group, time of occurrence post ectoparasiticides application should be compared among treatment groups using appropriate statistics. Such comparisons provide an assessment of the equality of survival distribution among the treatment groups. Frequencies and percentages of animals that died or had other adverse events should be presented for the different treatment groups and compared within and between the groups using appropriate statistics.

7.2 Primary Efficacy Variable

The difference between the average geometrical means of ectoparasite counts for the control product and the Investigational product should be the primary measure of efficacy for the Investigational product. The group geometrical mean ectoparasite counts and standard deviation will be calculated for each experimental group of animals at the different time points. The knock-down effect following counts will then be categorized as effective or ineffective. Interpretation and implications of these results [e.g., efficacy of 90% suppression of baseline ectoparasite density achieved or not] should be discussed in the Final study reports [FSRs].

7.3 Secondary Efficacy Variable: Invitro Efficacy

7.4 The *in vitro* efficacy of both Control Product (CP) and Investigational Veterinary Product [IVP] should be compared as outlined in standard FAO 2004 guidelines for resistance management and integrated parasite control in ruminants (https://www.fao.org/3/ag014e/ag014e.pdf) **Primary Dip Wash Stability Variable**

7.4.1 Plunge dip tanks should be sampled at initial charging and replenishment, according to the manufacturer's label claim for the trial period and the quality [concentration and contents] of the dip wash samples qualitatively and quantitatively analyzed using appropriate analytical methods.

7.4.2 To take the most representative sample of each dip, 30 to 50 stirrer animals should first be moved through the dip then collect the first sample. These stirrer animals should be re-dipped and the second sample collected. Thereafter, dipping of the rest of the animals (mop) continues, and the frequency of subsequent sampling should be as per the manufacturer's label claim. In each case the dip sample should be taken as the last animal (as per the manufacturers claim) is still moving towards the exit end of the dip when there is still agitation in the dip tank and the active substances of ectoparasiticide are uniformly distributed. For example, if a farmer is dipping animals in groups of a100, every 100th animal is considered the last in that group. The sample should be taken at the "jump-in" end of the dip at a depth of about 1 meter (to avoid hair and froth at the top of the dip). Dip wash samples should not be taken from the "walk-out" end of the plunge dip tanks to avoid sampling very dilute dip wash returning from the draining pen.

7.4.3 Wide-necked 500mL glass or plastic autoclavable bottles should be used as sample bottles to avoid hair and debris that often seat across narrow necked sample bottles. These should be fastened to the dip tank calibration stick using a strap and the sample bottle quickly dipped into the dip tank at the "jump-in end. Filled dip wash sample bottles should be securely sealed with plastic tape around the lid, packed in the foam container which should also be securely taped, and then further packed in a small box containing absorbent material to soak up any spillage. The delivery box should be labeled with the name and postal address of the dip owner, physical location and number of samples. The Dip wash sample bottle(s) when delivered to the laboratory should be labelled with the Name of the Plunge Dip tank owner, Dip wash Sample number, dip capacity, number of animals dipped, The Location [District] of the dip, brand name of the Acaricide used, Date of Sampling and the telephone contact of the submitting personnel.

7.5 Interpretation of Stability Results

To interpret stability results, the investigator should use the Certificate of analysis of the in-use [test batches] batches for the CP and IVP. Note that in the dip wash, the declared CoA ingredients' concentrations should be reduced by the dilution rate recommended by the manufacturer [e.g. by a thousand-fold if the dilution is a 1:1000 parts]. A product will be declared stable if the dip wash active substances concentration of the ectoparasiticide lies within 95% of the declared manufacturer's ranges while in use.

8.0 Efficacy Field Trials

8.1 Field trials are normally carried out on identified infested herds. Preferably, herds should not have been treated with any ectoparasiticides (acaricidal or insecticidal spray, pour-on, injection or drench) unless a sufficient washout period has elapsed to guarantee the absence of residual efficacy from any previous treatment prior to the trial.

8.2 Preferably domestic ruminants should only be infested with ectoparasites belonging to the same order, i.e. infestation with lice only and not with lice and mites. However, it is acceptable for more than one species to be present. In this case, all species should be documented and the dose and treatment schemes should be known for each ectoparasite species. The product should cover all ectoparasite species present or relevant at the moment of treatment and be carried out in accordance with the label recommendations of the final product.

8.3 The number of trials to be conducted and animals involved in each trial will depend on the ectoparasite species, the geographical location and local/regional situations and ectoparasiticide mode of application. However, under the MRP, trials should be conducted in 2 different countries (taking into consideration geographical and climatic variations), whereby each of the participating countries should be required to conduct the EFT in different seasons. It is suggested that the duration of the study should lead to generation of sufficient data for acceptable statistical analysis, preferably three application cycles for an ectoparasiticide applied as per the label claim.

8.4 The choice of sampling times should be justified e.g. in respect to the seasonal or daily time of maximum infestation with ectoparasites, considering sites of predilection. Efficacy should be demonstrated in at least two different common breeds to represent the target population putting in consideration of the hair/fur cover.

8.5 For topical products (e.g. spray, pour-on), the effects of coat length and density should be considered. Climatic conditions (rainfall, relative humidity, sunshine etc.), and faecal contamination, dirtiness of the coat should be documented to assess any effect of these parameters, if relevant

8.6 Where a claim for control of infestation is made, the period of time it takes to achieve control and the period over which control is achieved must be demonstrated.

8.7 At the end of the trial period as indicated by the applicant, the overall efficacy of ectoparasiticides in treating infestation in domestic animals should be achieved as follows:

For fleas: approximately 100%
For lice: approximately 100%
For mites: approximately 100% for Sarcoptes scabiei and, if possible, ≥ 90% for other mange mites
For ticks: ≥ 90%
For Diptera: 80-100% (preferably ≥ 90%)

8.7.1 For larval arthropods: 80-100% (preferably ≥ 90%)

8.8 Where indicated and justified, clinical parameters (e.g reduction pruritis, healing of skin lesions etc.) may be used to support the efficacy of a product.

8.9 Where efficacy is less than the above, no claim should be made unless the applicant can demonstrate that the degree of efficacy achieved is better than or comparable with current alternatives. All claims for efficacy of the product against particular species of ectoparasites must be demonstrated and method of study validated.

9.0 Special Requirements-Ectoparasite Species-Specific Information Mites (Chorioptes bovis / Psoroptes bovis / Psoroptes ovis / Sarcoptes sp. / Demodex bovis / Neotrombicula sp.) and Lice (E.g. Linognathus vituli / Solenopotes capillatus / Haematopinus eurysternus / Bovicola (Damalinia) bovis)

9.1 Efficacy Field Trials

9.1.1 Efficacy should be assessed using herds naturally infested with mites, and should utilize a Critical Study Group (CSG), within the herd, comprising at least 15 domestic ruminants each carrying an infestation of at least 25 live mites and showing clinical signs, at the time of treatment. For those ectoparasite species where these numbers might not be feasible e.g. Sarcoptes and Demodex, the number of domestic ruminants used must be justified. The CSG domestic ruminants should be individually identified by tags.

9.1.2 Each animal in the CSG should be visually inspected prior to treatment and at intervals post-treatment until the end of the assessment period (usually at least two complete ectoparasite life cycles post-treatment) when any lesions should be evaluated by measuring length and width of each lesion. Additionally, each animal should be inspected for the presence of live mites and where appropriate, all stages of development should be present to indicate an active infestation. An estimate should be made of mite numbers made along the periphery of each lesion by parting the coat at regular intervals over the body. The predilection sites of all domestic ruminants in the CSG should also be examined for the presence of live mites at the start and termination of the trial. If appropriate, skin scrapings should be taken from all unresolved lesion areas and examined for live mites.

10.0 Tick (e.g. Ixodes spp. / Dermacentor spp. / Rhipicephalus spp. / Haemaphysalis spp. / *Boophilus annulatus*)

10.1 Efficacy Field Trials

Field trials are carried out in herds, which are carrying natural infestations of ticks. See also section 6.4

10.2 Flies

11.0 (Non-biting flies – *Musca domestica* / *Hydrotea irritans* [Head Fly] and Biting Flies –*Stomoxys calcitrans* [Stable Fly] and Culicoides Sp. [Biting Midges] and Warbles [*Hypoderma bovis* / *H. lineatum*])

11.1 **Efficacy Field Trials**

11.2 **Flies**

Where trials involve different regions, pastures should be comparable with respect to topography and insect activity. Meteorological variables such as temperature, wind-force, relative humidity, presence and absence of sunshine or rainfall should be monitored throughout the trial. The studies should include a positive control group of animals using appropriate product. Appropriate distance between groups should be maintained to avoid cross contamination.

Baseline apparent density of flies should be recorded prior to treatment and then at weekly intervals after treatment. Pre-defined areas should be chosen depending on the behaviour of the fly-species and areas should be marked on a body map in the protocol. The study period depends on the treatment period claimed by the applicant.

The species and number of flies on the animal can be determined by visual counting (with the aid of binoculars) or by making photographs of pre-defined areas (including predilection sites for the different fly species) of the animal's body.

The differences between treated and control animals should be statistically analyzed; the duration of the fly season should be taken into account when noting any reduction in fly numbers in response to treatment.

12.0 Warbles

Domestic ruminants can be selected from herds with a history of warble infestation at a time when the larvae are expected to be in the first instar stage. During the subsequent period of emergence, the numbers of warbles parasitizing animals in treated and Positive-control groups can be compared.

13.0 Different Topical Delivery Methods

Products for topical use include shampoos, aerosols, spot-on, pour-on or dust formulations, ear tags, collars, clips, dipping or spray-race formulations, etc.

While the general requirements also apply to products for topical use, it is necessary to take into account interactions between treatment and regional climatic conditions during the course of the trial. In particular, the applicant should consider the need for additional studies as follows:

13.1 The effect of rainfall at various intervals before, during and after treatment;

13.2 The effect of sunshine and hot weather under monitored conditions during and after treatment;

13.3 The effect of dilution factors with dipping;

13.4 The effect of washing and bathing during the treatment period;

13.5 The effects of hair length and thickness of coat;

13.6 The effect of dirtiness of animal coat and the effect of dirtying of preparations

13.7 Dipping formulations) during the treatment of groups;

13.8 The effect of self-grooming or mutual grooming of treated animals;

13.9 Different body sizes of target animals treated with a standard dose formulation;

13.10 Effects on the quality of fleece or hide and impact on tanning or processing. Ideally, side effects and adverse effects of the product should be monitored during the trial and for several days afterwards. Where secondary pharmacodynamic effects are seen, a study on the dose/effect relationship may be required.

13.11 Insecticide-delivery systems (e.g. collars, ear tags etc.)

13.12 If the applicant claims that the product will be effective for a seasonal period of pest activity, then the trial must be conducted over the entire season.

13.13 Evaluation will be based on efficacy in controlling infestation with ectoparasites at the time stated by comparison with control animals, where relevant.

13.14 Controls and treated animals should occupy separate lots within the same area throughout the trial. Groups of animals should be maintained under such conditions to guarantee comparable ectoparasite loads but exclude interference between treatments and controls.

14.0 Other Considerations

In the design of efficacy studies, the following must be taken into account:

14.1 The kind of effect(s) exerted by the active substance(s) (e.g. flushing out, repellent, killing, anti-feeding or detaching effect, insect growth regulating effect, larvicidal, ovicidal, adulticidal or pupicidal effect);

14.2 Occurrence and susceptibility of ectoparasites in different geographic and climatic regions;

14.3 Control of ectoparasite-related diseases if indicated;

14.4 Safety of the target animals;

14.5 Pharmacokinetic behaviour of the substance under investigation;

14.6 Data on drug resistance of ectoparasite species, where available;

14.7 Products intended for the treatment of ectoparasitic conditions may affect the environment, etc. Therefore, due regard should be given in respect of operator, consumer and environmental safety.

14.8 For fixed combination products containing two or more active substances, it will be necessary to assess the potential advantages in the control of ectoparasites against possible disadvantages (e.g. synergistic or additive actions; antagonism; substitution of effects;

non-effect (overkill), taking into account the guidance on Fixed Combination Products.

References

Good Clinical Practice for the Conduct of Clinical Trials on Veterinary Medicinal Products (VICH – guideline, 2000).

Guidelines for Demonstration of Efficacy of Ectoparasiticidess- Directive 81/852/EEC as amended.

Guideline On Specific Efficacy Requirements for Ectoparasiticidess in ruminants.

WAAVP Guideline for evaluating the efficacy of parasiticides against ectoparasites of ruminants

ANNEXES

ANNEX I: PROCEDURE FOR CONDUCTING EFFICACY FIELD TRIALS IN THE EAC REGION

1.0 Ectoparasiticides Trial Product

1.1 All un-registered ectoparasiticides intended for registration shall be tested under local field conditions within the EAC Partner States to ascertain their efficacy, stability and safety in the indicated animal's species

1.2 Appropriate in vitro tests (bioassays) using the investigational product should be conducted to determine the level of susceptibility of ectoparasites from the study site before initiation of the trial.

1.3 All trials shall be conducted using the final formulation intended for marketing in region.

1.4 An application to import trial products shall be made by the Sponsor or by an authorized company or a Contracted Research Organization with a permanent address in the EAC Partner State and according to specific regulations governing importation of samples.

2.0 Efficacy Trial of Ectoparasiticides Intended for Registration in the Region

2.1 Minimum Requirements for Efficacy Trials:

2.1.1 All trials shall be conducted and supervised by qualified and experienced personnel as determined by the sponsor, & regulatory authorities within the Partner States.

2.1.2 All trials shall be replicated, with a minimum of two replicates: each replicate corresponding to either agro-ecological zone or production systems [or a hybrid of the two] in the participating partner states.

2.1.3 All registration applications will be accompanied by *in vitro* efficacy results (refer to section 1.1 above) from a recognized laboratory in the EAC or any other reference laboratories and efficacy field trial results from two agro-ecological zone or production systems (or a hybrid of the two) in the participating partner states.

2.1.4 Given that there are available standard of care ectoparasiticides in the EAC, all field trials involving ectoparasiticides will be positive controlled and blinded (double/single as is practicable). Trials must include a standard registered (reference) product for comparison purposes. Sometimes no standard product may exist – e.g. when a new formulation is being tested for the first time for registration. Under these circumstances it is still possible to include a standard (reference) registered product, the use of which is intended to give the same control result as the new product/formulation (e.g., 80 - 100% control of a specific ectoparasite species or application type or combination of both).

2.1.5 Residual surface sprays are normally used for indoor applications. Where the label makes mention of exterior use, field trials are required. Since this guideline is for outdoor/field trials only, indoor applications studies have been omitted.

2.1.6 If an ectoparasiticide is registered for use in one of partner states without following these harmonized EAC guidelines, the ectoparasiticide shall be retested [safety, stability, and efficacy] under field conditions of the Partner State where registration is being sought.

3.0 Submission of Application to Conduct Ectoparasiticide Trials

3.1 A Contract Research Organization (CRO) shall be appointed by the Sponsor based on the criteria set out in annex III (CRO Information and Responsibilities).

3.2 The Application shall indicate the complete address of the Contracted Research Organization.

3.3 The application for authorization to conduct a trial shall be made in the format and numbering set out in the Trial Application Form specified in annex II of these guidelines. An application for a trial license, other data, particulars, supporting documents, labels and package inserts shall be in EAC official languages.

3.4 The text and diagrams in the application must be clear and legible.

3.5 Each section in the field trial application form shall be cross-referenced to the detail in the field trial protocol, investigators brochure, and other appended documents.

3.6 Only one copy of completed form shall be submitted for each application.

3.7 An application for authorization to conduct a trial shall be accompanied by a non-refundable application fee as determined by a competent authority in a participating Partner State.

4.0 Confidentiality

4.1 The Competent Authority shall maintain the confidentiality of any information submitted as part of a trial application, supporting documents or associated correspondence according to the non-disclosure agreement clause of the confidentiality agreement.

5.0 Evaluation of Application

5.1 The application shall be vetted for completeness and shall be deemed complete if it includes;

5.2 The filled in Trial Application Form (annex II),

5.3 The Contracted Research Organization administrative information form (annex III),

5.4 The Format for Ectoparasiticide Efficacy, safety and Stability Field trial Protocol (Annex XI)

5.5 A complete checklist of required EFT application documents (Annex XII)

5.6 Proof of payment of trial fees and all necessary documentations (appendices, attachments, and any other information that may be demanded by the Authority).

5.7 Data from trials conducted from other countries on the same product, submitted to support the application.

5.8 The data to represent nationally and internationally acceptable standards i.e. VICH for GCP guideline and any other applicable guidelines and regulations

6.0 Application Reference Number

6.1 The competent authority shall issue an acknowledgement of receipt of a complete application with a reference number for each application received.

6.2 The reference number shall be quoted in all correspondence concerning the application.

7.0 Supplementary information and Update

7.1 Any new information available on the product such as adverse effects, change of manufacturer shall be reported in writing to the Competent Authority(ies).

7.2 The Contracted Research Organization shall immediately inform the Competent Authority(ies) of any changes that may affect the conduct and outcome of the trial.

7.3 The Contracted Research Organization and the Competent Authority(ies) shall inform either party about circumstances that may lead to the amendment of the trial application when necessary and the sponsor too shall be informed of the decision.

7.4 The Competent Authority shall request for further supplementary data or documentation when appropriate.

7.5 Supplementary information shall be given to the Competent Authority(ies) in case of additional quantity of trial product(s), additional trial site(s), change in trial sites, additional manufacturing site or re-packer, change of port of entry, and change of Contracted Research Organization, extension of product's shelf life accordingly, according to the respective roles as stipulated on this section of Supplementary Information and Update of this guideline.

8.0 Expert Review

8.1 When circumstances warrant, the application shall be reviewed by an EAC Ad-hoc committee of experts.

8.2 There shall be a confidentiality agreement with the reviewers to ensure that the contents of the application remain confidential.

8.3 The reviewers shall not have direct contact with the applicant, CRO or Sponsor and all correspondences shall be directed to the competent Authority.

8.4 The report and recommendations of the reviewers shall be considered by the competent Authority.

9.0 Final Decision

9.1 The Competent Authority reserves the right to approve or ask for amendment or reject the trial application.

9.2 The Competent Authority shall communicate the decision made to the applicant in writing and in case of rejection give reasons.

9.3 The applicant may appeal unfavorable decision to the relevant Competent Authority using the set-up appeal systems.

10.0 Responsibilities of the Stakeholders in Conduct of Ectoparasiticides Trials

10.1 Responsibilities of the Sponsor

These should be as described in the VICH GCLP guidelines, section 4 < https://www.ema.europa.eu/en/documents/scientific-guideline/vich-gl9-good-clinical-practices-step-7_en.pdf >Responsibilities of Contract Research Organization

10.2 These should be as described in the VICH GCLP guidelines, section 4.3<https://www.ema.europa.eu/en/documents/scientific-guideline/vich-gl9- good-clinical-practices-step-7_en.pdf >

11.0 Monitoring of Ectoparasiticides Trials by the Authority

11.1 Inspection of Trial Sites

11.1.1 The selected representatives of the EAC monitoring and evaluation team of TWG shall conduct inspection/ audit of Efficacy Field trials studies.

11.1.2 The audit shall include but not be limited to compliance with the approved protocol and Good Clinical and laboratory practices.

11.1.3 The inspections shall take place at the discretion of the Competent Authority including but not limited to:

11.1.4 Before commencement of the trial

11.1.5 At predetermined intervals

11.2 Reports of Suspected Adverse Events

11.2.1 The CRO shall report to the Competent Authority all suspected adverse events in writing within 48 hours.

11.2.2 The Competent Authority shall inform the sponsor in writing about the suspected adverse drug events after causality assessment.

11.2.3 Additional follow up information on the suspected adverse drug events shall be made available to the Competent Authority as soon as possible, but in any case, not later than fifteen calendar days.

11.3 Progress and Final Trial Reports

11.3.1 There shall be 3-monthly progress and/or a final report as in form in **(Annex VII)** of this guideline.

11.3.2 The contacted Research Organization shall submit the final report within 1 months from the date of completion of the trial.

11.3.3 The progress report shall include:

11.3.4 The number of animals and frequency of treatment;

11.3.5 The number and type of suspected adverse events reported;

11.3.6 The number of discontinued animals and the reason for discontinuation; and

11.3.7 The quantity of investigational product used.

11.4 Accountability and Disposal of the Investigational Product

11.4.1 An accountability and disposal report of the investigational product shall be submitted to the Competent Authority within 3 months from completion of the trial.

11.4.2 The report shall also include:

11.4.3 Date the trial started and ended;

11.4.4 Trial license number;

11.4.5 Trial certificate for the relevant site;

11.4.6 Date and quantity received for each investigational product;

11.4.7 Balance of the investigational product;

11.4.8 Product destruction certificate, and or written evidence of re-export of the unused product supplies to the country of origin (whichever is applicable).

11.5 Post-trial Review

11.5.1 The interim and final report from the trial shall be submitted to the Competent Authority for consideration.

11.5.2 The format of the report shall be as provided in the protocol used in the trial.

11.6 Archiving

11.6.1 The Authority, the Contracted Research Organization and the Sponsor shall archive and ensure the safety of all the documents related to the trial.

11.6.2 The Contracted Research Organization and the Sponsor shall inform the Competent Authority in writing prior to destroying the documents.

11.6.3 Documents shall be retained for as long as the product is on market.

12.0 Conditions for Application for a Trial License

12.1 Notification of Change of Information to Competent Authority

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

12.2 Discontinuation of the Trial

12.2.1 The trial license holder shall inform the Competent Authority of any decision to discontinue the trial to which the license relates and shall state the reason for the decision.

12.2.2 Where a trial is discontinued, the trial license holder shall return the trial license to the Competent Authority as soon as possible.

ANNEX II: TRIAL APPLICATION FORMAT/FORM

1.0 The Ectoparasiticides Trial Application Format (ETAF)

Introduction

The online application for permission to conduct research in the EAC Partner States, and the paper application are provided in accordance with the national regulatory Competent Authority submission pathway for such applications.

An application for authorization to conduct a field trial shall be made by a sponsor, who must be one of the following:

i. The Patent holder/Applicant and/or Manufacturer
ii. A licensed person/Local Technical Representative of the Patent holder or the ectoparasiticide manufacturer.

2.0 The Patent holder/Applicant and/or Manufacturer. A licensed person/Local Technical Representative of the Patent holder or the ectoparasiticide manufacturer.

Authorised Local Technical Representative (LTR) in EAC Partner States

Partner State	Name of Local Technical Representative	Address of Local Technical Representative
Add rows as needed		

In those cases, where Investigator submits the field trial application, the Investigator must submit a power of attorney verifying his/her appointment as investigator or a letter of authorization to conduct the field trial on behalf of the sponsor.

Furthermore, the Guide to Field Trial Conduct indicates that based on the field trial agreement between the sponsor and the principal investigator (PI), the competent Authority will liaise with the in-country PI representing the sponsor. The PI should be an East African resident and should be licensed by a relevant body in the region.

3.0 Identification of the Trial

3.1 Title of the study

3.2 Contact person and contact details

3.3 Product/application MRP number.

3.4 Declaration of intent signed by the Contracted Research Organization

We, the undersigned have submitted all the required documentation and have disclosed all the information required for approval of this application.

We have developed the Protocol and read the Investigators brochure, appended.

We agree to ensure that the trial will be conducted according to the Protocol and all legal, ethical and regulatory requirements in the EAC trial country.

CRO Institutional Officer:

Name date:

Signature

Designation

Principal Investigator:

Name date:

Signature:

Designation

4.0 Basic Administrative Data on the Application

Name and address of the registered office of the Applicant

Particulars	Sponsor	Manufacturer	Applicant
Name			
Physical address			
Postal address			
Telephone number			
Email			
Fax			

5.0 Trial Products

5.1 Product Information

5.1.1 Trade name, Manufacturer-site for the trial batch only, identifier or name, International Nonproprietary Names (INN) and active substances, complete composition, potency and presentation.

5.1.2 Registration number (if product is already in another Partner State)

5.1.3 Withdrawal period for offal and milk

5.1.4 Release specifications and tests. Include Certificate of Analysis.

5.1.5 Antidotes if applicable

5.1.6 Approved package inserts to be appended to application.

5.1.7 Details of handling trial product.

5.1.8 Shipping, delivery and distribution of trial product.

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

5.1.10 Dispensing trial products and waste disposal procedures.

5.1.11 Packaging and labeling of the trial products

5.1.12 Estimates of quantities for which an import is needed

5.1.13 Evidence of manufacture under conditions compliant with the current codes of good manufacturing practice.

5.2 Comparator product information

5.2.1 Trade name, Manufacturer -site for trial batch only, identifier number, International Nonproprietary Names [INN] & active substances, complete composition, potency, and presentation

5.2.2 Registration number (if product is already registered in another partner state)

5.2.3 Withdraw period for offals & milk

5.2.4 Release specifications and tests. Include Certificate of Analysis.

5.2.5 Antidotes if applicable

Note:

Sponsor shall source for comparator products, Researcher and Research institutions should not know the name of the product(coded). The container for comparator & investigational may not be same which may have effect to the product,

5.2.6 Evidence of manufacture under conditions compliant with current codes of good manufacturing practice

5.2.7 Details of handling trial product.

5.2.8 Shipping, delivery, and distribution of trial product.

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

5.2.10 Dispensing and waste disposal procedures.

5.2.11 Packaging and labeling details.

5.2.12 Estimates of quantities for which an import is needed

6.0 History of previous and in-progress trials for the Investigative Product

6.1 The Sponsor will provide the list/titles of of previous trials with this (or similar) trial product in EAC

6.2 Include a letter or certificate from the regulatory authorities in other Partner States where previous trials have been undertaken (including those in-progress) that these trials have been Good Clinical Practice (GCP) compliant.

6.3 Append interim or final report-summaries of these trials to this application. (This may be in the investigators brochure).

ANNEX III: THE CONTRACTED RESEARCH ORGANIZATION

1.0 Administrative Information

For each site, list the following:

2.0 Address of the CRO

Name	
Physical address	
Contact person (Director)	
Declaration of capacity & interests	

2.1 Site Identifier (Name)

Physical address: (Name and GPS coordinates)

Telephone & fax numbers

E-mail address

2.2 Description of the Site Facility & Staff

(a) Infrastructure on the site;

(b) Facility for special examination (if required);

(c) Capacity to collect, prepare, store and transport field samples;

(d) Storage and handling facility for the trial product; and

(e) Name and qualification of person with responsibility for dispensing trial product.

2.3 Site Investigators

Site Principal Investigator	Name	
	Qualifications	
	Contact details	
	Physical address	
	Declaration of capacity & interests	
Site Sub-investigator and Trial-specific support staff	Name	
	Qualifications	
	Contact details	
	Physical address	
	Declaration of capacity & interests	

2.4 Site Sub-investigator and trial-specific support staff

Name	
Qualifications	
Contact details	
Physical address	
Declaration of capacity & interests	

2.5 For animal farm sites

(a) Name and contact details of the administrator or farmer;

(b) Append signed letter of agreement for trial to take place.

2.6 Append signed agreement between the Investigating Institution and the Sponsor or CRO.

2.7 Trial Animals

2.7.1 Number of animals will be determined by number of sites as stipulated in the table below

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

2.7.2 Duration of the study; its start and end, should be as stipulated in study protocol

2.7.3 The intended compensation in case of loss or injury to the animals in the trial shall be based on understanding between the applicant and the farmer.

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

2.8 Trial monitoring and reports

2.8.1 Describe the safety and monitoring plan for each site.

2.8.2 Describe the system to be used to detect, record, assign causality and the actions for adverse events.

2.8.3 Describe the actions to be taken following reports of suspected adverse events.

2.8.4 Date for submission of the interim reports.

2.8.5 Date for submission of the final report

2.9 Insurance (where applicable)

2.9.1 Procure insurance to cover the study animals during the duration of study.

2.9.2 Procure professional indemnity insurance for the investigating team.

2.10 Description of the Trial

2.10.1.1 Provide brief description of trial title

2.10.1.2 Provide background information and a summarized rationale for this trial, including its relevance to the East African region. This should include:

(a) The problem statement and the justification of the trial;

(b) Properties of the trial product- hypothesis for action

(c) Description of risks of the protocol and the potential harms of the trial product.

(d) Summary report that establishes probable safety and efficacy of the investigational product in animals.

(e) 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.

(f) Published reviews or reports relevant to the indicated ectoparasiticides and this type of product

2.11 Objectives of this trial (List as primary and secondary objectives and provide justification)

2.12 Trial design (The applicant is to provide a description and justification for each component);

2.13 The eligibility of the animals involved in the trial in relation to:

(a) Inclusion criteria - list and justify each

(b) Exclusion criteria - list and justify each

2.14 The treatment regimens for each trial animal group.

2.15 Follow-up, sampling collection and monitoring plans; (immediate monitoring - intermediate monitoring - long term monitoring).

2.16 Outcome measurements and analysis

2.17 Describe each outcome or variable (including safety and efficacy)

2.18 Describe the samples that will be collected and the analyses to be conducted on each sample

2.19 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).

2.20 All statistical analysis of the results should be within the WAAVP guidelines unless justified.

2.21 Provide full details if any sub-studies are intended

2.22 Indicate whether field samples will be stored for any period beyond the duration of this trial

2.23 Provide justification for such archiving?

2.24 What controls are to be placed on their confidentiality and possible future use?

2.25 Informed consent from animal owners.

2.26 Append a copy of informed consent from animal owners.

2.27 Are there separate informed consent from animal owners for sub-studies.

2.28 Publication policy

2.29 Provide details of the investigators and Sponsors intentions and freedom to publish the outcomes of this trial.

ANNEX IV: INFORMED CONSENT PROCESS

1.0 General Requirement for Informed Consent Process

It is important for a researcher to obtain informed consent from the animal owners including farmers, breeders and institutions, from where trial's animals are sourced. No animals shall be involved in a study unless the researcher has obtained prior informed consent from the relevant individuals/institutions that own the animals. A researcher shall ensure that the animal owner or institution has sufficient understanding of the relevant information and knows the consequences of permitting the use of their animals in the trials and be given opportunity to consider whether to allow participation of their animals or not.

All communications with the animal's owner or their representatives shall be in a language understandable to all the parties. The researcher, sponsor, or its agents shall be held liable of any loss or damage during the field trial.

2.0 Key components of the Informed Consent Form

The information to be included in the informed consent form shall include the following:

a) A statement that the trial has been approved by a competent Authority in the EAC Partner State where it is to be conducted;

b) A description of any other procedures that are experimental;

c) Trial description and the estimated duration;

d) The approximate number of animals to be involved in the trial;

e) A description of any reasonably foreseeable risks or discomforts that the animal may experience.

f) The benefit of the trial.

g) Names and contact details of individual(s) who should be contacted at any time in case of questions about the animal welfare, including the sponsors and the institution of affiliation for the researchers;

h) An assurance that participation is voluntary;

i) A detail about compensation and veterinary treatment available if injury occurs;

j) The nature, form, and extent of compensation for loss of production, injury or deaths.

k) Provision for a witness at appropriate to the informed consent process, especially for illiterate animal owners.

3.0 Documentation of Informed Consent Process:

The information to be included in the informed consent form, which is provided to each potential animal owner, shall include the following:

a) A statement that this is a study rather than provision of veterinary care; that the study involves research and or teaching; an explanation about the study; the estimated length of time that the animal will take in the study; a description of the study procedures, and identification of any other procedures that are experimental.
b) A description of any reasonably foreseeable risks or discomforts that the animal may experience.
c) A description of the benefits to the animal or community that may reasonably be expected to result from the study.
d) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the animal.
e) A statement about compensation and veterinary treatment available if injury occurs and, what they consist of and where further information may be obtained.
f) Names and contact details of individual(s) who should be contacted at any time in case of questions about the study, and animal welfare. The individual(s) should be able to communicate in a language understandable by the animal owners or should be able to promptly secure the services of an interpreter to assist in responding to questions raised by the animal owners.
g) A statement that participation is voluntary, that refusal to participate will not result in a penalty or a loss of benefits to which the animal owner is otherwise entitled, and that the animal owner may discontinue participation at any time without penalty or loss of benefits to which the animal owner is otherwise entitled.
h) Where applicable, a statement of how the study will provide veterinary services to the animals.
i) The nature, form, and extent of compensation for loss of production, injury, or death of the animal. This compensation could be in form of pre-paid insurance cover.
j) A brief description of sponsors of the study and the institution of affiliation for the scientists.
k) A statement that animal owners will get feedback on findings and progress of the study, and that any new information that affects the study or data that has veterinary relevance (including incidental findings) will be made available to animal owners and or their veterinary care providers.
l) Where necessary, provision for a witness at appropriate specific stages

of the informed consent process, for example, in the case of illiterate animal owners.

m) A statement that the study has been approved by an accredited EAC member state-based Institutional Animal Care and Use Committees [IACUC].

Any of the following shall be provided to the animal owner, whenever appropriate, based on the nature and conduct of the study:

i. A statement that a particular treatment or procedure under study may involve risk to the animal or to the embryo or fetus if the animal is or may become pregnant, and that the risk is currently unforeseeable.
ii. An explanation of circumstances under which the scientist may terminate the animal's participation, whether the owner consents to such termination.
iii. An explanation of any additional costs to the animal owner that may result from his or her participation in the study.
iv. A statement explaining the consequences of the animal owner's decision to withdraw from the study. The study animal may be withdrawn at any time without further notice. However, animal owners should be provided with a description of the procedures that are to be followed to give notice of their animals' withdrawal.
v. A statement that significant new findings obtained during the course of the study, whether by the scientist or others that may relate to the animal owners' willingness to continue his or her participation, shall be provided to the animal owner in a timely manner.
vi. The approximate number of animals to be involved in the study.
vii. Whether, when how and for how long any of the products or interventions proven by the study to be safe and effective will be made available to the animal owners at the end of the study and whether they will be expected to pay for them.
viii. With regards to research involving the collection of biological materials, an explanation should be provided on how specimens will be managed at the end of the study. If the samples will be stored for future use, separate consent should be obtained.

ANNEX V: DECLARATION FORM

Format for Declaration by the Investigators

Trial protocol number. . . . .
Name: .....
Role in trial .....
Trial title: .....

A current Curriculum Vitae is attached.

I am aware of the responsibilities of my role as ..... in trial number . . . . . as required by the legal, ethical and regulatory requirements of (State the name of the country in the EAC).

I am fully aware and fully responsible for attached Protocol, investigators brochure and supporting documentation and I will comply with the procedures and requirements included in them.

I have read the attached trial application form as submitted to the National Competent Authority in the East African Partner State of .....and confirm that the information is complete, true and accurate, and conform to the protocol and supporting documentation.

I will not commence with this trial before written authorization has been received from the National Competent Authority and other government bodies as may be required. I will provide the national Competent Authority and other relevant bodies with reports as required.

I will obtain Informed consent from all animal owners participating in the trial. I will ensure that every animal in the trial will be treated ethically.

I will ensure that the District/Provincial Veterinary Officer and the area veterinarian are aware and involved in the trial.

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 trial.

Initials: . . . .

I DECLARE: I have not previously been associated with any trial that has been terminated, or study-site that was closed, due to failure to comply with Good Clinical Practice for the conduct of trials on veterinary ectoparasiticide products.
Initials:.....
SIGNED .....DATE .....
WITNESS:.....NAME .....DATE .....

ANNEX VI: LABELLING TRIAL PRODUCTS

Format for Labelling Trial Products

Outer/carton labels & Unit Pack

The following information shall be presented on the labeling of the product for trial. In addition, the information on the carton pack and particularly that on the inner pack should ensure the possibility of single or double blinding:

Parameters	Outer/carton Labels	Unit Pack
Study No. or Protocol	√	√
Group code	√	√
Product name or code	√	√
Dosage form	√ **	√ **
Name of active substance(s)	√ **	√ **
Strength of active substance(s)	√ **	√ **
Dilution for different species	√	√
Batch number	√ **	√ **
Manufacturing date or retest date	√	√
Expiry date	√	√
For Trial Use Only		
Name and address of manufacturer or final release or product owner (corporate address) or 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.

ANNEX VII: STUDY REPORT

Format for Study Report

1. TITLE
2. STUDY NUMBER
    - 2.1 Sponsor reference
    - 2.2 CRO study number
3. PROJECT MANAGEMENT AND STUDY SITE
    - 3.1 Contract Research Organization (Project Management)
    - 3.2 Study sites selection and location
4. STUDY CONTACTS
    - 4.1 Sponsor Organization
    - 4.2 Sponsor Representative
    - 4.3 Sponsor Monitor
    - 4.4 Statutory Monitor
    - 4.5 Investigator
    - 4.6 Assistant Investigator
    - 4.7 Quality Assurance
    - 4.8 Attending Veterinarian
    - 4.9 Statistician
    - 4.10 Technical Manager
5. LABORATORIES

5.1 For Bioassays

5.2 Analytical

6. OBJECTIVE(S) OF THE STUDY

6.1 General objectives

6.2 Specific objectives

7. RATIONALE AND JUSTIFICATION OF THE STUDY
8. SCHEDULE OF EVENTS

8.1 Field trial dates

9. STUDY DESIGN

9.1 Type of study and overall study design

9.2 Study layout

9.3 Randomization procedures: ranking and allocation.

9.4 Experimental unit and justification

9.5 Blinding

10. ANIMAL SELECTION AND IDENTIFICATION
11. INCLUSION, EXCLUSION AND POST-INCLUSION REMOVAL

11.1 Inclusion and exclusion criteria

- 11.2 Post-inclusion removal criteria of study animals
    - 11.2.1 Criteria for removal

11.2.2 Procedures for removal of ruminant from the tri
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12. ANIMAL MANAGEMENT AND HOUSING
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12.2 Management of feed and water
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18.5 Primary variable; stability
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19.2 Immediate adverse reactions upon topical administration of IVP and ICVP
19.3 Field Efficacy of the IVP and ICVP
19.4 Invitro efficacy of the IVP and ICVP
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2. Daily efficacy results not included in-Text Figures (Appendix B)

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4. Investigator statement of clinical compliance & declaration of conflict-of-interest (Appendix D)

5. Monitor certification of clinical compliance (Appendix E)

6. Quality assurance statement (Appendix F)

7. Amended Protocol, deviations and Notes to File (Appendix G)

ANNEX VIII: STUDY SAFETY AND STABILIY REPORT

Safety and Product Stability Report

Date:

The Head Competent Authority

Address

Tel:

< Trial Protocol Title and Protocol Number>

<EAC product code/national reference number>

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

a) Number of animals screened: < insert number>
b) Number of animals randomized: <insert number>
c) Number of animals discontinued: < insert number>
d) Reasons for discontinuation: <insert number>
e) Reasons for discontinuation: <List of individual discontinued animals
f) Number of animals completed study: < insert number>
g) Number of Suspected adverse events: < insert number>
h) Number of endpoints: <insert number if applicable, if not, to be removed>
i) Last batch of ectoparasiticide supplies collected back from site: < insert date>
j) Last batch of ectoparasiticide supplies sent back to < originating site> for destruction: <insert date>; if local destruction, attach copy of the destruction certificate.
k) List of any changes in trial personnel – including full Curriculum Vitae and declaration
l) List of monitor and audit reports to date.

ANNEX IX: FORMAT FOR PRINCIPAL INVESTIGATOR'S BROCHURE

Investigator Brochure (to be provided by the sponsor to the CRO/ Investigator)

Name of sponsor

Product Name

Chemical and generic (if approved)

Trade name (if legally permissible and desired by the sponsor)

INVESTIGATOR'S BROCHURE

Edition number

Release date

Previous edition and its numbers

Dates of previous editions

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   4.4. Investigational Product Excipients
5. Non-Clinical Studies
   5.1. Nonclinical Pharmacology

   5.2. Pharma Kinetics and Product Metabolism in Animals
      5.2.1. Absorption, Distribution, And Excretion
      5.2.2. Biotransformation

5.2.3. Effects on Enzymes and Other Biochemical Parameters

5.3. Toxicological Data on The Active and Formulated Pesticide

5.3.1. Acute Toxicity: Oral-Oral Single Dose LD50

5.3.1.1 Mode of Toxic Action

5.3.1.2 Percutaneous Skin Penetration, And Absorption, Dermal LD50

5.3.1.3 Sub-Chronic Toxicity Tests on Rodent (Rat) And One Non-Rodent Species

5.4 Chronic Toxicity

5.4.1 Laboratory Animal Pesticide Long-Term Oral Toxicity and Carcinogenicity

5.4.2 Mutagenicity Studies

5.4.3 Reproductive Toxicity

5.4.4 Multigeneration Studies in Mammals Over a Minimum of Two Generations

5.5 Metabolic Pathways

5.5.1 Safety and Efficacy

5.5.1.1 Side Effects and Incompatibilities

5.5.1.2 Overdose in Animals

5.5.1.3 Reproductive Safety and Teratogenicity

5.5.1.4 Carcinogenicity

5.5.2 Marketing Experience

6. Summary of Data and Guidance for The Investigator

7. Appendixes

ANNEX X: AUTHORIZATION LETTER

Letter of Authorization from Manufacturer to conduct the field trial

Date: ……

1. Manufacturer's Name) ……

A company operating under the laws of ……, located in ……

Local company name and address

Tel No: ……

Fax No:……

E-mail: ……

2. CRO name and address

Tel No: ……
Fax No: ……
E-mail: ……

A company operating under the laws of ……, located in__

To conduct filed trial for our product(s) in the East African Partner State of: ……

The CRO above will henceforth apply for Trial License in the East African Partner State above for the Sponsor Protocol No. ……

CRO Protocol reference No: ……

These reference Numbers have been assigned to this field trial on this day ----------Month ---------- year_____

(The CRO address) is authorized to be the Trial License Holder and will be responsible for all matters pertaining to the Trial License application for the above-mentioned trial protocol.

Yours faithfully.

……

Authorized name & signature

ANNEX XI: FORMAT FOR THE ECTOPARASITICIDE EFFICACY, SAFETY AND STABILITY FIELD TRIAL PROTOCOL TEMPLATE

This template is prepared to conform to 3 which the user can access via the link below;

https://www.ema.europa.eu/en/vich-gl9-good-clinical-practices-scientific-guideline

1. Title of the field trial that should have elements of the study design
2. Study number
   - 2.1. Sponsor Reference
   - 2.2. CRO Study Number
3. Project management and study site
   - 3.1. Contract Research Organization (Project Management)
   - 3.2. Study Sites Selection and Location
4. Study contacts
   - 4.1. Sponsor Organization
   - 4.2. Sponsor Representative
   - 4.3. Sponsor Monitor
   - 4.4. Statutory [from departments of Veterinary Services] Monitor
   - 4.5. Investigator
   - 4.6. Assistant Investigator
   - 4.7. Quality Assurance
   - 4.8. Attending Veterinarian
   - 4.9. Statistician
   - 4.10. Sponsor Technical Representative
5. Laboratories
6. Field trial Objectives
   - 6.1. General Objectives
   - 6.2. Specific Objectives
7. Rationale and justification of the study
8. Schedule of events
   - 8.1. Proposed Dates
9. Study design
   - 9.1. Type of Study and Overall Study Design
   - 9.2. Study Layout
   - 9.3. Randomization Procedures: Ranking and Allocation
   - 9.4. Experimental Unit and Justification
   - 9.5. Blinding
10. Animal selection and identification

11. Inclusion, exclusion and post-inclusion removal
11.1. Inclusion and Exclusion Criteria
11.2. Post-Inclusion Removal Criteria of Study Animals
11.2.1. Criteria for Removal
11.2.2. Procedures for Removal of Animal from The Trial
11.2.3. Fate of Animal Removed from The Study
12. Animal management and housing
12.1. Animal Containment
12.2. Management of Feed and Water
12.3. Health Care and Concomitant Therapy
12.4. Special Conditions and Restraint
13. Environmental monitoring
13.1. Environment and In-Contact Personnel Protection
13.2. Veterinary Product [Cp and Ivps] Handling and Storage
14. Investigational and control veterinary products
14.1. Investigational Veterinary Product
14.2. Control Product
15. Veterinary product administration
15.1. Investigational Veterinary Product/Control Product Application
15.1.1. Frequency and Duration of Application
15.1.2. Dilution Rates [if applicable]
15.1.3. Justification of Application Route and Dilution Rates (IVP/CP)
15.1.4. Method and Route of Application (Ivp/Cp)
15.1.5. Precautions for Personnel
15.1.6. Precautions to Ensure ectoparasiticide application in Compliance with The Approved Protocol
16. IVP and study animal accountability
16.1. Study Animal Accountability
16.1.1. Euthanasia of terminally sick animals
16.1.2. Disposal of Euthanized Animals
16.2. Investigational Veterinary Product
16.3. Control Product Accountability
17. Assessments of safety, efficacy, and stability
17.1. General Health Observations
17.2. Ectoparasite counting |burden determination
17.3. Sample collection for invitro testing
17.4. Mortality and Necropsy
17.5. Stability Testing [If applicable]
18. STATISTICAL METHODS
18.1. Sample Size Calculation
18.2. Primary Variable: Safety
18.3. Primary Variable: Efficacy
18.4. Secondary Variable: Invitro Efficacy
18.5. Description and measurement of pprimary Variable of Stability
18.6. Statistical Methodologies
18.6.1. Statistical Unit
18.7. Data Management

19. Handling of records
19.1. Procedures for The Recording, Processing and Handling of Study Documentation
19.2. Records to be retained by Investigator
19.2.1. Personnel List, Signatures and Duties [Delegation of Duties Log]
19.3. Retention of Records after Completion of The Study
19.4. Final Report description
20. Adverse events
21. Operational matters
21.1. Monitoring
21.2. Changes to the Approved Protocol
21.2.1. Approved Protocol Amendment
21.2.2. Deviation from Amended Protocol
21.3. Animal Ethics
22. Quality standards
23. References

ANNEX XII: CHECKLIST OF REQUIRED DOCUMENTS

Item No.	Requirement	*Yes or No
1.	Proof of payment	
2.	Applications for import and/or export of materials	
3.	Trial Application Form	
4.	GCP|GLP Standard Trial Protocol	
5.	Investigators Brochure	
6.	Consent Form that includes compensation for mortalities associated with the trial products at current market rates	
7.	Certificate of Good Manufacturing Practice manufacture of the trial product or other evidence of manufacture quality, safety and consistency	
8.	Package insert/s for other trial products	
9.	Name and address of delegated laboratories	
10.	Signed and completed Declarations by all Investigators form.	
11.	Full, legible copies of key, peer-reviewed published articles supporting the application.	
12.	Sample of the label for the trial products	
13.	Letter of authorization from the manufacturer/product owner	
14.	Data on dosage and any other relevant information	
15.	Field Trial Agreement between the Sponsor and the Principal Investigator	

16.	Other supporting documents.	

*If you complete No for any of the above documents the application is incomplete, and you need to provide these non-discretionary documents

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 a Competent Authority recognized by EAC Partner State.
- Or the statement on GMP can be issued by the Quality Assurance Department where the product is manufactured.
- For local product, the manufacturing license is required.
- For a comparator product, a retention certificate from the relevant competent authority is required:

Approvals of study protocols should be submitted along with the Trial Application to the National Authority.

1. **Required Documents by the Competent Authority Inspector at the Port of Entry for Conduct of Ectoparasiticides Trials**

   To be supplied by the Sponsor for use by the Competent Authority Inspector at the port of entry to authorize the importation of the trial product

Importation and Release of Investigational Products			
Checklist of required documentation			
Are the following documents attached and correct, as indicated√		Yes	No
1.	A copy of national Competent Authority letter of approval of trial		
2.	CoA to reflect at least the following information:		
3.	Product name or code		
4.	Name of company / Sponsor		
5.	Batch number		
6.	Expiry date		

7.	Date of issue		
8.	Signature, qualification, and title of responsible person		
9.	Results of physical and analytical tests		
10.	A copy of valid Certificate of Manufacture issued by the competent Regulatory Competent Authority in the country of origin		
11.	Application device included (if applicable)		
12.	The label clearly indicates Labeling: outer packaging, immediate container		
13.	That the product is trial material, e.g. "For use in trial only"		
14.	Product name or unique code (if blinded)		
15.	The Storage temperature is stated		
16.	The Storage conditions indicated (e.g. protection from light)		
17.	The Batch number is stated		
18.	The Date of manufacture is stated		
19.	The Expiry date is stated		
20.	Details of Sponsor`s contacts are included		
21.	The physical condition of the consignment is acceptable		

If you complete **No** to any of the above you will most likely be denied import permit. Please provide all documents stated above

References

For additional information about the harmonized test guidelines and to access the guidelines electronically, please go to https://www.epa.gov/test-guidelines-ectoparasiticides-and-toxic-substances

2. Document Revision History

Date of revision	Revision number	Document Number	Author(s)	Changes made and/or reasons for revision
	0			
	1			
	2			

End of Document