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StandardGuide for Laboratory Information Management Systems (LIMS)[1]

This standard is issued under the fixed designation E1578; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide covers issues commonly encountered at all stages in the life cycle of Laboratory Information Management Systems from inception to retirement. The sub-sections that follow describe details of scope of this document in specific areas.

1.2 *High Level Purpose*—The purpose of this guide includes: *(1)* help educate new users of Laboratory Information Management Systems (LIMS), *(2)* provide standard terminology that can be used by LIMS vendors and end users, *(3)* establish minimum requirements for primary LIMS functions, *(4)* provide guidance for the specification, evaluation, cost justification, implementation, project management, training, and documentation, and *(5)* provide an example of a LIMS function checklist.

1.3 *LIMS Definition*—The term Laboratory Information Management Systems (LIMS) describes the class of computer systems designed to manage laboratory information.

1.4 *Laboratory Categories*—The spectrum of laboratories that employ LIMS is wide spread. The following break down provides an overview of the laboratory categories that use LIMS as well as examples of laboratories in each category.

1.4.1 *General Laboratories:*
1.4.1.1 Standards (ASTM, IEEE, ISO), and
1.4.1.2 Government (EPA, FDA, JPL, NASA, NRC, USDA, FERC).
1.4.2 *Environmental:*
1.4.2.1 Environmental Monitoring.
1.4.3 *Life Science Laboratories:*
1.4.3.1 Biotechnology,
1.4.3.2 Diagnostic,
1.4.3.3 Healthcare Medical,
1.4.3.4 Devices, and
1.4.3.5 Pharmaceuticals Vet/Animal.
1.4.4 *Heavy Industry Laboratories:*
1.4.4.1 Energy & Resources,
1.4.4.2 Manufacturing & Construction,
1.4.4.3 Materials & Chemicals, and
1.4.4.4 Transportation & Shipping.
1.4.5 *Food & Beverage Laboratories:*
1.4.5.1 Agriculture,
1.4.5.2 Beverages,
1.4.5.3 Food, and
1.4.5.4 Food Service & Hospitality.
1.4.6 *Public Sector Laboratories:*
1.4.6.1 Law Enforcement,
1.4.6.2 State & Local Government,
1.4.6.3 Education, and
1.4.6.4 Public Utilities (Water, Electric, Waste Treatment).
1.4.7 *Laboratory Size:*
1.4.7.1 This guide covers topics regarding LIMS for a range of laboratory sizes ranging from small with simple requirements to large multi-site/global laboratories with complex requirements. Although the guide addresses complex issues that impact primarily large LIMS implementations, laboratories of all sizes will find this guide useful. The implementation times and recommendations listed in this guide are directed at medium and large laboratories.

1.5 *Integration*—Integration between LIMS and other external systems (document management, chromatography data systems, laboratory instruments, spectroscopic data systems, Enterprise Resource Planning (ERP), Manufacturing Execution Systems (MES), Corrective Action and Preventative Action (CAPA), Electronic Laboratory Notebooks (ELNs) and data archive) provides significant business benefits to any laboratory. Integration between LIMS and other external systems is discussed at a high level in this guide including data interchange and XML standards.

1.6 *Lifecycle Phases*—The LIMS lifecycle described in this guide includes the following phases: *(1)* project initiation, *(2)* requirements analysis, *(3)* design, *(4)* build/configure, *(5)* test and commission, *(6)* operation and maintenance, and *(7)* retirement. This guide is intended to provide an understanding of the LIMS system life cycle and good practices for each of the activities. It will help first time LIMS implementers plan and manage their LIMS projects while seasoned LIMS users may use the LIMS system life cycle to maintain existing LIMS and prepare for the implementation of the next generation LIMS.

[1] This guide is under the jurisdiction of ASTM Committee E13 on Molecular Spectroscopy and Separation Science and is the direct responsibility of Subcommittee E13.15 on Analytical Data.

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1.7 *Audience*—This guide has been created with the needs of the following stakeholders in mind: *(1)* end users of LIMS, *(2)* implementers of LIMS, *(3)* quality personnel, *(4)* information technology personnel, *(5)* LIMS vendors, *(6)* instrument vendors, *(7)* individuals who must approve LIMS funding, *(8)* LIMS application support specialists, and *(9)* software test/validation specialist. Information contained in this guide will benefit a broad audience of people who work or interact with a laboratory. New LIMS users can use this guide to understand the purpose and functions of LIMS. The guide can also help prospective LIMS users in understanding terminology, configurations, features, design, benefits and costs. Individuals who are purchasing a LIMS may use this guide to identify functions that are recommended for specific laboratory environments. Research and Development staff of commercial LIMS vendors may use the guide as a tool to evaluate, identify, and potentially improve the capabilities of their products. LIMS vendor sales staff may use the guide to represent functions of their LIMS product to prospective customers in more generic and product neutral terms.

1.8 *Out of Scope*—The full description and use of systems mentioned in this guide within the context of interfaces to LIMS are beyond the scope of this standard. Examples of these systems include Chromatography Data Systems (CDS), Electronic Laboratory Notebooks (ELN), Data Archive, Scientific Data Management Systems (SDMS), Enterprise Resource Planning (ERP), Manufacturing Execution Systems (MES) and Electronic Document Management Systems (EDMS).

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E1340 Guide for Rapid Prototyping of Information Systems

E1947 Specification for Analytical Data Interchange Protocol for Chromatographic Data

E1948 Guide for Analytical Data Interchange Protocol for Chromatographic Data

E2066 Guide for Validation of Laboratory Information Management Systems

E2077 Specification for Analytical Data Interchange Protocol for Mass Spectrometric Data

E2078 Guide for Analytical Data Interchange Protocol for Mass Spectrometric Data

2.2 *ANSI Standards:*[3]

ANSI HL7 Arden Syntax for Medical Logic Systems

2.3 *EPA Data Standards:*[4]

40 CFR 160 Code of Regulations, 54 FR 34067, August 17, 1989

40 CFR 792 Code of Regulations, 54 FR 34043, August 17, 1989

EPA 2185 Good Automated Laboratory Practices Principles and Guidance to Regulations For Ensuring Data Integrity In Automated Laboratory Operations with Implementation Guidance, 1995 Edition

2.4 *FDA Regulations:*[5]

FDA 21CFR Part 11 Code of Regulations, 57 FR 32185, July 21, 1992

2.5 *GAMP:*[6]

GAMP 4 Good Automated Manufacturing Practice (GAMP) Guide for Validation of Automated Systems in Pharmaceutical Manufacture, ISPE, December 2001

GAMP Good Practice Guide Validation of Laboratory Computerized Systems, April 2005 (this is a supplement to the GAMP 4 document)

GAMP GPG IT Infrastructure Control and Compliance, ISPE, September 2005

2.6 *IEEE Standards:*[7]

IEEE 829 1998 IEEE Standard for Software Test Documentation

IEEE 830 1998 Recommended Practice for Software Requirements Specifications

IEEE 1008 1987 IEEE Standard for Software Unit Testing

IEEE 1012 2004 IEEE Standard for Software Verification and Validation

IEEE 1028 1997 IEEE Standard for Software Reviews

IEEE 1063 2001 IEEE Standard for Software User Documentation

2.7 *Instrument Interface Standards:*

AnIML (Analytical Information Markup Language) an emerging standard for laboratory instruments covering multiple analytical techniques. The E13.15 subcommittee is responsible for the development of this standard.[8]

NetCDF (Network Common Data Form) an interface for array-oriented data access and a library that provides an implementation of the interface. The netCDF library also defines a machine-independent format for representing scientific data. Together, the interface, library, and format support the creation, access, and sharing of scientific data. Unidata Program Center at the University Corporation for Atmospheric Research (UCAR).[9]

Staged Electronic Data Deliverable (SEDD) EPA—eXtensible Markup Language (XML)—joint standard developed by US EPA Office of Superfund Remediation and Technology Innovation (OSRTI) Analytical Services Branch (ASB)and US Army Corps of Engineers (US ACE)[10]

[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

[4] Available from United States Environmental Protection Agency (EPA), Ariel Rios Bldg., 1200 Pennsylvania Ave., NW, Washington, DC 20460, http://www.epa.gov.

[5] Available from Food and Drug Administration (FDA), 5600 Fishers Ln., Rockville, MD 20857, http://www.fda.gov.

[6] Available from the International Society for Pharmaceutical Engineering (ISPE), 3109 W. Dr. Martin Luther King, Jr. Blvd., Suite 250, Tampa, FL 33607-6240, http://www.ispe.org.

[7] Available from Institute of Electrical and Electronics Engineers, Inc. (IEEE), 445 Hoes Ln., P.O. Box 1331, Piscataway, NJ 08854-1331, http://www.ieee.org.

[8] Schaefer, B. A., Poetz, D., and Kramer, G. W., "Documenting Laboratory Workflows Using the Analytical Information Markup Language," *Journal of the Association for Laboratory Automation*, Vol 9, No. 6, 2004, pp. 375–381, and http://animl.sourceforge.net.

[9] Available from UCAR: http://www.unidata.ucar.edu/software/netcdf.

[10] Available from US EPA: http://www.epa.gov/superfund/programs/clp/sedd.htm.

ISO/IES 12207 Subcommittee for Electronic Data Standards (SEDS), reference spectroscopic databases sponsored by the International Union of Pure and Applied Chemistry (IUPAC) and standards related to the Joint Committee on Atomic and Molecular Physical Data (JCAMP) and JCAMP-DX (XML in the chemistry area) ISO Standards ISO/IEC 12207 Information technology—Software life cycle processes, as amended by ISO/IEC 12207 AMD2[11]

2.8 *NRC Standards:*[12]

FDA CFR Pa rt 21 10 Code of Federal Regulations (CFR) Part 21.42 FR 28893, June 6, 1977

FDA CFR Part 50, Appendix B 10 Code of Federal Regulations (CFR) Part 50 Appendix B. 35 FR 10499, June 27, 1970, as amended at 36 FR 18301, Sept. 11, 1971; 40 FR 3210D, Jan. 20, 1975

FDA CFR Part 50, Appendix E 10 Code of Federal Regulations (CFR) Part 50 Appendix E. 45 FR 55410, Aug. 19, 1980, et sequentia as amended

FDA CFR Part 50, Appendix K 10 Code of Federal Regulations (CFR) Part 50 Appendix K. 21 FR 355, Jan. 19, 1956, unless otherwise noted

3. Terminology

3.1 This guide defines terminology used in the LIMS field. Section 3.2 defines LIMS terms specific to this guide. Users of this document should request a terminology list from each vendor with a cross reference to the terms used in this guide.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *CAPA, n*—acronym for corrective action, preventative action.

3.2.2 *Chromatography Data System (CDS), n*—computer system used to acquire, analyze, store and report information from chromatography instruments.

3.2.3 *EDMS, n*—acronym for electronic document management system.

3.2.4 *ELN, n*—acronym for electronic laboratory notebook. computer system designed to replace paper laboratory notebooks.

3.2.4.1 *Discussion*—Lab notebooks in general are used by scientists and technicians to document research, experiments and procedures performed in a laboratory. A lab notebook is often maintained to be a legal document and may be used in a court of law as evidence. Similar to an inventor's notebook, the lab notebook is also often referred to in patent prosecution and intellectual property litigation. Electronic laboratory notebooks enable electronic access to information including searching, data capture from instruments and collaboration between laboratory personnel and personnel outside the laboratory.

3.2.4.2 *Discussion*—ELNs can be divided into two categories: specific ELNs contain features designed to work with specific applications, scientific instrumentation or data types. Refer to laboratory exectuion system (LES) as an example of a specific ELN. Cross-disciplinary ELNs or generic ELNs are designed to support access to all data and information that needs to be recorded in a lab notebook.

3.2.5 *ERP, n*—acronym for enterprise resource planning.

3.2.6 *GALP, n*—the GALPs are a union of federal regulations, policies, and guidance documents. Several of the GALP provisions are embodied in EPA's Good Laboratory Practice Standards (GLPs). The GLPs are regulations that govern the management and conduct of most nonclinical laboratory studies submitted to EPA's office of Toxic Substances and its Office of Pesticide Programs. Reference EPA 2185.

3.2.7 *GAMP, n*—acronym for good automated manufacturing practice.

3.2.8 *LES, n*—acronym for laboratory execution system. Computer system employed in the laboratory at the analyst work level to aid in step enforcement for laboratory test method execution.

3.2.8.1 *Discussion*—Laboratory execution systems (LES) are a sub class of electronic laboratory notebooks (ELNs) that focus on step execution of defined laboratory test methods. The LES are typically employed in Quality Control laboratories that have defined test methods. The functionality of LES and LIMS overlap in the areas of result entry, instrument integration and specification flagging. Deployment options include LES and LIMS systems deployed as an integrated solution, LIMS only or LES only (for limited functions).

3.2.9 *Laboratory Information Management System (LIMS), n—(1)* acronym for laboratory information management System. Computer application(s) software and hardware that can acquire, analyze, report, and manage data and information in the laboratory; *(2)* computer software that is used in the laboratory for the management of samples, test results, laboratory users, instruments, standards and other laboratory functions such as invoicing, plate management, stability LIMS, work flow automation; and *(3)* a class of application software which handles storing and managing of information generated by laboratory processes. These systems are used to manage laboratory processes including defining master data, sample management and chain of custody, work assignment, instrument and equipment management, standard and reagent management, scheduled sample collection and testing, result entry, result review, reporting, trending and business rule enforcement. These systems interface with laboratory instruments (for example, chromatography data systems (CDS), spectrophotometers and balances) and other information systems such enterprise resource planning (ERP), manufacturing execution systems (MES), or health care based laboratory information systems). A LIMS is a highly flexible application, which can be configured or customized to facilitate a wide variety of laboratory workflow models.

3.2.10 *LIMS configuration, n*—refers to the process of preparing the LIMS for use in a particular laboratory. It typically involves using an interface provided by the vendor to enter information that describes the types of samples, analytical methods, specifications, etc. used in the laboratory.

[11] Available from International Organization for Standardization (ISO), 1, ch. de la Voie-Creuse, Case postale 56, CH-1211, Geneva 20, Switzerland, http://www.iso.ch.

[12] Available from U.S. Nuclear Regulatory Commission (NRC), Washington, DC 20555-0001, http://www.nrc.gov.

3.2.11 *LIMS customization, n*—refers to the process of modifying the LIMS to meet the requirements of a particular laboratory. It typically involves adding tables, modifying table structures and writing code or programs to alter the behavior of the LIMS.

3.2.12 *metadata, n—(1)* data about data; and *(2)* information that describes another set of data.

3.2.12.1 *Discussion*—Metadata in the LIMS context typically includes all data that supports a test result that is recorded in a LIMS. Examples include for a pH test, a pH result can be supported by metadata including what instrument was used, what is the calibration date of the instrument, what standard buffer solutions (reagents) were used to calibrate the pH probe sensor and the expiration dates for the standard solutions. sample

3.2.13 *sample registration, n*—the process of registering samples in a LIMS.

3.2.14 *SDMS, n*—acronym for scientific data management system.

3.2.15 *spectroscopic data systems, n*—computer system used to process, visualize, interpret, store and report information from spectroscopic and non-chromatographic instruments.

3.2.16 *static tables, n*—descriptive LIMS database tables where templates, tests, calculations, specifications, and related information are defined and stored (commonly found in "look up/reference/dictionary" tables).

3.2.16.1 *Discussion*—LIMS stores look up information to speed sample registration and test assignments. Generally prior to sample registration the static tables need to be configured. Some LIMS implementations can enter static table information directly from the sample registration step. Synonyms of static tables include master data and configuration data.

4. Significance and Use

4.1 *Relevance*—This guide is intended to educate those in the intended audience on many aspects of LIMS. Specifically, the guide may:

4.1.1 Help educate new users of LIMS;

4.1.2 Help educate general audiences in laboratories and other organizations that use LIMS;

4.1.3 Help educate instrument manufactures and producers of other commonly interfaced systems;

4.1.4 Provide standard terminology that can be used by LIMS vendors and end users;

4.1.5 Establish a minimum set of requirements for primary LIMS functions;

4.1.6 Provide guidance on the tasks performed and documentation created in the specification, evaluation, cost justification, implementation, project management, training, and documentation of LIMS; and

4.1.7 Provide high-level guidance for the integration of LIMS with the most commonly integrated systems such as laboratory instruments, CDS, ERP, ELN, SDMS and so forth.

4.2 *How Used*—This guide is intended to be used by all stakeholders involved in any aspect of LIMS implementation or maintenance.

4.2.1 It is intended to be used throughout the LIMS life cycle by individuals or groups responsible for LIMS including specification, build/configuration, validation, use, upgrades, retirement/decommissioning.

4.2.2 It is also intended to provide an example of a LIMS function checklist.

5. LIMS Concept Model—Graphic Picture of Functionality

NOTE 1—The LIMS primary functions, integration points, life cycle and industry segments are described in Fig. 1.

5.1 *LIMS Concept Model—High Level*—The core LIMS functions cover a wide range of laboratory workflows, information management and integration with other enterprise computer systems. These core LIMS functions are illustrated in the LIMS box. Integration with LIMS and a number of external systems, instruments, reporting tools and automated test tools are illustrated by the boxes above and below the LIMS box in Fig. 1.

5.2 *LIMS Concept Model—Mid Level*—The LIMS functions and their relationship with external systems, extended LIMS functions and future LIMS functions is illustrated in Fig. 2. The diagram defines:

5.2.1 Core LIMS functions (LC) with sub-divisions of LC-1.X Operations and LC-2.X Support;

5.2.2 Extended LIMS functions are described by items listed in boxes LE-X;

5.2.3 Systems external to LIMS are illustrated with boxes coded with E; and

5.2.4 Future LIMS functions are described in boxes coded with LF.

5.3 *LIMS Life Cycle Phases*—Fig. 3 defines the high level LIMS life cycle phases of *(1)* initial LIMS implementation, *(2)* LIMS operations, and *(3)* system maintenance. Each of these primary phases is further decomposed into primary functions. The numbering scheme use matches the mid level definitions in Fig. 2 and also tie to the requirements section located in Appendix X1.

5.4 *LIMS Concept Model—Industry Segments*—All laboratories require basic LIMS work flow including sample registration, assignment of tests, entry of results, review and approval and reporting. Laboratories in various industries may require additional functionality to meet special workflow requirements. An environmental laboratory for example may require tracking of sample containers, processing of samples in batches with control samples, instrument integration to address the number of components reported, and multiple levels of review. There also may be specific reporting requirements. Fig. 4 illustrates some of the additional functions that may be required to address the needs of laboratories in particular industry segments. The functions illustrated would be over and above the basic laboratory workflow.

6. LIMS Workflow and Sample Lifecycle

6.1 *LIMS Workflow Introduction*—The LIMS workflow model (see Fig. 5) provides a generic representation of the process flow in a typical laboratory. The purpose of the work flow diagram is to elucidate the LIMS functions and interaction

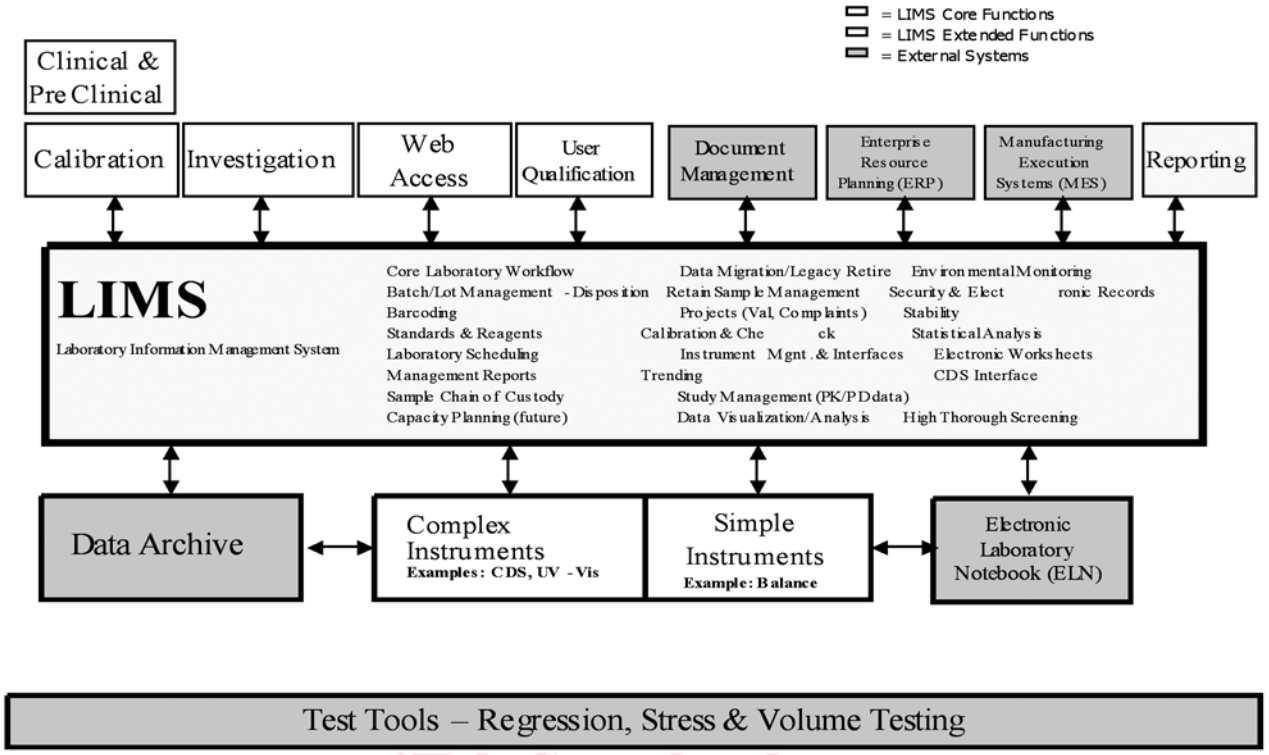

FIG. 1 LIMS Concept Model—High Level

points with typical laboratory work processes (processing of samples, analysis and reporting). Specific laboratory requirements will vary widely from one laboratory to another. The definition and composition of a sample or collection of samples will also be specific to an individual's laboratory, and will change significantly from industry to industry. The individual's own laboratory workflow and sample definition should be defined as part of the LIMS life cycle. Fig. 5 explains the basic LIMS functions and workflow interactions. The numbers in the parentheses in 6.2 refer to specific workflow processes (bubbles) in Fig. 5, which in turn relate to the areas shown in the LIMS concepts models (Figs. 1-4) in Section 5. To provide clear examples of what may be performed in each of the work flow model functions, items from all levels of the LIMS concept model are used. The description in 6.2 does not include every concept model function and is not limited to a particular level.

6.2 *Generic LIMS Workflow*—Fig. 5 shows both the logical dataflow through the LIMS process in combination with the corresponding physical sample processes. Each box in Fig. 5 is uniquely numbered (cross reference toFig. 2 and described in detail in subsequent sections.

6.3 *LIMS Functional Areas*—The following section describes the generic LIMS workflow steps as outlined in Fig. 5. Each step is described with a cross reference to Fig. 2. The index number show in parentheses refers to both Fig. 2 and the Appendix X1.

6.3.1 *Sample Registration (LC-1.1):*

6.3.1.1 The initiation of a request for testing/sampling starts the process. Examples of sample requests include manual forms, electronic forms, phone requests, web requests, process-driven requests, time or calendar-based requests, ad-hoc requests, and LIMS-generated requests. Information obtained from the sample request includes biographical, client, requested test(s), and safety information. Some LIMS implementations allow the laboratory to pre-log or post-log samples or the client to pre-log samples through a web portal.

6.3.1.2 The LIMS must first be properly configured and the relatively fixed information about personnel, customers, tests, reports, and the like must be entered into the static tables. After the LIMS is configured, the process begins with a sample registration. The LIMS assigns a unique number to each sample that is registered. The unique number can be a sequential integer or a user-defined sequence. Multiple samples that are submitted together for registration can be logically linked in the LIMS. For example, all samples for a particular customer. The system will normally provide functionality to capture descriptive information about the sample(s) such as who submitted the sample(s), costs, sample description, and what tests are to be performed on the sample. Other information may also be important, such as the priority of the tests, what level of accuracy and precision of testing is needed, what hazards the sample might present to the laboratory personnel, what approximate levels of components are expected, and what should be done with the sample when analysis is complete. Sample registration can precede or follow physical sample

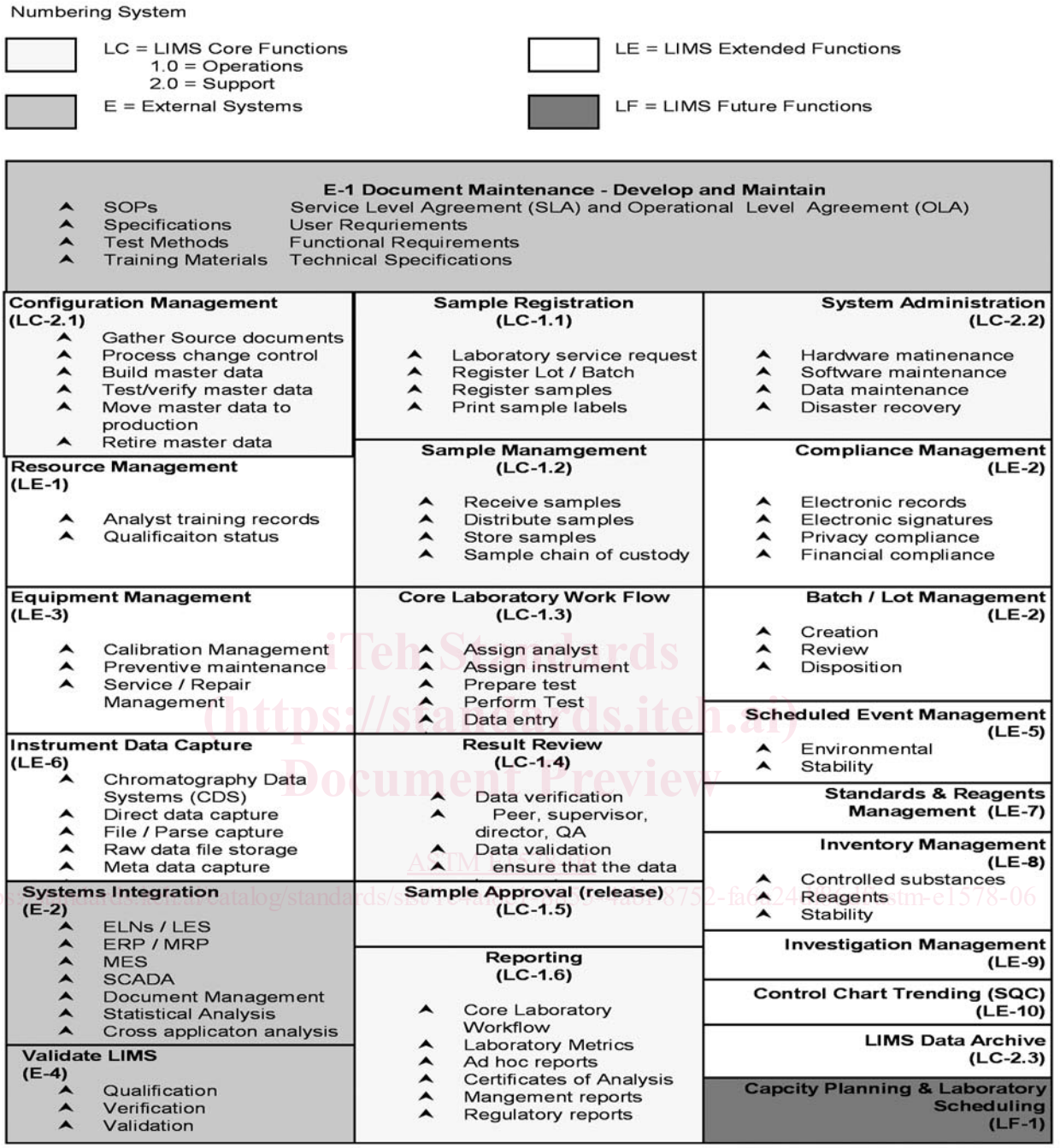

FIG. 2 LIMS Concept Model—Mid Level—Requirements Structure

collection. The LIMS sample registration function should be a simple, straightforward process with an intuitive and efficient user interface.

6.3.1.3 A confirmation report is often issued to ensure users the system accepted the sample order. LIMS statuses are updated for the sample/order. The system needs to record the fact that an order was made (for keeping operational metrics) and when it was made so the system can track the time intervals for the remaining steps of the process. This will also allow laboratory management to determine turnaround time, sample status and various overdue conditions.

6.3.2 *Sample Management (LC-1.2):*

6.3.2.1 *Sample Collection (LC-1.2.1)*—Sample collection may be a manual, automated, or robotic process. The sample collection can be assisted by the LIMS (post sample registration) in some environments by printing collection lists and generating labels (bar code) for the sample containers. Sample collection can precede sample registration or follow sample registration; the actual order will vary from laboratory to laboratory. LIMS statuses can be updated (post sample registration) during the sample collection step. The LIMS can provide information on how to collect samples, specific sample

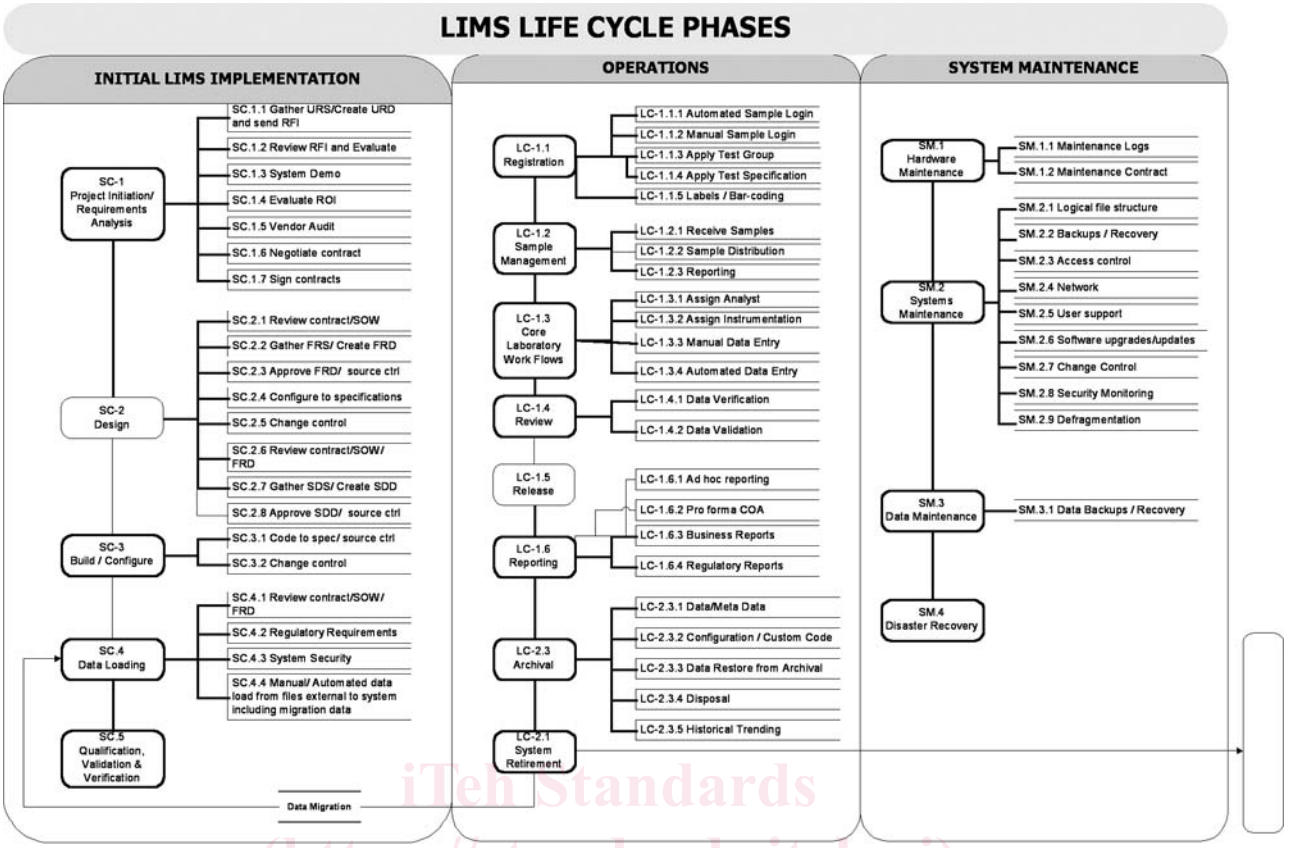

FIG. 3 LIMS Life Cycle Phases

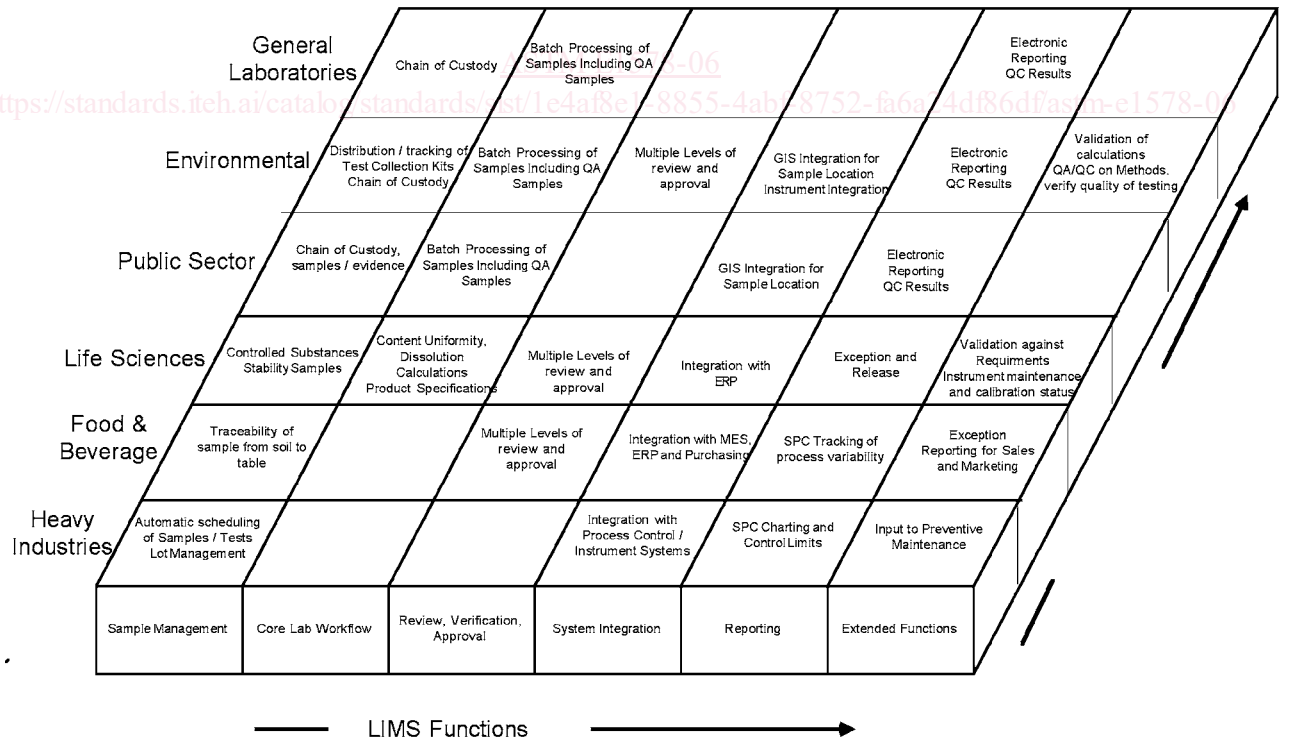

FIG. 4 LIMS Needs by Industry Segment

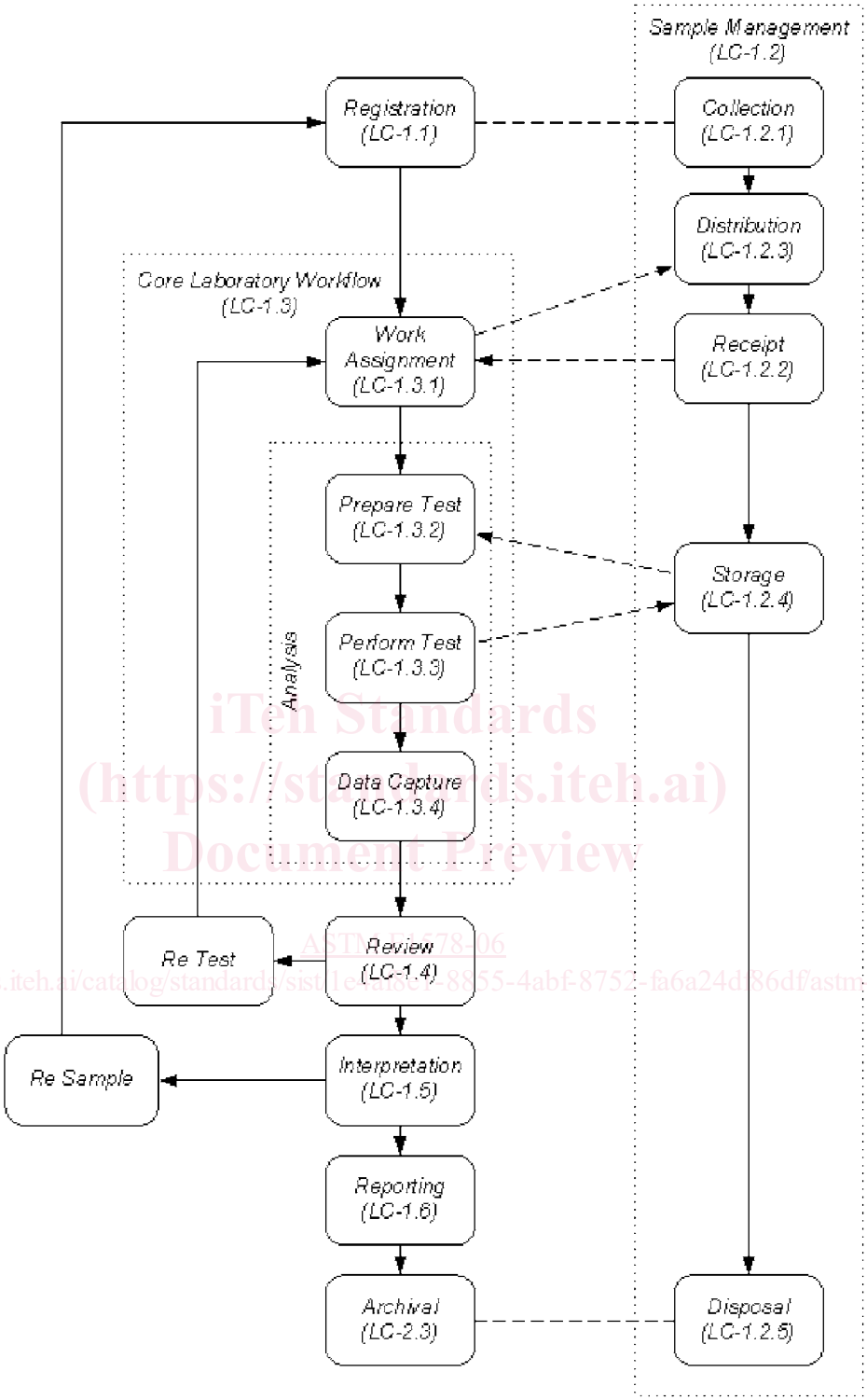

FIG. 5 Generic LIMS Workflow

plans, container and preservation requirements, safety (Material Safety Data Sheets (MSDS)) information, sample storage requirements, and sample routing information. Chain of custody for the sample can be tracked by the LIMS, although this may not supplant legal chain of custody requirements.

6.3.2.2 *Sample Receipt (LC-1.2.2)*—The physical receipt of samples in the lab is recorded in the system. The receipt process includes the important LIMS functions of sample registration (if samples were not registered in LIMS prior to sample collection), initial sample checking and labeling.

Sample orders or groups of samples may be checked against customer or project sampling requirements. Additional information such as the number of samples received and the arrival time may be recorded and the status of samples may be updated for the sample/order from logged to received. Where collection lists are used, a missed sample report may be used to indicate those samples that could not be obtained for whatever reason. The customer may be issued a receipt to confirm delivery of the sample.

6.3.2.3 It may be necessary to divide the sample into sub-samples or aliquots for simultaneous analysis at different workstations or laboratories. The LIMS specifies the aliquot requirements for a sample based on the tests to be performed on it. Sample problems may be noted and recorded at this point. There may be insufficient sample for the test to be performed or to prepare the individual aliquots needed for multiple tests. Other problems with the samples may be observed and recorded such as a unexpected color or physical state. Some samples may require a preliminary treatment such as addition of a preservative. If so, instructions can be presented to a technician to ensure correct performance of this step. The LIMS should be flexible enough to allow these checks to be performed and documented during the sample registration process or by technician prior to sample preparation or testing. LIMS should also assign a unique laboratory identifier for each sample received or each aliquot generated and print an appropriate label for each.

6.3.2.4 *Distribute Samples (LC-1.2.3)*—The distribution process includes important LIMS functions of work list, sample routing and custody. Chain-of-custody may be required to provide documented evidence of control and traceability of custody of sample containers and their contents. Examples of situations where chain-of-custody requirements may be encountered include handling of controlled substances, pieces of evidence (forensic) supporting legal court cases, or radioactive materials. The LIMS should provide a listing of all the tests that must be performed and may even provide details to the technician regarding aliquots required for each test, the amount of material required, and where samples are to be sent. The sample or any aliquot may be sent to a workstation in the laboratory or off site to a remote facility for analysis. The date and time of sample distribution is important since it designates when the sample becomes available to the various laboratory workstations for analysis. Sample status may be updated to indicate samples are available for analysis at this time as well.

6.3.2.5 *Store/Retrieve Samples (LC-1.2.4)*—Samples or any aliquots that might have been prepared can be retained in fixed storage rooms/locations while awaiting analysis. LIMS statuses are updated for the sample/order. Inventories can be maintained for reference samples, laboratories reagents, standards, QC samples, time-based samples (shelf life stability), in addition to normal samples.

6.3.2.6 *Dispose of Samples (LC-1.2.5)*—The proper documentation of sample disposal following analysis is an increasing concern. The LIMS can be used to track final sample disposition and waste removal.

6.3.3 *Work Assignment (LC-1.3.1):*

6.3.3.1 *Schedule Work (LC-1.3.1)*—The LIMS may be configured to automatically group samples into runs or sequences and to schedule work (tests) for each sample/order or it may be configured to allow authorized users to perform these functions manually. The LIMS may be configured to add laboratory standards, control samples, and QC samples to the scheduled work flow or it may be configured to allow authorized users to manually insert standards and control samples.

6.3.4 *Analysis*—Analysis contains multiple subjects. Subjects addressed in Analysis include sample preparation, measurement, QC samples, and data capture. The analysis activity will vary from laboratory to laboratory. Fig. 5 also shows a re-test and re-sample loop. A more detailed discussion of these topics follows:

6.3.4.1 *Prepare Test (LC-1.3.2)*—Most samples need some preparation before analysis. In addition, some samples may require that preliminary processing steps be performed prior to creating aliquots of the sample for preparation. The LIMS may be configured to provide sample preparation directions for these preliminary processing and sample preparation steps. The LIMS may also be configured to automatically insert into a sequence of unknown samples, the standards and blanks needed to calibrate or verify operation of the preparation method. The LIMS may be configured to compute experimental factors (dilution factor or actual weight) from this data. Alternatively, these types of parameters may be calculated outside of LIMS and manually entered by the technician. All samples, standards and QC samples that undergo these preliminary processing or preparation steps, or both, need to be uniquely identified. QC samples can include spikes, spike duplicates, blanks, and sample duplicates. How LIMS will assist in the proper tracking of these QC samples needs to be carefully examined. The LIMS should maintain links between all such QC samples and their associated unknown samples. The QC sample associations can be determined by the technician, who manually groups the samples in LIMS, or the LIMS may be configured to automatically batch unknown and control samples standards based on some criteria such as the method or instrumentation to be used. Any irregularities or exceptions encountered during preparation may be entered as preparation notes that can be displayed on printed reports or on screen and may help explain any unusual results obtained later in the process. LIMS statuses are updated for the sample/order to indicate that sample preparation has been completed. These associations can be determined by the technician who informs the LIMS, or by the LIMS which tells the technician. They can be tagged on to the reports and may help explain any unusual results. LIMS statuses are updated for the sample/order. After sample preparation, the analyst may use functionality available in the LIMS to put the prepared samples and associated standards and QC samples into a specific sequence in which they need to be measured. Alternatively the LIMS may be configured to automatically order samples and control standards into a sequence based upon the method and instrumentation to be used. Additional standards and QC samples may need to be added and tracked by the LIMS at this point. These

additional standards and QC samples need to be uniquely identified in LIMS and linked properly to their associated regular samples.

6.3.4.2 *Perform Test (LC 1.3.3)*—Certain supporting metadata should be collected as part of the measurement process. This may include instrument settings, any additional standards, QC samples and blanks used, and any irregularities, difficulties, and unusual behavior observed. This information helps document the procedures used, and may help explain unusual results. Test results/determinations are the main output of the measurement process. Intermediate and final test results for the samples, standards and their associated QC samples may be reported out in hard copy or electronic formats, or both. In addition, the measurement process may produce values for additional internal blanks, standards, and instrument self-checks. The concepts of what is raw data and what needs to be retained for legal evidence may be defined differently for each client or agency involved.

6.3.4.3 In cases where instruments are bi-directionally interfaced to LIMS, the sequence of unknown samples and control standards may be transferred to the instrument to streamline instrument setup prior to analysis. The sequence may include information such as sample ID, sample weight, dilution factor or other pertinent information. The sequence information may be saved in a formatted electronic file created by LIMS and loaded into the instrument software by way of a file import function. Alternatively, sequences may be printed onto worksheets with bar codes and the sample sequence quickly loaded into the instrument software by scanning bar codes from the printed worksheet or by scanning bar codes on prepared sample containers. Where no interface is present, sequences may need to be manually entered into an instrument system by an analyst or a printed worksheet may be used to manually record test results.

6.3.4.4 *Data Capture (LC-1.3.4)*—The results of the measurement must be entered into the LIMS. The amount of the supporting measurement data to be transferred to the LIMS should be carefully evaluated. As clients request that more of this supporting measurement data be reported, the LIMS should have the capability to acquire, store and report more of this supporting data. It may be entered by way of electronic interfaces or, in low volume applications, typed in by technicians. When a test result/determination is entered, the statuses of the sample/order and result determination are updated. The management functions record the fact and times that results were captured so that they can keep statistics of work accomplished and track the progress of each test order. Audit trails record biographical information about each LIMS transaction. Direct instrument integration with the LIMS is critical to fully realizing the business benefits of the LIMS implementation. Instrument integration takes place within box LC-1.3.4.

6.3.5 *Test Review (LC-1.4):*

6.3.5.1 *Test Result Review and Interpretation*—A laboratory may require that each test result undergo one or more levels of documented review and interpretation. The LIMS should be designed to document at least two levels of review. The original sample result would normally be reviewed and interpreted by the primary technician. This review would be documented in the LIMS. A laboratory may require that results be reviewed by a second qualified person (this is industry specific and dependent on regulatory requirements) to ensure that the results were properly entered and interpreted. To help in this process, the LIMS may show the results for standards and blanks in addition to sample results. The technician can judge whether the method was in control. The LIMS can show summaries of work done for review. Unusual or out-of-range results can be flagged for more careful scrutiny. If normal values are known for the substance being tested, they can be displayed. Results outside of normal can be highlighted or displayed separately for closer review. The LIMS can enforce laboratory SOPs that require the reviewer to be a different person from the tester. Corrections or changes to LIMS data can be made during the verification step. Changes to LIMS results should be audit trailed and a reason given for why a correction has been made. Audit trails should contain original data and all changes to the result record including date/time of change, who made the change, and the reason for the change. In some cases, the LIMS can provide a review by exception paradigm where results meeting specifications or within acceptable limits are passed automatically through test review and only unexpected test results are queued for manual review. Results can be approved, changing the result status. A test (one or more determinations) can be scheduled for re-test, or if that is not possible, the result can simply be marked as invalid. Electronic signatures may be used to confirm changes in status to the LIMS records if the regulations or guidelines require this. Management functions need to know when results are verified—another milestone in the progress of a test/sample/order. LIMS statuses are updated for the sample/order. Not all LIMS implementations require audit trails. The LIMS implementer needs to determine whether audit trails are important, what information should be audited, and whether reasons for changes should be recorded.

6.3.5.2 *Re-Test Loop*—Retests can be initiated at multiple points in the LIMS work flow. Fig. 5 shows possible re-test paths. A re-test is defined as one or more additional determinations on the original sample/order container. These retests would normally be ordered if a given test was suspected to fail for reasons that may include failed quality control parameters, instrument malfunction or technical judgment. The LIMS should document each retest along with an appropriate justification.

6.3.5.3 *Re-Sample Loop*—Re-samples can be initiated at multiple points in the LIMS work flow. Fig. 5 shows possible re-sample paths. A re-sample is defined as one or more additional samples. The LIMS needs to establish forward and backward links to samples that are added by way of the re-sample loop. These resamples would normally be ordered if a given sample was suspected to fail for reasons that may include where insufficient sample was available for a retest, technician judgment that the original sample was not appropriate for the test performed, or to confirm a test failure.

6.3.6 *Sample Approval (LC-1.5):*

6.3.6.1 A laboratory may require that each sample undergo a documented approval process. The LIMS should be designed to document this process. The laboratory exists to generate

information for the parent/client organization. Some of the LIMS today are configured to better assist that ultimate purpose. They may organize and configure results to make interpretation and decision-making easier. This can be done by combining results from many samples, adding additional non-laboratory-generated information to the reports or Certificates of Analysis, and including generic information related to the test or activity that caused the samples to be analyzed in the first place. Analysis is frequently done to confirm quality or properties of a material. In this case, material specifications can be entered into the LIMS so that results can be checked against acceptable values. Electronic Signatures may be used to confirm results or authorize changes in status to the LIMS records. Sometimes statistical routines can be used with collections of results to determine trends and make other conclusions. Spectral libraries can be used to identify materials. Artificial intelligence is used in some cases to help understand the results. LIMS statuses are updated for the sample/order.

6.3.6.2 The output of the approval segment can be reports, Certificates of Analysis, decisions based on predefined criteria, or direct process control actions.

NOTE 2—In many cases the interpretation function will coincide with the reporting process. In many LIMS data are interpreted in a reported format either in electronic of paper forms.

6.3.7 *Reporting (LC-1.6)*—Once test results are verified, both external and internal reports can be generated.

6.3.7.1 Test results, along with QC data, can be reported to the customer. This can take a variety of forms, including hardcopy reports, electronic data deliverables, and web-based systems. The report generators within a given LIMS need to be flexible to accommodate the different reporting needs of individual clients. The LIMS should come with preprogrammed formats for the most common hardcopy and electronic reporting formats. Conventional Certificates of Analysis are commonly required to be reported as an example of a hardcopy report. Many clients are now relying on the use of various electronic formats that support the transfer of data from the LIMS database to the client's database using electronic transfer formats such as XML.

6.3.7.2 Reports can include summaries for internal laboratory use by management. Management functions are told when the reports are issued, because this marks the end of the turn-around time. LIMS statuses are updated for the sample/order. By collecting statistics and time-stamps at various points in the process, reports can be prepared for laboratory managers. Number of samples processed at each workstation by shift, day of week, and hour of day can be prepared. This can help identify peak demands, roadblocks, and other problems. It provides good documentation to justify new instruments or personnel. Turnaround times document the laboratory's responsiveness to customer needs. Overdue results and work remaining in the system help managers to determine how well the laboratory is responding to current demands. Personnel time accounting can be tracked by the time each sample is at each workstation. This can be used to bill by project, and to monitor personnel performance. The number of tests done can be used to estimate the consumption of reagents and supplies. Instrument calibration and maintenance records can be maintained and reported by the LIMS.

6.3.7.3 Quality control reports can also be prepared for internal laboratory use. Statistical reports can be generated to evaluate the performance of a given method within the laboratory. Control charts can be generated based on analysis of specific QC samples. The QC ranges as derived from these control charts can be used to set the limits as used by the laboratory to evaluate their internal processes or used to compare how the laboratory's performance compares to the published performance of a given method. Some clients require that these statistical ranges also be reported to them.

6.4 *LIMS Data Model:*

6.4.1 *Types of Data*—The database technology employed by LIMS varies with each vendor and implementer. The LIMS database tables are divided into two broad areas: *(1)* LIMS static database tables where descriptive information is defined (for example, profiles, tests, calculations, specifications, and related information (commonly found in "look up/reference/dictionary" tables)) and *(2)* dynamic tables where sample and result/determination information is stored as samples are logged and results are entered. The terms static and dynamic represent general characterization of LIMS database tables reflecting the frequency of changes to the data. The LIMS user needs to closely study how the current laboratory information organization and work flow match the two database areas (static and dynamic). The time required to implement a LIMS is dependent on tools and structure of the static database tables.

6.4.2 *Statuses*—LIMS are capable of maintaining information on the status of samples, individual test/determinations, comparison of results to specifications, verification of results, approval of samples/orders, and much more. Status information is updated as each LIMS transaction takes place. The functions/work flows all have an impact on LIMS status information. Examples of sample/order statuses include: unavailable, available, and received in the lab, testing in progress, suspended, complete, approved, and rejected. Examples of test/determination statuses include: available, complete, approved, out of specification.

6.4.3 *Data Load and Migration*—A LIMS is capable of maintaining information for a broad range of business and laboratory data required for the effective operation of the laboratory. LIMS contains data that not only reflects the current operation state of the laboratory but also historical information on past performance and events. Where LIMS is introduced into an environment where a LIMS system has not previously been deployed, much of the information typically managed in the LIMS will exist in the form of paper documentation or disparate electronic sources such as documents, spreadsheets or specialized databases. When implementing the LIMS this data need to be loaded into the new LIMS system to provide the base configuration. Static data are always loaded into the LIMS as part of the LIMS deployment lifecycle. The decision on how to deal with historical dynamic data should be evaluated on the basis of risk. Appropriate strategies for dealing with this data include migration, preservation and archival. Where an existing LIMS is being replaced with a new solution, it may be possible to migrate data from the source