Innovations in Molecular Lab Operation

Lessons in the Best Ways to Blend Automation, Lean Workflow, and Paperless Processes

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Disclosure

- **Member of the Strategic Advisory Board of Sunquest Information Systems**

Lecture Objectives

- To review the current status of molecular diagnostic testing technology as it is available for the clinical laboratory
- To present the opportunities for Lean enhancement opportunities in the molecular diagnostics laboratory
- To discuss the impact that automation of molecular testing is having upon the decision-making for laboratories considering the addition of such testing to their menu of offerings
- To present data illustrating the impact of a Lean reorganization of a molecular diagnostics laboratory
- To describe the features of a laboratory information system molecular testing module intended to simplify and eliminate errors from the testing process

Today's Reality

- All U.S. healthcare organizations are coping with increasing pressure to contain costs
- In the laboratory this means invoking ways to optimize testing, leverage information technology, and improve productivity
- Automation is a major step in the right direction to achieve these goals, but you must also make the best use of your available laboratory resources

http://consciouslifenews.com

What are Molecular Diagnostics and Why Should We Care About Them?

- Molecular diagnostics involve the detection of DNA/RNA sequences to obtain clinical information
- For infectious diseases, assay targets are signature sequences unique to specific pathogens
- These assays are becoming the tests of choice owing to their superior sensitivity, specificity, and shorter turnaround times
- Molecular assays are rapidly changing the testing landscape for diagnosis of infectious and genetic diseases

http://www.kerismith.com

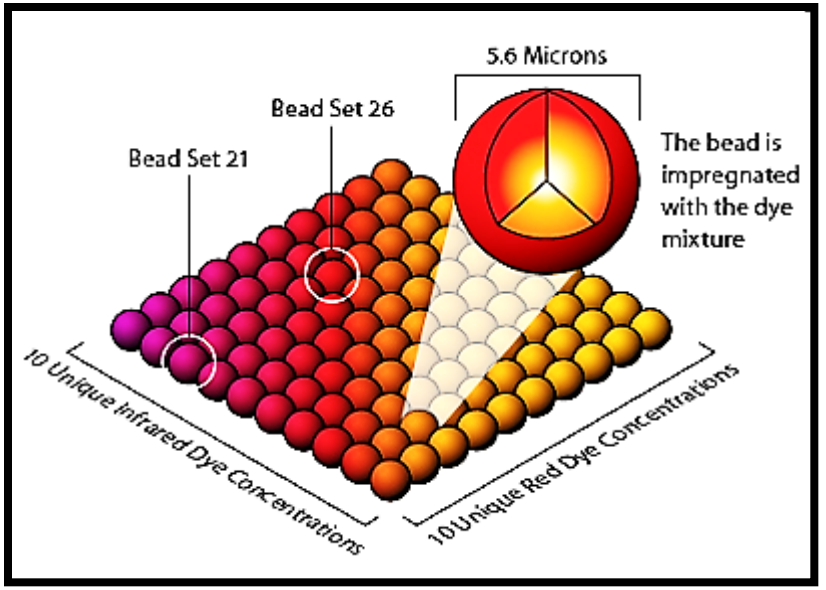
Enter the Molecular Era

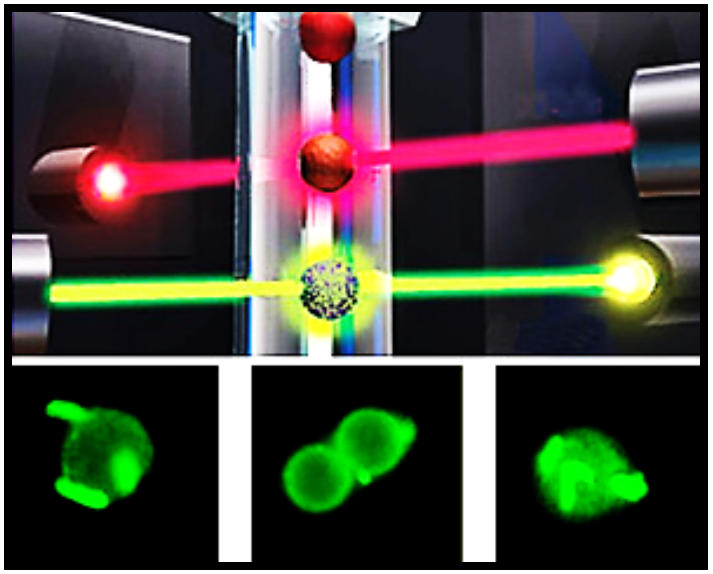
- The molecular era began in the 1980s with assays for bacterial ribosomal RNA
- Next came adaptation of research amplification assays (e.g. PCR) for use in clinical laboratories
- Then the development of automated testing platforms and detection of amplified targets in “real-time” made molecular testing feasible for a wider cross-section of laboratories
- Today we have multiplex assays, partial/whole genome sequencing assays, and microarray assays that are ushering in yet a new generation of diagnostic testing

http://3.bp.blogspot.com

Detection of Targets by Multiplex PCR

- Multiplex PCR involves amplification of many targets simultaneously in one reaction
- The Luminex xTAG® assay detects the amplified targets by hybridization with probes bound to dyed microspheres
- The microspheres are interrogated in a flow cytometer with dual lasers to identify the color dyes in each particle and the reporter dye attached to amplified targets





http://www.pri.wur.nl

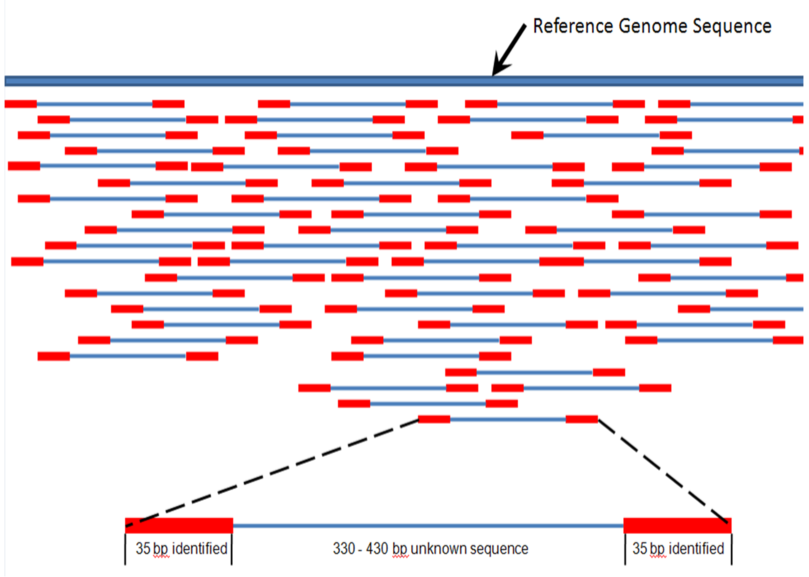
Pathogen Detection by Microarray Testing

- Thousands of DNA oligomer "capture probes" of known specificity are immobilized on the solid surface of a silicon chip
- Fluorescent dye-labeled amplified targets hybridize to the "capture probes", are washed, and then scanned with UV light to detect the resultant fluorescence
- Infectious disease microarray testing is a molecular analog of culture in that hundreds or even thousands of pathogens can be sought simultaneously in a specimen

http://www.tessarae.com

Sequencing for Recognition of Genes and Gene Mutations

- Targeted sequencing of single genes is used for phylogenetic studies and for detection of mutations
- Next-generation sequencing of partial or whole genomes is achieved by parallelizing the sequencing process, yielding thousands or even millions of overlapping sequences
- Pathogenic microorganisms can be identified, virulence factors recognized, and antibiotic resistance detected



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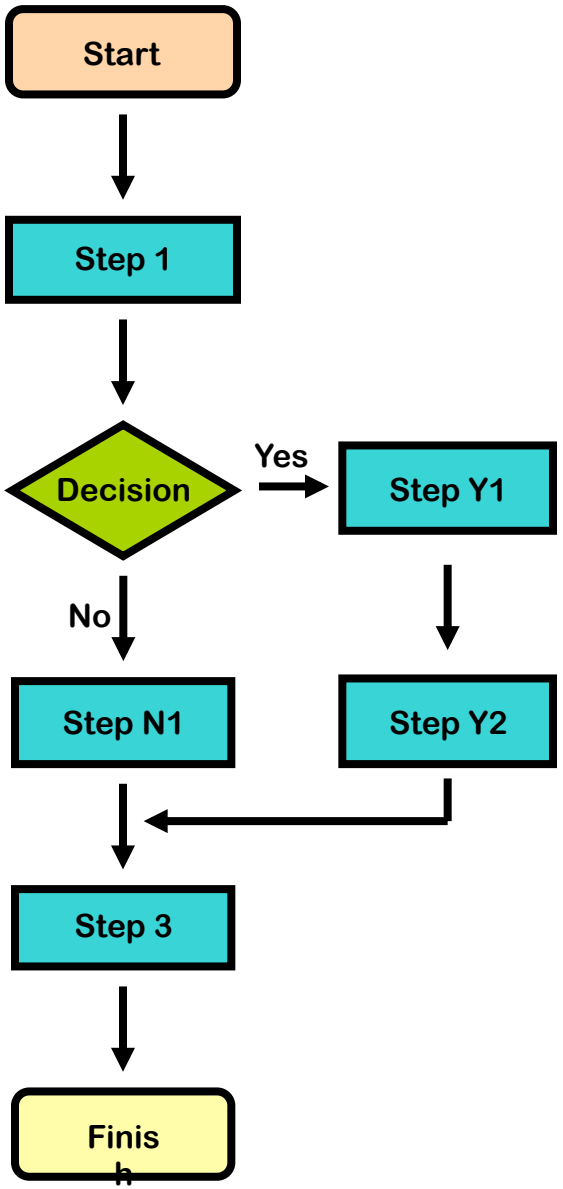
Healthcare and LEAN

- LEAN principles may be applied to processes that can be mapped as a series of discrete steps
- Healthcare in general, and laboratory testing in particular, are especially amenable to LEAN assessment and improvement
  - Some of the estimated $850 billion per year of waste in the U.S. healthcare system can be attributed to hospital laboratories
  - A LEAN overhaul of the hospital laboratory involves carefully analyzing each step in its processes, eliminating wasteful activity and inactivity, and developing revised processes in which each step adds value

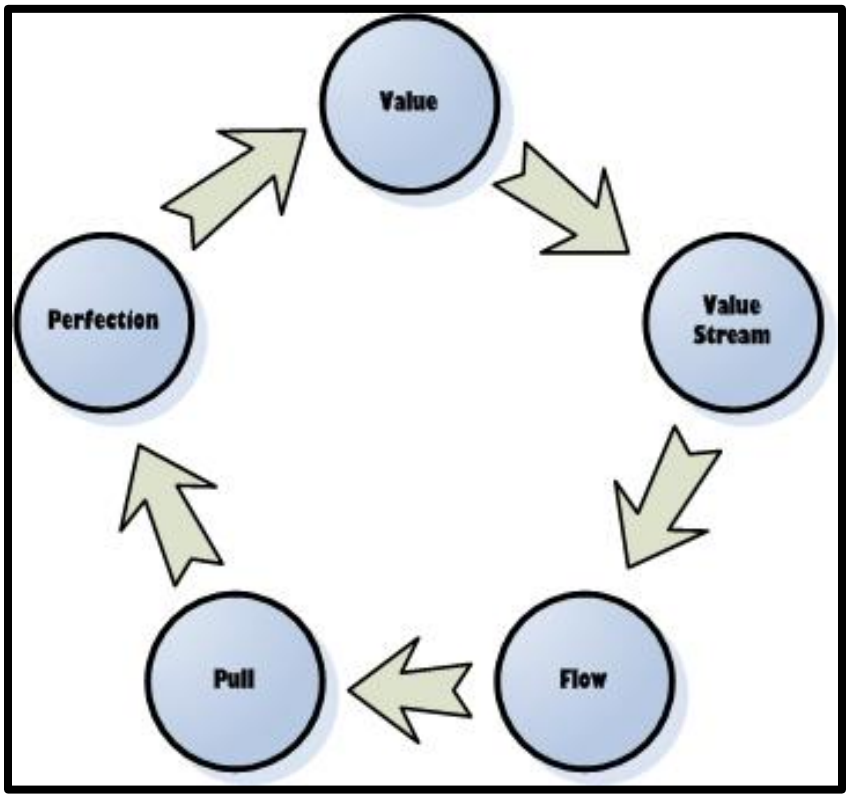


Laboratory Testing and LEAN

- The main objective of a LEAN laboratory reorganization is to deliver the highest quality test results, at the lowest cost, within the shortest timeframe, and all the while improving patient outcomes
- The deliverables of a successful LEAN reorganization include:
  - Improved operational performance
  - More standardized processes
  - Fewer errors
  - Lower test costs
  - Better employee morale
  - Enhanced patient management

Lean and the Molecular Diagnostics Lab

- The complexity of molecular testing lends itself well to Lean-based enhancement
- The Lean assessment evaluates existing testing processes and maps them to readily analyzed value streams
- Guided by Lean principles, a careful analysis of the value streams identifies non-value-added steps and wasteful activities that can be eliminated from testing algorithms



http://www.anticlue.net

Opportunities for Improvement

- The Lean analysis will reveal opportunities for automating testing, reducing turn-around times and lowering operational expenses
- Workload balancing, decreasing laboratory worker stress, and improved use of laboratory space are additional benefits to be realized
- Other goals include creation of work cells to eliminate unnecessary motion while standardizing test methods to lessen error rates

http://hbculifestyle.com

Automation in Molecular Diagnostics

- While automated approaches to laboratory testing are commonplace in the clinical chemistry and hematology laboratories, molecular testing remains primarily a collection of manual procedures
- A small number of automated "sample-to-result" testing platforms exist, but they are restricted primarily to diagnosis of a limited number of infectious diseases
- What are lacking and are currently under development are integrated automated approaches to molecular diagnostic testing as we know it today

Journal of Clinical Microbiology

Automation in Clinical Microbiology

Paul P. Bourbeau and Nathan A. Ledeboer
J. Clin. Microbiol. 2013, 51(6):1658. DOI: 10.1128/JCM.00301-13.
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Why Automate Molecular Testing?

- Current molecular testing is manual, laborious and essentially non-standardized leading to errors that impact patient safety
- Shortages of highly-skilled molecular diagnostics technologists exist in many parts of the world – there is a "graying" of the laboratory workforce
- Lean strategies for laboratory testing call for greater reliance on automation to streamline this testing workflow

LEAN Microbiology

Laboratory Automation Case Study

- ARUP Laboratories in Salt Lake City, UT is generally regarded as the most automated clinical laboratory in North America
- This automation has contributed significantly to improving ARUP's quality, turnaround time, efficiency, and profitability
  - Since 1998, lost specimens have declined by 80 percent to near Six Sigma levels
  - Turnaround times have been reduced by 30 percent
  - Productivity in laboratory sections served by automation has more than doubled

ARUP®
LABORATORIES

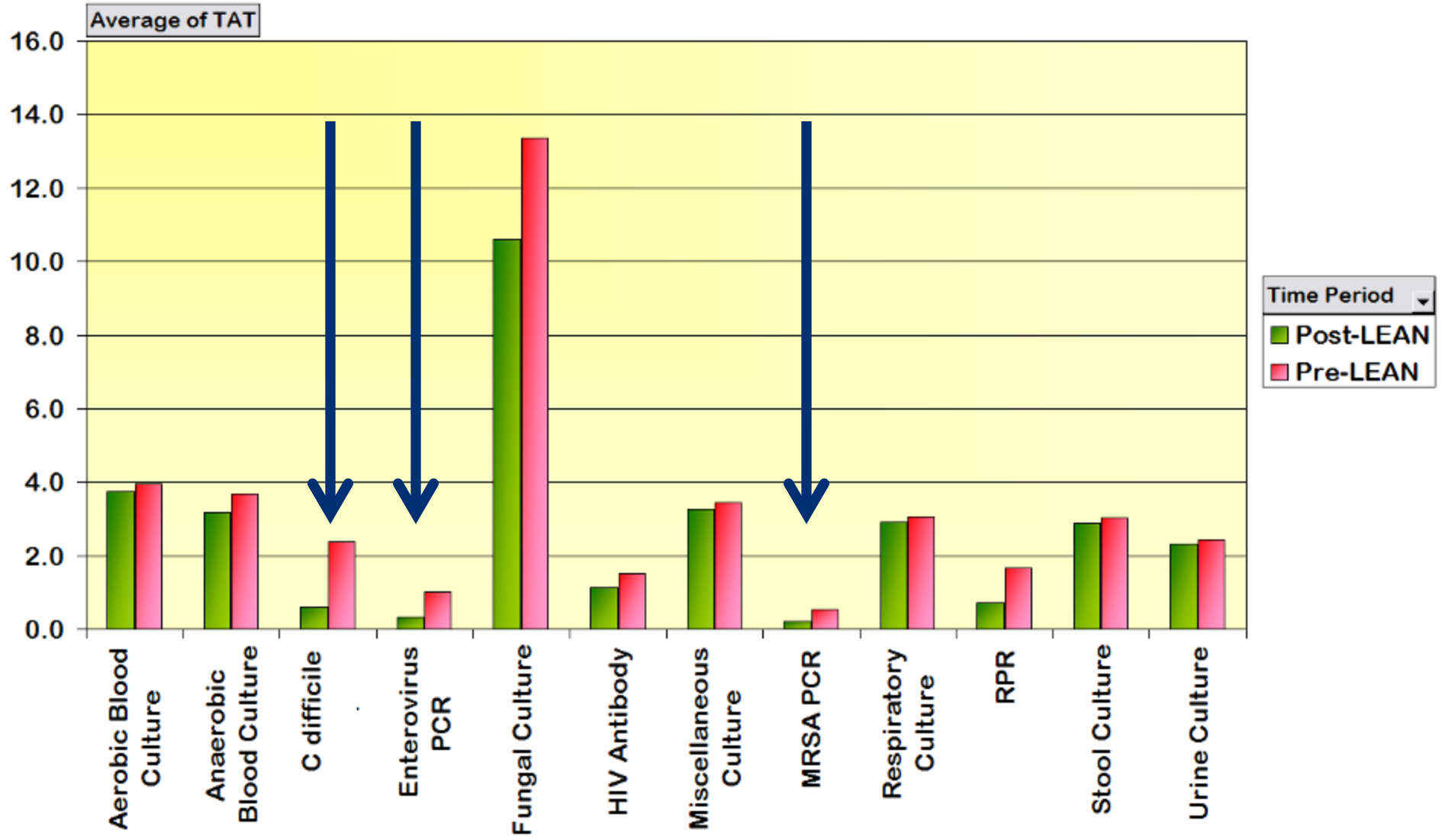
ARUP Experience with Automation

Organizational benefits	Before automation—1998	After automation—2010
Increased capacity for growth	200,000 specimens per month	970,000 specimens per month
Decreased error rates for common human-based errors	11 lost specimens per 100,000	<2 lost specimens per 100,000
Improved (or steady state) turnaround time despite growth	4,000 billed units per technical employee per quarter	8,406 billed units per technical employee per quarter
		30 percent reduction in median turnaround time
		31 percent reduction in 95th percentile turnaround time

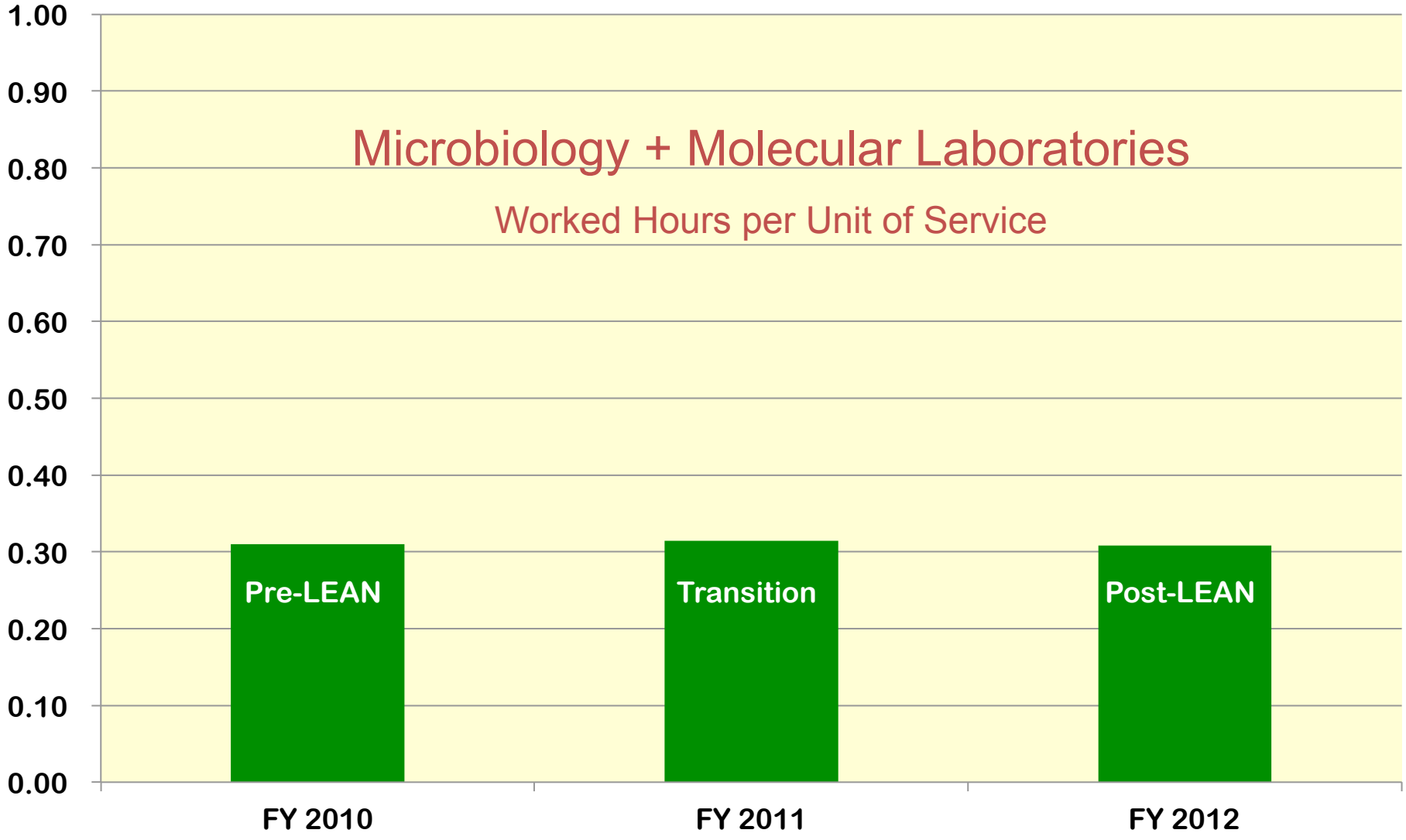
http://aruplab.com/Testing-Information/QualityCompliance/white_papers/Compliance

Impact of LEAN on Turnaround Time

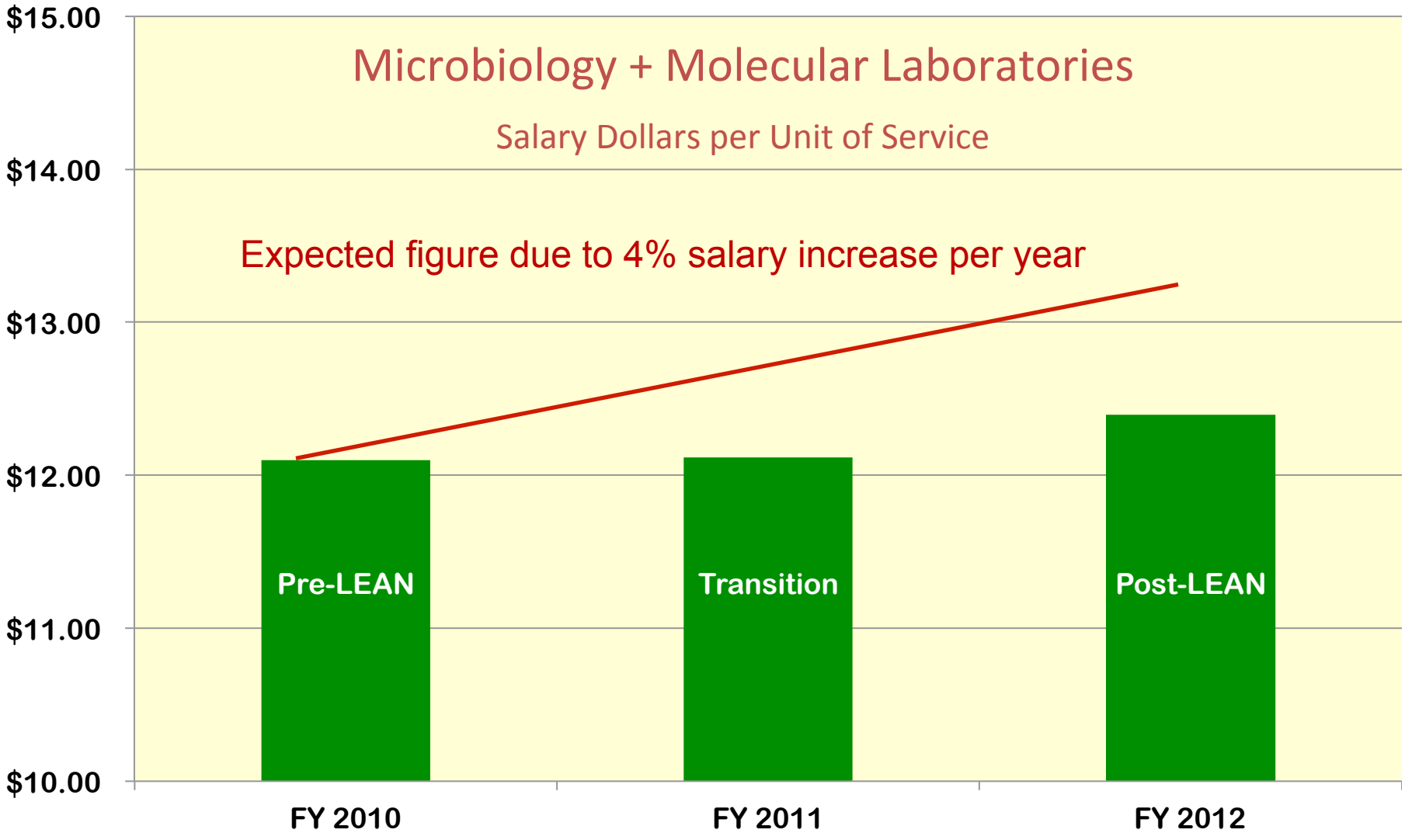
Six Month Period Post-LEAN versus the Same Six Month Period Pre-LEAN



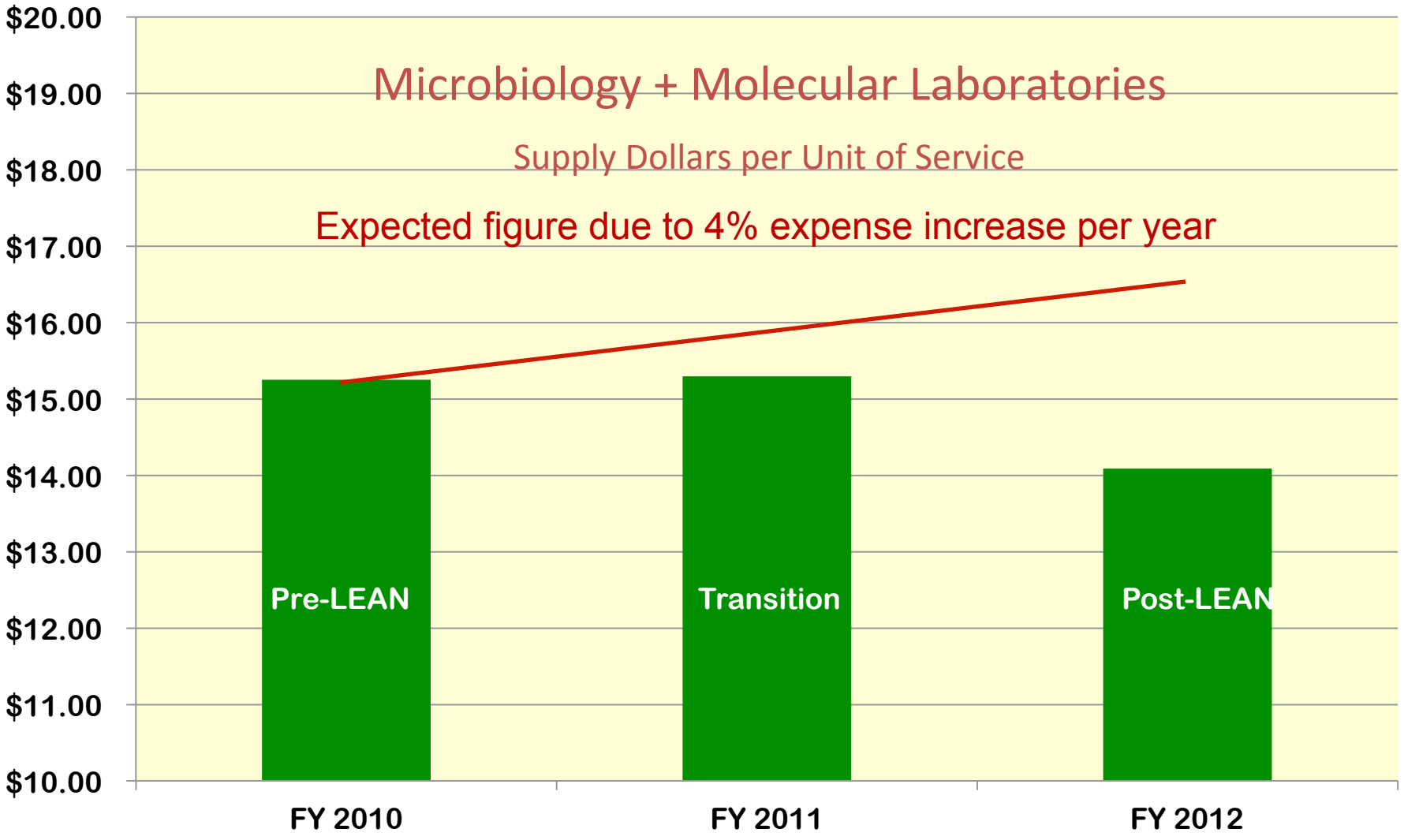
Comparability of Workload Complexity



Impact of LEAN on Staff Efficiency



Impact of LEAN on Supply Expenses



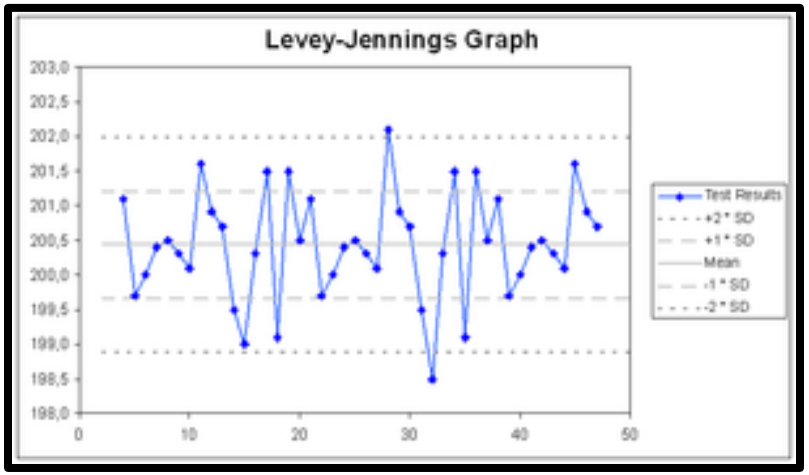
The LIS and Molecular Diagnostics

- None of the currently commercially available laboratory information systems were designed to handle today's complex molecular testing
- The challenge for laboratorians has been how to adapt legacy systems to handle the unique workflow and results reporting concerns for this testing
- The new molecular module from Sunquest Information Systems is an example of a big step in the right direction

http://www.digitalstructuresgroup.com

Molecular Module Features (1)

- Molecular testing protocol management
  - Assays can be performed based on pre-defined plans with data captured in the system during the workflow
- Assay materials inventory management
  - Inventory of assay materials is auto-decremented during use
  - Supplies available for use are visible to the test performer along with expiration dates
- Quality control management
  - Quality control data are maintained on-line for Levey-Jennings and Westgard rules analysis



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Molecular Module Features (2)

- **Tray map preparation**
  - Tray map rules for a testing protocol are easily created
  - The rules are applied to patient samples to create a tray map
  - The assay reagent volumes needed per tray can be calculated per protocol to eliminate human error in preparing the correct amount of master mix for a batch of tests
- **Assay results review**
  - Rules can be applied to assay results to highlight clinically significant findings
  - Negative results can be entered automatically leaving only positive results to be entered manually
- **Instrument interface capability**

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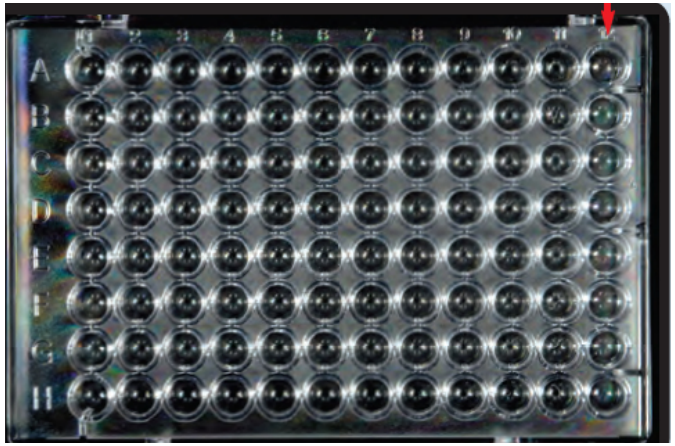

Forecast for Hospital Laboratories

- Careful thought must be given to the future when considering the expenditure of large amounts of money on current technology
- The laboratory of tomorrow will become increasingly more dependent upon molecular approaches for diagnosing and managing patients with infectious and genetic diseases
- The tools we are using today will not disappear, but will become minor activities of the laboratory in the future

http://mutamorphosis.org

Projections for the Future

- Automation of molecular testing will enable increasing numbers of laboratories to join this testing revolution
- Molecular testing will become more standardized and amenable to Lean-based improvement
- LIS vendors will add the processing power, storage capacity, and system flexibility to handle complex molecular testing or risk losing major market-share

http://plusmood.com