

Reference No. \_\_\_\_\_

## TERMS OF REFERENCE

**Project Title:** Procurement of Professional Services for the Full Health Technology Assessment of Osimertinib for EGFR-positive non-small cell lung cancer (NSCLC)

**Funding Source:** DOST GAA for the Health Technology Assessment implementation

### I. Background

Pursuant to the Universal Health Care (UHC) Act, all health technologies that the government will implement and cover shall undergo health technology assessment (HTA). This aims to ensure the rational utilization of various health technologies that will be funded by the government.

In this regard, a collaborative approach in HTA, through the commissioning of independent academic teams via the HTA research network to conduct the topic assessments as stipulated in the HTA Process Guide, will streamline the work on evidence reviews and accelerate the delivery of much-needed advice by decision-makers and health policy makers. In 2022, the HTA Council started to commission assessments of priority health technologies through research partners to complement the current internal capacity for HTA.

This project is therefore being undertaken to facilitate the conduct of the full health technology assessment (clinical assessment, economic assessment, ethical, legal, social, and health systems impact assessment) for Osimertinib for Epidermal Growth Factor Receptor (EGFR)-positive non-small cell lung cancer (NSCLC), to be appraised by the HTA Council in developing their financing recommendations to DOH and/or PhilHealth.

This topic underwent an eligibility assessment for possible accelerated HTA track, where recommendations from the WHO Model List of Essential Medicines, and local and international clinical practice guidelines were reviewed to establish its use as standard of care for the treatment of EGFR-positive NSCLC. While it is considered as standard of care, the HTA Council concluded that a full assessment is needed to determine the additional value of Osimertinib, given its higher cost compared to other tyrosine kinase inhibitors (TKIs) for EGFR-positive NSCLC reviewed (i.e., Erlotinib, Gefitinib, and Afatinib). Additionally, new clinical evidence must be reviewed to update the local DOH-approved clinical practice guideline on lung cancer.

This specific Terms of Reference (TOR) is for the contracting of the external full HTA. The external assessment group (EAG) to be selected shall conduct the HTA based on the guidelines stated in this TOR, which is based on the HTA Methods Guide, to ensure that evidence outputs are of high quality and can be used as evidentiary basis for the HTA Council in developing recommendations to DOH and PhilHealth policy-makers on coverage/financing decisions.

## II. Objectives

### A. General Objective

To determine the clinical, economic, and ELSHI impact of **Osimertinib** as adjuvant treatment for early-stage EGFR-positive non-small cell lung cancer (NSCLC) after tumor resection, as first-line treatment for locally advanced or metastatic EGFR-positive NSCLC (with subgroup analysis for brain metastasis), and as subsequent therapy for NSCLC patients who have progressed on first- and second-generation EGFR TKIs, to guide the HTA Council in the development of the HTA recommendation on coverage and financing decisions of DOH and PhilHealth.

### B. Specific Objectives

#### 1. Clinical Assessment

- a. To determine the appropriate Population, Intervention, Comparator, and Outcome (PICO) for the assessment topic
- b. To determine the critical clinical outcomes and their corresponding minimal important difference (MID) to be used as the decision threshold for interpreting review findings
- c. To determine the clinical evidence synthesis methodology track\* through an initial scoping of evidence

*\*Possible clinical evidence synthesis tracks depending on the existing evidence:*

- i. de novo systematic review with meta-analysis or network meta-analysis*
  - ii. updating of an existing systematic review with meta-analysis or network meta-analysis*
  - iii. adoption of an updated systematic review with meta-analysis or network meta-analysis*
- d. To appraise evidence based on the final methodology track\*, through the use of the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Approach
  - e. To determine the clinical impact (i.e. efficacy and safety for drugs) of the health technology of interest based on the synthesized evidence
  - f. To identify relevant international policies and guidelines on the use of the health technology of interest
  - g. To determine the applicability and usefulness of additional evidence that may be submitted by nominators and stakeholders, and incorporate meritable additional evidence

#### 2. Economic Assessment

- a. To determine the value for money of Osimertinib for EGFR-positive non-small cell lung cancer
- b. To determine the budget impact of Osimertinib for EGFR-positive non-small cell lung cancer
- c. To determine the household financial impact of non-small cell lung cancer

#### 3. Ethical, Legal, Social, and Health Systems Impact Assessment

- a. To determine the ethical, legal, social, and health systems impact of Osimertinib for EGFR-positive non-small cell lung cancer

### III. Scope of Work and Expected Outputs and Deliverables

1. Implement the research project as per the developed and approved (with technical and ethical clearances, if applicable) research proposals;
2. Submit all research project deliverables according to the prescribed timelines below and following the forms or templates as prescribed in the Official Call Guide, incorporating the HTA Process Guide and Methods Guide;

Phase	Output(s)	Timeline
<b>A. Alignment</b>	<ol style="list-style-type: none"> <li>1. Alignment meeting before inception report submission</li>   <li>2. Approved inception report               <ul style="list-style-type: none"> <li>- Methodological Plan</li> <li>- Detailed budget proposal</li> <li>- Detailed and Feasible Work Plan</li> </ul> </li> </ol>	<p><b><u>Month 1:</u></b> <i>Within 7 calendar days after signing of the Memorandum of Agreement</i></p> <p><i>Within 7 calendar days after the alignment meeting</i></p>
<b>B. Clinical Assessment</b>		
B.1. Research Question Finalization	<ol style="list-style-type: none"> <li>1. Stakeholder-validated PICO, including the proposed critical outcome/s and their corresponding importance ranking for HTA Council vetting and approval, with information required from the <u>HTA Methods Guide Annex 3</u></li> <li>2. PICO Consultation Report, with information required from the <u>HTA Methods Guide Annex 4</u></li> </ol>	<p><b><u>Month 2:</u></b> <i>Within 30 calendar days after the approval of the inception report</i></p>

		3. HTA Council approval of stakeholder-validated PICO ( <i>through meeting or ad ref</i> )	
B.2. Methodology Track Finalization	<ol style="list-style-type: none"> <li>1. Scoping of evidence to set MID thresholds</li> <li>2. Scoping of clinical evidence report and proposed clinical evidence synthesis methodology track before proceeding to assessment</li> <li>3. Meeting with HTA Council Core and/or Subcommittee to present the proposed MID as decision threshold for each critical outcome and proposed methodology track</li> </ol>	<p><b><u>Month 3:</u></b>  <i>Within 30 calendar days after the approval of the PICO/Research Questions</i></p>	
B.3. Presentation of Clinical Assessment	<ol style="list-style-type: none"> <li>1. Draft Clinical Assessment Report prior to the presentation meetings <ul style="list-style-type: none"> <li>- Clinical assessment</li> <li>- Guideline review</li> </ul> </li> <li>2. Evidence slides for the presentation to the HTA Council Subcommittee</li> <li>3. Meetings to present findings: EAG presentation of findings to the HTA Council Subcommittee</li> </ol>	<p><b><u>Month 4:</u></b>  <i>Within 30 calendar days after the approval of the proposed final evidence synthesis methodology track and MID</i></p> <p><b><u>Month 5:</u></b>  <i>Within 14 calendar days after the HTA Philippines sent the comments on the draft Final Report</i></p> <p><i>Note: There may be more than one EAG presentation to the HTA Council Subcommittee (SC), depending on the quantity and complexity of SC comments to be addressed by the EAG. Subcommittee-level should be</i></p>	

		<i>resolved to finalize revisions in the assessment report, the clinical judgment and the relevant clinical input parameters for the economic assessment.</i>
<b>C. Economic Assessment (conducted simultaneously with the ELSHI Assessment after clinical assessment is completed, with HTA Council-approved judgment)</b>		
C.1. Scoping of Economic Evaluation Studies	Scoping of economic evidence report, which will include the following: <ul style="list-style-type: none"> <li>- Initial scoping of existing economic evaluations</li> <li>- Final Methodological Plan (<i>based on the findings of the initial scoping of existing economic evaluations</i>)</li> </ul>	<b><u>Month 6:</u></b> <i>Within 30 calendar days after finalization of the clinical judgment</i>
C.2. Finalization of Economic Model and Input Parameters	<i>Initial</i> Economic Assessment Report including: <ul style="list-style-type: none"> <li>- Approved model to be used for the economic evaluation and BIA</li> <li>- Approved input parameters</li> </ul>	<b><u>Month 7 to 8:</u></b> <i>Within 60 calendar days after finalization of methodological plan</i>
C.3. Presentation of Economic Assessment	<ol style="list-style-type: none"> <li>1. Draft Economic Assessment Report prior to the presentation meetings <ul style="list-style-type: none"> <li>- Economic Evaluation</li> <li>- Budget Impact</li> <li>- Household Financial Impact</li> </ul> </li> <li>2. Meetings to present findings: EAG presentation of findings to the HTA Council Subcommittee</li> </ol>	<b><u>Month 9:</u></b> <i>Within 30 calendar days after the approval of model and input parameters</i>  <b><u>Month 10:</u></b> <i>Within 14 calendar days after the HTA Philippines sent the comments on the draft Economic Assessment Report</i>

		<p><b>Note:</b> There may be more than one EAG presentation to the HTA Council Subcommittee (SC), depending on the quantity and complexity of SC comments to be addressed by the EAG. Subcommittee-level comments should be resolved to finalize revisions in the assessment report and the economic assessment judgment</p>
<p><b>D. ELSHI Assessment (done simultaneously with the Economic Assessment)</b></p>		
D.1. Scoping of ELSHI studies	<p>Scoping of ELSHI evidence report, which will include the following:</p> <ul style="list-style-type: none"> <li>- Initial scoping of existing ELSHI studies</li> <li>- Final Methodological Plan (based on the findings of the initial scoping of existing ELSHI studies)</li> </ul>	<p><b>Month 6:</b> Within 30 calendar days after finalization of the clinical judgment</p>
D.2. Qualitative Systematic Review	<p>Qualitative systematic review</p> <ul style="list-style-type: none"> <li>- Methodology</li> <li>- Final included studies with extraction</li> <li>- Results of evidence appraisal</li> <li>- Synthesis of evidence</li> </ul>	<p><b>Month 7:</b> Within 30 calendar days after submission of scoping of evidence</p>
D.3. Primary data collection	<p>Primary data collection report</p> <ul style="list-style-type: none"> <li>- Ethics review</li> <li>- Data collection guide</li> <li>- Methodology</li> <li>- Coding analysis and transcript after primary data gathering</li> <li>- Results</li> </ul>	<p><b>Month 7:</b> Within 30 calendar days after submission of scoping of evidence</p>
D.4. Presentation of ELSHI Assessment	<p>1. Draft ELSHI Assessment Report prior to the presentation meetings</p>	<p><b>Month 8 to 9:</b> Within 60 calendar days after the submission of QSR and/or primary data collection report</p>

	<p>2. Meetings to present findings: EAG presentation of findings to the HTA Council Subcommittee</p>	<p><b>Month 10:</b> <i>Within 14 calendar days after the HTA Philippines sent the comments on the draft Final Report</i></p> <p><b>Note:</b> <i>There may be more than one EAG presentation to the HTA Council Subcommittee (SC), depending on the quantity and complexity of SC comments to be addressed by the EAG. Subcommittee-level should be resolved to finalize revisions in the assessment report and the ELSHI assessment judgment</i></p>
<p><b>E. Finalization</b></p>	<p>1. HTAC meeting</p> <ul style="list-style-type: none"> <li>- The EAG can also be invited as resource persons (if necessary) during the HTA Council Subcommittee Presentation to the Core Committee</li> </ul> <p>2. Final report for clinical, economic, and ELSHI assessments</p> <p><b>Note:</b> For topics with appeals from the stakeholder consultation period the Final Assessment Report must have already included the appraisal of new evidence that may be received from appellants during the stakeholder consultation phase.</p>	<p><b>Month 11:</b> <i>Within 15 calendar days after finalization of economic and ELSHI judgments</i></p> <p><b>Month 12:</b> <i>Within 15 calendar days after finalization of HTAC preliminary recommendation or HTAC final recommendation</i></p>

**Note:** *Timelines may vary as all the outputs are subject to review of the HTA Philippines which may require revisions in order to comply with the HTA Methods Guides.*

3. Provide regular updates following the prescribed timelines to HTA Council and Staff on the status of the assessment through electronic mails and/or checkpoint meetings;
4. Closely coordinate with the HTA Council for any issues or advice/ guidance needed in the activities within the project;
5. Submit the final HTA Council-approved technical report one month before end of project
6. By the end of the contract, ensure submission of all deliverables according to the specifications indicated in Section VIII.B.

#### **IV. Project Duration**

These Terms of Reference shall take effect upon signing by both Parties hereto and shall remain effective for *1 year and 1 month* (12 months project implementation + 1 month to complete all final deliverables and process payment) upon signing of the Memorandum of Agreement/Contract.

#### **V. Project Delays**

Except for delays resulting from circumstances beyond the control of the parties, such as, but not limited to, force majeure and others of similar nature, no extension of the project period shall be allowed.

Where such uncontrollable situations, however, arise, extension may be allowed at no additional cost. In instances when the HTA Council fails to meet its obligations to the implementing agency (i.e., review of reports within the agreed time), they will be granted a no-cost extension equivalent to the length of delay caused by the HTA Council. In instances when the project team experiences unforeseen delays, scope creeps, resource constraints, and the like, only one (1) no-cost extension may be granted. The number of days of no-cost extension shall be determined by the HTA Council, which should be equivalent to delays that are considered valid based on the justification provided by the commissioned project team. All requests for no-cost extension shall be justified and shall be expressed in writing to HTA Council and HTA Council Staff for consideration. HTA Council and HTA Council Staff, in turn, shall review and decide upon all requests for no-cost extension from the external assessment group (EAG).

The HTA Council shall institute measures to hold implementing agency/partner research institutions accountable for the timely submission of their project deliverables, which includes the discontinuance of payments, following provisions under RA 12009 Section 71.3.

## **VI. Intellectual Property Rights and Publication of Assessments**

Pursuant to Section 16, Article VII of Republic Act no. 10055, otherwise known as the "Philippine Technology Transfer Act of 2009" and Rule 5 Chapter II of its implementing rules and regulations (IRR), ownership of intellectual property (IP)/intellectual property rights (IPR) of research projects that are fully-funded by the DOST rests with the research institution or the proponent/investigator unless a written document assigning the IP/IPR ownership to DOST-HTA Council and Staff has been provided. The disclosure of personal and sensitive personal information/data gathered under the project is covered by the Republic Act 10173 - Data Privacy Act of 2012.

In order to protect public interest, the ownership of all intellectual property and intellectual property rights (IP/IPR) resulting from projects covered by this TOR shall be made in favor of the DOST-HTA Council and Staff.

In case the consultant intends to publish the methods and results of the assessment, the DOST HTA Council shall provide clearance for the dissemination of DOST-funded research outputs in research-related meetings/fora/workshops/conferences or to publish in academic journals, the DOST HTA Council shall provide clearance, provided the following conditions are complied with:

- 1) The DOST-HTA Council has been informed in writing of the intent to publish/present the research;
- 2) All expected deliverables and outputs have been submitted to the DOST-HTA Council Staff and accepted by the DOST HTA Council;
- 3) Due acknowledgement has been given to the DOST-HTA Council and Council Staff for its role and participation in supporting the research project; and,
- 4) Required disclaimer (see below) is included in the presentation or published report.

*“This article/report reflects the points of view and thoughts of the authors’, and the information, conclusions, and recommendations presented must not be interpreted as those of the Department of Science and Technology HTA Council and Staff. The material presented here however is done in the spirit of promoting open access and meaningful dialogue for policy/plan/program improvement, and the responsibility for its interpretation and use lies with the reader.”*

The DOST-HTA Council and Council Staff reserve the right to use all the data and findings of the PROJECT in the pursuit of their respective official functions.

## **VII. Implementation Agreement**

A. Contact persons:

All communications and reports must be addressed to:

**ANNE JULIENNE GENUINO-MARFORI, RPh, MSc**  
Chief Science Research Specialist  
Health Technology Assessment Council

B. Reporting obligations, notices, and approval process, including minimum or essential reports' contents

Deliverable	Technical and formatting requirements
Inception Report	<ol style="list-style-type: none"> <li>1. Title</li> <li>2. Protocol information</li> <li>3. Background</li> <li>4. Research question</li> <li>5. Methodological Plan <ol style="list-style-type: none"> <li>a. Clinical Assessment</li> <li>b. Economic Assessment</li> <li>c. ELSHI Assessment</li> </ol> </li> <li>6. References</li> <li>7. Annexes</li> <li>8. Declarations</li> <li>9. Budget and Timelines</li> </ol>
Stakeholder-consulted PICO	<ul style="list-style-type: none"> <li>● PICO Consultation Report which includes the proposed PICO, including the proposed critical outcome/s, for HTAC approval and finalization (Refer to <u>HTA MG Annexes 3 and 4</u> for the content of the PICO Development Report and RQ Setting Stakeholder Consultation report)</li> </ul>
Scoping of evidence report	<ol style="list-style-type: none"> <li>1. Cover page (Research Title; Name and Signature, Designation and Affiliation of Research Lead; Date of Submission)</li> <li>2. Background <ul style="list-style-type: none"> <li>- Health problem and clinical management options</li> <li>- Description, technical characteristics, and use of the health technologies</li> </ul> </li> <li>3. Methodology of Scoping</li> <li>4. Results of Scoping</li> <li>5. Proposed methodological plan</li> <li>6. Annexes (if applicable)</li> <li>7. References</li> </ol>
Assessment Reports	Refer to HTA Methods Guides Annexes: <ul style="list-style-type: none"> <li>- Clinical Assessment Report: Annex 10</li> <li>- Economic Assessment Report: Annex 11</li> <li>- ELSHI Assessment Report: Annex 12</li> </ul>
Checkpoint meetings, as necessary	N/A

**Note:** Any undelivered outputs itemized in the Terms of References (TOR) and HTA Philippines' Interim second edition of the HTA Philippines Methods Guide shall be subjected to computation of liquidated damages for any delays.

**VIII. External Assessment Group (EAG) Qualification and Project Sites**

Philippine Universities/colleges, research agencies/institutions and other health-related agencies with the capacity to manage health research projects to be led by a researcher with at least a Master's degree in a relevant field and with at least 2 years of experience in health research. To be qualified to proceed with research commissioning, research or academic institutions must submit a proposal following the guidelines posted on the Call Guide, and approved by the HTA Council.

The project sites will be identified by the proponents and should be reflected on the proposal to be submitted to the Department of Science and Technology (if applicable).

**IX. Budget Proposal:**

**TWO MILLION TWO HUNDRED SEVENTY THOUSAND PESOS ONLY  
(PHP 2,270,000.00)**


**X. Terms of Payment**

Release	% of Fund	Requirements	Timelines
1st tranche	15%	<ul style="list-style-type: none"> <li>Approved Inception report</li> </ul> Percent completion of the project: 15%	1 month after signing of contract
2nd tranche	25%	<ul style="list-style-type: none"> <li>Finalized Research Question</li> <li>PICO Consultation Report</li> <li>Scoping of clinical evidence report</li> </ul> Percent completion of the project: 40%	3 months after signing of contract
3rd tranche	10%	<ul style="list-style-type: none"> <li>Draft clinical assessment report</li> <li>Presentation of the clinical evidence by the consultant through a meeting</li> </ul> Percent completion of the	5 months after signing of contract

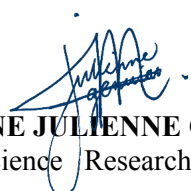
		project: 50%	
4th tranche	25%	<ul style="list-style-type: none"> <li>• Scoping of economic evaluation studies</li> <li>• Approved economic model and input parameters</li> <li>• Scoping of ELSHI studies</li> </ul> <p>Percent completion of the project: 75%</p>	8 months after signing of contract
5th	15%	<ul style="list-style-type: none"> <li>• Draft economic and ELSHI assessment report</li> <li>• Presentation of the economic and ELSHI evidence by the consultant through a meeting</li> </ul>	10 months after the signing of the contract
6th tranche	10%	<ul style="list-style-type: none"> <li>• Approved final clinical, economic, and ELSHI assessment reports</li> </ul> <p>Percent completion of the project: 100%</p>	12 months after signing of contract

Project outputs should be submitted to the HTA Council.

This is to certify that this project is prioritized by the Health Technology Assessment Council in the 2025 HTA research agenda and is approved by the HTA Council to be conducted by an external assessment group.

Certified by:   
**JACINTO BLAS V. MANTARING III, MD, MSc**  
 Chairperson, Health Technology Assessment Council

This is to certify that this partnership with detailed scopes of work, specified in this TOR, is chargeable against the DOST-GAA funds.

Recommending approval:   
**MS. ANNE JULIENNE G. MARFORI, RPh, MSc**  
 Chief Science Research Specialist, Health Technology Assessment Council