TERMS AND CONDITIONS

LABORATORY SERVICES FOR STABILITY STUDY OF ULASIMANG BATO 500 MG TABLET OF THE PITAHC TACLOBAN HERBAL PROCESSING PLANT

I. BACKGROUND AND RATIONALE

The Philippine Institute of Traditional and Alternative Health Care (PITAHC) is the lead agency in the research and development, promotion and advocacy, and development of standards on traditional and complementary medicine (T&CM); and the Institute ensures its accessibility, availability, sustainability and integration into the national health care. system.

The Institute has three (3) existing Herbal Processing Plants located in Cagayan Valley, Tacloban and Davao. In the past, these HPPs produced Lagundi and Sambong tablets and supplied the Department of Health (D0 OH) offices, hospitals, and other local government agencies.

Currently, PITAHC has a licensing agreement with the University of the Philippines (UP) Manila for five (5) herbal medicines, under which PITAHC has secured a non-exclusive license for the commercial development, production, manufacture, use, and sale of the licensed goods. One of the licensed products is the Ulasimang Bato 500 mg Tablet.

Shelf-life testing, also known as stability testing, is an assessment of a product's functioning, acceptability, safety, effectiveness, and stability over time in order to determine or verify its expiration date.

The Philippine Institute of Traditional and Alternative Health Care (PITAHC - Tacloban) is responsible for ensuring the safety, efficacy, and quality of herbal medicine being produced. As part of this mission, PITAHC Tacloban requests laboratory assistance to undertake a Stability Study on Ulasimang bato. These services are vital for determining the product's stability and quality throughout time. The service will include a variety of testing to guarantee product quality and safety. The results of these laboratory services for the Ulasimang bato 500 mg tablet developed by PITAHC-THPP will be critical for its FDA registration.

II. OBJECTIVES

The General Objective of this project is to render service of a third-party provider for laboratory services for PITAHC THPP's Ulasimang bato 500 mg tablet for FDA registration.

The specific objectives of this project are as follows:

a. To conduct the stability study on three samples of lot or batch of Ulasimang bato over 0, 3, 6, 12, 18, and 24 months

b. To evaluate the physical and chemical properties of the samples at different time intervals, including weight variation, moisture content, tablet hardness, friability, disintegration, TLC profiling, and organoleptic properties.
c. To assess the microbial load of the samples, including testing for Total Aerobic Count (TAC), Total Yeast and Mold (TYM), Escherichia coli (*E. coli)*, Pseudomonas aeruginosa, Enterobacteria, Staphylococcus aureus, and Salmonella spp.
d. To determine the levels of heavy metals, including lead, cadmium, arsenic, and mercury in the samples.

III. METHODOLOGY

The main purpose of this_project is to conduct the analytical tests necessary to assess the quality of *Ulasimang bato* tablets upon manufacturing and over defined time periods as defined in the regulatory requirements in FDA A.O. 172 s. 2004 ("Guidelines on the Registration of Herbal Medicine").

1. Physicochemical and Microbiological Analysis of the Raw Material

The quality of the raw material (*Peperomiae Pellucidae Herba Pulveratum*) shall be assessed against the set of physicochemical and microbiological technical specifications defined in the Philippine Pharmacopoeia, as seen in **Table 1** below.

Table 1. Technical specifications for *Peperomiae Pellucidae Herba Pulveratum*

Parameter	Specification	Test Method
Macroscopic Description	Conforms to morphological description of *Peperomia pellucida* in Philippine Pharmacopoeia	Taxonomic Description
Botanical Identity	Certification Available from Registered Herbarium	Taxonomic Description
Organoleptic Description	Greenish-brown to brown fine powder with characteristic odor	Sensory Evaluation
Ash Content Total Ash Acid-insoluble Ash Water-soluble Ash	 NMT 27% NMT 8% NMT 16%	 Gravimetry Gravimetry Gravimetry
Extractives Content Ethanol-soluble Extractives Water-soluble Extractives	 NLT 5% NLT 25%	 Gravimetry Gravimetry
Moisture Content	NMT 10%	Gravimetry
Heavy Metals Content Lead Cadmium Mercury Arsenic	 NMT 10 ppm NMT 0.3 ppm NMT 0.5 ppm NMT 0.3 ppm	 AAS / ICP-MS AAS / ICP-MS AAS / ICP-MS AAS / ICP-MS
Pesticide Residue Organochlorine Organophosphate Carbamate	 Absent Absent Absent	 HPLC HPLC HPLC
Foreign Matter	NMT 2%	
Microbial Limits Aerobic Plate Count Yeast and Mold Count *Escherichia coli* *Salmonella* spp. *Staphylococcus aureus* Other Enterobacteriaceae	 NMT 1 x 10^5 NMT 1 x 10^3 Absent Absent Absent NMT 1 x 10^3	 Microbial Enumeration Microbial Enumeration Microbial Enumeration Microbial Enumeration Microbial Enumeration Microbial Enumeration
Aflatoxin Content Total Aflatoxin Aflatoxin B1	 NMT 20 ppb NMT 10 ppb	 ELISA ELISA
Identification Test	Conforms to Phytochemical Profile for *Peperomia pellucida*	TLC

2. Physicochemical and Microbiological Analysis of Finished Product

The quality of the finished product (*Peperomiae pellucidae* Tablet) shall be assessed against the set of physicochemical and microbiological technical specifications defined in the Philippine Pharmacopoeia, as seen in **Table 2** below.

Table 2. Technical specifications for *Peperomiae pellucidae Tablet*

Parameter	Specification	Test Method
Organoleptic Description	Plain, uncoated, brown tablets with characteristic pungent odor	Sensory Evaluation
Moisture Content	NMT 10%	Gravimetry
pH	Informative	Conductivity
Microbial Limits		
Aerobic	NMT 1 x 10^5	Microbial Enumeration
	NMT 1 x 10^3	Microbial Enumeration
Plate Count	Absent	Microbial Enumeration
Yeast and Mold Count	Absent	Microbial Enumeration
Escherichia coli	Absent	Microbial Enumeration
Salmonella spp.	Absent	Microbial Enumeration
Staphylococcus aureus	NMT 1 x 10^3	Microbial Enumeration
Pseudomonas aeruginosa		
Other Enterobacteriaceae		
Identification Test	Conforms to Phytochemical Profile for *Peperomia pellucida*	TLC
Weight Variation	675 mg ± 5% RSD	Gravimetry
Disintegration Time	NMT 30 mins	Disintegration Test
Hardness	<98 N	Hardness Test
Friability	<1.0%	Friability Test

3. Nutritional Analysis of Finished Product

In addition to the physicochemical and microbiological parameters of the finished product, nutritional analysis will be conducted to assess the nutritional value of the drug product and to provide additional data in the preparation of the Certificate of Analysis of the finished product. **Table 3** below shall define the parameters to be assessed. Nutritional analysis shall be conducted on the finished product and shall not constitute a parameter for stability study.

Table 3. Technical specifications for nutritional analysis.

Parameter	Specification	Test Method
Calories		
Total Calories	Informative	Calculation
Calories from Fat	Informative	Calculation
Fat Content		
Total Fat	Informative	FAO Food 14/7-1986
Saturated Fat	Informative	FAO Food 14/7-1986
Trans Fat	Informative	FAO Food 14/7-1986
Cholesterol	Informative	FAO Food 14/7-1986
Sodium	Informative	AAS / ICP-MS
Potassium	Informative	AAS / ICP-MS
Carbohydrate Content		
Total Carbohydrates	Informative	AOAC 986.25
Dietary Fiber	Informative	AOAC 986.25
Sugar	Informative	AOAC 986.25
Protein Content	Informative	FAO Food 14/7-1986

4. Accelerated Stability Study

A six-month stability study under accelerated IVB climatic zone conditions (40°C ± 2°C / 35% RH ± 5% RH) shall be conducted on two (2) distinct production or commercial scale batches of *Ulasimang bato* tablets following the ASEAN Guideline on Stability of Drug Product (R1) using the minimum recommended testing frequency of **0th, 3rd, and 6th** month testing. The parameters defined in Section III-2 ("Physicochemical and Microbiological Analysis of Finished Product") shall constitute the specification of the product to be assessed throughout the course of the stability study. The contract service provider shall define the minimum number of samples (including contingency samples) to be provided by DOH-PITAHC necessary to conduct the stability study. For each batch tested, the contract service provider must provide and issue a **Stability Study Protocol**. The project manager from DOH-PITAHC shall be notified within 7-14 working days from the release of the result regarding any deviations or out-of-specification (OOS) results from the protocol.

5. Long Term Stability Study

A twelve-month stability study under standard IVB climatic zone conditions (30°C ± 2°C / 35% RH ± 5% RH) shall be conducted on two (2) distinct production or commercial scale batches of *Ulasimang bato* tablets following the ASEAN Guideline on Stability of Drug Product (R1) using the minimum recommended testing frequency of **0th, 3rd, 6th, 9th, and 12th** month testing. The parameters defined in Section III-2 ("Physicochemical and Microbiological

Analysis of Finished Product") shall constitute the specification of the product to be assessed throughout the course of the stability study. The contract service provider shall define the minimum number of samples (including contingency samples) to be provided by DOH-PITAHC necessary to conduct the stability study. For each batch tested, the contract service provider must provide and issue a **Stability Study Protocol**. The project manager from DOH-PITAHC shall be notified within 7-14 working days from the release of the result regarding any deviations or out-of-specification (OOS) results from the protocol.

6. Data Presentation

Data for all physicochemical, microbiological, and nutritional analyses shall be summarized into a **Report of Analysis (RoA)** and an electronic copy of a corresponding **Certificate of Analysis (CoA)** shall be issued to the Project Manager from DOH-PITAHC within 7-14 working days upon complete availability of results for all test parameters listed in the CoA.

For stability study results, a CoA shall be issued for each stability testing time point in the study period, an electronic copy of which shall be sent to the Project Manager from DOH-PITAHC within 7-14 working days upon complete availability of results for all test parameters listed in the CoA. An accompanying **Technical Summary Report** shall also be included with an interpretation of the data observed as of the period of testing.

Upon completion of the stability study, a **Stability Study Summary Sheet** briefly detailing the main results of the study shall be provided to the Project Manager from DOH-PITAHC within 7-14 working days upon complete availability of results. An accompanying **Technical Summary Report** shall also be included with a final interpretation of the data observed as of the end of the study.

7. Sample and Data Retention

A minimum retention sample size of 10.0 g shall be retained and stored at -40°C for each sampling interval throughout the duration of the stability study to serve as a reference for use in identification tests. A minimum retention sample size equivalent to three (3) additional testing points for accelerated, and eight (8) additional testing points for long term, shall be included in the stability study.

Data generated from the study shall be retained and made accessible to DOH-PITAHC for a period of four (4) years following the end of the contract of service, after which all data shall be destroyed in a manner deemed appropriate by the contract service provider.

All unrefrigerated unused stability study samples shall be destroyed within two (2) years from the end of the contract of service, in a manner deemed appropriate by the contract service provider.

All refrigerated samples shall be destroyed within one (1) year from the end of the contract of service, in a manner deemed appropriate by the contract service provider.

IV. SCOPE OF WORK

A. Responsibilities of the Service Provider:

To meet the above-mentioned objectives, the Service Provider should be able to:

1. Implement the project on the design/development the institutional contracting mechanism;
2. Providing an accelerated storage chamber capable of simulating conditions for 18-24 months of storage.
3. Conducting weight variation tests to assess the uniformity of weight among tablets.
4. Performing moisture content analysis to determine the moisture content of the samples.
5. Testing tablet hardness and friability to evaluate the mechanical strength of the tablets.
6. Conducting disintegration tests to assess the time taken for tablets to disintegrate.
7. Performing TLC profiling to identify and quantify the active constituents of Ulasimang bato.
8. Assessing microbial load through testing for TAC, TYM, E. coli, P. aeruginosa, Enterobacteria, S. aureus, and Salmonella spp.
9. Testing for heavy metals, including lead, cadmium, arsenic, and mercury, to ensure compliance with safety standards.
10. Conducting organoleptic tests to evaluate the sensory properties of the samples. and help clients answer specialized business questions with its market research.

B. Responsibilities of the PITAHC

1. Allocate the amount of Php700,000.00 inclusive of applicable taxes, chargeable against the funds of PITAHC- THPP and Research and Development Division, the disbursement of which shall follow the schedule of payment;
2. PITAHC through the PITAHC-THPP and R&DD shall oversee the overall conduct of this project;
3. Responsible for the timely provision of access, information, decision-making which are necessary for the achievement of the project
4. Make prompt review of the work produced and presented by the Service Provider in the different phases of the project;

5. Review and evaluate all the technical progress reports and final report submitted by Service Provider;
6. Process payment on schedules as stated in the section VI of this term;
7. Issue certification of final acceptance and recommendation for payment.

V. QUALIFICATIONS FOR SERVICE PROVIDER

1. The Service Provider must possess the following qualifications:

   a. Service Provider must have a valid FDA License to Operate (LTO) and certified with Current Good Manufacturing Practices (cGMP);
   b. Product development team lead must be a graduate of BS Pharmacy, Chemistry, Biotechnology or equivalent;
   c. Certification that bidder has at least 10-year experience in providing verifiable data, analysis in the pharmaceutical sector, locally and globally;
   d. Service Provider must have an experience dealing with Government Owned and Controlled Corporations (GOCCs) State Universities, and/or national government agencies in the provision of market share data/information and analysis;
   e. Service Provider must have an experience with working with pharmaceutical companies in product development and contract manufacturing

VI. APPROVED BUDGET FOR THE CONTRACT (ABC) AND PAYMENT SCHEDULE

1. The approved budget for the contract is Seven Hundred Thousand Pesos (Php 700,000.00).
2. For and in consideration of the services of the Service Provider, PITAHC shall make the following payment tranches:

PAYMENT TRANCHE	ACCOMPLISHMENT	PERCENT	AMOUNT
1st (within 2 weeks from the submission of inception report)	1. Acceptance of Notice to Proceed 2. Signed contract of service 3. Submission of Inception Report (Stability Study Protocol)	15%	105,000.00
2nd (Delivery of progress reports within 3 months from the submission of the inception report)	Submission of Progress Report/s (4 hard copies with electronic copy) Report on the initial phase of stability study, on"0 & 3 month" condition (long term and accelerated) a. Detailed analyses of physical and chemical properties, including weight variation, moisture content, tablet	45%	315,000.00

PAYMENT TRANCHE	ACCOMPLISHMENT	PERCENT	AMOUNT
	hardness, friability, disintegration, TLC profiling, and organoleptic properties. b. Microbial load analysis reports, including results for TAC, TYM, E. coli, P. aeruginosa, Enterobacteria, S. aureus, and Salmonella spp. c. Heavy metal testing reports, providing levels of lead, cadmium, arsenic, and mercury in the samples.		
3rd (Delivery of progress reports within 3 months from the submission of the latest progress reports)	Report on the initial phase of stability study, on"6 month" condition (long term and accelerated) a. Detailed analyses of physical and chemical properties, including weight variation, moisture content, tablet hardness, friability, disintegration, TLC profiling, and organoleptic properties. b. Microbial load analysis reports, including results for TAC, TYM, E. coli, P. aeruginosa, Enterobacteria, S. aureus, and Salmonella spp. c. Heavy metal testing reports, providing levels of lead, cadmium, arsenic, and mercury in the samples.	30%	210,000.00
Final (Delivery of final reports within 3 months from the submission of the latest progress reports)	Submission of Final Report a. Detailed analyses of physical and chemical properties, including weight variation, moisture content, tablet hardness, friability, disintegration, TLC profiling, and organoleptic properties. b. Microbial load analysis reports, including results for TAC, TYM, E. coli, P. aeruginosa, Enterobacteria, S. aureus, and Salmonella spp. c. Heavy metal testing reports, providing levels of lead, cadmium, arsenic, and mercury in the samples. d. Recommendations based on the findings, including any necessary actions to maintain or improve product quality	10%	70,000.00
	TOTAL ABC		700,000.00

3. Payments shall be based on the completion of the above-mentioned activities and submission of required deliverables/reports subject to acceptance of the authorized representative of the Head of the Procuring Entity.

VII. DURATION OF ENGAGEMENT AND IMPLEMENTING ARRANGEMENT

The engagement shall be completed within nine (9) months from the receipt of the Notice to Proceed (NTP).

The PITAHC Research and Development Division and Tacloban HPP shall be the focal office in this engagement and the highest oversight authority.

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Director General

MARIA VENUS K. APOLONIO, RPh
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MICHAEL D. JUNSAY, RPh, CPS, MBAH
OIC, Research and Development

VIII. CONFIDENTIALITY

The Service Provider shall not use (except for PITAHC's benefit) or divulge to anyone-either during the term of this Agreement or thereafter - any of the PITAHC's trade secrets, the proprietary information, or other proprietary data, personal information covered by the Data Privacy Act, or information of any kind whatsoever acquired by the Service Provider in carrying out the terms of this agreement. In this regard, the Service Provider shall:

1. Warrant, represent and undertake reliability of the service required;
2. Agree to hold the proprietary information in strict confidence;
3. Agree not to reproduce, transcribe or disclose the proprietary information to third parties without prior written approval from the CLIENT; and
4. Uphold strict confidentiality of all information that will come to Service Provider knowledge.

IX. TERMINATION

The PITAHC may, in case of material default on the part of the Service Provider, terminate the contract, through written notice to the Service Provider at least thirty (30) days prior to the termination, and that the Service Provider failed to resolve the fault within the conditions and period specified in the Notice. The CLIENT shall only be liable to pay the Service Provider on the accomplishments delivered prior to the termination of the contract, and shall not in any way, prevent or prejudice any other claims which the parties may have against each other.

X. OTHER DOCUMENTARY REQUIREMENTS

1. List of Proposed completed and ongoing projects; and
2. List of technical personnel with their Curriculum Vitae indicating the relevant training and certification, and Professional Licenses, if applicable.

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