President's Emergency Plan for AIDS Relief

Laboratory Information System (LIS)
High Level Requirements

APHL ASSOCIATION OF
PUBLIC HEALTH LABORATORIES

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Legal Notice

This document contains information that is proprietary and confidential for the Association of Public Health Laboratories.

Section 1. About the LIS Documents

This High-Level Requirements Document is one component of a set of documents is provided by the Association of Public Health Laboratories (APHL) in support of the activities of the President's Emergency Plan for AIDS Relief (Emergency Plan) for the purpose of enhancing laboratory testing for the treatment and prevention of HIV infections and AIDS. The U.S. President's Emergency Plan for AIDS Relief through the Office of the Global AIDS Coordinator (OGAC) has provided funding for this project. This document is a cooperative effort of APHL and its contractor DiagnosisONE, Inc., with technical guidance from the Centers for Disease Control and Prevention.

1.1.   Acknowledgments

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Comments, questions, and other correspondence regarding these documents may be sent to APHL in care of Patina Zarcone, Director, Strategic Initiatives and Research, at pzarcone@aphl.org. Information and assistance regarding the use of these documents by country HIV/AIDS programs or national laboratory programs may be sent to APHL in care of Ralph Timperi, Acting Director, Global Health Programs, at rtimperi@aphl.org.

1.2.   About This Document

This document is one component of a nested set of resources developed by the APHL to support the development of Laboratory Information Systems (LIS) in resource-limited settings. Users of this document are encouraged to become familiar with the content of each of these references. We recommend that the users start with the Guidebook to familiarize themselves with the overall approach being described in this set of references.

This document identifies these aspects of LIS:

- Identifies and describes the high level software requirements for a GAP/Emergency Plan LIS.
- Describes the functional, system and operational requirements of adequate system solutions.
- Documents all assumptions made in the development of requirements.
- Identifies dependencies and contingencies.

1.3.   Revision History

No changes are to be made to the requirements described within this document unless approved and documented as an amendment to this document.

Date	Revision	Description
01-18-2005	1.0	Initial draft release
03-09-2005	1.1	Draft Release - Updated look and feel - Updated laboratory levels to match the WHO categorization - Updated text of individual requirements - Added Maintenance Management section
10-24-2005	2.0	Initial public release - Updated look and feel - Updated Introduction, Preface, and Executive Summary sections to fit with other documents in LIS Implementation set

Section 2. Executive Summary

2.1. Introduction

The goal of this document is to systematically list required functions of these LIS to enable effective project definition and timely implementation of an appropriate LIS. These are called High Level Requirements documents as they provide a broad overview of what the LIS should be able to do and not 'how' these functions will be performed. The LIS selected can be a Commercial-Of-The-Shelf (COTS) product, a built-to-specification solution or a combination of these two that will meet specific program needs and be compatible with other systems.

This document identifies these aspects of LIS:

- Identifies and describes the high level software requirements for a GAP/Emergency Plan LIS.

- Describes the functional, system and operational requirements of adequate system solutions.

- Documents all assumptions made in the development of requirements.

- Identifies dependencies and contingencies.

The overarching goal of this project is to help identify appropriate solutions for different country programs. Because there has been demonstrable progress already in implementing LIS solutions to meet in-country local needs, we will evaluate these initiatives to document lessons learned and successes to incorporate this knowledge and experience into this document.

For more information about the requirements gathering stage of this project, please see Appendix A of the Guidebook.

2.2. The Process

The process of selecting and deploying a Laboratory Information System (LIS) in the GAP/Emergency Plan countries consisted of the following steps:

1. Produce a high level requirements document (this document) that describes the functional, system and operational requirements for the LIS based on interactions between LIS experts and country experts. In contrast to the high level requirements, a detailed level requirements document would be used by IT groups to develop an LIS.

2. Host a conference to review the documents with country representatives and solicit feedback as to its accuracy and relevance to conditions with in the countries.

3. Survey and produce a list of systems and/or vendors qualified to provide the needed systems and services to the country representatives.

4. Produce a system selection toolkit that incorporates the appropriate sections of this document, the list of potential systems/vendors, and provides a mechanism for the country representatives to evaluate the recommended systems and select those systems that best meet their specific needs.

2.3. Goals

The following are the goals for this High Level Requirements Document:

1. Capture the functional, system and operational requirements for the GAP LIS at a high level.

2. Capture the high level solution features that will support the user interaction with the GAP LIS.

3. Capture what the system should do and not how it will do it.

2.4. Non-Goals

The following lists what this document is not intended to do:

1. Identify requirements that are not directly relevant to the GAP LIS such as hospital management.

2. Identify detailed operating procedures of laboratories.

3. List all possible vendors that provide software systems that might meet the requirements of some appropriate solutions, in whole or in part.

4. Recommend specific vendors for specific GAP country LIS solutions.

5. Provide in-depth functional and operational characteristics of a LIS.

6. Describe design aspects of the LIS including object models or database schemas.

Section 3. Functional Requirements

This section captures the high level features and functionality of the LIS. The first part of this section (denoted 3.1, Laboratory Staff) is designed for use by laboratory personnel to determine what functions the LIS must perform to satisfy the needs of their laboratories. The second part of this section (denoted 3.2, Information Technology Staff) provides more details regarding functionality that would be useful to an individual with IT knowledge to assist lab personnel in reviewing and selecting appropriate systems.

In general, to suit the various needs of different types of laboratories the system needs to be modular. The simplest module with limited functionality shall require minimal technical expertise from the operator and allow simple commands. Similarly the most advanced version should have full capabilities for managing a central referral or national reference laboratory. In addition it shall have capabilities to request and show the results of tests done at these facilities.

3.1.   Laboratory Staff

We have grouped the various functions that a LIS should be able to perform into categories. Not all categories are essential for every level of lab. To find out more about which functions are suited for a certain level, please refer to the LIS Toolkit.

1.   User Accounts

This function allows different users to have access to the LIS based upon their role in the organization and the data they need access to. Users can log in using a username and a password. This enables a certain amount of security in the system so that non-authorized users cannot have access to lab information or be able to change any data. Also users can be added or deleted at any time.

2.   Patient Management

The LIS maintains information on all individuals that are assigned any tests in the lab. Certain users may be able to change patient information depending on their roles. The patient management function allows for all lab tests done for a specific person over time to be linked to that particular individual.

3.   Provider Management

Providers are either individuals or organizations that submit specimens for testing to a lab. The LIS keeps a record of all providers that have the ability to send specimens and receive results.

4.   Test Catalog Management

The LIS manages all the tests and procedures that are carried out by the lab, allowing for different tests to be grouped into categories if needed. Tests may be identified using standard codes such as LOINC (Logical Observations Identifiers Names and Codes) or CPT (Current Procedural Terminology). The LIS allows for tests to be added, deleted or modified from the Test Catalog.

5.   Request Management

This function allows maintenance of all requests for lab services to be performed. A request consists of a specific test or tests to be performed and other associated data. A request is also linked to a specific individual.

6.   Specimen Management

The LIS allows for information regarding the handling of specimens from the time they are received at the lab all the way to disposal. Unique identification, including labeling of the sample and all of its aliquots, is required so that results can be matched back to the originating sample. Additionally, samples may be sent to third parties for confirmatory testing or as overflow.

7.   Specimen Tracking Management

Besides the sequential processing from receiving through testing, specimens and samples may spend time in intermediate storage, as well as be stored for subsequent testing following the initial

testing or stored as evidence. Long-term specimen and sample storage may also be required, including products/organisms grown from them. This LIS keeps track of every stage that the specimen goes through including registration, short term and long term storage.

8. Testing Management

This includes the functional requirements of the processes after a specimen has been received and registered in the LIS and before the result data is available for dissemination. Manual entry of results or automatic capture from a lab instrument, flagging of abnormal values etc are all required functions of the LIS.

9. Scheduling Management

This function allows for prioritizing and processing the test workload. The LIS is able to manage urgent requests, sample holding time, and other factors relating to the timely processing of the test requests.

10. Results Management

The LIS maintains information related to the test results including entry and reporting. Users have limited access to results based on their roles and only certain individuals will have the authority to modify results. Reference ranges are also included.

11. Reports Management

The LIS will generate and deliver reports in either hard copy or electronic format to authorized users. These reports will be stored or generated ad hoc and will allow the user to view data on requests received, specimens registered, pending results, workload etc. The user will be able to define the types of reports they need.

12. Quality Control Management

The system maintains quality control checking (directly from instruments or via manual input) and cumulative weekly and monthly quality control reports. The laboratory will define QC parameters and features test procedure type.

13. Maintenance Management

This function allows for managing the maintenance of laboratory equipment, maintenance records etc including reminders for maintenance

14. Billing Management

For Labs that bill their patients or need to bill insurance, the LIS will obtain billing information from the submitter requesting the test or other entities, tabulate the items to be billed, apply appropriate billing rates, and create the invoices and supporting billing documentation.

15. Inventory Management

The LIS provide capability to manage various aspects of inventory control such as ordering, tracking, and distribution for all items inventoried by a laboratory. Examples include specimen and sample collection kits, testing kits, lab supplies, chemicals, equipment, and forms.

16. Localization Management

This function allows for the LIS to be set up taking into consideration the local environment such as language, date format, currency etc. This will be country specific.

17. Alert Management

This function allows for alerts to be generated based on certain criteria – such as a lab result that is significantly below normal, liver toxicity indications, etc.

3.2. Information Technology Staff

This section provides more detailed requirements for the LIS using the same categories mentioned above under 'Laboratory Staff' but with information useful for IT personnel assisting in the selection of systems. The requirements are grouped logically in several feature sets. Each feature set represents a software component and it is designated by the term **Management**. The term Management is used to summarize the functionality needed to create, read, update, delete, search and list items. An item may be a user account, patient profile, specimen, order, report, etc.

3.2.1. User Account Management

This section covers the functional requirements for managing the various LIS user accounts.

3.2.1.1.   User Online Access

1.   The LIS provides online (while connected to a local or remote server) access to various laboratory personnel

2.   Online access to the LIS is granted only through dedicated user accounts

3.   The system maintains list of user accounts

4.   A user account consists of the following components:

     a.   User Profile – contains user contact information

     b.   User Credentials – contains user authentication (identity confirmation) information

     c.   User Role – Defines user authorization and privileges

5.   The system allows authorized users to manage user accounts.

3.2.1.2.   User Profile

1.   A user profile contains the following contact information

     a.   Person full name including last (family), first (given) and middle names

     b.   Gender

     c.   Title

     d.   Organization or department the person works for

     e.   One or more postal addresses such as work, mailing, etc.

     f.   One or more telecommunication addresses such as telephone, fax, email, etc

     g.   A specific site/laboratory identifier to which the user belongs to in the case of a centralized LIS that is used by several laboratories

2.   The system allows authorized users to manage user profiles

3.   The user may be allowed to manage his/her profile.

3.2.1.3.   User Credentials

1.   User credentials consist of the following information:

     a.   A unique username, and

     b.   A password

2.   The system stores user credentials in encrypted format for security purposes

3.   The system requests the user to enter designated username and password, i.e. login using provided credentials, whenever the user tries to access the LIS

4. The system authenticates user credentials, i.e. validates the provided username and password against the stored ones, upon user login attempt

5. The system allows access to authenticated users

6. The system allows authorized users to manage user credentials

7. The user may be allowed to manage his/her credentials.

3.2.1.4. User Role

1. A user role defines user authorization and should reflect the person's title/job in the laboratory

2. Example user roles are:

   a. Laboratory Clerk – Interact with the system to enter patient, specimen and order information

   b. Laboratory Technician – Interact with the system to review orders and enter test results

   c. Laboratory Manager– Interact with the system to create user accounts and review their work

   d. System Administrator – A type of IT operations personnel that configures the system, schedules job runs and backs up the system data

3. A user role represents a list of LIS features to which the user has been granted access, i.e. privileges

4. Every user account is assigned a user role

5. The system allows authorized users to manage user roles

6. The system allows authorized users to manage user role privileges.

3.3.   Patient Management

This section covers the functional requirements for managing the patient profiles.

1. The system maintains list of patient profiles

2. The patient profile consists of, but not limited to, the following

   a. A unique patient identifier (internal LIS ID)

   b. Sending provider patient identification (patient ID as known to the provider)

   c. Full name including last (family), first (given) and middle names

   d. Mother's maiden name

   e. Also Known As (AKA)

   f. Previously known as

   g. Gender

   h. Date of birth

   i. Government assigned identification

   j. One or more postal addresses such as residence, work, mailing, etc.

   k. One or more telecommunication addresses such telephone, fax, email, etc.

3. The system allows authorized users to add additional profile fields such as birthplace, race, ethnicity, tribe, religion, etc.

4. Creating a patient profile is deemed patient registration

5. A patient registration may be a:

    a. Standalone process at the time of the patient reception, or

    b. Sub process of data entry during the collection of the specimen, or

    c. Sub process of the request data entry

6. The system allows authorized users to manage patient profiles.

3.4.   Provider Management

This section covers the functional requirements for managing the provider profiles.

1. A provider is the healthcare organization that sends a laboratory order on behalf of a patient to a laboratory supported by the LIS

2. The system maintains list of provider profiles

3. A provider may be a doctor office, a clinic, a hospital, another laboratory, etc.

4. The provider profile consists of, but not limited to, the following

    a. A unique provider identifier (internal LIS ID or code)

    b. Provider organization name

    c. Department

    d. One or more postal addresses such as physical, mailing, etc.

    e. One or more telecommunication addresses such telephone, fax, email, etc.

5. The system allows authorized users to manage provider profiles.

3.5.   Test Catalog Management

This section covers the functional requirements for managing the test catalog.

1. The system maintains one or more catalogs of all the offered testing services, i.e. tests or procedures, at any specific laboratory supported by the LIS

2. Tests may be grouped in one or more categories and sub-categories in a catalog

3. A catalog test entry consists of, but not limited to, the following:

    a. A unique test identifier/code, preferably adhering to a recognized coding standard such as:

        i.   Logical Observations Identifiers Names and Codes (LOINC), or

        ii. Current Procedural Terminology (CPT)

    b. Test name

    c. List of other tests in the case of a test panel.

4. The system allows authorized users to assign one or more test catalogs to a laboratory

5. The system allows authorized users to manage the test catalogs

6. The system allows authorized users to import the test catalogs.

3.6.   Request Management

This section covers the functional requirements associated with the processes needed to initiate testing at a specific laboratory.

1. The system maintains list of requests.

2. The LIS request is a request to perform laboratory testing services by the receiving laboratory.

3. Once a request is accepted, vs. rejected, by authorized personnel, it becomes an order.

4. The process of request creation is also known as order entry.

5. The system supports the capture of standard request data fields needed by all laboratories supported by the LIS.

6. The system allows additional data fields to be captured as needed by a laboratory and or test procedure.

7. A request consists of, but not limited to, the following:

    a. A unique request identifier

    b. A unique accession number; in many case is the same as the request identifier

    c. Priority indicator

    d. Patient information

    e. Provider information

    f. List of tests to be performed

    g. Specimen information

8. The system supports local and remote accessioning, both registration and order entry.

9. The system generates specimen accession numbers that are definable by laboratory, or test procedure category.

10. Search existing patient profiles during request creation to select/match the current request patient based on certain criteria such as a government assigned ID, name, gender, date of birth, birth place, etc.

11. The system supports barcode label printing via:

    a. Online direct connection

    b. Modem connection

    c. Intranet or Internet using Browser technology

12. The system requests minimum demographic input during request creation and allows the remaining request information to be input later.

13. The required fields to be entered during request creation will be determined by test procedure type by the laboratory.

14. Test procedures can be identified by users for selection and addition to a request during order entry via:

    a. Character search on partial entry of test procedure name, or

    b. Selection from a laboratory specific catalog

15. The system presents the user specimen sources specific to the selected test procedures

16. Selection from a laboratory specific catalog The system calculates automatically essential request parameters using existing patient data, e.g. enter date of birth and system calculates age

17. The system checks for duplicate order entry based upon the test procedure currently active orders, inactive or already performed orders

18. The system validates all entered data to ensure accuracy using methods such as check digits, range check, consistency check, format check

19. Reflex testing, i.e. the ability to automatically order test procedures based on predefined criteria

20. Register blinded samples, which are user definable and can be tracked and reported on statistical reports

21. Request add-on tests to specimens that may be already registered and in storage

22. The system allows authorized users to manage the requests.

3.7.   Specimen Management

This section describes the requirements of handling specimens and samples that must be tracked from the time they are received at the laboratory thru to disposal. Unique identification of the sample and all of its aliquots is required so that results can be matched back to the originating sample. Additionally, samples may be sent to third parties for confirmatory testing or as overflow. In instances where chain of custody documentation is required, the laboratory must be able to document custody of the specimen or sample from receipt through disposal or return to the submitter or other agency.

Mid and long term storage requirements of specimens are described in the next section.

3.7.1. Specimen Registration

1. All specimens received at a laboratory must be registered using the LIS

2. Specimens may be barcode labeled in the field or at registration

3. The specimen shall be scanned into the LIS at registration if labeled in the field

4. The specimen information captured at registration consists of the following:

   a.   Date/time of collection

   b.   Date/time of field registration

   c.   Date/time of shipment

   d.   Date/time of registration

   e.   Name of person entering data

   f.   Specimen type

   g.   Field identifier of specimen

   h.   Submitter identifier

   i.   Tests required

   j.   Container type

   k.   Condition of specimen

   l.   Approximate temperature of specimen

   m.   Volume of specimen, if applicable

   n.   Patient demographic data

   o.   If anything is missing, what and why (if known)

   p.   Accept/reject specimen based on predefined criteria

   q.   If specimens are associated with a specific out break, which one

   r.   If specimen is a quality control specimen

5. Unique specimen identifier to be assigned at specimen registration

6. Create a request for a specimen that is being sent to an external laboratory. During this process the LIS should produce:

   • An LIS assigned accession number

- A user-defined number of specimen labels that would include; accession number (human readable and barcode format), patients name, submitter and test ordered or organism suspected.
- Referral laboratory request form with appropriate data entered during test request entry.

3.7.2. Specimen Labeling

1. Create user-definable specimen barcode labels by laboratory, test procedure category and include the data elements to be printed on the label.

2. At a minimum, all labels will contain the specimen identifier in barcode and numeric form

3. Other data elements that could be included on the label (based on laboratory preference) are patient name, submitter code, date of birth, priority, sex, collection date and time, and date and the time a specimen was registered into the laboratory

4. The number of labels that print per specimen will be definable by laboratory by test procedure category

5. Once a specimen has been registered a label will be printed with the following information:

    a. Specimen identifier

    b. Unique laboratory identifier

    c. Submitter identifier

    d. Patient identifier

6. Field applied labels includes:

    a. Field location

    b. Patient identifier

    c. Date/Time

7. Labels contain a specimen type code to allow for the visual identification of specimens

8. Specimens that are aliquoted or separated will have the same specimen identifier with a unique extension

9. Re-print specimen labels as needed

10. Print additional barcode labels during request creation by test procedure category with a suffix attached to the specimen number to identify the additional assays. Additional assays may be another simple/rapid assay, an ELISA based assay, a PCR based assay or a flowcytometric assay

11. Print additional barcode labels as needed during the testing process by test procedure category with a suffix attached to the specimen number to identify the additional assays.

12. Additional assay barcode labels are user-definable by laboratory, test procedure category and should include the data elements to be printed on the label. At a minimum, all labels will contain the specimen identifier suffix barcode and numeric form. Other data elements that could be included on the label are patient name, submitter code, date of birth, priority, sex, etc.

13. The number of labels that print per specimen will be definable by GAP laboratory by test procedure category

14. Additional specimen identifier and suffix is designed to fit on a single line on the label so that they can be scanned for identification in one motion.

3.7.3. Shipment Forms

1. The system allow for the generation of shipment forms for shipment along with the specimen.

2. The shipment form shall contain at least the following information:

    a. Date of collection

    b. Field number of specimen

    c. Volume of each specimen, if applicable

    d. Date/time of shipment

    e. Submitter ID

    f. Number of specimens shipped

    g. Type of specimens.

    h. Any specific transport conditions, if applicable.

3.7.4. Shipment Receipt

1. The system shall generate shipment receipt forms to be provided to the delivery person at the time a specimen is received at a laboratory.

2. The shipment receipt shall include at least the following information:

    a. Number of specimens received

    b. Date/time of receipt

    c. Person receiving the specimens.

3.7.5. Referral Laboratory (send outs) Specimen

1. Track specimen sent to Referral Laboratories and produce reports that identify the referral laboratory by test group

2. Track pending results (not yet received from the referral laboratory)

3. Track test procedures that have gone beyond the normal testing time

4. Enter a non reportable or reportable comment when a report is received from the referral laboratory that would complete the test procedure held in the LIS

5. Scan referral laboratory report into LIS when received from the referral laboratory and have it linked to the system specimen record

6. Generate a duplicate referral laboratory result report upon request from the initial submitter

7. Generate statistical data regarding information sent to referral laboratories via management reports ad hoc queries

8. The system sends orders to and receives results from referral laboratory electronically

9. Patient results that are not received electronically from a reference laboratory are entered manually into the LIS

10. Optionally, enter reference ranges as part of the manual result entry process.

3.7.6. Specimen Processing

1. Process specimens selected using one of the following criterion:

    a. Specimens registered as batch from a submitter

      b.   Range of unique IDs selected by lab tech

      c.   Selected sequentially, one by one

      d.   Based on date collected or date received

2. Assign a rejection reason if a specimen is rejected

3. Track specimens assigned to permanent storage.

3.8.   Specimen Tracking Management

Besides the sequential processing from receiving through testing, specimens and samples may spend time in intermediate storage, as well as be stored for subsequent testing following the initial testing or stored as evidence. Long-term specimen and sample storage may also be required, including products/organisms grown from them. The specimen goes thru the following process:

1. Registration (accept shipment). On receipt the specimen is registered

2. A short term storage area is designated for specimen where they will be assigned before and during testing

3. After testing is complete specimens are assigned to permanent long term storage.

3.8.1. Specimen Storage

1. Define unique storage units and subunits such as facilities, rooms, racks, freezers, shelves and boxes

2. Assign a specimen to a storage unit

3. Indicate the consumption of a specimen

4. Indicate the return of a specimen

5. Allow for Specimen shipment

6. Indicate the discarding of a specimen

7. Checkout stored specimens

8. Check in of checked out specimens

9. Search for a specific specimen.

3.8.2. Specimen Retrieval

1. Whenever a specimen is retrieved from storage, the system accepts the following information:

      a.   Number of thaws

      b.   Initial volume of specimen

      c.   Initial temperature of freezer

      d.   Date time of retrieval

      e.   Final volume of specimen

      f.   Final temperature when specimen is placed in freezer

      g.   Date/time when specimen is placed in freezer.

3.8.3. Specimen Long Term Storage

1. Capture the date/time and volume of specimen when it is assigned to long term storage

2. Enter a discard date to be assigned to each specimen based on:

      a.   Submitter ID

      b.   Type of specimen

3.   Capture the storage location of each specimen

4.   Each Specimen is a room number or refrigerator number (if applicable), rack number, shelf number and box number for long term storage.

3.8.4. Specimen Short Term Storage

1.   Each Specimen shall be assigned a rack number, shelf number and box number for short term storage.

2.   The system periodically captures the temperature of the cold room

3.   The system captures the date/time a specimen is added to or removed from the cold room.

3.9. Testing Management

This section covers the functional requirements of the processes after a specimen has been received and registered in the LIS and before the result data is available for dissemination.

1.   Support different data types including: single test results, multiple test results, test comments, etc.

2.   Automatic capture of workload and test procedure statistics. Statistics is available by:

      a.   Test

      b.   Patient identifier

      c.   Laboratory

4.   Identify and track specimens that are sent to reference laboratories

5.   A specimen has a status field denoting whether a test is pending, in progress or completed

6.   Produce daily management workflow documents that can be printed or displayed by laboratory, test, workstation, date and date range, etc.

7.   Documents are user definable by laboratory, test procedure category. Examples:

      a.   Work lists - produced automatically by the system, or manually set up by analyst, for batch processing, by wanding specimen (with barcode accession number), to be placed on a work list or instrument load list

      b.   Pending procedure report

      c.   Unverified result reports

      d.   On demand or scheduled logs of completed tests

      e.   On demand or scheduled logs of positive and reactive results

8.   Flag abnormal, critical and absurd values

9.   Capture all test data regardless of whether a test was successful or failed

10. Flag by Delta values that can be set by user definable criteria such as 50% change in a test value, in addition to critical alerts

11. Age and/or sex adjusted reference ranges

12. Access patient demographic, clinical data and orders during result entry

13. Enter textual results by:

      a.   Selecting predefined responses from a table

      b.   Entering part of a data string and having a predefined response displayed

14. Define testing units and format to be used for each test procedure result entry

15. Send notification to user at result entry that a critical result(s) or control outlier is present, as such:

    a. Notification attempts must be documented.

    b. Unsuccessful critical result notification attempts made during result entry must be captured.

    c. Audit trail of all successful and unsuccessful notification attempts.

16. Capture the date/time, specimen type and ID and the user name/ID of the person performing the test

17. Capture the volume of each aliquot

18. Enter the following information when conducting a test:

    a. Worklist number

    b. Plate number

    c. Lot number/Kit number/Expiry date.

19. Keep a record of bench processes, for example the date/time when monoclonal antibodies or fixatives are added to a specimen

20. Review previous results for a patient if that is required to perform a test

21. Interface to major lab instruments

22. Print outstanding specimen log by identifying the time interval in days

23. Track which instrument performed any specific test

24. Track whether a test result was entered manually, imported from a file or read directly from an instrument

25. Update the system with routing information (laboratory to which a *sample* is directed) and status code

26. Route specimens/aliquots associated with a test request submittal to multiple laboratories

27. Allow Reflex testing, i.e. the ability to automatically order test procedures based on predefined test results

28. The result entry verification procedures are user definable by laboratory, test, or employee (Analyst)

29. The system tracks the identity of the analyst performing and/or completing the test procedure along with the date and time performed

30. If a test fails for some reason the system captures a reason for the failure and allow for retesting from the same specimen

31. If the specimen is determined to be unusable for retesting for any reason the system captures the reason and request a redraw of the specimen from the patient

32. Note ambiguous results of any test in the test result data

33. Support manual inquiry or automatic review of other laboratory data before releasing results

34. Maintain a complete audit trail of the result process

35. The audit trail includes the following:

    a. Date and time of event change and initial result entry.

    b. Record each step that occurred in the processing of a test procedure

      c.   User who performed the step.

3.9.1. Specific to HIV Specimens

1. For HIV specimens workflow is based on the following recommendations by WHO/CDC/APHL:

   a. Serologic diagnosis of HIV infection is based on a multi-test algorithm for detecting antibodies to HIV

   b. Two simple/rapid diagnostic assays or one rapid assay and an enzyme immunosorbent assay (EIA) may be used for initial evaluation

   c. Confirmatory tests such as Western blot (WB) may be used to confirm infection in samples that are initially reactive on conventional EIAs.

2. System shall allow for User-definable and procedure specific:

   a. Assay setups with User-define instrument or manual defaults based on type of test, type of assay and source and specimen type.

   b. Serial testing or parallel testing setups with user-define defaults based on local testing practices, source and specimen type, assay type as needed.

   c. Test log summary information.

   d. Daily review information including:

      i. Test Request for initial assay (Rapid assay A1)

      ii. Resulting of Rapid Assay

      iii. A screen dedicated to first line rapid assay A1 that summarize all test results as positive, negative and if relevant indeterminate or error.

      iv. Suggestion of confirmatory tests such as another rapid assay based on a different technology rapid assay A2, EIA or western blot (WB).

3. Maintain anonymity of patients if required

4. Identify which tests, such as WB, PCR or Flow cytometry with CD4 counts or CD4:CD8 ratio, need to be performed

5. Support batch result reporting of tests that are negative

6. Support the issuing of preliminary, final, supplemental and corrected and result reports

7. Clearly identify and access specimens, sub-specimen, various assays and their daily readings from a common screen

8. Work log entry must be streamlined to allow for easy entry of data without the need to use the mouse to move around the workcard

9. Sort specimens based on the type of specimen, ordering facility, ordering physician or care provider

10. Sort specimens based on patient name, sex, location, batch, reference lab, type of assay, type of result i.e. positive, negative indeterminate. Ability to sort by CD 4 counts CD4:CD8 ratio, critical lab results

11. Submit test results for physician review.

3.10. Scheduling Management

This section captures the functional requirements dealing with prioritizing and processing the test workload. Scheduling factors include request urgency, sample holding time, and other factors relating to the timely processing of the test requests. This section covers: adding requests received, prioritizing requests, removing requests that have been completed, and publishing test schedules.

1. Add test requests and samples received and accepted by PHL to specific test schedule

2. Add in-house generated tests to schedule

3. Assign a submitter priority to a specific test

4. Assign priority by type of test

5. Generate internal priority based on holding times, number of days since receipt, and other factors associated with sample

6. Adjust priorities

7. Organize test "queue" by priority

8. Automatically delete tests from the schedule once the result has been entered in the PHL-LIS (and restore if needed)

9. Manually delete a test request from the schedule/batch (and restore if needed) or delete an entire batch

10. Select tests for diversion to mutual assistance laboratory and create file of diverted tests

11. Create packing lists and other documentation for diverted tests

12. Adjust holding times based on extractions and other reasons

13. Divert samples to another area in-house based on a trigger from a completed test for subsequent testing

14. Calculate daily processing capacity for each test; adjusted by instrument availability and personnel availability [future phase]

15. Translate workload into N-day "rolling schedule" based on capacity limits where N is the number of days ahead of current date the user wants to include in the display

16. Track test loads in the schedule at the specific instrument level

17. Indicate which tests have been passed through to another laboratory (mutual assistance situation, etc.)

18. Record, either electronically or manually, test results for tests performed by another (either a reference or a mutual assistance) laboratory and indicate name of person who performed the test utilizing HL7 and other standard formats as appropriate

19. Create subsequent test requests from a given test request

20. Flag overdue test requests based on schedule and notify submitter

21. Provide reports of test processing time by priority

22. Provide test status reports.

3.11. Results Management

This section covers the functional requirements of the acquisition, management, editing and delivery of test results data.

1. Access to results data shall be based on User Roles and Privileges

2. Support searching and editing results data

3. The automatic faxing or e-mailing of reports via laboratory-defined, submitter-specific schedules

4. Ability to import results in electronic formats into the LIS

5. User-definable result reports by laboratory, test and submitter and be able to produce reports on either pre-printed forms or using free form laser printers and postscript printing. For mailing purposes, reports would be sorted by submitter and include the submitter's address. Alternatively, the system would print a submitter slip-sheet with the address for each batch of submitter reports. Result report production should be available in either an on-going, real-time process or printed on-demand in batches. The system will flag printed reports allowing for reprinting in the event of a problem.

6. Highlight abnormal and critical results. Critical data and delta values should be highlighted differently from abnormal data.

7. Print reference ranges, which are age, sex and specimen-type specific.

8. Allow for the inquiry of results from users outside the laboratory with proper security clearance. The system maintains an audit trail of all data accessed.

9. Support the storage and retrieval of all reports. Corrected reports should show highlighted changes

10. The ability to print interim reports that contain preliminary result findings.

    a. Support the issuance of multiple interim reports on the same specimen and the same test

    b. Each interim report for the test contains each preliminary finding and the date it was reported.

    c. When a final report is produced, it contains all preliminary findings along with the date they were reported, as well as the final result

11. Print multiple copies of a report for additional submitters.

12. Generate a notification that an additional report is needed and to whom it should be sent to should be able initiated:

    a. At any time during the order entry process.

    b. During the editing of a specimen record.

13. When multiple tests are ordered on the same specimen, the LIS support the option by laboratory, by test, or by submitter to either:

    a. Issue an interim report with available results and an indication that a test is pending and will follow.

    b. Interim reports would be issued until all tests are complete for that specimen and each interim report will contain all completed test results to date, along with indication any test that are pending.

    c. When all tests are completed, a final report will be issued which contains all completed disease/test results, or

    d. Hold all test results for a specimen until all work is complete and a final report issued

14. When a final report has been issued and the submitter asks for additional testing on the same specimen , the LIS supports the option by laboratory, by test, or by submitter to either:

    a. Issue a report with the new test results only, or

    b. Issue a report containing new test results and previously reports disease/test results

15. Correct result data and retain a clearly marked on-line record of the original and corrected reports with functionality to print a complete archived copy of the patient report including original reference ranges and interpretative comments

16. Review all test data before they are released.

3.12. Reports Management

This section lists the requirements for test report generation and delivery. Reports may be delivered in hard copy or electronic formats to authorized users. Examples of reports that the system should be able to produce are:

1. Management and statistical reports must be retrievable for:

   a. A single Laboratory or test

   b. User defined groups of Tests or Laboratories

   c. All Laboratories

2. Reports can be either displayed (viewed on a monitor) or printed

3. Management and statistical report functions permit:

   a. The user development of specific ad hoc reports via the use of standard SQL tools. This should include all system data, i.e. all patient demographic and historical information

   b. Download user-selected information to other systems

   c. Access to information is based upon user role that would only allow access to data for specific laboratories, functions, and test procedures.

3.12.1. Generated Reports

1. Order Entry Statistics Report - Summary

   Description: Provide summary data of how many Order Entry records were input into the system in a given date range for a particular submitter or all submitters. This report is used by Management to track number of specimens being entered into the system.

2. Order Entry Statistics Report - Detail

   Description: Retrieve Order Entry statistics details for Order Entry. The report provides a detail list of Order Entry records input into the system in a given date range for a particular submitter or all submitters. Management uses this report to track list of specimens being entered into the system.

3. Specimen Registration Report

   Description: Retrieve information about any and all specimens registered. There are several kinds of registration reports:

   - Date/time and type of specimens received
   - If the specimens are being received on timely basis
   - If the specimens are complete and appropriately packed and shipped etc.

4. Pending Results Report

   Description: Retrieve incomplete test logs that show incomplete tests in the system. There are several kinds of incomplete:

   - If the results have not been verified and accepted
   - If the tests have been ordered but none have been performed
   - If a test procedure has gone beyond the normal turnaround time as defined for each test procedure in the system.

   This report lists all such incomplete results available in the system, to help track statistics for the same and lists incomplete tests chronologically with oldest test procedure first or by another user definable sort.

5. Positive Results Report

    Description: Retrieve statistics details for Positive Test results in the system for any given time period.

6. Patient History Report

    Description: Retrieve a specific patient's test results in the system for any given time period.

7. Incomplete Order Entry Statistics Report

    Description: Report all records in the system that has incomplete Order Entry. This list is used to communicate with the submitters to get additional data for specific records to enable completion of Order Entry.

8. Specimens Received Statistics Report

    Description: Retrieve a detail list of all specimens received for a given date range in the laboratory.

9. Workload Statistics Report

    Description: List a summary of the following for the given time period in days, hours etc (to help organize workflow), submitter and test:
    - Patient Samples received in the lab
    - Results reported in the lab
    - Repeats performed in the lab
    - Rejected Test Results in the lab
    - QC samples tested in the lab
    - Incomplete Test Results in the lab.

10. Unsatisfactory Results Report

    Description: Generate a count of all Unsatisfactory Results in the system for a given time period, submitter and test.

11. Amended Results Report

    Description: Retrieve list of Amended results in the system, i.e. results that have been modified since verification process was completed for the test result.

12. Turnaround Times Report

    Description: Generate a list of average turnaround time between various points in the ordering and testing process.

13. Incomplete Worksheets Report

    Description: Generate a list of incomplete worksheets in the system.

14. Where appropriate above reports should be able to be selected for:
    a. Date range
    b. Test procedure (selection by drop down, partial entry of test procedure name)
    c. A single submitter (selection by drop down, partial entry of submitter name, support for submitter levels)
    d. A user defined group of submitters
    e. All submitters.

15. The system provides data mining techniques that allows for the on going review of the database to uncover significant trends

16. Production of either on demand or scheduled logs of important test data such as:

- Cases that are positive and show results suggestive of liver and renal toxicity by user definable criteria

- Cases that are positive and show signs of resistance to treatment either by increasing viral loads or decreasing CD 4 counts or total leucocyte count and total lymphocyte count as surrogates for CD 4 counts and CD4:CD8 ratio.

3.13. Quality Control Management

The system must maintain, both on-line and manually, quality control checking (both instruments and manual input) and cumulative weekly and monthly quality control reports. QC parameters and features must be user definable by laboratory, test procedure type. QC software must:

1. Be able to define control samples (lot number, lot status, manufacturer / preparer, preparation/receipt data, expiry date, and test parameters by method and organism strain ID.

2. Have the capability to define reagents (lot number, lot status, expiration date, concentration, manufacturer / preparer, preparation/receipt date, storage conditions, etc.).

3. Be able to define instruments (model name and number, manufacturer, serial number, property number, location & installation date.

4. Allow for user-defined criteria for evaluating QC results for each control, reagent, and instrument parameter.

5. Handle statistics (mean, SD, CV) that can be manually defined, calculated on demand, or continually updated. Statistical outliers detection should be performed during calculation of statistics.

6. Enable the user to define the layout and frequency for each/any standard or control as they are found in worksheets and load lists.

7. Permit the entry of control results as desired by the user in addition to or instead of, using automatic prompts

8. Allow QC results to be entered either manually or through an instrument interface.

9. Allow personnel to edit manually entered QC results prior to final acceptance and provide an audit trail of edits.

10. Notify the analyst of any QC results that fall outside user-defined criteria (i.e. outliers or trends as defined by user). Allow for the entry of a narrative comment, allowing analyst to enter a probable cause, and a response to the unacceptable results with the corrective action being documented.

11. Provide the option of suspending patient results until supervisor intervention when QC results fail defined criteria.

12. Be capable of displaying a visual warning of reagent expiration or pending expiration.

13. Allow QC results to be viewed on-line or printed in either graphic or trend format. Support the production of statistical plotting and graphing aids, i.e. Levey-Jennings chart, scatter graph etc.

14. Allow for QC data review. For any individual piece of QC data, the system must be able to identify, allow for review, and track the following information:

- The person who documented and accepted the QC result

- The date/time the result was documented

- The criteria used to evaluate the result

- Any criteria that failed

- The statistical range or endpoint in effect when result was documented

- The assignable cause/corrective action comments
- Supervisor intervention and any supervisor/director review comments documented against the result.

15. Instrument identification and printed graphs w/ text.

16. Allow any/all QC data to be available for statistical evaluation. I.e. have statistics reporting that will list calculated mean, SD, & CV for user-selected time period and user-selected control test parameters, instrument function checks, etc.

17. Must have the ability to set date parameters on a lab/test procedure basis for storing data and associated information. Must have the ability to link archival patient results and test procedure specific worksheets/work cards to appropriate QC results and lot numbers

18. Allow reagent verification checks to be recorded and evaluated based on user-defined criteria.

3.14. Maintenance Management

This section covers the functional requirements associated with managing the maintenance of laboratory equipment.

1. The system maintains list of equipment maintenance records

2. The maintenance record consists of, but not limited, to the following:

    a. Equipment name

    b. Equipment manufacturer

    c. Equipment model

    d. Equipment serial number

    e. Equipment location

    f. Dates or interval of required maintenance

    g. Date maintenance was performed

    h. Problems identified during maintenance

    i. Corrective actions taken to resolve problems and when

3. The system issues reminders for maintenance

4. The system allows authorized users to manage the maintenance records.

3.15. Billing Management

This section covers the requirements associated with obtaining billing information from the submitter or other entities, tabulating the items to be billed, applying appropriate billing rates, and creating the invoices and supporting billing documentation.

1. Maintaining pricing of the laboratory offered tests

2. Extending lines of credit (LOC) to customers

3. Generating customer invoices

4. Accounting for customer payments

5. Generating financial reports

6. Capture and maintain submitter billing address and responsible party information

7. Specify which services are included under a given contract agreement and tag each service with a active/inactive flag (or timestamp each unique set of services active under the agreement

for any given service provision date. The term "service" is used rather than "test" to include training fees, annual license fees, etc.)

8. Capture and maintain agreed upon charges for specific services if different than standard billing rates

9. Select specific billing ledger entries and create submitter specific billing invoices

10. Create hard copy invoices grouped by submitter

11. Create electronic billing invoices in lieu of paper

12. Track billing and payment status

13. Create billing reports by submitter, timeframe, service and other key parameters

14. Track grants & contract services and associated fees

15. Create reports for non-billable services indicating dollar value by grant/contract based on standard costs

16. Report on test billing – what tests have been billed and the amount billed by selected time period

17. Associate a fixed cost with a specific test and/or group of tests plus allow for new fixed costs to be added to the system when price increases are put into effect. Price increases should not distort the historical records for billing. In addition to fixed costs, there needs to be an allowance for each test if a surcharge for extra time spent during testing needs to be added

18. Add in a surcharge to the fixed cost depending on the priority code assigned to the test request

19. Accommodate billing/purchase order identification numbers plus client identification, test identification, date completed, plus several other identifiers.

20. Allow billing data to be produced by date range and client

21. Produce costs by client either as tests completed or projected costs for tests requested but not yet completed

22. Summarize costs in multiple ways, such as purchase order number, client, billing codes, etc.

23. Void the cost of a test for valid reasons.

3.16. Inventory Management

This section covers aspects of inventory control such as ordering, tracking, and distribution for all items inventoried by a laboratory. Examples include specimen and sample collection kits, testing kits, lab supplies, chemicals, equipment, and forms. Collection kit management includes order processing, component and kit assembly tracking, and assembled kit inventory tracking activities including lot number and expiration date tracking for QC purposes.

1. For the purposes of inventory management, a supply is a tangible item or a product used to before, during and after the test process, and it covers consumable and durable goods, including:

   a. Test Media

   b. Test kits

   c. Control re-agents

   d. Paper forms such as request forms, shipment forms, etc.

   e. Containers for specimen

   f. Label rolls

   g. Masks

      h.   Gauze pads

      i.   Tapes

      j.   Bandages

2. Define unique storage units (and possible subunits) – hospitals, labs, clinics, facilities, bins, shelves, etc.

3. Define item/product properties such as part number/SKU, name, description, manufacturer, date of manufacture, shelf life/expiration date, UOM, quantity, STD pack, Bundle, serialized, etc.

4. Set inventory levels, quantities, at a storage unit

5. Define consumer/project/customer specific catalogs and bills of materials

6. Assign supplies to a storage unit

7. Move/transfer a supply between storage units

8. Consume a supply

9. Return a supply

10. Supply shipment

11. Receive/acknowledge supply shipment

12. Discard a supply

13. Checkout stored supply

14. Check in checked out supply

15. Reconcile supply

16. Manage product suppliers (distributors and manufacturers)

17. Manage warehouses

18. The warehouse consists of the following information:

      a.   Name of the warehouse.

      b.   Unique identifier of the warehouse.

      c.   Description of the warehouse.

      d.   Contact information for the warehouse including name, address and telephone number.

      e.   Owning Supplier.

19. Associate a warehouse to a product supplier

20. Assign product fulfillment to a supplier's warehouse

21. Create inventory replenishment requests for a site

22. An inventory replenishment request consists of the following:

      a.   Requisition Number – System generated.

      b.   Requisition Creation Date – System generated.

      c.   Contact information of entity that creates the request – System provided based on user login if manually created, otherwise from record if the request is system generated.

      d.   The site shipping address – System provided from preset site settings on record.

      e.   List of line items – Product part number and name from the site predefined Bill Of Materials.

       f.   Line item quantity – Manually entered or system generated.

23. Review inventory replenishment requests for a site

24. Approve inventory replenishment requests for a site

25. Schedule inventory replenishment requests for a site based on per product site inventory capacity (AKA Order Point) and minimum reorder level threshold

26. Receive email notifications when site employees or the FMS issue new materials replenishment requests

27. View inter-site inventory movement requests

28. View inventory levels for all tracked materials at a site

29. View the inventory levels of any secure materials removed and returned from and to the safe at participating sites

30. View inventory levels of the materials on hand at a participating site

31. View inventory levels of the materials actually used by a participating site

32. View inventory levels of materials returned and scrapped by sites

33. View inventory levels for all tracked materials for a warehouse

34. View inventory levels of materials received from the manufacturers at a warehouse

35. Run, view and print a Serial Number Reconciliation report. The report shows any noted reasons for discrepancies

36. Run, view and print an Inventory Capacity versus Actual usage per site report.

3.17. Localization Management

This section captures the functional requirement that pertain to localization of the deployed LIS. Localization of the system is GAP country specific and includes, but not limited to, the setting the following:

1. Language(s)

2. Calendar

3. Date and time format

4. Currency denomination and format

5. Acceptable payment methods

6. Available shipping carriers

7. Additional user-define data fields.

3.18. Alert Management

A critical lab value is defined as one which represents a patho-physiological state at such variance to normal as to be potentially life-threatening or which requires immediate attention.

These may include CD4 counts below a certain value, tests indicative of liver and renal toxicity and significant rise in viral loads.

Section 4. System Requirements

This section is targeted at the IT and operations personnel who are responsible for the selection and implementation of the LIS. This and the subsequent sections cover the hardware and software components necessary for the successful deployment and operation of the LIS.

4.1.   Software Architecture

The architecture must adhere to open standards, follow multi-tier architecture and service-oriented architecture (SOA).

4.1.1. Multi-Tier Architecture

The LIS must follow multi-tier approach to application architecture as depicted for example in Figure 1, where a tier is a logical partition with a unique responsibility in the system.
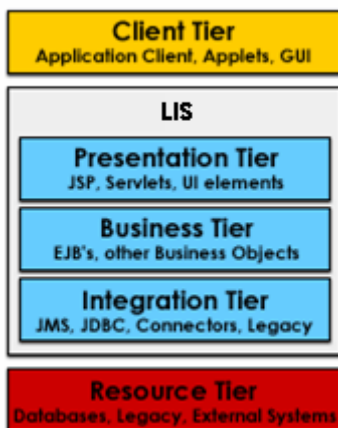

Figure 1 – Multi-tier Application Architecture

The multi-tier architecture provides the ability to fully employ load balancing and failover capabilities of the LIS application.

The rest of this section describes the various tiers in more details and the benefits of the multi-tier application architecture.

4.1.1.1.   The Tiers

4.1.1.1.1.   Client Tier

This tier represents all client devices and systems accessing the LIS. A client can be a web browser, an application, a Java applet, an ActiveX control, a WAP phone, etc.

4.1.1.1.2.   Presentation Tier

This tier encapsulates the presentation logic required to service the clients that access the LIS. The presentation tier intercepts the client requests, provides single sign-on, session management and accesses business services, constructs the response, and delivers the response to the client.

4.1.1.1.3.   Business Tier

This tier provides the business services and features required by the LIS clients. The tier contains the business data and business logic. The business data should be accessible as class objects and all business processing for the LIS should be centralized into this tier. All persisted objects should be isolated from the physical database schema to ensure that applications are portable in the event of database vendor or schema changes.

4.1.1.1.4.   Integration Tier

This tier provides communication with external resources and systems, such as data stores and legacy applications. The business tier is coupled with the integration tier whenever the business objects require data or services that reside in the resource tier.

4.1.1.1.5.   Resource Tier

This tier contains the business data and external resources such as databases, legacy systems, other value-add systems, and external services such as payment processors and shipping carriers.

4.1.1.2.   Benefits of Multi-Tier Architecture

The multi-tier architecture provides these advantages:

- **Improved Performance**: Employing server load balancing by separating the various LIS tiers provides more options for distributing the load of the web application across multiple server machines and improving the performance.

- **Higher Availability**: By utilizing additional LIS server instances in a clustered configuration, the multi-tier architecture has fewer points of failure than the basic single-tier or two-tier architectures, making the application highly available and more reliable.

- **Higher Scalability**: Handle growing future volume and performance requirements by adding additional servers for any of the congested tiers with negligible downtime and without the need for further programming.

- **Improved Security Options**: By separating the presentation and business tiers onto separate clusters, firewall policies can be created to places only the presentation tier cluster in the DMZ. Servers hosting clustered business tier can be further protected by denying direct access from untrusted clients.

4.1.2. Service-Oriented Architecture

SOA is a standards-based organizational and design methodology that more closely aligns IT with business processes using a collection of shared services on a network. Using standard interfaces that help mask the underlying technical complexity of the IT environment, SOA enables greater re-use of IT assets. This results in more rapid development and more reliable delivery of new and enhanced business services.

SOA is valuable to enterprises that need to solve business-critical problems using information technology, including enterprises that want to minimize redundant infrastructure and create a common business interface across customer and employee systems; businesses that need to personalize information to users based on roles and workflows; and organizations that want to use the Internet to boost customer satisfaction and access via personal computers and mobile devices.

4.1.2.1.   Business Benefits of Service-Oriented Architecture

Enterprises that adopt a service-driven approach experience the following business benefits:

- **Efficiency**: Transform business processes from siloed, replicated processes into highly leveraged, shared services that cost less to maintain.

- **Responsiveness**: Rapid adaptation and delivery of key business services to meet market demands for increased service levels to customers, employees, and partners.

- **Adaptability**: More effectively rollout changes throughout the business with minimal complexity and effort, saving time and money.

4.1.2.2.   IT Benefits of Service-Oriented Architecture

Enterprises that adopt a service-driven approach experience the following IT benefits:

- **Reduced Complexity**: Standards-based compatibility versus point-to-point integration reduces complexity

- **Increased Reuse**: More efficient application/project development and delivery through the reuse of shared services, previously developed and deployed

- **Legacy Integration**: Leveraging Legacy applications as re-usable services lowers the cost of maintenance and integration.

4.1.3. Standards Compliance

The following table summarizes the technical open standards requirements for the LIS.

Model Area	Standards	Impact
Service Access and Delivery Service transport	**TCP/IP** - Transmission Control Protocol / Internet Protocol **FTP** - File Transfer Protocol **LDAP**- Lightweight Directory Access Protocol	Standardizes the way information is sent between network entities
Component Framework Presentation/Interface	**HTML** - Hypertext Markup Language **XML** - Extensible Markup Language **HTTP** - Hypertext Transfer Protocol **HTTPS** - Secure Hypertext Transfer Protocol	Standardizes the way information is exchanged between applications
Service Interface and Integration Service discovery and description	**WSDL** - Web Services Description Language **UDDI** - Universal Description, Discovery and Integration	Standardizes on the way Web services are described and discovered
Service Interface and Integration Interoperability	**SOAP** - Simple Object Access Protocol	Standardizes the way interoperability between different software applications is achieved

4.1.4. Platform

While there are many LISs successfully deployed worldwide that were developed using various technologies such as MUMPS, it is desirable that this LIS be developed using the latest technologies. The two technologies that most current systems are developed in are either Sun Microsystems' Java 2 Enterprise Edition (J2EE) or Microsoft's .NET Framework (.NET) platforms.

The main technical difference between the two platforms can be summarized as that .NET is tied to Microsoft's Windows platform, VB.NET (including ASP.NET) and the C# programming languages for development, while J2EE is an open industry standard founded on Sun's Java language which can run on various platforms such as UNIX, Linux, and Microsoft Windows.

The major operational divide between .NET and J2EE usually boils down to a matter of productivity versus scalability. Java is traditionally seen as more scalable, robust and reliable, while .NET is more productive and easier to use.

4.2.   Operating System

The LIS must use established and non-proprietary computer operating systems for both clients and servers.

The list of operating systems recommended for server side applications includes recent versions of:

- Microsoft Windows Server, or
- UNIX – Sun Solaris, IBM AIX or HP-UX, or
- Linux

The list of operating systems recommended for client personal computers and devices includes recent versions of:

- Microsoft Windows for PCs
- Microsoft Windows CE for mobile devices

4.3.   Database

The LIS must use established and non-proprietary database server engines. The list of database servers recommended for enterprise LIS applications used at the national, provincial and district levels includes recent versions of:

- Oracle Database Server, or
- Microsoft SQL Server, or
- IBM DB2, or
- Open source MySQL.

The list of database servers recommended for stand-alone LIS applications used at the local and clinic levels includes recent versions of:

- Microsoft Access
- Open source MySQL.

A tool that can be used for building applications and is non proprietary but uses the Access database engine is Epi Info 3.2 (Windows).

4.4.   Connectivity

The LIS will be providing critical services to the GAP users and their clients. Therefore, there is a need to have the LIS support data exchange with various clients and systems that operate on a multitude of disparate platforms; this would include any case study specific software and reporting formats from CDC.

4.4.1. Client Tier

To achieve connectivity between the Client Tier and the LIS, the LIS should support one or more of the following protocols:

- **Transmission Control Protocol / Internet Protocol (TCP/IP)**: Used as the underlying protocol for all Internet based communications.
- **File Transfer Protocol (FTP)**: Used to transfer batch files from and to the LIS.
- **Hyper-Text Transfer Protocol (HTTP)**: Used to communicate with client Internet browsers and web services clients.
- **Hyper-Text Transfer Protocol over Secure Socket Layer (SSL) (HTTPS)**: Used to secure HTTP communication by utilizing encryption keys.
- **Wireless Access Protocol (WAP)**: Used to communicate with mobile devices such as Personal Digital Assistants (PDA), handheld PCs and smart phones.

4.4.2. Resource Tier

To achieve connectivity between the LIS and the LIS, the LIS must support one or more of the following protocols:

- **TCP/IP**: Used as the underlying protocol for all Internet based communications.
- **HTTP**: Used to communicate with external web-based systems.
- **HTTPS**: Used to secure communication with external web-based systems by utilizing encryption keys.
- **Simple Mail Transfer Protocol (SMTP)**: Used to send email to various clients and systems.
- **Lightweight Directory Access Protocol (LDAP)**: Used to communicate user authentication, authorization and groups with and LDAP compliant.
- **Open Database Connectivity (ODBC)**: Is an open standard application programming interface (API) for accessing databases.
- **Java Database Connectivity (JDBC)**: Is an application program interface (API) specification for connecting programs written in Java to the data in popular databases.

4.4.3. Data Message Format

The LIS must support the following data message formats:

- **Hyper-Text Markup Language (HTML)**: Used to describe the content of a Web page, mainly text and graphic images, only in terms of how it is to be displayed and interacted with using an Internet browser.
- **Extensible Markup Language (XML)**: Describes the content in terms of what data is being described. XML is used to describe file contents and communication with web services.
- **Health Level 7 (HL7)**: An ANSI standard for healthcare specific data exchange between computer applications. The name comes from "Health Level 7", which refers to the top layer (Level 7) of the Open Systems Interconnection (OSI) layer protocol for the health environment.
- **Flat File**: Includes proprietary formats or designated character delimited formats. The LIS must provide capabilities to parse, map or create such flat files depending whether the file is to be imported or exported.

4.5.   Security

The system-wide security must support the following:

- Compliance with the HIPAA privacy regulations.
- User authentication by maintaining unique and encrypted user ID and password per system user.
- User authorization by maintaining a role based system security matrix identifying users and their access rights i.e. Laboratories, tests procedures and results, software modules, programs, devices and specific data groups or elements.
- Lightweight Directory Access Protocol (LDAP) to store user authentication and authorization.
- Security to data field level.
- The ability to lock a terminal after user-defined number of unsuccessful login attempts is exceeded.
- Assignment of temporary passwords with automatic expiration.
- Administration procedures to add change and remove security passwords or individuals' access rights.

- An audit trail of failed attempts to log into system/application.

- Encrypted e-mail for auto e-mailed reports.

4.6. External Interface Specifications

To complete this section, more information is required to determine existing legacy systems, current and future external systems per country.

Section 5. Operational Requirements

This section relates to issues regarding the deployment and operation of the LIS. While many of these requirements are not part of the core LIS these issues none the less need to be addressed by the laboratory team in conjunction with the LIS vendor. How the LIS vendor recommends addressing these issues can have a significant effect on the lab's cost and capabilities over the lifetime of the LIS deployment.

5.1.   Operations Monitoring

Comprehensive monitoring of the entire production LIS environment (hardware, network, application, OS, security, etc) is critical. An effective monitoring solution can often predict and fix problems before they adversely affect the end users of the application. An effective monitoring system should be implemented and operated by support personnel. The monitoring system is outside the scope of the LIS system. The following items should be considered when implementing a monitoring system:

- Event reporting
- Application events reporting

    - Customer sessions
    - Web site hits including source IP address

- System Monitoring:

    - System up/down
    - CPU utilization
    - Disk Space utilization
    - Memory utilization
    - Windows 2000 Services monitoring
    - SNMP capability to monitor external devices (routers, etc)
    - Event log scanning to capture events (security, errors, etc)
    - Web server monitoring
    - Network activity (traffic in/out).

5.2.   Browser Support

The LIS should supports Microsoft Internet Explorer version 5.5 and above.

5.3.   Security

5.3.1. Server Configuration

Server user login accounts should be limited to few trusted personnel involved in the setup and/or maintenance of the LIS application.

5.3.2. Virus Protection

An anti-virus application should be installed, running and kept up to date with virus signatures on all LIS servers, and should be configured to perform weekly full scans of the system. The anti-virus application should also be configured to automatically trigger alerts to support personnel in the event of virus detection.

The virus signature files should be kept up to date automatically via a central Security Server. The central security server should poll the Antivirus vendor's site daily for signature updates. When an update is available, it is downloaded to the server or workstation automatically. The LIS servers and workstations should be configured to poll the security server each hour for signature updates. If available, it will automatically install on the server or workstation.

This automated process ensures that updates are as timely as possible and it requires no manual involvement from the System Administration staff.

5.3.3. Network Configuration

The LIS production server should be hosted in a DMZ behind an Internet firewall that enforces and monitors all Internet traffic to the application.

The LIS servers should be configured to open only the TCP/IP ports that are required by the application.

5.3.4. Encrypted User Communication

The production system will require the installation of Secure Socket Layer (SSL) certificate using strong 128-bit Key encryption on the Application Server. SSL provides encrypted transmission of any data being exchanged between the server running the LIS and the client system (Internet browser). Without SSL, sensitive data such as passwords and patient information would be transmitted as clear text and would thus not be protected from hack attacks.

5.3.5. User Authentication

The system needs to authenticate, enforce and maintain unique system wide user id and password credentials, for every user that has been granted access to the system. The application should only allow authenticated users access to system. The issuance of user ids and passwords to users for online access should be limited to selected group of authorized users..

The system automatically logs off users after a certain amount of inactivity.

All user passwords in the database are encrypted and can be deciphered only by backend server modules. All passwords are transmitted and stored in encrypted fashion.

5.3.6. User Authorization

Every user that has been granted access to the LIS must be assigned a specific *Role* to play in the system. The user role defines a set of privileges for the particular user. These privileges in turn indicate to the application whether to grant or deny particular user access to specific functionality in the application. The LSI must support the assignment of different roles to different users.

5.3.7. Audit trail

The system needs to track and log all critical interactions with the user including capturing the identity of the user, the user's action, and the timestamp of the action. Sample user interactions include:

- User successful and failed login attempts

- Updates to user profile such as name, credentials, address and contact information

- Creation and updates to patient profiles

- Viewing patient medical history and/or test results

- Creation of orders by user

- Order updates by the user

- Creation of test reports by user

- Creation, review and updates of billing information and statements.

Critical factors for a successful deployment include the following:

- Clearly defined project teams and roles assumed by appropriate individuals within each organization.

- Availability of necessary staff participation to assist in the deployment and training needs.

- Availability of necessary staff participation in this effort and providing additional staff members as necessary.

- Timely and effective communications.

- Effective management of the deployment and training plan.

When ready for system installation, a formal deployment plan should be developed that addresses the critical issues related to a successful deployment. A recommended approach for a deployment would include the following items:

- Define the deployment teams

- Establish a release to production criteria that will allow the final software to migrate to the production environment. Criteria should include the following:

- There are no Open regression bugs.
- There are no Open bugs with a severity 1 or 2.
- Test cases performed during the Integration and System Test phases have passed.
- There are no discrepancies between the version released to the staging and production environments and the version used during the final regression testing.
- The User Acceptance Test (UAT) was successfully completed.
- UAT issues were addressed.
-
- Setup the production hardware, software and network environments

- Once the final software is deployed in the production environment, the following high level tests should be run to validate the system setup and ensure all system are functioning as expected. It will not be necessary to run the entire test suite in the production environment from a functionality viewpoint, but only a subset.

  - **Network** – Test that all servers are networked correctly and are able to communicate via the preset protocols and ports.

  - **System Accessibility** – Test the accessibility of the LIS application via the preset URL for both internal and remote users.

  - **Application Communications** – Ensures all applications running in the various environments can successfully communicate via the preset protocols and ports.

  - **Systems Integration** – Ensures the LIS and any related applications function well in the same environment.

  - **Security** – Test SSL encryption between a client (user) browser and the server hosting the LIS web server.

  - **Application Security** – Test various layers of security within the LIS application including:

    - Passwords are fully encrypted within the database

    - User authentication

  - **Operating System Server Security** – Analyze system and security logs to ensure that the integrity of the system and network are maintained:

    - Operating system event logs

    - Database audit logs

    - Virus protection logs (if available)

    - Application monitoring logs

    - Application server logs

  - **Internal Users** – Ensures a typical internal user can successfully access the LIS application, save data, and print from the application

- **Remote Users** – Ensures a typical remote user can successfully access the LIS application, save data, and view the printable screens/reports

- **Printing** – Includes sending the printable test reports and billing statements to a printer already installed on the user's computer (local or network).

- **File Upload/Download** (if required) -Test upload/download of files from a source to the LIS application.

- **Application Tuning** – The applications may require some tuning to maximize the performance based on the traffic and load experienced during the testing phase in the production environment.

- **Restoration** – Once testing is completed, the database and all initial settings will be restored.

- Plan data migration

- Handle legacy orders

- Restore production data in the production environment, (create users, roles, etc.)

- Go live with a pilot deployment that includes a limited number of users to minimize the support effort required in the initial phases of deployment

- Generate release notes and documentation changes

- Go live

Production support must be in place to ensure the system is operational and monitored during business hours, and can be attended to when required. In addition to the high level deployment plan, a detailed deployment checklist should also be developed. This checklist should include all necessary tasks related to the installation, configuration, testing, etc of the LIS system.

5.4. Support

Ongoing support for the LIS deployment falls under both the vendor (or other entity that created the system also referred to as 'vendor' here) who will have to continue to provide support, maintenance and upgrades for the LIS and under the lab's IS group who will be responsible for the day to day running of the system.

In selecting a vendor special consideration should be given to the vendor's ability to deploy support personnel at a reasonable cost and in relative proximity to the GAP country. This means that the GAP country should not be reliant on support personnel that are based only in North America or Europe. The vendor should be expected to provide resources from locations within South Asia or Africa.

The GAP countries might also give consideration to creating regional support centers that can provide second line support to Users of groups of two, three or four countries locally.

Ongoing first line support will be provided by IT staff that is directly controlled by the Public Health or other related departments within the GAP countries. Deploying and providing ongoing operational support for the LIS by these groups will require skills that span across the following disciplines:

- Operations Personnel

- System Administration

- Network Administration

- Database Administration

- Quality Assurance personnel.

5.4.1. Hosting

The LIS server infrastructure should be hosted in a controlled environment with adequate power, physical security, cooling, and UPS battery backup in the event of temporary power interruption.

5.4.2. Incident Processing and Tracking

The selected vendor shall define a technical support process to enable the lab to submit support requests in the event of problems or issues with the LIS. Incidents should be able to be submitted either by phone, email, or using a web form. The Support system should have the ability to track support incidents that are submitted via either of these methods. Once the customer submits a technical inquiry to the support organization, an "Incident" is generated. An Incident is the processing of a technical inquiry or the attempt to solve a technical problem, regardless of the number of required phone calls or e-mails. Opened Incidents remain open until a solution is achieved or the incidents closed upon mutual agreement with the Customer.

The lab shall determine the urgency of the support inquiry in coordination with the support organization. The Support engineer may use his or her reasonable discretion to change the processing order of inquiries in case of identical urgency and priority, or for reasons of efficiency, provided that the postponed Customer does not suffer any significant disadvantages.

An example of such a schedule is listed below and should be defined in a service level agreement.

Urgency Levels	Specification	Response Time
Level 1 – Critical	Database server or failure of LIS Software components or major system problem causing entire application to be unavailable.	< 1 business hour
Level 2 – High	Error/issue causing an interruption of business, or possibly causing server failure. Portion of application may be unavailable. Temporary workaround may be possible.	< 4 business hours
Level 3 – Low	A problem affecting the production in the long term, but not causing immediate failure. Workaround is possible.	< 8 business hours

5.4.3. Application Software Maintenance

Procedures for change control need to be put in place to address the following types of application software upgrades:

- Critical bugs related to the LIS application should be resolved in a timely fashion. Such bugs may result in erronous data and don't usually have a workaround. The implementation and deployment timelines will be mutually agreed upon.

- Implemention of any minor enhancements or updates related to the application. Such enhancements do not include major database or other infrastructure and design changes. The implementation and deployment timelines will be mutually agreed upon.

5.5.   Training

Adequate training must be performed before authorized users are allowed to use the system in a production environment. The following approach is recommended to achieve the training goals:

- Create training material based on the delivered user documentation,

- Train the trainers (if necessary). How to use the software, including system setup and configuration, system maintenance and other routine operations. The training will be directed towards system users as well as the system administration and technical support staff personnel.

- Training sessions should be performed on the staging environment,

- Use simulated/test data (patient demographics, results, etc.) that will not be maintained after the training is completed,

- Track and address issues raised during the training phase.

5.6.   Backups and Disaster Recovery Plan

The LIS should have the capability to perform routine backups of the data in the system. The LIS must have the ability to do both manual and scheduled data backups. The data backups must be done to a storage media that can be stored off-site and should also provide for the ability to do backups to remote connected devices as well, for example a Storage Area Network (SAN) architecture in the future. The system must provide for data restore and recovery capabilities as well.

5.7.   Data-Entry Procedures While System Is Down

In case of a system or database breakdown the users must have the ability to manually accession the specimens and enter data into a separate local database or tool designed for temporary use. Upon successful restoration of the database following the outage there must be a mechanism to transmit the manually collected data to the LIS system or reenter it with the assigned accession numbers.

Section 6. Documentation

Documentation will include sufficient and detailed documentation for a general laboratory user as well as necessary details for the specialty laboratories as appropriate. The specific documenataion guides shall be provided to cover the needs of the following users.

6.1.   Installation and Administration

The installation guide shall be detailed enough to provide system's administrators with all of the information necessary to install and bring the application live in a production environment. The documentation shall list all utilities and tools necessary for the proper administration of the LIS. These tools shall cover management and administration of the LIS database, the user interface, and any auxiliary programs integrated into the delivered LIS.

6.2.   User Guide

Laboratory User documentation shall be sufficient and detailed enough to allow different levels of lab users to perform their functions with out having to rely overly much on external support.

6.3.   Online Help

The system shall provide context-sensitive online help at the data field level.

6.4.   Training

The system vendor shall submit a training plan which shall include the cost (if any), course titles, a summary of content, and state the position/qualifications of the target audience. Training shall be provided on two levels; LIS system maintenance and system operation designed for IT staff and; user training, designed for laboratory personnel that will be using the LIS on a day-to-day basis.

6.5.   Operations – troubleshooting, escalation procedures, knowledge database

Systems Administration documentation shall include information on trouble shooting and support escalation procedures. The system must also provide a centrally managed, web based knowledge database that users can access to get the latest information on trouble shooting, support, bugs, updates etc.

Section 7. Glossary

This section lists the definitions of the various clinical and technical acronyms and abbreviations terms used throughout the document.

Emergency Plan — An abbreviation for the President's Emergency Plan for AIDS Relief. While used frequently in the "AIDS world" as shorthand for the U.S. government's initiative to fight international HIV/AIDS, it should be used sparingly in documents prepared for broader external audiences. "Emergency Plan" is the preferred second reference for the "President's Emergency Plan for AIDS Relief" in a press release or announcement. This helps to ensure that the emergency nature of the initiative gets consistently communicated (and not lost in an acronym) to those who are less familiar with the program. Other acceptable second references include "the American people" and "the U.S. government."

Emergency Plan Country — 123 countries receive U.S. government funding for HIV/AIDS. All of the programs supported by this funding are under the authority of the Office of the U.S. Global AIDS Coordinator and are considered part of the President's Emergency Plan for AIDS Relief. They can be referred to, especially internally, as PEPFAR countries.

Focus Country — Out of the 123 Emergency Plan countries there are fifteen "focus countries," accounting for nearly 50 percent of the infections worldwide. A focus country is not a country in which the U.S. has special interest; the USG is interested in HIV/AIDS in every country. A focus country is one in which the USG has committed the resources needed to support the full national scale-up of prevention, treatment and care programs. The focus countries are Botswana, Cote d'Ivoire, Ethiopia, Guyana, Haiti, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Vietnam and Zambia.

Encounter — A patient specimen arriving at GAP for testing.

FTP — File Transfer Protocol.

HL7 — Health Level 7: An ANSI standard for healthcare specific data exchange between computer applications. The name comes from "Health Level 7", which refers to the top layer (Level 7) of the Open Systems Interconnection (OSI) layer protocol for the health environment.

HTML — Hyper-Text Markup Language: Used to describe the content of a Web page, mainly text and graphic images, only in terms of how it is to be displayed and interacted with using an Internet browser.

HTTP — Hyper-Text Transfer Protocol.

HTTPS — Hyper-Text Transfer Protocol over Secure Socket Layer.

JDBC — Java Database Connectivity: Is an application program interface (API) specification for connecting programs written in Java to the data in popular databases.

LDAP — Lightweight Directory Access Protocol.

Loadlist — A document (hardcopy or electronic) used by laboratory analysts to load and position groups of specimens for testing an instrument (i.e. BD ProbeTec, plate reader, etc.) or for loading a plate (TPPA) for reading.

LOINC — The Logical Observation Identifiers Names and Codes (LOINC) database provides a standard set of universal names and codes for identifying individual laboratory results (e.g. Hemoglobin, Serum Sodium concentration), clinical observations (e.g. Discharge Diagnosis, Diastolic blood pressure) and diagnostic study observations, (e.g. PR-interval, Cardiac echo left ventricular diameter, Chest x-ray impression).

MPI — A Master Patient Index is used to identify patient. Social Security number could be used; however, the MPI is usually calculated based upon patient demographic information. Questionable matches are brought to the attention of the person placing the order for clarification.

ODBC — Open Database Connectivity: Is an open standard application programming interface (API) for accessing databases.

SMTP — Simple Mail Transfer Protocol.

SNOMED — Systemized Nomenclature of Medicine.

SQL — Structured Query Language (SQL allows GAP users to access data in relational database management systems, such as Oracle, Sybase, Informix, Microsoft SQL Server, Access, and others, by allowing users to describe the data the user wishes to see. SQL also allows users to define the data in a database, and manipulate that data.

SSL — Secure Socket Layer.

TCP/IP — Transmission Control Protocol / Internet Protocol.

User — The user as defined in this report can be anyone that has access to the function described with appropriate security clearance.

User Definable (User defined or User Definition) — The ability for LIS user to define information i.e. selectable data lists, worksheets, worklists, etc. that would be given to the developers to implement.

WAP — Wireless Access Protocol.

Workcard — A document (hardcopy or electronic) used by microbiology analysts to record findings of readings and conformation tests (non –reportable) for a particular specimen.

Worklist — A document (hardcopy or electronic) used by laboratory analysts to organize groups of specimens for testing and recording results.

XML — Extensible Markup Language: Describes the content in terms of what data is being described. XML is used to describe file contents and communication with web services.

Section 8. References

The following documents were referenced in the creation of this document:

DHHS Global AIDS Program Trip Report, dated 8/20/2003 by Reshma Kakkar, CDC, Atlanta – Requirements gathering for lightweight clinical system, Addis Ababa, Ethiopia, August 11-15, 2003.

Functional Specifications Document – National Microbiology Reference Laboratory, in collaboration with CDC-Zimbabwe, dated 2/24/2003.

Several WHO and CDC documents – The original documents can be found at the DiagnosisONE CDC/APHL portal http://extranet.diagnosisone.com/sites/aphlcdc/default.aspx.

Commonwealth of Massachusetts – Enterprise Information Technology Architecture Enterprise Technical Reference Model document Version 1.0.

Appendix A. World Health Organization HIV Working Group Report

A Technical Working Group meeting on development of a toolkit for HIV/AIDS diagnostic support was held on 30-31 August 2001 at the headquarters of the World Health Organization (WHO) in Geneva. Participants included experts in virology, hematology and coordinators of HIV/AIDS antiretroviral projects at country level.

The WHO working group has described methodologies and testing facilities and needs in under-developed countries. The Working Group report stated:

In contrast to those in industrialized countries, most patients from resource-limited countries are already in an advanced stage of the disease when they are identified as HIV-positive and treatment is initiated. The diagnosis of HIV infect ion is often delayed due to the lack of voluntary counseling and testing (VCT) services and an absence of information. Therefore patients in resource-limited countries are more likely to have coexisting morbidity which may affect the choice of therapy, and may limit the scope of the potential spectrum of drug interactions and toxicity.

The President's Emergency Plan establishes the aggressive goal of providing treatment over the next five years to at least 2 million people living with HIV/AIDS in countries bearing some of the greatest burdens of the disease.

Due to the high cost of Antiretroviral (ARV) treatment, the complexity of the regimens, and the rapid emergence of resistant viruses when treatment regimens are not optimal, reliable laboratory diagnostic and monitoring services have to be in place when introduction of ARVs treatment is considered.

Initiation of ARV treatment requires the following:
- Appropriate diagnosis of HIV infection
- Recognition of opportunistic infections
- Determination of the immune status of the patient

Monitoring ARV treatment requires:
- Monitoring of immune status
- Recognition of opportunistic infections
- Monitoring of adverse affects from the drugs
- Monitoring of viral load in some cases
- Detection of resistant HIV variants in some cases

The discussion below covers which laboratory tests can/should be done at the different laboratory levels using which technology. Emphasis was put on the identification of minimum requirements at the various levels for diagnosis of HIV infection and initiation and monitoring of patients receiving ARV. Elaborated below are mainly the specific ARV-associated issues required in addition to the basic routine diagnostic tests.

These issues have been divided into three different levels: central/referral, provincial/district and peripheral/primary health care (PHC) level. The basic information regarding the various levels is summarized in Table 1 below.

Peripheral Level

It is assumed that the activities at this level can be performed without regular supply of electricity. Diagnosis of HIV infection can be performed by simple/rapid (S/R) antibody tests.

Although VCT facilities are being scaled up in many countries, only a few PHC clinics actually carry out HIV diagnostics on site. However, mechanisms for referring both samples and potentially HIV-positive patients to the district/provincial laboratory should be in place. Diagnosis of some of the opportunistic infections (OI) can be made by simple light microscopy. A White Blood Cell (WBC) count and differential analysis can also be carried out by microscopy. Hemoglobin levels can be measured at this level of health facilities. In the longer perspective, it is anticipated that many persons receiving ARV drugs will take their medicines at home, with the nearest health facility providing the necessary support and facilitating basic clinical follow-up.

Essential equipment includes a light microscope (usually available at this level) and a refrigerator (storage of reagents). These facilities may or may not be able to support the deployment of even basic computers. In those facilities where PCs cannot be deployed paper based processes might need to be modified so as to ensure that the data collected can be integrated with the LIS deployed at the other levels.

Provincial/District Level Laboratories

WHO working group discussed the basic requirements for diagnosis of HIV infection and the introduction of ARV at this level, and agreed that diagnosis based on S/R tests or ELISAs and a CD4+ T-cell determination in most circumstances is sufficient for initiation of ARV. An HIV antibody testing algorithm can be based on S/R assays only, provided that the combination of assays chosen is carefully designed. The choice of S/R tests or ELISAs (or combinations thereof) depends largely on the volume of samples to be tested, availability of equipment and training level of staff. CD4+ T-cell counts should preferably be performed by use of alternative methods (e.g. Dynabeads) at this level. In addition, whole blood counts need to be performed here. Due to the high cost and degree of sophistication of available assays, a wide use of HIV plasma viral load measurements at this stage is not recommended. However, when the clinical status (including decreasing CD4+ T-cell levels) of a patient receiving ARV indicates a treatment failure, logistics should exist for referral of the patient or samples to a setting with facilities for analyses of viral load and/or viral resistance (see below).

The provincial/district level should also have facilities to monitor ARV side effects (renal and liver function tests) and opportunistic infections such as TB (sputum microcopy), cryptococcosis (Ag test), toxoplasmosis (Ag test) and pneumocystis carinii pneumonia (wet mount microscopy).

Essential equipment includes a light microscope, preferably an immunofluorescence (IF) microscope (e.g. for Dynabeads), a centrifuge, refrigerator and freezer (-20 o C). It was pointed out that plasma samples for subsequent plasma HIV RNA analyses should preferably be stored at -70° C. Moreover, it is better to send non-separated whole blood samples to a laboratory which has -70 ° C freezers to store the separated plasma sample.

For adults, TB diagnosis can be done by sputum microscopy at this level. For early diagnosis of HIV infection in infants (under 12 months), samples have to be referred to the central/referral laboratory for PCR or p24Ag assay. Dried blood samples collected on filter paper would facilitate this strategy. Some institutions may choose to follow up children born to HIV-infected women at around one year of age (when the maternal antibodies have disappeared), using conventional HIV antibody tests. However, this approach does not provide the necessary information for decisions regarding breast versus bottle feeding, or for providing prophylaxis to the newborns.

At the provincial/district level, staff should include doctor(s) with special training in ARV, laboratory technologist(s), laboratory technicians, counselors, nurses, a pharmacist (for drug dispensing) and an officer in charge of monitoring records, data and information systems. Staff should be trained for, and possess equipment and reagents to diagnose and monitor the efficacy of ARV treatment.

Central Referral Laboratories

It was concluded that a distinction should be made between national reference laboratories and central/referral laboratories. The former usually have a more supervisory, quality assurance role while the latter will be more directly involved in the advanced diagnostics of HIV-infected individuals. In some cases, the reference and central referral laboratory will be the same. At the central level, in-depth knowledge of the various methodologies used at all levels should be available. This is important for technical discussions, supervision and problem solving, etc.

Diagnosis of HIV infection should also be done by serology, i.e. ELISA and/or simple rapid tests for screening as well as for confirmation. The need for a western blot (WB) assay for confirmation is limited and not recommended here. However, due to previous experience and current interest, some laboratories may wish to keep WBs as one of their options for complicated samples. Lymphocyte subset determinations (CD4+/CD8+ T-cell counts) will probably be done by flow cytometry at this level, due to an anticipated high throughput of samples. However, these laboratories should also have knowledge and experience of alternative methods such as the Dynabeads assay and Cyto-sphere.

Methodology for complete hematology analyses and monitoring of side effects (renal and liver function tests) should be available. Diagnostics for OIs should be available, including Ag tests for cryptococcus, toxoplasmosis, PCP and TB cultures.

The central referral laboratories may have facilities for HIV nucleic acid amplification testing (NAT), both in a qualitative (early detection) or quantitative (viral load) form.

Although expensive and cumbersome, there are currently no alternatives except for the p24Ag assay for early diagnosis in children. Analyses for viral resistance may be performed at this level but it was also suggested that these analyses are even further centralized to a few regional and/or international centers. It was concluded that surveillance for viral resistance on a population basis, rather than individual testing of a large number of persons receiving ARV, would probably suffice at this stage. Constant vigilance for the occurrence of resistant HIV variants remains of utmost importance. The diagnostics of OIs greatly improves with access to at least X-ray and ultrasound. MRI is preferable to CT, but both are very expensive alternatives.

Special equipment needed includes a flow cytometer, -70 o C freezer, PCR equipment, TB culture facilities and radiological equipment.

Staff should include doctors with specialized ARV training, laboratory technologists and technicians with specialized training in immunology, viral load measurements, etc.

Other categories with university education such as (micro) biologists and chemists may also be of interest.

	Central (referral) level	US $	Provincial/district level	US $	PHC level	US $
Diagnosis of HIV infection	Simple rapid test and ELISA ELISA equipment (incubator, washer, reader)	5 2000-5000 each	Simple rapid test and/or ELISA ELISA equipment (incubator, washer, reader)	5 2000-5000 each	Simple rapid test	5
CD4+ T-cell measurements	Flow cytometry Flow cytometer e.g. Dynabeads assay (light or IF microscopy)	10-20 40-80,000 8-10 2000-5000	e.g. Dynabeads assay (light or IFL microscopy) or referral to central level	8-10 2000-5000	sample referral only	
HIV plasma viral load	NAT-like commercial assays PCR equipment and laboratory facilities	30-100 35,000	Sample referral only		--	
Viral resistance (optional)	In-house reagents (or sample referral) PCR equipment and adapted laboratory facilities		Sample referral only		--	
Adverse effects	To be determined		To be determined		To be determined	
Opportunistic infections	To be determined		To be determined		To be determined	

Table 1 – Summary of basic requirements for laboratory monitoring of ARV: reagents, equipment and costs, August 2001.

WHO Report on Commercially Available HIV Assays

Another WHO/UNAIDS report issued in January 1999 surveyed the operational characteristics of commercially available HIV assays and, of pertinence here, available testing strategies. The following discussion provides a brief overview of the available testing strategies.

The diagnosis of HIV infection is usually made on the basis of the detection of antibodies to HIV. Serological tests for detecting antibodies to HIV are generally classified as **screening tests** (sometimes referred to as **initial** tests) or **confirmatory tests** (sometimes referred to as **supplemental** tests). Initial tests provide the presumptive identification of antibody-positive specimens, and supplemental tests are used to confirm whether specimens found reactive with a particular screening test contain antibodies specific to HIV.

The most widely used screening tests are **ELISAs** as they are the most appropriate for screening large numbers of specimens on a daily basis, e.g. blood donations. The earliest assays used purified HIV lysates (1st generation), and often lacked sensitivity and specificity. Improved assays based on recombinant proteins and/or synthetic peptides, which also enabled the production of combined HIV-1/HIV-2 assays became rapidly available (2 nd generation). The so-called 3rd generation or sandwich ELISAs, which use labeled antigen as conjugate, are extremely sensitive and have reduced the window period considerably.

A variety of simple, instrument-free initial tests are now available, including agglutination, immunofiltration (flow through tests) immunochromatographic (lateral flow tests) and dipstick tests. Specimens and reagents are often added by means of a dropper to the test device. A positive result is indicated by the appearance of a coloured dot or line, or shows an agglutination pattern. Most of these tests can be performed in less than 10 minutes, and are therefore called **simple/rapid (S/R) assays**.

Other simple tests are less rapid and their procedures require 30 minutes to 2 hours. The results are read visually. In general, these tests are most suitable for use in laboratories that have limited facilities and process low numbers of specimens daily.

When a single screening assay is used for testing in a population with a very low prevalence of HIV infection, the probability that a person is infected when a positive test result is obtained (i.e., the positive predictive value) is very low, since the majority of people with positive results are not infected. This problem occurs even when a test with high specificity is used. Accuracy can be improved if a second supplemental test is used to retest all those samples found positive by the first test. Those found negative by the test are considered negative for antibodies to HIV.

The most commonly used confirmatory test was the Western blot (WB). However, its use has proven to be very expensive and can, under some conditions, produce a relatively large number of indeterminate results. Similar assays, generically called Line immuno-assays (LIAs), based on recombinant proteins and/or synthetic peptides capable of detecting antibodies to specific HIV-1 and/or HIV-2 proteins, have been developed. Examples of this technology include the INNOLIA, Pepti-Lav, and RIBA assays. In general, these assays produce fewer indeterminate results as compared to WB, but are equally expensive. Studies have shown that combinations of ELISAs or S/R assays can provide results as reliable as the WB at a much lower cost. WHO and UNAIDS therefore recommend that countries consider testing strategies which use ELISAs and S/R assays rather than ELISA/WB for HIV antibody detection.

Objective of testing		Prevalences of infection	Testing strategy
Transfusion/transplant safety		All prevalences	I
Surveillance		>10%	I
		≤10%	II
Diagnosis	Clinical signs/ symptoms of HIV infection[1]	>30%	I
		≤30%	II
	Asymptomatic	>10%	II
		≤10%	III

Table 2 - UNAIDS and WHO recommendations for HIV testing strategies according to test objective and prevalence of infection in the sample population.

UNAIDS and WHO recommend three testing strategies, which have been recently updated, to maximize accuracy while minimizing cost. Which strategy is most appropriate will depend on the objective of the test and the prevalence of HIV in the population, as shown in Table 2 and Figure 2.
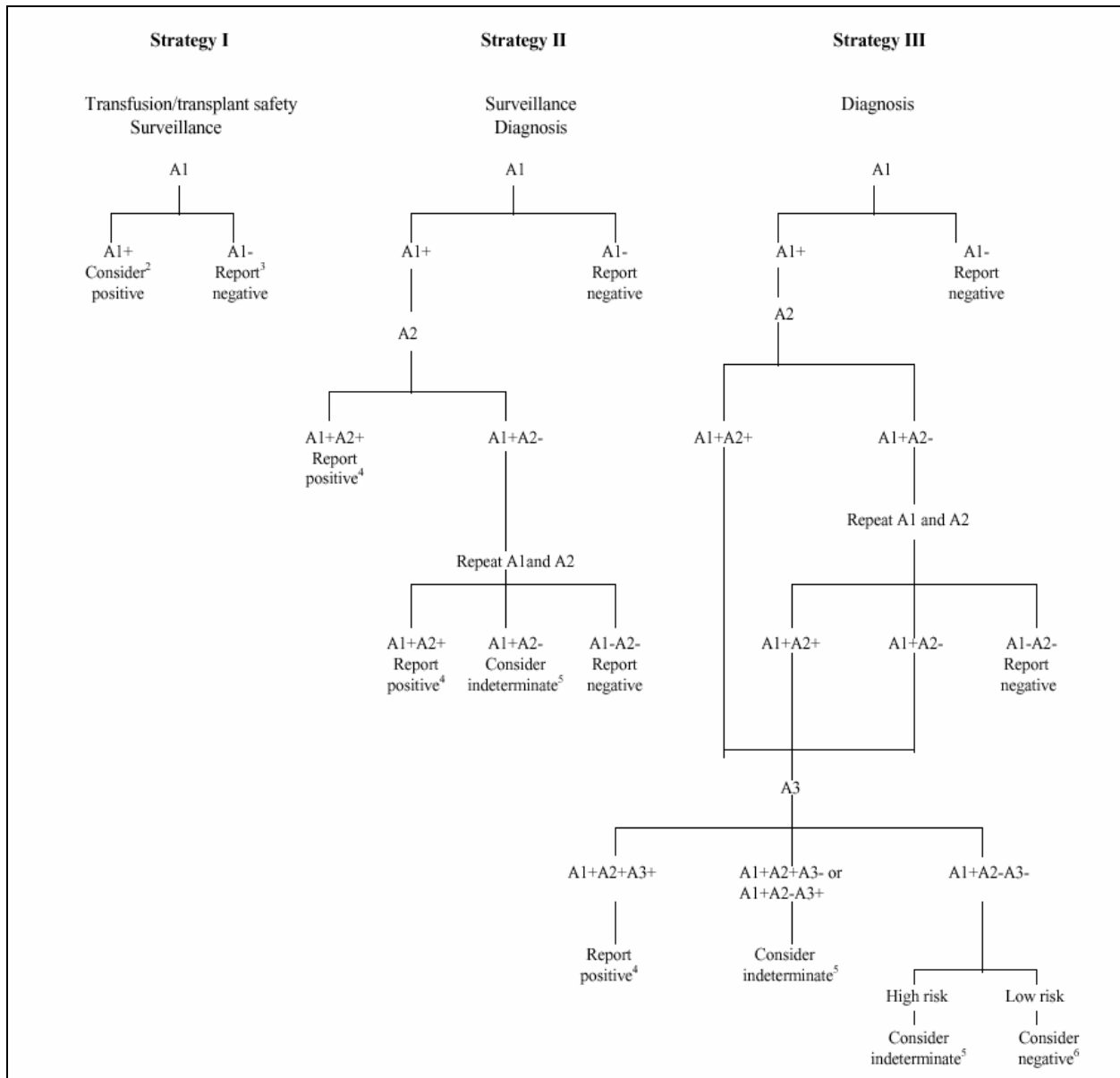
Figure 2 – WHO/UNAIDS recommended HIV testing strategies.