Note: This draft is only intended as a copy for comments during the stakeholder consultation period of the proposed guidelines. The content of this draft may change and does not prejudge any policy nor decision of the FDA. Citation of any text in this draft, for purposes other than the submission of comments as indicated in the issued announcement, is not recommended.

FDA CIRCULAR
No. _____

SUBJECT : **Guidelines on the Filing and Submission of Acceptable Variations on Protocols and Non-standard Protocols for the Review and Pre-Approval by the Food and Drug Administration Prior to the Conduct of Bio-efficacy Test Studies of Household Pesticides for the Purposes of Securing a Certificate of Product Registration**

I. RATIONALE

Pesticide registration involves an evaluation of comprehensive scientific data demonstrating that a pesticide is effective for its intended purposes and does not pose an unacceptable risk to human or animal health or the environment. In particular, the aspect of pesticide registration which reviews the effectiveness of a pesticide is the technical evaluation of the submitted bio-efficacy study. Following Department of Health (DOH) Administrative Order (AO) No. 2019-0008, entitled, "New Rules and Regulations in the Registration of Household Pesticide Products and their Active Ingredients", accepted protocols have been identified and that any deviation from standard protocols require sufficient and compelling justification to ensure soundness of the method and the reliability to produce data to support product claims.

In the course of the implementation of the said AO, updates to the internationally-accepted standards suggest that changes to the list of accepted protocols must be made. Additionally, an assessment of the implementation of the AO showed that pesticide registration applications were found to display deficiencies in the submitted bio-efficacy test study which resulted in disapproved applications. Such applications displayed failure to substantiate claims and failure to justify modifications to accepted standards. In order to assist market authorization applicants, promote regulatory compliance, and ensure the efficient use of resources, this Circular hereby establishes the pre-approval process for modified and non-standard bio-efficacy test protocols.

II. OBJECTIVES

This Circular aims to improve the regulatory compliance of pesticide registration applications and facilitate the same through the establishment of a pathway for the review and pre-approval of non-standard and modified bio-efficacy test protocols, which will be submitted in support of pesticide registration under DOH AO No. 2019-0008.

III. SCOPE

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This Circular shall cover household pesticide products pursuant to the definition and scope provided by DOH AO No. 2019-0008 and the establishments that are engaged in the manufacture, importation, exportation, sale, offer for sale, distribution, donation, transfer, and where applicable, the use, testing, promotion, advertising, or sponsorship of such household pesticide products.

IV. GENERAL GUIDELINES

A. The applicant for pesticide registration shall be a holder of a valid License to Operate (LTO) as a Household Pesticide Establishment issued by the FDA. Consequently, applicants seeking the review and approval of its non-standard or modified test protocol shall also be a licensed Household Pesticide Establishment.

B. All household pesticides shall preferably be tested in accordance with existing accepted protocols as listed in Annex A. Bio-efficacy tests conducted in strict adherence to existing accepted protocol shall directly proceed to pesticide registration under DOH AO No. 2019-0008.

C. Where a bio-efficacy test to be conducted for the purposes of applying for a household pesticide registration utilizes a non-standard protocol or where justifiable circumstances require deviations from accepted test protocols, licensed household pesticide establishments shall submit the said modified or non-standard test protocol to the FDA for review and approval prior the conduct of the bio-efficacy test study and any subsequent pesticide registration.

D. Applications for the pre-approval of non-standard and modified bio-efficacy test protocols shall be filed following the procedure outlined in Section V.A. and the requirements provided in Section V.B.

E. Market authorization holders (MAHs) intending to use and strictly apply a bio-efficacy protocol previously approved following these Guidelines for a different pesticide registration application may conduct and present data on bio-efficacy studies generated using the accepted protocol; Provided, the product type, intended use and manner of use shall be similar to as the previously approved bio-efficacy protocol; Provided, further, that that the market authorization applicant of the pesticide registration application shall be the same as the applicant of the previously approved bio-efficacy protocol.

V. SPECIFIC GUIDELINES

Applications for pre-approval of bio-efficacy test protocols shall be filed in accordance with the following procedure and requirements:

A. Filing of an application

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Each application shall contain a single protocol which is a modification of an existing protocol or a non-standard protocol. An application shall be filed following the procedure outlined in Annex B. An application is considered final upon submission of complete requirements, following pre-assessment, including payment of the required fees and charges. Incomplete applications shall be returned to the applicant.

A successful filing following pre-assessment shall not be construed as an approval of the application, wherein the comprehensive evaluation for correctness and compliance to administrative and technical standards is performed in the evaluation step.

B. Documentary Requirements

1. Letter of Intent specifying the reason for utilizing a non-standard or modified bio-efficacy test protocol
2. Integrated application form
3. Valid LTO
4. Copy of official receipt
5. Test Protocol

The test protocols shall contain the information as listed in Annex C.

C. Evaluation

The evaluation of the submitted test protocols shall be based on the correctness, accuracy, and compliance with administrative and technical standards of the submitted documents.

D. Processing time

The duration of the review and pre-approval of the submitted test protocols shall be twenty (20) working days. The processing time may be extended for the same number of days with prior notice to the applicant.

E. Fees and Charges

An application fee of Php 500, and the corresponding Legal Research Fee, shall be charged for applications for the review and pre-approval of test protocols, following DOH AO No. 50 s. 2001.

F. Result of application

The result of the application shall be issued by the FDA to the email address of the applicant declared in the application form.

VI. TRANSITORY PROVISIONS

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Applications submitted prior the effectivity of this issuance shall be processed in accordance with DOH AO No. 2019-0008. Upon effectivity of this Circular, new applications shall adhere to the guidelines set forth in this Circular.

VII. PENALTY CLAUSE

Applicable sanctions or regulatory actions shall be imposed upon those found in violation of the provisions of this Circular.

VIII. REPEALING CLAUSE

All other administrative issuances, bureau circulars and memoranda and other regulations inconsistent with this Order are hereby withdrawn, repealed and/or revoked accordingly.

IX. SEPARABILITY CLAUSE

The provisions of this Memorandum are hereby declared separable and in the event of any such provision/s is/are declared invalid or unenforceable, the validity of enforceability of the remaining portions or provisions which are not affected, shall remain in full force and in effect.

X. EFFECTIVITY

This Circular shall take effect fifteen (15) days after its publication in a newspaper of general circulation and filing with the University of the Philippines Law Center Office of the National Administrative Register.

FRANCISCO T. DUQUE III, MD, MSc
Secretary of Health

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ANNEX A

List of Bio-efficacy Test Studies with accepted Test Protocol/s

1. Human Mosquito Repellent
   - 1.1 WHO Guidelines for Efficacy Testing of Mosquito Repellents for Human Skin
   - 1.2 OPPTS 810.3700: Insect Repellents to be Applied to Human Skin
   - 1.3 MS 1497:2007: Household Insecticide Products – Personal Mosquito Repellent – Evaluation Method for Biological Efficacy (First revision)

2. Insecticides
   - 2.1 WHO Guidelines for Efficacy Testing of Insecticides for Indoor and Outdoor Ground-Applied Space Spray Applications (May also be used for houseflies)
   - 2.2 ECHA Appendix 18 "List of Currently Available Standard Test Methods for Product Type 18 Insecticides/Acaricides and Product Type 19 Repellents/Attractants (As Far as They Concern Insects and Other Arthropods)"
   - 2.3 OCSPP 810.3500: Premises Treatments
   - 2.4 WHO Guidelines for Testing Mosquito Adulticides for Indoor Residual Spraying and Treatment of Mosquito Nets (May also be used for houseflies)
   - 2.5 MS 1911: Part 1: 2006: Household Insecticide Products – Evaluation Method for Biological Efficacy – Part 1: Glass Chamber Method
   - 2.6 MS 1911: Part 2: 2006: Household Insecticide Products – Evaluation Method Biological Efficacy – Part 2: Peet Grady Method
   - 2.7 MS 1911: Part 3: 2006: Household Insecticide Products – Evaluation Method for Biological Efficacy – Part 3: Cylinder Method
   - 2.8 MS 1911: Part 4: 2006: Household Insecticide Products – Evaluation Method for Biological Efficacy – Part 4: Plaque Method
   - 2.9 MS 1984: 2007: Laboratory Colonisation of Insects of Public Health Importance – Guidelines
   - 2.10 MS 1985: 2007: Household Insecticide Products – Ant Bait – Evaluation Method for Biological Efficacy
   - 2.11 MS 1986: 2007: Household Insecticide Products – Containerised Ant Bait – Specification
   - 2.12 MS 1326: Part 3:2007: Household Insecticide Products – Cockroach Bait – Evaluation Method for Biological Efficacy (Second revision)
   - 2.13 MS 1326-2:2010: Household Insecticide Products – Containerised Cockroach Bait – Specification (First revision)

3. Insecticidal Net
   - 3. 1 WHO Guidelines for Laboratory and Field Testing of Long-Lasting Insecticide Nets

4. Mosquito Coils, Vaporizer Mats, Liquid Vaporizers Ambient Emanators and Aerosols
   - 4.1 WHO Guidelines for Efficacy Testing of Household Insecticide Products
   - 4.2 MS 23 PART 1 2006: Household Insecticide Product – Physical, Chemical and Biological Efficacy Requirements – Mosquito Coil (Fourth revision)
   - 4.3 MS1044:2012: Household insecticide products – Mosquito vapourising mat – Specification (Second revision)

4.4 MS 1255:2006: Household Insecticide Products – Physical, Chemical and Biological Efficacy Requirements – Surface and Direct Spray Aerosol (First revision)

4.5 MS 1257:2010 Household Insecticide Products – Aerosol Against Flying Insects – Specification (First revision)

5. Mosquito Larvicide

5.1 WHO Guidelines for Laboratory and Field Testing of Mosquito Larvicides

6. Termiticide, Wood preservative and Termite baits

6.1 ASTM D3345: Standard Test Method for Laboratory Evaluation of Solid Wood for Resistance to Termites, ASTM D3345-17 (West Conshohocken, PA: ASTM International, approved January 1, 2017), https://doi.org/10.1520/D3345-17

6.2 OPPTS 810.3800: Method for Efficacy Testing of Termite Baits

6.3 OPPTS 810.3600: Structural Treatment

The afore-mentioned list of bio-efficacy test studies with accepted test protocols may be amended or updated as determined by FDA.

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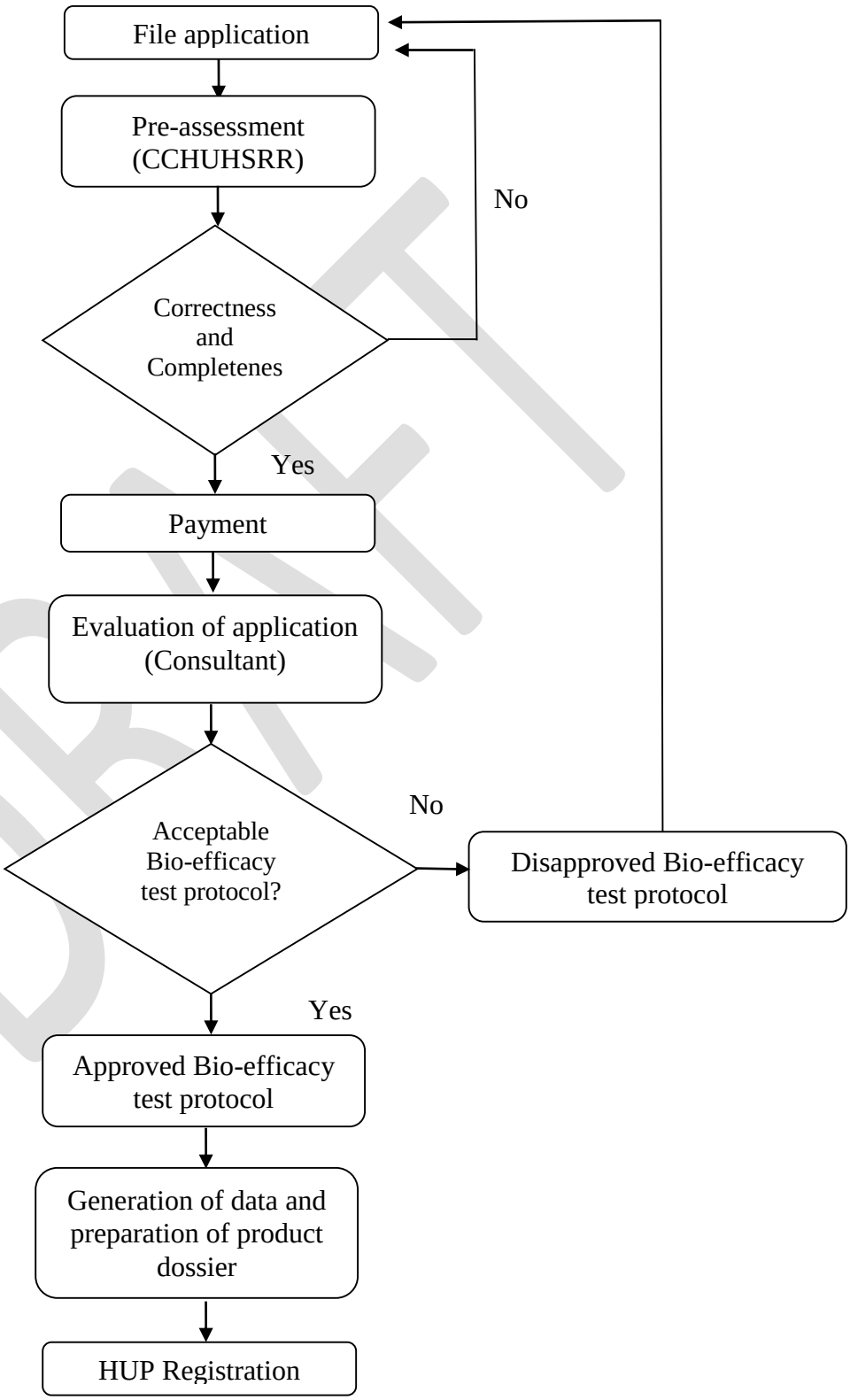
ANNEX B
Step-by-step Application Procedure

1. Pathways for pre-approval of Bio-efficacy test protocols



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2. Application procedure for the review and pre-approval of test protocols:

2.1 Applicant sends a request for schedule of submission of application requirements to FDAC (fdac.pacd@fda.gov.ph). Requests for schedule may be submitted from Monday to Friday. The schedule of the applications for pre-assessment is on Thursdays, except for Holidays, from 8AM to 12NN.

2.2 Applicant submits the application requirements for pre-assessment to FDAC (fdac.pacd@fda.gov.ph) on the day of the schedule, from 8AM to 12NN. Only applications with complete requirements pre-assessed by the Center shall proceed to payment.

2.3 Applicant pays for the corresponding fee.

2.4 Applicant submits the paid application (electronic copies of the complete requirements) to FDAC (fdac.pacd@fda.gov.ph).

2.5 The FDA forwards the application to the Center.

2.5 The Center receives and forwards the application to Center's HUP Consultant.

2.6 The Center's HUP Consultant evaluates the correctness of the documents and renders the final decision.

2.8 Releasing of the final issued document.

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ANNEX C
Test Protocol Content

The test protocol/s shall contain the following information:

Background (combining the introduction, objective and literature review)	Information on the Product • product owner • product classification • formulation type • identity and concentration of the active ingredient/s • available information on the efficacy of the active ingredient/s against the intended target pest • available information on the toxicity of the active ingredients, both acute and chronic toxicity • available information on resistance and cross-resistance of target pests against the active ingredient/s • information whether the test/s have been previously accepted by other regulatory agency Purpose of the proposed test • specific claim of the household pesticide (includes field of use, mode of application, target pest/s, dilution rate, application rate, frequency of re-application) Justification/Reason for the modified or non-standard protocol • Existing accepted protocol, if available • compelling reason for the modification or use of non-standard test protocol

Methodology	Test Duration
	Test insect/s
	• species (in binomial nomenclature)
	• source (i.e. laboratory-reared, wild-collected)
	  • rearing technique for laboratory-reared target insect/s including environmental conditions and food
	• age and sex
	Positive Control
	• registered HUP product with the same active ingredient/s or active ingredient belonging from the same chemical family
	• include the HSR number
	Negative Control
	Test Procedure including but not limited to:
	• environmental conditions
	• acclimatization of test insect/s
	• mode of application
	• dilution rate,
	• application rate
	• size of the test
	  • number of test insect/s per replicate
	  • number of replicates (min. of 3)
	• test area / facility / equipment

	• laboratory trial: design of chamber including material and dimension, cleaning/washing protocol, etc • field trial: plot size, selection criteria for the test location, equipment design, cleaning/washing protocol, etc • schedule of observation • efficacy Parameter • in case of modified protocol, include a description of the modifications made in their respective sections Statistical Analysis In case human subjects are part of the proposed test protocol, include the selection criteria, copy of informed consent form, certification/approval from a Research Ethics Committee
References	Include in-text citation, reference list at the end of the document and pdf copies of the references

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