



INTERNATIONAL MEETING ON AUTOMATED COMPLIANCE SYSTEMS

May 18-19, 2005 - Princeton, NJ

Program Highlights

On May 18 and 19, 2005, over 100 people attended the second annual IMACS conference. The conference blended strategic and tactical presentations by leaders from the pharmaceutical and related industries. The strategic messages highlighted the industry challenges and then created a vision, urgency and strategy to automate laboratory compliance through highly compliant paperless operations. The tactical presentations described a range of successful implementations including integration among dependent IT solutions. Included are practical recommendations on implementation programs and examples of compelling productivity, cycle time and compliance impacts.

During the conference, a consistent theme developed. The key elements included:

- ❑ Pharma and its related industries face unique challenges requiring multifaceted solutions ranging from new product discovery through dramatic improvements in productivity and cycle times throughout their organizations. Action is urgently needed!
- ❑ Paperless operations, enabled by validated electronic systems, must replace paper-based manual systems prone to human error and, thereby, requiring layers of redundant checking to ensure data integrity.
- ❑ Paperless initiatives require investing funds and resources. Successful paperless initiatives do not simply replace manual with automated techniques. To gain full advantage they require related SOP, information flow and workflow reviews. The good news is that these reviews can streamline current processes and identify ambiguities, inconsistencies and opportunities to upgrade legacy processes around current “best practices”.
- ❑ Successful laboratory automated compliance delivers compelling results:
 - Testing time reduced by 25% and more.
 - Review times reduced by 50% and more.
 - Dramatically reduced errors – reports of total elimination.
 - Cycle times reduced by 35% to 50%
 - The analysts “love it”.

**To learn more, please read the following highlights.
Need more details, please request the complete presentations.**

Challenges, Vision, Urgency and Strategy:

“The Pharmaceutical Industry – Hero or Villain?”

Myra N. Williams – Former Vice President and CIO Glaxo Inc.

New Strategies are needed - R&D/Manufacturing Imperatives

- ❑ Rethink innovation throughout the corporation all the way to patients
 - R&D and manufacturing productivity
 - Sales force effectiveness
 - Direct-to-Consumer Advertising
- ❑ Focus on staff excellence – seek innovators and entrepreneurs; hold accountable.
- ❑ Improve project selection, prioritization, and portfolio analysis.
- ❑ Identify failures early.
- ❑ Make more effective use of outsourcing & partnerships.
- ❑ Define opportunities for major enhancements in productivity and cost effectiveness.
- ❑ Become skilled at managing cultural change.
- ❑ Plan strategically to create a shared vision.

Keys to success.

- ❑ Hiring the right people and creating an environment conducive to innovation.
- ❑ Selecting the right projects, and providing the resources required for success.
- ❑ Using information technology to accelerate projects through automation and knowledge management.

Conclusion.

Success in the pharmaceutical industry will require innovation in making major productivity improvements, understanding of how to manage change, and strategic use of informatics.

“Visions and Strategy for Pharmaceutical QA Compliance and Productivity”

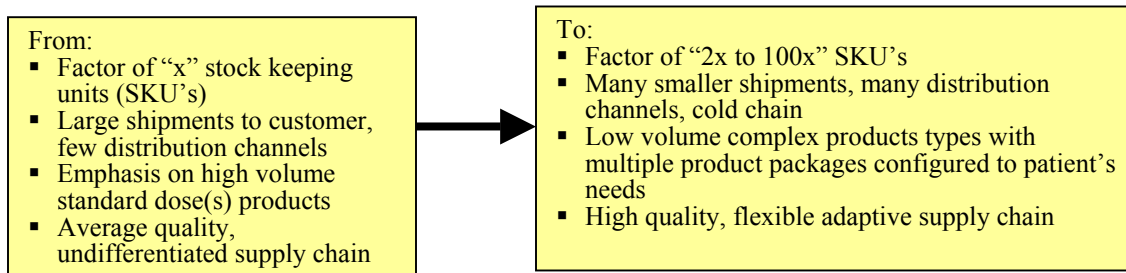
Brian Graeff, Senior Director of Quality Assurance, AstraZeneca, Westborough, MA.USA

The Analyst’s Role – How it has changed – Complexity has increased dramatically

Notebook rules, Calculations/Verifications, Corrections, Equipment-calibration dates, Test Solutions-Prep. and Expiration dates, Retests, Errors and Investigations.

The game has changed: We used to all be winners; sharing different slices of the pie - now there are winners and losers. We have to fight for our piece.

Changing product types causing a major shift in complexity (Courtesy of IBM):



Principles for Risk Management

- ❑ Cannot apply risk models and risk assessment to poorly understood processes
- ❑ Risk assessment is proactive process to determine risk areas, prioritize and mitigate
- ❑ Risk assessment is not: “Which GMPs do I need to really adhere to?”

“FDA’s Desired State and the Paperless Laboratory”

Jerome P. Skelly,
Adjunct Professor, Biopharmaceutics and Pharmaceutical Consultant
Former FDA Executive

Today’s situation:

- ❑ Most labs today use a combination of various existing electronic systems.
- ❑ Problems:
 - Redundancy
 - Inefficiency
 - Reports stored in manual lab books.
 - Lack of data mining or filtering.

The FDA’s desired state:

- ❑ Complete change in the regulatory process – complete electronic submissions
Paperless laboratory is part of the process.
- ❑ All the road signs are in place.
- ❑ All one has to do is read them.
- ❑ When the FDA is convinced that it is possible, you will see the regulation.

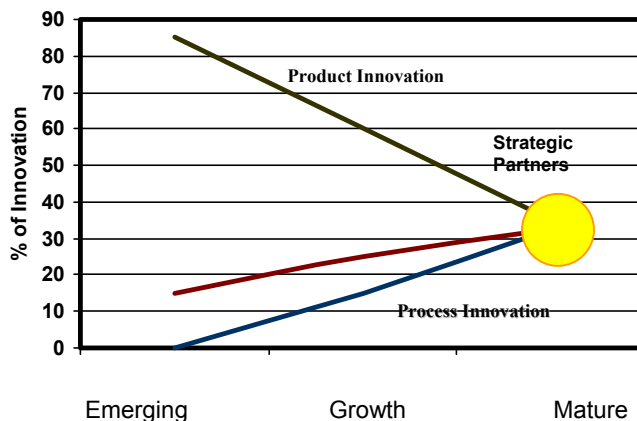
The Paperless Lab is here

“Renewing Innovation – In the Maturing Pharmaceutical Industry”

Frank Zenie – Chairman VelQuest, Former President Zymark and Waters

- ❑ Virtually all-successful businesses build their success through innovation.
- ❑ The types of innovation, however, must change as the industry matures.
- ❑ “Above all, innovation is not invention. It is a term of economics not technology”.
“Management, Tasks, Responsibilities and Practices”, Peter F. Drucker, 1973
- ❑ IMACS Mission = “Automated Compliance” - “Automated Compliance” is actually code for:
 - Replacing slow, inefficient paper-based processes with fast, efficient, and validated electronic processes And, while you’re at it:
 - Re-engineering your methods and processes to adopt “Best Practices”.
- ❑ As technology-based industries mature, product innovation, branding and process innovation become strategic partners!

Innovation Portfolio – Industry Maturity



- ❑ It's the innovation portfolio that changes as an industry matures.
- ❑ Future leaders in the maturing pharmaceutical industry will deploy an innovation portfolio including product, branding and process innovation.
- ❑ Today's leaders are very good at product innovation and branding. They are just learning, however, about process innovation.
- ❑ Yes, you can make a difference! Bring the IMACS message back to your colleagues.

Some Solutions and their Impact:

“Impact of an Automated Laboratory Compliance System”
Michael Stroz, Director QA Lab Automation and Technology
AstraZeneca, Westborough, MA USA

How Does Technology Fit?

- ❑ Today's available technology permits all critical parameters to be recorded, stored in a secure environment, measured, trended, and analyzed
- ❑ Sharing of data between systems, groups, and sites is relatively easy
- ❑ By establishing a model that utilizes today's technology with an eye to other departments and future enhancements is important
- ❑ Manufacturing systems must be linked with laboratory systems, that are linked to electronic batch records and batch scheduling and raw material procurement
- ❑ Manufacturing must be linked to R&D

AstraZeneca Status:

- ❑ System (SmartLab) went live October 1, 2003 in conjunction with LIMS
- ❑ Conversion of methods for 3 products are complete
- ❑ In all, 32 methods have been rolled out in the laboratory (OCM and Test)

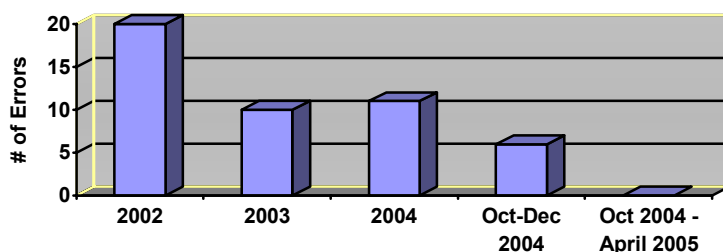
Impact:

- ❑ Overall Product A Time Savings - A total savings of approximately 79 hours per week of analyst time per week based on 15 batches per week

<u>Analytical Method</u>	<u>Manual (Hr)</u>	<u>Electronic (Hr)</u>	<u>Savings (Hr)</u>	<u>Weekly Savings 15 Batches/Wk</u>
Color, pH, Osmolality, ID	12.25	12.25	0	0
Particle Size & Appearance				
Agglomerates	3.0	2.5	0.5	5.5
Assay/CU	9.0	7.0	2.0	22.5
EDTA	8.0	7.5	0.5	5.5
Degradation & Impurities – 3 Tests	28.0	26.0 (est.)	2.0	22.5
Data Review	8.0	6.0	2.0	22.5
Total	68.25	61.25	7.0	78.5

- ❑ Product B Time Savings - A total savings of approximately 14 hours per week of analyst time per week based on 2.5 batches per week
- ❑ Error Reduction (documentation, transcription, calculation) - For SmartLab coded methods, errors have been reduced to zero

Calculating, Transcription and Labelling Errors



- ❑ Data Review - Reviewers benefit by having all of the data centralized and in electronic format for review. Only manual inputs, chromatography interpretation, and that the right file is attached must be checked.

Analyst's Perception – "When you're done, you're done."

"Electronic Laboratory Notebooks – their Application in a High Volume QC Laboratory"

Dennis McDaid, QC Manager, Forest Laboratories, Ireland

- ❑ QC testing typically took 6 days.
- ❑ QC testing already had significant investment in robotics for automated Dissolution and Content Uniformity testing
- ❑ No LIMS in place thus large volume of paperwork generated and signed off by analysts.
- ❑ **Target of 3-4 days envisaged as being possible**

Current Situation – Review Time:

- ❑ QC Review of paperwork, including photo-copying and compiling batch results typically 2-3 days
- ❑ Huge volume of paper being handled and reviewed as part of process.
- ❑ **Target of 1 day envisaged as being possible**

Needs Assessment – Solutions:

- ❑ Virtual printer for capture of human readable data able to apply E-sigs – *NuGenesis Unify/Vision*
- ❑ ELN system to network remaining instruments, and to capture sample preparation (meta-data) and non-instrumental test results – *VelQuest SmartLab*
- ❑ LIMS - *VelQuest SmartLab*

Key Features – SmartLab:

- ❑ Developed separate methods for common standards and reagents
- ❑ Possible to place limits on numerical inputs. Not just for OOS / atypical detection. Avoids silly errors and increases compliance
- ❑ Calibration dates for instruments included
- ❑ Step by step of procedure completed by analyst in predetermined order. Results are not manually entered but calculated or imported
- ❑ Once test completed, data is immediately ready for review
- ❑ System checks the data. Flags if any data is missing, was re-collected or was OOS / atypical / out of trend.
- ❑ Review effort can be concentrated towards selected steps / data that merit more attention.

Performing LIMS functions within SmartLab:

- ❑ Set up 2 types of procedure in SmartLab
 - Sample administration procedure for samples
 - Execution procedures for actual tests
- ❑ Sample is logged into Admin Manager which automatically releases all tests to be performed and populates key sample data
- ❑ Results of testing are sent back to sample administration and allows automatic generation of

- laboratory report or Certificate of Analysis
- ❑ Query database for sample progress, cycle times, trend reporting.....
- ❑ Generate tailor made reports using Crystal Reports

Use of SmartLab made purchase of stand-alone LIMS unnecessary

Results:

- ❑ % Savings vary depending on activity and complexity etc. but generally are:
 - 30 to 50% reduction in testing time and
 - 50 to 70% reduction in review / approval time

“Rapid Implementation of SmartLab in an R&D Laboratory”

**Mitchell Hollander, Senior Research Investigator,
Bristol-Myers Squibb Medical Imaging, Billerica, MA USA**

Expected Benefits:

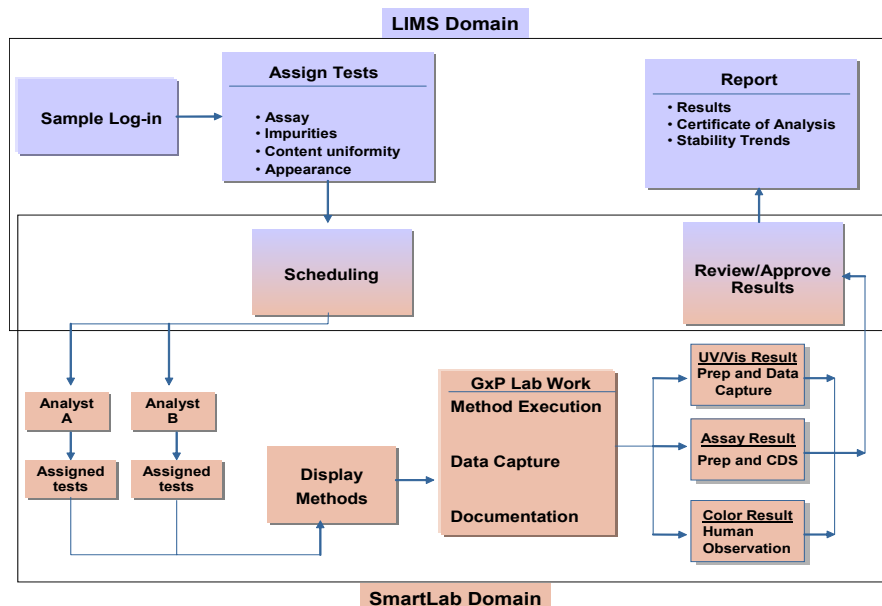
- ❑ Enforce procedure steps
- ❑ Reduce transcription, hand calculations, mistakes
- ❑ Reduce checking, rework, cycle time
- ❑ Lower compliance risk, cost of compliance

Potential for Increased Efficiency

(Example based on one stability program that is phasing down. Subsequent programs will increase work load.)

Stage of stability testing program	Time required to Complete GxP related activities (Hours)	Potential time savings with paperless system (25% to 50%)	Resources liberated for other program needs
First Year	10,200 (5 FTE)	2,550 – 5,100 hours	1.25 – 2.5 FTE
Second Year	4,080 (2 FTE)	1,020 – 2,040 hours	0.5 – 1 FTE
Third Year	2,040 (1 FTE)	510 – 1,020 hours	0.25 – 0.5 FTE
		Average for 3 year period	0.7 – 1.3 FTE

Information/Work Flow SmartLab - LIMS



Project Approval Contingent on 6 Month Implementation

Implementation Plan – Limited Scope:

- 16 analytical methods
- 11 interfaced instruments
- 8 networked instruments
- Interfaces to LIMS and chromatography data system (CDS)
- Wireless network implementation
- Computer system validation

Successes:

- Removed many manual calculations and transcriptions
- Eliminated use of Excel for one method
- Drastically cut down on paperwork
- Analysts and reviewers are saving time

Lessons Learned:

- All knowledge is not embedded in the written method
- Don't save the hardest method(s) for last
- Simplify methods – do you really need all those contingencies?
- You can never provide too many example reports for parsing

User Reaction:

- Very favorable overall!
- Users were nervous before go-live
- Many positive comments after

We did it! - Live: April 6, 2005

“The Paperless Laboratory

Metrology and Analysis in an R&D Environment”

Paul Cowcher, Manager, Technical Support Department

Napp Pharmaceuticals Research, Cambridge,, UK

What are we using SmartLab for?

- Established methods still in R&D
 - HPLC identification & assay & related substances
 - HPLC CR dissolution
 - Moisture content
 - Physical determinations
- Instrument calibration and verification procedures
 - Balance verifications
 - Dissolution system verifications
 - pH meter calibrations
 - TOC analyzer method
- Custom reports to review performance.

Implementation Experiences – Process:

- Make use of the technology
- Project scope document
- Project plan
- Prepare
- Vendor audit
- System development

Summary:

- Involve the potential users at an early stage – sell the product to them
- Evaluate the best approach to verify methods and procedures and run them – make sure it does what you want it to do
- In-build sufficient method flexibility but remember the process flow of your operation

*System go-live only 12-months after initiation
Users wanted to use it, •Users liked it!*

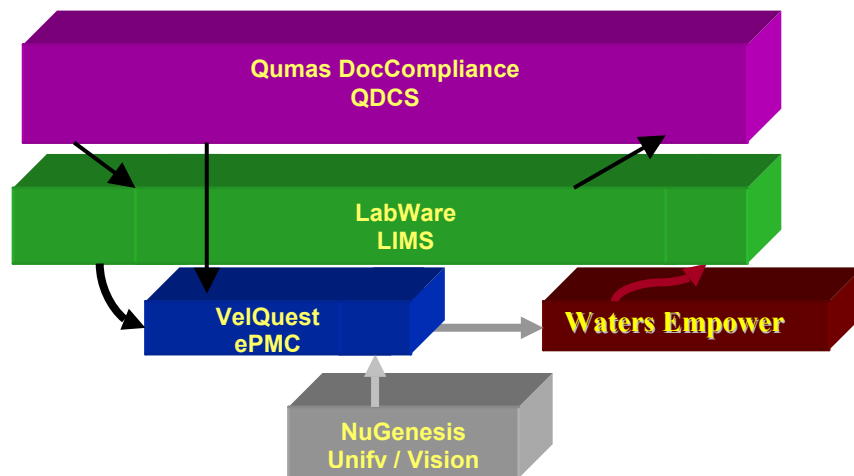
“The Paperless Lab – Making it Worth the Effort”

**Lane Gehrlein, Senior Director Analytical R&D
Purdue Pharma, Ardsley, NY USA**

The GMP Paper Avalanche:

- ❑ Test Methods
- ❑ Specifications
- ❑ Stability Reports
- ❑ Certificates of Analysis
- ❑ Assay Records
- ❑ Laboratory Notebooks

The Purdue Paperless Laboratory Environment



e-Process Management and Compliance - e-PMC now SmartLab:

- ❑ Only the current version of test method available to chemists
- ❑ Data entry/capture either directly from instrument or manually via laptop
- ❑ System requires all data – reagent info, sample weights, pH, etc.
- ❑ All data displayed onto a reviewer screen, colored flags denote status
- ❑ Secure Access – Account name, password, multiple levels of access
- ❑ Fully accessible for data review, electronic signature, full audit trail

Pros:

- ❑ Follows the method step by step, no missed entries e.g. reagent lot #/exp date
- ❑ No chance of using an outdated version of the method

- ❑ Little or no manual data entry e.g. balance weights transferred electronically
- ❑ Allows for quick and thorough peer review - all issues/missing data are flagged

Cons:

- ❑ Training needed to code methods – solvent prep only, lab investigations
- ❑ Not easily adaptable to experimental work – don't toss out the notebooks yet

Application Example - Physical Inventory via ePMC - Realized Benefits

- ❑ Met all requirements of process, with several improvements
 - Improved reporting over paper process
 - No transcription of data: counts entered once at time of counting
 - Automated calculations
- ❑ Documented evidence of tight control
 - Praised by Internal Auditing Function
- ❑ Greatly reduced reconciliation time
 - System set up in four weeks
 - Several weeks of recounting and reconciliation reduced to several days
 - Overall process reduced from four months to one month

Application Example – Instrument Calibration Management

- ❑ All data generated during calibration are collected in one system
- ❑ Out of tolerance results automatically flagged
- ❑ Instrument calibration procedures run using the same tools as test methods
 - No need for additional training
 - No need for additional system validation and infrastructure
- ❑ Calibration procedures easily converted to ePMC

“The SmartLab Method Conversion Process”

Thomas Bonitz, Director, Instrument and Systems Services

Par Pharmaceutical, Inc., Spring Valley, NY USA

- ❑ The User Requirements Process
- ❑ Requirements Gathering Team (not teams)
 - Gain the in depth analysis of your processes from the bench level chemists to the managers and review process
- ❑ Monographs come in all shapes and sizes
 - Many lack detailed instructions
 - One paragraph = 2 to 3 pages of code - Work sheet type
 - One Paragraph = 100 pages of code - Dissolution S1-S3, standard sharing, standard check failures linked to SOP
- ❑ Template approach
 - All procedures have the same look/feel
 - Reduces training requirements
 - Reduces Coding Errors
 - Review “view” is the same
 - Re-use Validation Docs
- ❑ System Capabilities and “Feature Creep”
 - Something captured as a single line in a note book can result in huge amounts of work
50% of the coding was performed to capture events that might take place less than 1% of the time
 - Standard Sharing

Then the monograph gets updated

- ❑ System Suitability Test
 - Chemist tests method for suitability at bench level.
 - Data is collected and entered in the notebook and via Smart Lab.
 - Typically the Smart Lab Procedure Conversion Guru will accompany the chemist on this run through.
- ❑ A note about Change Control
 - Make sure you have “friends” in the technical writing group
 - Once a monograph has a Smart Lab procedure associated with it, the same change control used for the monograph should trigger and track the change on the Smart Lab Side
 - Make it automatic

The Return on Investment

- ❑ Obvious Benefits
 - Every Chemist performs the tests the same way.
 - Procedure is complete before submitting for review.
 - Review of data is formatted.
 - Review by exception is possible.
 - Best practices and compliance are forced at the bench
 - Green Chemist almost equals Senior Chemist
- ❑ Not So Obvious Benefits:
 - Complete and exhaustive review of Laboratory Procedures - nSOPs, Monographs, Policies
 - Statistical review of capabilities - identify problematic procedures, instruments and Chemists

“Physical Integration: System Ergonomics in a Paperless Laboratory Environment”

Michael VanTyne, Director, Information Systems

Tandem Laboratories, Salt Lake City, UT USA

er-go-nom-ics - an applied science concerned with designing and arranging things people use so that the people and things interact most efficiently and safely. Making equipment accommodate your work instead of working to accommodate your equipment

Using a Process-Oriented Approach:

- ❑ Focus on interactions, communication, workflow, review by exception
- ❑ Process management – provides a structure within which procedure standardization is enforced
- ❑ Analytical and predictive process management – users know what is coming next:
B always follows A and usually takes ‘x’ amount of time.
- ❑ Facilitates generation of metrics and planning of workflow
- ❑ Contend with the fact that some job functions may become less efficient while making the greater process more effective

Reality

- ❑ Pen and paper is simple, familiar, reliable and is easy to install
- ❑ Usage of a system may be incidental to a user’s actual job function
- ❑ Most lab personnel are tasked with putting information into a system
- ❑ Most people need to see a killer application for them; ‘what makes my job easier or better’?

Electronic Notebooks:

- ❑ Creates opportunities and functionality that would not otherwise exist
- ❑ Cross-checking relational data
- ❑ Elimination of review
- ❑ Electronic interfacing with equipment
- ❑ Print just-in-time labels
- ❑ Provides session persistence - Ability for a user to work on a system in one lab location, physically move to another location and continue system interaction where they left off

Wireless tablets:

- Pros:
 - Portability
- Cons:
 - Expensive
 - Poor screen visibility
 - Form factor
 - Vulnerable to breakage
 - Management of wireless infrastructure

Citrix Metaframe Server:

- Advantages:
 - Enhances GxP compliance
 - Configuration management and change control
 - Improved security
 - Ease of application management
 - Patches, upgrades and validation

“Brief Overview of Legal Issues Surrounding ELN Records”

Colin Sandercock, HellerEhrman, Washington, DC USA

- An ER should evidence with a reasonable degree of confidence:
 - Who created it?
 - When was it created?
 - What was its content when it was created?
 - Whether it can be reproduced in human readable form?
- Courts consistently find admissible - ERs not inherently less reliable (presumed trustworthy)
 - ERs routinely qualify as "business records"
 - Party proffering ER must prove it trustworthy
 - Opponent are allowed to explore accuracy and how the ER was created and maintained
 - Record management procedures will be critical if the ER seems “fishy”
- Establish a Credible ER System - Credibility of ERs may be critical to winning
 - Admissibility irrelevant if credibility impugned
 - Credibility depends on how the ER is created, stored and reproduced in human readable form
 - Implement (1) technology and (2) records management procedures to ensure reliable ERs
 - Rigorously follow ER policies and procedures to prevent credibility attack
- Prepare Early
 - Have counsel review your system and documentation before litigation arises
 - Prepare to explain your ER system to a judge and/or jury
 - Consider making system documentation understandable -- at least in part -- to the judge/jury
 - Judges are "gatekeepers"; prepare from the outset of the case to get ERs into evidence

“Developing a Lab IT Strategy for Improved Laboratory Performance”

Guy R. Talbot, President, GR Talbot Consulting – Edgewater, NJ USA

An Effective IT Strategy for the Labs:

- ❑ How will the laboratory performance be better when we are done?
- ❑ What IT tools will facilitate this improvement?
- ❑ What is the plan to achieve these improvements?
- ❑ What will we need to do differently when we are done?

In other words: Are we doing the right things?

Common problems affecting IT projects for the laboratory:

- ❑ Unintelligible requirements documents
- ❑ Continual scope creep, with late project discovery of undiscovered critical requirements
- ❑ Seemingly arbitrary vendor selection
- ❑ Interminable validation phases
- ❑ Inexhaustible appetite for laboratory staff participation

Sound familiar?

Common problems caused by IT projects for the laboratory:

- ❑ Increased management of paper records
 - Affecting parts of lab operations not directly covered by the project
- ❑ Introduction of new manual data transcription tasks
 - Often found at the boundaries of system implementation
- ❑ Institutionalization of bad practices
 - Often that could have been eliminated with introduction of the system
- ❑ Overwhelmed laboratory staff
 - Asked to absorb too much change in too little time

Components of Good IT Strategy for the Labs:

1. Common understanding of the laboratory process
2. Clear articulation of the desired performance outcomes
3. High level description of the new system architecture
4. Well defined set of projects required to achieve the desired business outcomes
5. Plan to manage the impact on the organization

Summary:

- ❑ An IT Strategy helps us do the right things when implementing integrated systems for the lab
- ❑ An effective IT strategy should help prevent, or at least minimize, many of the problems that traditionally plague laboratory IT projects
- ❑ A good IT strategy focuses on business process improvements, not just technology deployment. Otherwise, you have no way of know if your doing the right things.

“Remediation Technology for the Laboratories”

**Angela Anderson, Project Manager, Global Information Technology
Schering Plough, Kenilworth, NJ USA**

Situation: Business Critical Instruments/Systems with Outdated Software

Regulatory Challenges - 21 CFR Part 11 – Legacy systems lacked:

- Audit Trail
- Security Compliance

How SmartShell helped:

- Provided the Audit Trail / History
- Provided Security Controls

Installation Challenges:

- Corporate IT standards require Oracle databases on dedicated UNIX servers
- Tight deadline: timely delivery to receive new servers and to qualify
- “Locked-down” Windows 2000 image is a key part of our remediation strategy

Application Server Install:

- New VMWare Session created on existing server
- Disk space allocated from existing Storage Area Network
- No new hardware required
- Repository for reports – VQ Printer
- Instrument data
 - Mirror of data from Client PC directory (Shadow Mode instruments)
 - Original data saved directly from instruments (Block Local Mode - 2 instruments)

Client Install:

- PC attached to instrument
- Mostly Shadow Mode - Network latency and reliability while transmitting data
- Access Control
- Access Repository – reports print PDF

IMACS Experience and Insight Panel

Robert Femia - Par Pharmaceutical

W. Stephen Conder - Bristol-Myers Squibb

Danlin Wu - Purdue Pharma

Michael Stroz – AstraZeneca

Thomas Bonitz – Par Pharmaceutical

Dennis McDaid – Forest Laboratories

- Invest time in the planning and method review process. This is a great opportunity to identify and correct ambiguous wording and to clarify techniques to be used and data to be acquired.
- Go for the quick win – management benefits and user-friendly environment.
- Build a small, dedicated implementation team. Best source is experienced lab people who have added computer skills.
- Vendors should create a method library to simplify implementation and encourage standardization around best practices.
- Do not try to automate every contingency – permit manual operations for rare occurrences.