CLINICAL RESEARCH PROTOCOL

Protocol Number: MA25H0501 **Version:** v1.0 **Date:** November 19, 2025

1. GENERAL INFORMATION

Protocol Title: Guided **U**se of **A**rtificial Intelligence for **R**isk **D**etection of **P**ulmonary Hypertension in Surgery (GUARD-PH Trial): A Prospective, Open-Label, Randomized Controlled Trial of an Artificial Intelligence-Enabled Electrocardiography System for Preoperative Detection of Pulmonary Hypertension and Related Diseases

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Study Site: Taipei Veterans General Hospital, Taiwan

2. INTRODUCTION

2.1 Background Information Pulmonary Hypertension (PH) is defined as a mean pulmonary arterial pressure (mPAP) > 20 mmHg at rest. It is a condition with significant morbidity and mortality, particularly in patients undergoing surgery. The prevalence of PH is estimated at 1% in the global population and up to 10% in those over 65. Left heart disease and lung disease are the leading causes. Patients with PH face significantly higher risks of perioperative mortality and major cardiovascular events (8.3% vs. 2.0%) compared to those without PH. However, early diagnosis is often delayed due to non-specific symptoms. A screening tool to identify high-risk patients preoperatively could allow for timely intervention and risk reduction.

2.2 Research Motivation The "TAIMedImg" Pulmonary Hypertension Detection System (TAIMedImg PHDS) is an AI-enabled software that analyzes 12-lead ECGs to detect PH. It has demonstrated high diagnostic performance (AUC 0.83-0.92) in multi-center tests and received Taiwan FDA approval (License No. 008156) in 2025. This study aims to evaluate the clinical utility of this system in the preoperative setting.

3. STUDY OBJECTIVES

3.1 Primary Objective To evaluate whether the use of the "TAIMedImg" Pulmonary Hypertension Detection System can assist in the early detection of preoperative PH and PH-related diseases, thereby potentially reducing surgical risks or mortality.

4. STUDY DESIGN

4.1 Study Type This is a prospective, open-label, randomized controlled trial.

4.2 Study Population

- **Participating Physicians:** Surgeons responsible for preoperative assessment.
- **ECG Subjects (Patients):** Patients undergoing preoperative ECG assessment for non-cardiac surgery.

4.3 Randomization ECG Subjects will be randomized in a 1:1 ratio into two groups:

- **Experimental Group:** The participating physician receives the standard ECG report **PLUS** the AI-generated PH risk assessment.
- **Control Group:** The participating physician receives **ONLY** the standard ECG report.

5. ENDPOINTS

5.1 Primary Efficacy Endpoint Incidence of newly diagnosed pulmonary hypertension (PH), defined as echocardiographic right ventricular systolic pressure (RVSP) > 50 mmHg, or cardiopulmonary conditions associated with or leading to PH, occurring after the index ECG and before surgery; for participants who do not undergo surgery, occurring within 90 days after the index ECG.

5.2 Secondary Efficacy Endpoints

All participants

- Cardiovascular and all-cause mortality within 90 days of enrollment.

In the patients receiving surgery after enrollment

- Incidence of surgical complications during hospitalization.
- Cardiovascular mortality rate during hospitalization.

- All-cause mortality rate during hospitalization.
- Length of hospital stay.

6. SUBJECT SELECTION

6.1 Inclusion Criteria (ECG Subjects)

- Age 18 to 80 years.
- Scheduled for non-cardiac surgery under general anesthesia.
- Scheduled for a routine preoperative ECG.
- Willing to provide medical records for research and sign informed consent.

6.2 Exclusion Criteria (ECG Subjects)

- Scheduled for emergency surgery.
- Refusal to participate or withdrawal of consent.
- Presence of specific comorbidities that interfere with ECG data collection (e.g., implanted pacemaker).

7. STUDY PROCEDURES

7.1 Screening and Enrollment (Day -180 to Day -1)

- Obtain informed consent.
- Randomize subjects (1:1).
- Collect baseline demographics, medical history, and preoperative examination results (blood tests, echocardiography, etc.).
- Perform ECG (analyzed by AI for the Experimental Group).

7.2 Surgery (Day 0)

- Record surgical details (anesthesia, blood loss, vitals).
- Record any surgical complications.

7.3 Postoperative Follow-up (Day 0 to Day 90)

- Collect data on hospital course, discharge diagnosis, and any new

cardiopulmonary diagnoses.

- Record survival status and adverse events up to 3 months post-operation.

8. STATISTICAL ANALYSIS

8.1 Sample Size Estimated sample size is **1,380 subjects** (690 per group) to achieve 80% power to detect a superiority margin of 0.5% in the diagnostic rate (assuming 0.5% in control vs. 3.0% in experimental group).

8.2 Statistical Methods

- **Primary Endpoint Analysis:** Two-proportion Z-test to compare the incidence rates between groups.
- **Secondary Endpoints:** Chi-square tests for categorical variables and T-tests/Wilcoxon rank sum tests for continuous variables. Kaplan-Meier survival analysis will be used for mortality endpoints.
- **Significance:** P-value < 0.05 is considered statistically significant.

9. ETHICAL CONSIDERATIONS

The study will be conducted in compliance with the Declaration of Helsinki and Good Clinical Practice (GCP). The protocol has been approved by the Institutional Review Board (IRB) of Taipei Veterans General Hospital (IRB No: 2025-10-004CCF). Informed consent will be obtained from all participating physicians and patients.

10. DATA HANDLING AND RECORD KEEPING

Data will be collected on Case Report Forms (CRF) and stored securely. Subject confidentiality will be maintained by using coded identifiers. All trial-related documents will be retained for 10 years after study completion.