STANDARD OPERATING PROCEDURE

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Written by: HTA Team

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Approved by: Sarvashni Moodliar

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GUIDELINES FOR HTA EVALUATIONS

1 TERMS OF REFERENCE FOR THE 'GUIDELINES FOR HTA EVALUATIONS'

This document outlines the procedures to follow when supplier or laboratories require to have an Invitro Diagnostic Medical Device evaluated.

- All new or modified technologies proposed to the NHLS; the supplier is required to meet with the NHLS HTA Unit prior to consultation with other NHLS staff members.
- All new technologies entering the NHLS; will make use of a single entry (i.e. the HTA Unit).
- To coordinate evaluations thereby improving processes and addressing duplication of work within NHLS laboratories.
- Providing guidance to NHLS laboratories with refererence to evaluation protocols and report templates to be followed.
- Ensuring evaluation documentation is safely kept for future reference and freely available to NHLS staff
- Implementing a structure in place for post-marketing surveillance ongoing safety, and efficacy of *Invitro Diagnostic Medical Device*

2 DEFINITIONS:

Evaluation: The systematic assessment of the relevance, adequacy, progress, efficiency or effectiveness of a project OR the process of determining the worth or significance of an activity.

Cost: An amount paid or required in payment for a purchase; a price.

Supplier: Indicates a vendor that provides goods or service to the NHLS. This supplier becomes a client to the HTA Unit upon applying for an evaluation.

Contract: An agreement between two or more parties, especially one that is written and enforceable by law.

Invitro Diagnostic medical device: 'Is any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information for patient care.

Analytes: An analyte is a substance or chemical constituent that is determined in an analytical procedure, such as a titration. For instance, in an immunoassay, the analyte may be the ligand or the binder, while in blood glucose testing, the analyte is glucose. In medicine, analyte often refers to the type of test being run on a patient, as the test is usually determining a chemical substance in the human body.

Timeframe: A period during which something takes place or is projected to occur:

Prorforma invoice: The cost before the evaluation is done.
Invoice issued before an order is placed or before the goods are delivered giving all the details and the cost of the goods

Ethics: As moral philosophy is a branch of philosophy that addresses questions about morality; that is: concepts such as good and evil, right and wrong, virtue and vice, justice, etc.

Protocol: A set of guidelines or rules.

Report: Written reports are documents which present focused, salient content to a specific audience. Reports are often used to display the result of an experiment, investigation, or inquiry.

Person: Includes a juristic person.

Methodologies: A methodology, is instantiated and materialized by a set of methods, techniques and tools. A tool is an instrument or apparatus that is necessary to the performance of some task. A methodology doesn't describe specific methods; nevertheless it does specify several processes that need to be followed. These processes constitute a generic framework. They may be broken down in sub-processes, they may be combined, or their sequence may change. However any task exercise must carry out these processes in one form or another.

Cost effective: This form of analysis seeks to determine the costs and effectiveness of surveillance and response strategies and activities. It can be used to compare similar or alternative strategies and activities to determine the relative degree to which they will obtain the desired objectives or outcomes. The preferred strategy or action is one that has the least cost to produce a given level of effectiveness, or provides the greatest effectiveness for a given level of cost.

Reference analyser: An analyser used as a point of of reference or forming the basis of an evaluation or assessment.

EP9: The CLSI EP9 Method Comparison (CLSI:EP9) is a statistically rigorous and rugged Protocol, excellent for preparing reports for regulatory agencies. It may also be used by a laboratory for rigorously evaluating methods. CLSI EP9 Method Comparison is designed to compare two methods which produce results with similar units. It is not designed to compare items with disparate units (i.e. mg/dL vs. IU/L).

EP10: The CLSI:EP10 Protocol evaluates linearity, recovery, drift, carryover and precision at three concentrations: low, medium and high.

3 PURPOSE

The purpose of the HTA Unit is to manage and coordinate all laboratory Invitro Diagnostics (IVD) evaluations within the NHLS.

4 OBJECTIVE

The objective is to give guidance to all NHLS persons and suppliers on the evaluation processes within the NHLS.

5 ROLES AND RESPONSIBILITIES

It is the role and responsibility of the HTA Unit, the Regional QA Manager, the designated Lab Manager and assigned Pathologist to ensure that the evaluation is conducted in accordance with the agreed upon protocol.

6 EVALUATION PROCESS

6.1. Types of evaluations: The requests that the HTA Unit may receive are outlined in Figure1.

Figure1. Types of evaluation requests

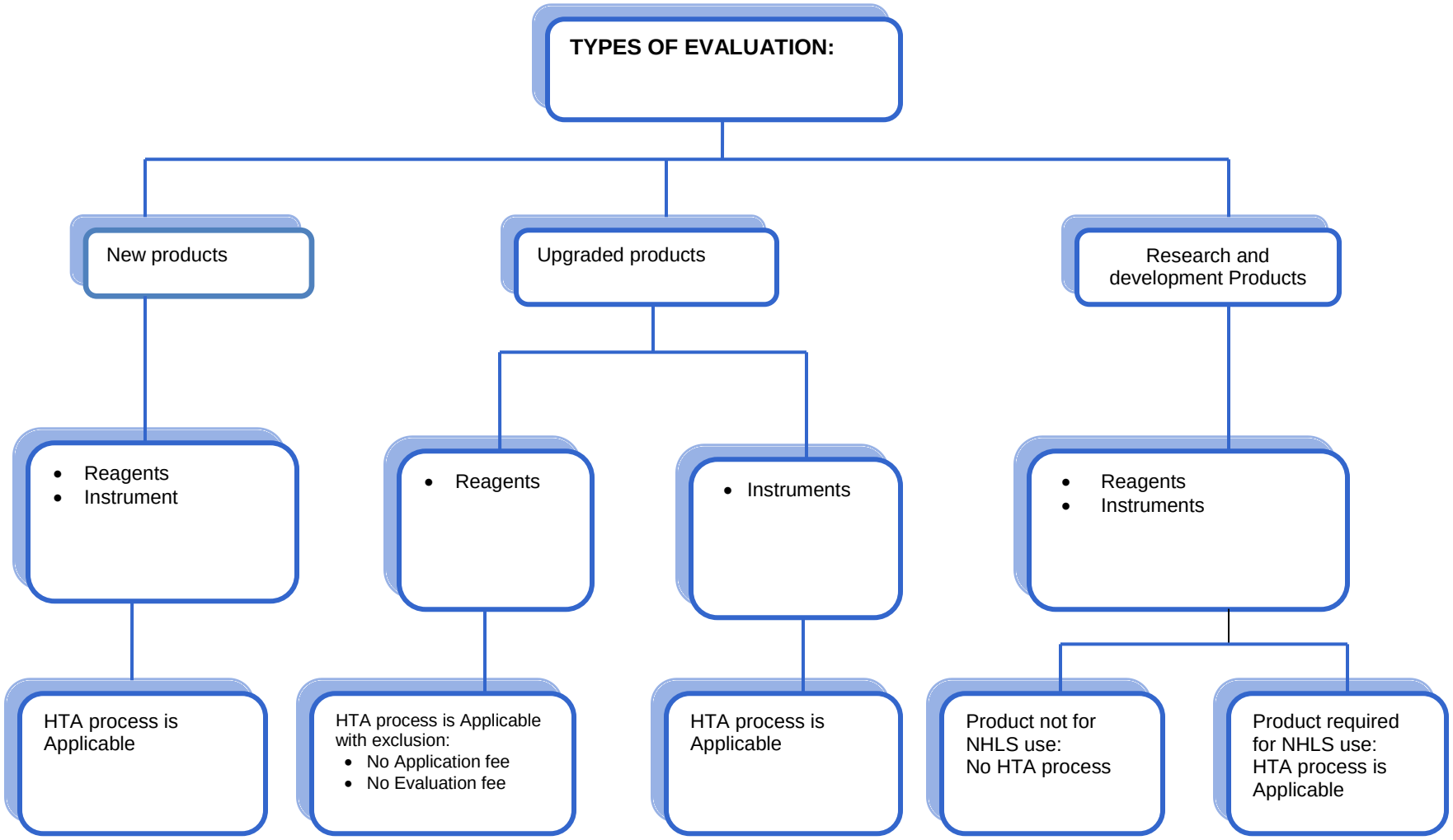
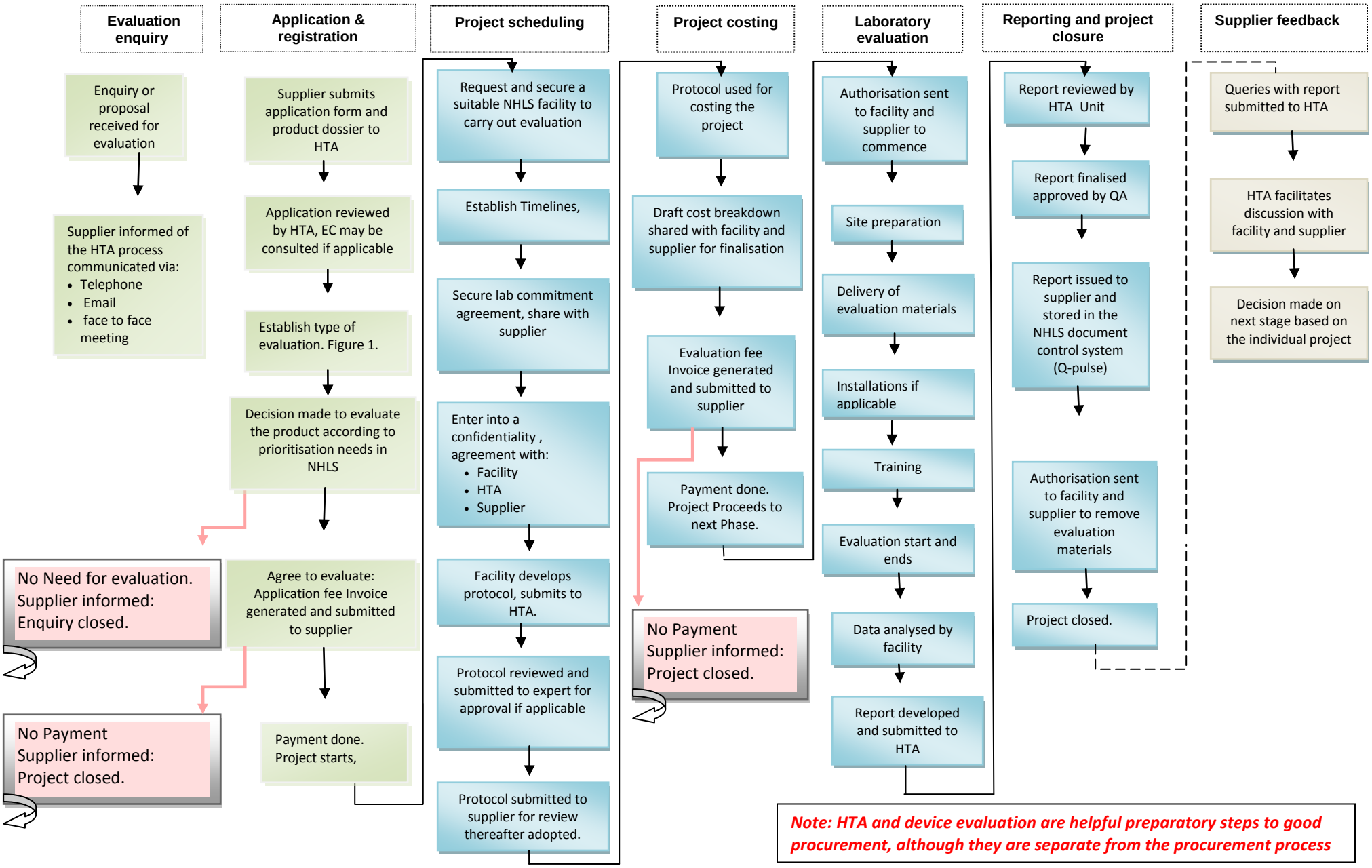


Figure 2. HTA projects process



6.2. An explanation of the evaluation process as illustrated in Figure 2.

6.2.1. Initial Meeting with interest supplier:

This is the first meeting the supplier will have with HTA Unit. At the meeting that the supplier will introduce their product/s to the HTA Unit. The HTA Unit will explain the process that will be followed namely: NHLS priority list and waiting period for evaluations; the timeframe for the evalution (dependant on the availability of several factors ie. a suitable evaluation site, materials/samples etc).

Matters to be addressed with the supplier at the intial meeting are as follows:

6.2.2. Costing: The supplier must be made aware that there will be costing involved in conducting the evaluation and this will include an Application and an Evaluation Fee.

6.2.3. Product Information: The supplier will be requested to provide the HTA Unit with product information including brochures. For automated analyzers check the system is opened or closed. Remember open systems fall outside our scope of evaluation at NHLS; unless the supplier is able to provide NHLS with reagents that are specific for the analyser and are responsible for the regent component of the contract.

6.2.4. Technical Support: Key component for the evaluation and technical support from the supplier should be readily available during the duration of the evalution...

6.2.5. Evaluators: Evaluations done outside the jurisdiction of the NHLS or by the supplier will not be endorsed by the HTA unit (i e acceptable for tender processes).

6.2.6. Analytes to be evaluated: Prior to the evaluation the contract must clearly state the analytes to be evaluated and this must be as per NHLS requirement based on repertoire of tests that NHLS provides.

6.2.7. Chain of communication: The chain of communication needs to be clearly defined between the NHLS and the supplier.

6.3. HTA Proposal

The supplier will then be requested to send a proposal for evaluation in writing to the HTA Unit. The NHLS will consider the proposal and provide the client with feedback.

6.4. HTA Application Form

6.4.1 An HTA Application Form(FMQ0022) is given to client for completion and returned to the HTA Unit.

6.4.2 A non-refundable application fee of R2500 must be submitted for all new Invitro Diagnostic Device (IVD) application.

6.4.3 *Note: There is no charge for reagent upgrades*.

6.5. Project number

The evaluation will be assigned a project number by HTA Unit and loaded onto the database.

6.6. Evaluation protocol

A standardised evaluation protocol is utilised based on discipline specific Expert Commitee /designate recommendation. If there are no suitable protocols available the HTA Unit will consult with the relevant expert to draft an evaluation protocol.

6.7. Evaluation Site

HTA Unit will then find a suitable site based on NHLS requirements; (HTA unit have a database of NHLS laboratories that may be suitable based on accreditation , PTS performance and technical expertise etc.). Once the selection has been made the HTA unit will contact the facility and

provide the facility with a site commitment form(FMQxxxx). At this stage, the staff assigned to handle the evaluations on the chosen site are identified and introduced to the HTA Unit. These are the people the HTA Unit will be communicating with throughout the evaluation process.

6.8. Timeframe:
HTA Unit will work with the evaluation site to monitor and to ensure that the agreed upon timeframe as per the contract are adhered to.

6.9. Costing:
6.9.1 The HTA Unit will then cost the evaluation project
6.9.2 The quotation will be worked out with costs as follows: Consumables (direct and indirect), labour and administrative charge.
6.9.3 Payment must be effected before the evaluation can start.
6.9.4 If the client rejects the quote, the process stops and the application is closed.
6.9.5 If the client agrees, the process will continue.

6.10. Ethics Approval:
The facility and HTA unit to ensure that the protocol has ethical approval (where applicable).

6.11. The evaluation preparations:
Preparations for evaluations will commence involving the following processes;

- At the start of the evaluation, the objective of the evaluation must be defined. The protocol used must be in line with this objective.
- A table comparing the methods used by the reference and the new method, will need to be compiled. Key components: stability of reagents, calibrators and controls, analyte stability periods and reference ranges.
- Checking for stability periods for the different analytes in the different sample types.
- HTA Unit and supplier are expected to conduct a site visit prior to the evaluation commencing (where relevant). The site visit confirmation report to be stored in the HTA database..
- Training of relevant staff on the new method/ instrument will commence.
- When training is complete the client will provide staff with proof of training.
- The criteria of acceptance must be based on the protocol used or validation sop.

6.12. Commencement of evaluation and monitoring:
The site is expected to provide an update on the project progress(a minimum of bimonthly) to HTA. The supplier should ensure a technical person is available for assistance during the course of the evaluation.

6.13. Report :
The report will be written by the evaluation site and signed off by the Technical Expert/ Pathologist overseeing the process. If the evaluation was performed at a non academic site, a Pathologist will be assigned to provide technical support during the evaluation. Where relevant the report may be issued to the Expert Committee for ratification.

6.14. Report Template

The report layout must be as below:

A) Covering Letter**:** This is the letter from the NHLS to the supplier.
- Ensure that the covering letter signed by the National QA Manager or designate.
- Ensure that the NHLS standard letter format is used for the letter.
- Ensure that the report is dated.

B) Index

The cover page is followed by a table of contents, page numbered consisting of:
- Table of contents
- Background to the study
- Method/s used
- Purpose of study
- Materials used
- Procedures followed
- Results
- Discussion and conclusion.

C) Background: Explaining when the study began, and the site where it was done.

D) Technology: List the analytes and the methods used on both the reference and the new analyser.

E) Purpose: Explains what we need to achieve through this study.

F) Materials used: List all the materials used for the evaluation.

G) Procedure: Explain what protocols were followed and the analytes assessed.

H) Results: HTA Unit makes use of the EP Evaluator to do statistical analysis of results. Each analyte will be listed together with results and the conclusions drawn. Reference range/s confirmed.

I) Discussion: Summary of what took place, what should have been done i.e. if process was not followed properly. What the recommendation is going forward.

J) Conclusion: A clear statement on what the conclusion on the evaluation is; i.e. if the instrument/ method is acceptable for use within NHLS. Criteria of acceptance of results must be stated.

7 THE SUPPLIERS RECORDS

HTA unit are to ensure all records for each project are kept on site and not accessible to unathorised staff. The records are to include the following:.

7.1 Proposal from the supplier
7.2 Records of intial meeting and register
7.3 Completed HTA questionnaire
7.4 Laboratory commitment form
7.5 Costing template
7.6 Protocol/s used and references
7.7 Confidentiality (supplier, site)
7.8 Contract
7.9 Risk Assessment (Were applicable)

7.10 Deviations from protocol (Were applicable)
7.11 The report
7.12 EP Evaluator printouts
7.13 Completed product validation/ Raw date to kept at evaluation site according to NHLS retention times
7.14 HTA Impact analysis (conducted if instrument is placed within the NHLS).
7.15 Proof of payment (application and evalution cost)
7.16 Qpulse E number allocation for evaluation report
7.17 HTA Checklist

8 SUBMISSION OF REPORT TO SUPPLIER

8.1 Ensure that the report is dated
8.2 Ensure that the report is signed by the National QA Manager or designate.
8.3 Forward to supplier.
8.4 Acknowledge receipt of report

9 POST EVALUATION ENQUIRIES

9.1 Queries with report submitted to HTA
9.2 HTA facilitates discussion with facility and supplier
9.3 Decision made on next stage based on the individual project

10 ENQUIRIES

Enquiries about this policy or recommendations can be made to the following email address: hta@nhls.ac.za

11 REFERENCE DOCUMENTS

11.1 HTA Application form - FMQ0022
11.2 Testing lab commitment form - FMQ 0024
11.3 Validation of test methods – new and relocated - GPQ0005
11.4 Protocol for instrument evaluations - GPQ0006
11.5 Protocol for instrument evaluations - GPQ0007
11.6 Confidentiality agreement - GPQOO34
11.7 Summary of Health Technology Assessment (HTA) Process - GPG0035
11.8 HTA Contract - GPQ0036
11.9 POLQ0003 - HTA Policy

Acknowledgement of Reading Form

Document number: _____ **Version Number:** _____

Title: _____

My signature confirms that I have read and understood the content of this document and relevant kit insert (where applicable).

Name	Signature	Date

Note to the Quality Rep: - This form must be filed for 5 years to provide audit traceability.

In the event of a dispute concerning this document, the electronic version stored on Q-Pulse will be deemed to be the correct version