Agaram TECHNOLOGIES

How Qualis LIMS helps Laboratories to fulfill ISO 15189 requirements

White Paper

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TABLE OF CONTENTS

INTRODUCTION

About IS0 15189 Standard and its importance

ISO 15189 is an international standard, prepared the International Organization for Standardization (popularly referred to as ISO, which brings together a worldwide federation of national standardization bodies to formulate standards), that specifies requirements for competence and quality that are specific for medical laboratories to meet both the technical competence and management system requirements necessary for delivering consistent technically valid results.

It is based upon ISO/IEC 17025 and ISO 9001 and deals with the important aspects and processes in a medical laboratory such as arrangements for examination requests, patient preparation, patient identification, collection of samples, transportation, storage, processing and examination of clinical samples, interpretation and reporting of results, etc.

Background

Medical Laboratories play an important role in the Health Care System. The results obtained from Medical Laboratories are critical for detection of disease in individuals and populations as well as for the proper treatment provided to the patients. Quality management has been around for long time and the quality management system (QMS) model has been adapted to the medical laboratory environment through the use of international standards such as ISO 15189.

Laboratory quality can be defined as accuracy, reliability, and timeliness of reported test results. To be useful, laboratory results must be as accurate as possible, all aspects of the laboratory operations must be reliable, and reporting must be timely. Some significant consequences of poor quality in the laboratory can include unnecessary treatment or treatment complications, failure to provide correct treatment, delayed diagnosis, and unnecessary follow-up diagnostic testing. These consequences result in increased cost in time and work, as well as poor patient outcomes.

All aspects of the laboratory operation—including the organizational structure, processes, and procedures— need to be attended to in a QMS. ISO 15189 is the international standard that sets the requirements for a quality management system in a medical laboratory environment.

How it will apply to Laboratories?

This standard is intended to be used in the most common disciplines of a medical laboratory for the purpose of providing information for the diagnosis, management, prevention and treatment of disease in, or assessment of the health of, human beings.

To understand what kind of laboratories will benefit by implementing ISO 151189 standards, we can look at the definition of medical and clinical laboratories as mentioned in ISO 15189 standards:

"… laboratory for biological, micro-biological, immunological, chemical, immuno-haematological, haematological, biophysical, cytological, pathological or other examination of materials derived from human body for the purpose of providing information for the diagnosis, prevention and treatment of disease in, or assessment of health of, human beings and which may provide a consultant advisory service covering all aspects of laboratory investigation including interpretation of results and advice on further appropriate investigation".

A note further states:

"*These examinations also include procedures for determining, measuring or otherwise describing the presence or absence of various substances or micro-organisms. Facilities which only collect or prepare specimens or act as mailing or distribution center, are not considered to be medical or clinical laboratories, although they may be part of a larger laboratory network or system"*

The medical and clinical laboratory services need the following tasks to be considered as per the standard:

"…..*arrangements for requisition, patient preparation, patient identification, collection of samples, transportation, storage, processing and examination of clinical samples, together with subsequent validation, interpretation, reporting and advice, in addition to the considerations of safety and ethics in medical laboratory work"*

ISO 15189 Accreditation

The medical and clinical laboratories that perform the services as described above can be benefited by obtaining ISO 15189 accreditation. They can do so with the help of professional accreditation body that has a full understanding of ISO 15189 Standards and that can assist and verify the requirements of any specific medical laboratory.

It is also to be noted that ISO 15189 is not equivalent to ISO 9001 (though both have many similarities), which needs to be accredited separately if required. Of course, many of ISO 15189 and ISO 9001 standards overlap and mutually beneficial while implementation of the standards.

Another important standard that can be focussed on is ISO 17025 which are technical competence ones upon which a lot of ISO 15189 standards are based. The laboratories can be benefitted a lot by obtaining both ISO 15189 and ISO 17025. Same as in the case of ISO 9001, if required, ISO 17925 needs to be accredited separately.

A few of the benefits of accreditation for Medical Laboratories and users are:

- ✓ International recognition
- ✓ Techniques are up to date
- ✓ Reliable and trusted results
- ✓ Confidence in the competency of staff
- ✓ Commitment for continuous improvement
- ✓ Risk mitigation measures are applied
- ✓ Traceability of measurement

OVERVIEW OF AGARAM'S QUALIS LIMS

About Qualis LIMS

Agaram Technologies' Qualis® LIMS (Laboratory Information Management System) is designed for use in manufacturing, Quality Control, R&D, analytical research and any testing laboratory. Qualis LIMS helps organization to manage the laboratory business process end-to-end, from sample receipt to COA generation, MIS and beyond.

It helps in streamlining the process with respect to laboratory investigations starting from tests and specifications management, ordering of tests, registration of samples, job allocation, results entry, approval, report generation, OOS, deviations recording, and document management. It provides a structured method to document the laboratory investigations besides handling the compliance requirements.

Qualis LIMS ensures that the laboratory organisation complies with regulations and standards namely 21 CFR Part 11, Eudralex Annex 11, ISO 17025, ISO 15189 and ALCOA data integrity. The advantages include paper-less record keeping system having high availability, easy access, accurate validation at various levels, easy tracking of records, data integrity, Audit trail information and authorised secured user access to data.

Qualis LIMS Core Product Features

1. **Sample Management** – It helps the laboratory users to receive, register and manage samples within LIMS application including barcode labelling

2. **Results and Release Management** – It helps the laboratory users to enter results and the details including inventory material usage using approval workflow and retest/recalculation features.

3. **Work Scheduling** – It helps the laboratory users to allocate tasks to human resources and reschedule them

4. **Test Grouping and Specification Management** – It helps the laboratory users to manage test and specification version and release controls, template-based hierarchy

5. **Instrument Management** – It helps the laboratory users to maintain the instrument details along with calibration schedule (for validation) and instrument usage log

6. **Training and Certification Management** – It helps the laboratory users to maintain training and competency records of human resources (to comply with GLP principles and ISO 17025 requirement)

7. **Inventory Management** – It helps the laboratory users to maintain and record the usage of material inventory (consumables, reagents, etc) along with expiry data for validation and re-order level

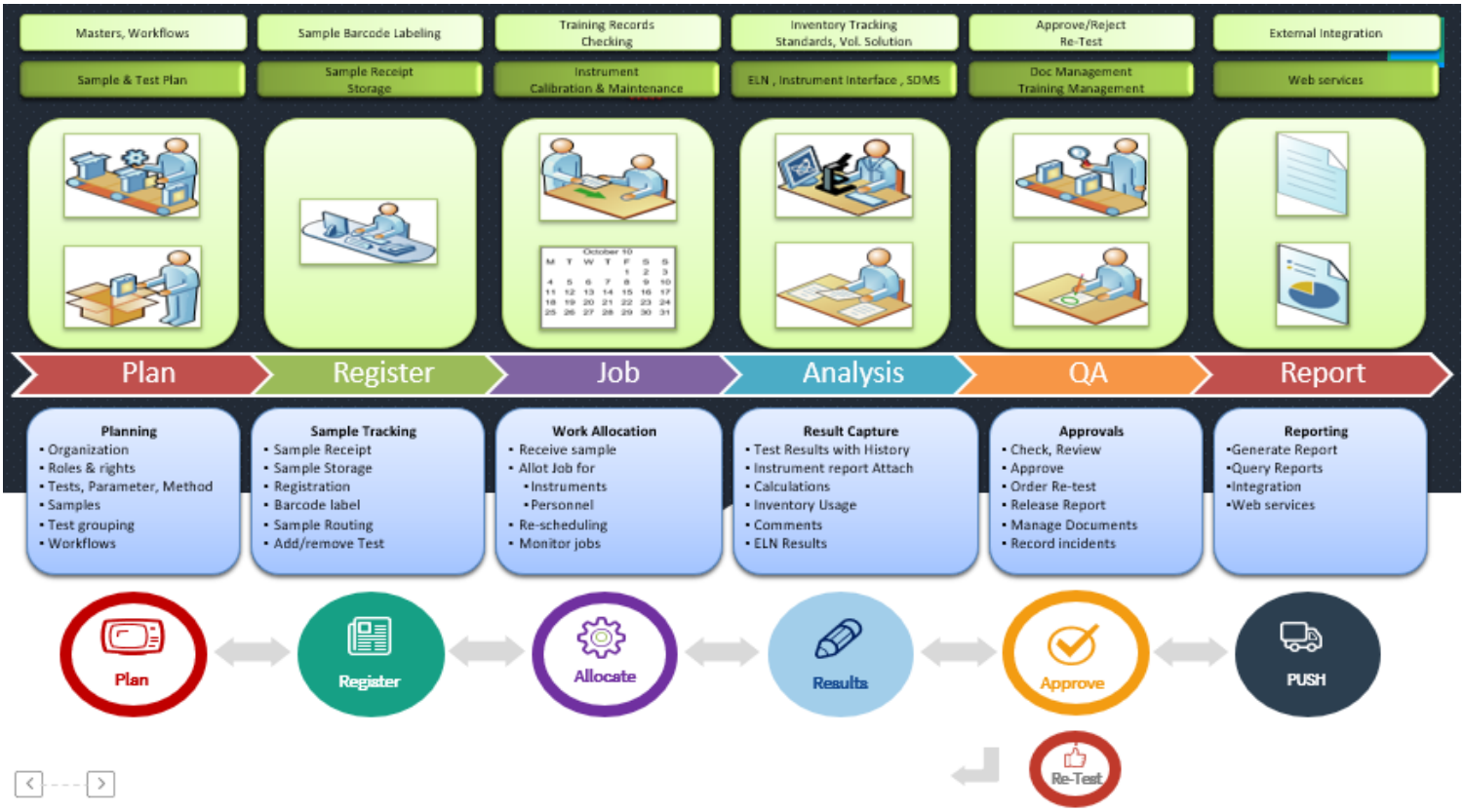
8. **Workflow** – Multi-level workflow configuration is used for better monitoring of the processes, approve the data, results (with electronic signature) and calculation and also to order re-test and re-calculation to achieve better quality and reliability.

9. **User Management** – It helps the laboratory users to setup control role-based access with password policy setup

10. **Reports, Alerts and Dashboards** – It helps the laboratory users to enable them to monitor the process and take pro-active action as required

11. **Audit Trail** – It helps the laboratory users to keep track of what, when, who, why changes take place and maintain the record of changed values with date/time and electronic signature

Overview of Qualis LIMS Process Flow



This is the overview of the sequence of process flow carried out in a typical lab. It involves: Planning, Registering, Job Allocation, Analysis or Testing, QA Verification and Approval followed by Output Report generation.

In Planning process, the master data is collected and configured in the system. Masters namely Organisation hierarchy, Users, their roles and rights, tests and specifications, workflow setup, etc are configured.

In Sample registration process, samples are collected, pre-registered, registered, labelled, stored, divided into subsamples and tests are associated.

In work allocation, the tests are assigned to the right users (using validation of users for their competency), right instruments (using validation of instruments for their calibration and maintenance status) and job scheduling.

The results are captured during the sample analysis by the Analyst and the results entry is by direct method or using instrument integration with the help of ELN/SDMS (either in simple manner or using complex calculation and parsing logic).

The results of the tests are routed typically to verifiers from QA Department who after verification approve or reject or request for recalculation/re-entry or re-do tests. Once reviewed, the results are routed for final approver, who approves and releases the final results.

Finally, the Certificate of Analysis (COA) report along with other reports are generated in the system and despatched to whosoever requires it.

Qualis LIMS Features and their benefits to the users

Qualis LIMS Feature	Benefits
Browser-based, Multi-site, secure architecture with high availability and scalability	Easy to use and maintain, cost-effective ownership and maintenance, time-savings by the way of easy Scalability, better user experience, highly productive use, increased customer confidence
Secured data access and with standards compliance	Error-free operation, Minimum manual intervention, cost and time savings, better control and transparency of data changes, better data protection, high reliability due to standards compliance, more user accountability, quicker trouble-shooting
Easy and controlled data access	Better and richer user experience due to simple interface, Time-savings due to faster data retrieval, Ensure more transparency and reliability of operations
Powerful Integration capabilities	Time and cost savings and better user experience due to reduced complexity of operations and maintenance, error-free operations, uniformity and consistency of data extraction and processing

ISO 15189 AND QUALIS LIMS SOLUTION

In this section, we shall see how Qualis LIMS helps laboratories to fulfil ISO 151189 requirements. We shall see the critical ISO 15189 clauses and the corresponding Qualis LIMS solution

ISO 15189 Standard Clause	Qualis LIMS Solution
Documentation **Clause 4.2.1** – *"Policies, processes, programmes, procedures and instructions shall be documented and communicated to all relevant personnel. The management shall ensure that the documents are understood and implemented."* **Clause 4.2.4** – *"All personnel shall be instructed on the use and application of the quality manual and all referenced documents, and of the requirements for their implementation. The quality manual shall be kept up to date under the authority and responsibility of an individual appointed to be responsible for quality by the laboratory management."*	Qualis LIMS allows users (with appropriate rights) to create documents (may be quality manual, policies, procedures, etc.), route it through an approval work flow and publish the same post approval, for reference by other approved users. It also has features for users to collaborate at the time of creation (by way of parallel work flows). The changes made to the document are version-controlled, electronically signed with unique id generation. This way, it ensures that obsolete documentation is not used in the operations of the laboratory.

Training **Clause 5.1.4(g)** – *"…ensure that there are sufficient qualified personnel with adequate documented training and experience to meet the needs of the laboratory;"*	Qualis LIMS Competence management allows to schedule training programs, invite participants and record the participants' progress. Reliability and quality results can be improved by assigning trained persons to the laboratory jobs. Functionality is available to ✓ Link training with analytical technique and instrument category. ✓ Configure Competency types (competent, certified, unskilled, for example) ✓ Assign competent individuals to specific tasks. ✓ Maintains training status of individuals. By maintaining the skill records of the laboratory personnel, Qualis LIMS ensures that only competent ones can be assigned the tasks.
Audits **Clause 4.14.1** – *"In order to verify that operations continue to comply with the requirements of the quality management system, internal audits of all elements of the system, both managerial and technical, shall be conducted at intervals defined by the system itself. The internal audit shall progressively address these elements and emphasize areas critically important to patient care."*	Qualis LIMS has an Audit Trail module which is used to record the actions such as: ✓ What was changed (the field and table that was modified)? ✓ When the change was made (the time and date)? ✓ Who made the change (the user name of person logged at the time of change)? ✓ Why it was changed (the reason for modification)? ✓ Contains Previous and New Values. ✓ Maintains separate log for system generated entries and user generated entries. A log is maintained separately for system and user generated entries using which review can

	be conducted on the tasks that have been performed in the system
Corrective and Preventive Action (CAPA) **Clause 4.10.1** – *"Procedures for corrective action shall include an investigative process to determine the underlying cause or causes of the problem. These shall, where appropriate, lead to preventive actions. Corrective action shall be appropriate to the magnitude of the problem and commensurate with possible risks."* **Clause 4.10.2** – *"Laboratory management shall document and implement any changes required to its operational procedures resulting from corrective action investigations."* **Clause 4.11.1** – *"Needed improvements and potential sources of nonconformities, either technical or concerning the quality management system, shall be identified.* *If preventive action is required, action plans shall be developed, implemented and monitored to reduce the likelihood of the occurrence of such nonconformities and to take advantage of the opportunities for improvement."*	Qualis LIMS has Out-of-Specification (OOS) investigation feature using which the Lab Analyst can generate Unique OOS id in case of result has OOS values. Those users with appropriate role can take against such OOS cases. Alerts can be triggered once such OOS case is created and reports can also be printed with all the relevant details. Time-frame can also be configured for OOS cases by the supervisor. When a deviation happens, not only alerts (in the form of emails can be configured), more importantly, the condition that led to the deviation can be investigated and approval work flow can be triggered for the corrective action. All the planned and unplanned deviations can be recorded with unique id. Deviations (non-conformities) can also be categorised (for example, Major or Minor) with time periods. CAPA records can be maintained and routed to appropriate QA/QC user for action/approval.

Management Review **Clause 4.15.1** – *"In order to ensure their continuing suitability and effectiveness in support of patient care and to introduce any necessary changes or improvements, laboratory management shall review the laboratory's quality management system and all of its medical services, including examination and advisory activities.* *The results of the review shall be incorporated into a plan that includes goals, objectives and action plans. A typical period for conducting a management review is once every twelve months."*	In order to achieve better monitoring, control of the processes as well as to achieve better quality results, Qualis LIMS has in-built approval workflow steps which can be configured to achieve: ✓ Multiple levels of approvals. ✓ Check individual test results, calculations performed, raw data captured etc. ✓ Marks the samples as reviewed/approved. ✓ Reject results ✓ Request a re-test/re-calculation. The data that is maintained in the system can be processed into a useful information in the form of views and reports as desired by the Laboratory users and system administrators. Qualis LIMS has a very powerful SQL query builder feature using which custom queries can be written. Using these queries (using filtering and rules logic), several useful reports/views can be generated and exported to excel for further analysis. Qualis LIMS home page comes with a configurable dashboard. These dashboards can be configured based on the user role. Example – For a lab supervisor, vital information such as the number of samples received, the status of the work allocated, completed, pending approval,

	released, etc. can be viewed in a directly and simply. Qualis LIMS has built-in alerts for users to act such as approvals (several types of approvals like specification, registration, results, document, and invoice), schedule reminders for calibration of instruments, report release, etc. Email alerts can be configured such that specific events will generate an automatic email to person who needs to receive the email.
Supplier Management **Clause 4.6.4 –** *"The laboratory shall evaluate suppliers of critical reagents, supplies and services that affect the quality of examinations and shall maintain records of these evaluations and list those approved."*	Qualis LIMS helps to maintain the Supplier details in the Supplier Master. The records of Supplier evaluation and results can be recorded in the Supplier Master. Qualis LIMS maintains a complete material inventory of the laboratory. This allows the laboratory to track and account of the material consumption, manage the expiry dates and ensure correct material usage. ✓ Provides categorization of material ✓ Maintain masters for all types of standards, volumetric solutions, reagents, chemicals, glassware, etc. ✓ Document and Track Input Reference Standard No., Batch #, Lot #, Qty., Unit, Expiry date, Storage condition, Purity, ROL, Open expiry days, etc.
Laboratory Equipment **Clause 5.3.2 –** *"…Laboratory management shall establish a programme that regularly monitors and*	Qualis LIMS Instrument Management module helps to maintain all instruments and equipments used across the laboratory. The following are the main features of the module:

demonstrates proper calibration and function of instruments, reagents, and analytical systems. It shall also have a documented and recorded programme of preventive maintenance (cf. 4.2.5), which, at a minimum, follows the manufacturer's recommendations" **Clause 5.3.5 –** *"Equipment shall be operated by authorised personnel only. Up-to-date instructions on the use and maintenance of equipment (including any relevant manuals and directions for use provided by the manufacturer of the equipment) shall be readily available to laboratory personnel"* *Clause 5.3.9 – "Whenever practicable, equipment under the control of the laboratory which requires calibration or verification shall be labelled or otherwise coded to indicate the status of calibration or verification and the date when recalibration or reverification is due."*	✓ Determine and maintain the status of the Calibration and maintenance instrument. ✓ Generate alerts through scheduler when the calibration is due ✓ Generate calibrated samples automatically. ✓ Record and document each and every calibration. ✓ Validation ensures that only calibrated instruments can be assigned for tests and users and goes through a workflow for approval. In Training and Competence module, it is configured in such a way that only trained users can use specific equipment/instrument.
Pre-examination Procedure **Clause 5.4.1 –** *"The request form shall contain information sufficient to identify the patient and the authorised requester, as well as providing pertinent clinical data"*	Test Masters with relevant attributes and parameters can be maintained based on test category and specific sections within the laboratory that will perform the tests. This will help to keep track of vital attributes of testing in the following way:

"The format of the request form (e.g., electronic or paper) and the manner in which requests are to be communicated to the laboratory should be determined in discussion with the users of laboratory services."

Clause 5.4.7 – *"All primary samples received shall be recorded in an accession book, worksheet, computer or other comparable system. The date and time of receipt of samples, as well as the identity of the receiving officer, shall be recorded"*

Clause 5.4.14 - *Samples shall be stored for a specified time, under conditions that ensuring stability of sample properties, to enable repetition of the examination after reporting of the result or for additional examinations.*

Examination Procedure

Clause 5.5.1 - *The laboratory shall use examination procedures, including those for selecting/ taking sample portions, which meet the needs of the users of laboratory services and are appropriate for the examinations*

Clause 5.5.2 - *The laboratory shall use only validated procedures for confirming that the examination*

- ✓ Tests can have one or multiple parameters
- ✓ Parameters can be numeric, character, pre-defined values, attachments etc.
- ✓ Tests can be linked to instruments, have rounding rules and analysis techniques, which, in turn are linked to user/personnel and training records
- ✓ Manages one or more material for each specification
- ✓ Provide several layers of hierarchy for quick access and easy maintenance as shown below

  Material > Group > Sub Group > Profile > Specification Version > Tests > Parameters > Limits.
- ✓ Document upload for each specification.

Sample Registration in Qualis LIMS begins with Chain of Custody which helps to keep track of the sample throughout its life cycle.

- ✓ Allows the samples [Raw Material, Intermediate and Finished Product] to register manually
- ✓ Automated Sample registration via file import and scheduler.
- ✓ Generate Unique Sample Number or an Analytical Request Number (AR Number)
- ✓ Appropriate profile and specification selection for each sample.
- ✓ Helps to set Testing priorities for samples.

Qualis LIMS Result entry module allows certified analysts to enter test results manually based on a sample number and test. The module provides

procedures are suitable for the intended use.	great flexibility and makes it easy for users to track the entries in the following ways: ✓ Automated result entry is provided via file import. ✓ Final results along with the instrument used with its identifier, usage time, and calibration status with test execution can be linked. ✓ Attach raw data and reports from the instrument for each test. ✓ Records and maintain status for Complete traceability of results ✓ Helps regulated laboratories to eliminate additional work, improve efficiency and be audit ready.
Quality Assurance of Examination **Clause 5.6.1 –** *"The laboratory shall design internal quality control systems that verify the attainment of the intended quality of results... Special attention should be paid to the elimination of mistakes in the process of handling samples, requests, examinations, reports, etc."*	Qualis LIMS approval workflow can be configured to achieve multiple levels of approvals and actions to be performed on approval actions. First level of approval post result entry is verified by personnel who can check individual test results, calculations performed, etc. Once verified the sample is marked as verified. The verifier can also reject the results and request a re-test/re-calculation. If found verified ok, the sample can move to Approver as in approval hierarchy preferably to personnel in in QA Department where it can be finally verified and final release/reject can be carried out.

Reporting of Results **Clause 5.8.1 –** *"Laboratory management shall be responsible for formatting reports. The format of the report form (i.e. electronic or paper) and the manner in which it is to be communicated from the laboratory should be determined in discussion with the users of laboratory services."* **Clause 5.8.3 – "***Results shall be legible, without mistakes in transcription and reported to persons authorised to receive and use medical information"*	In Qualis LIMS, once the tests have been approved and released, we need to create Certificate of Analysis (COA) Reports as the final step in the transaction workflow process. Qualis LIMS includes a dedicated reporting module and is pre-packaged with a set of commonly used reports. Reports can be easily configured to specific user requirements. Reporting module provides users with an easy-to-use interface to generate reports, lookup previously generated reports based on specific criteria.

CONCLUSION

ISO 15189 standards help medical and clinical laboratories in various industries to streamline quality and competence. Switching to automated processes that associated with quality and compliance can make medical and clinical laboratories more efficient than ever and more prepared to compete in an increasingly competitive life-science and healthcare environment.

ABOUT AGARAM TECHNOLOGIES PRIVATE LIMITED

Agaram Technologies has been stablished in 1998 with Headquarters in Chennai, India and has offices in USA, Europe and South Korea.

It is a leading provider of enterprise class Integrated Laboratory informatics software and solutions namely LIMS, QMS, ELN and SDMS.

Agaram provides integrated software solutions, consulting services, product support and training to laboratories in Pharmaceutical, Healthcare, Dairy, Food & Beverage, Chemical, Oil & Gas, Environmental, Contract Research Organization (CRO), Forensics, Agriculture and Bio-Banking Industry.

Agaram Technologies exclusively focuses on laboratory informatics products. It has earned a leadership position in this market by combining a world class customer experience with a powerful, yet simple and affordable suite of software products. These products have been organically built to seamlessly integrate all Laboratory related functions.

It is an ISO certified organization (ISO 9001:2015) in Design, Development, Implementation, Maintenance and Support of Laboratory Information and Analytical Instrumentation Software Products and Services.