EUROLABAUTOMATION'99 REVIEW

by Robin A. Felder, Ph.D.

The Second EuroLabAutomation conference was held this year in London, following on the highly successful 1998 conference in Oxford.

The London conference saw an increase in exhibitors and attendees, as well as offering the displays of the latest technology in the field. Delegates enjoyed a multi-track format of scientific lectures, from leaders in the field across Europe, and around the world.

This first installment of the Program Review deals with the clinical section of the meeting, Chaired by Dr. Michael Wheeler, of St. Thomas Hospital, London.

Mike Wheeler, Ph.D.
Consultant Clinical Scientist, Head of routine endocrinology, also head of the Medical Devices Agency Evaluation Unit

Dr. Wheeler described laboratory trends including the need for laboratories to replace capital with labor. Diagnostic kits have been replacing labor for over a decade, however, the increasing workload and increased need for labor requires innovative solutions beyond kits to increase efficiency. The advent of laboratory automation will provide the next level of efficiency especially with the assistance of expert system software.

Dr. Wheeler explained that his hospital has a plethora of sample reception points, many different request cards, and other inefficient systems that need to be rationalized before automation can be employed. Dr. Wheeler's staff examined their laboratory workflow and decided to buy the Beckman Coulter IDS system to address the needs of pre-analytical processing area. Dr. Wheeler described a range of technologies that his laboratory considered for purchase.

For example, the OLA series of instruments are available from Olympus in a variety of configurations depending on laboratory needs. Konelab and Bayer have produced relatively small conveyor belt systems (compared with the TLA systems). Partnerships have been forming in the industry such as the new partnership between Dade Behring for analytical systems and CLIDS in Finland for automation.

Modular automation systems have been produced by Bayer (the IMS workcell), and Abbott (the Architect series), and Roche (the MODULAR series). The advantages of modular systems are reduced costs of robotics, reduced size, but overall costs may be rather high.

Dr. Wheeler described the limitations of robotics including high cost, space consuming, and do not necessarily allow for system backup. Current automation systems do not accommodate small sample size and thus short samples and pediatric specimens must be handled manually.

Furthermore, despite recent standardization efforts, industry has not yet adopted the international standards resulting in interfacing problems.

Automation will also reduce the errors in laboratories. More than 50% of the errors in the lab are Preanalytical, 3.5% errors in data entry such as wrong destination, and 0.8% were due to missed analyses. All other errors were relatively insignificant.

Technology that can assure foolproof specimen collection and labeling can have a significant impact on reducing errors. Wireless LANs can assist with these labeling issues. AutoLog (Lynn Sharman, Director) is one system that allows data entry via patient credit card into the system that will eventually end up on the tube.

The AutoLog system includes AutoCard, AutoTrack, and AutoFile all reporting to AutoAudit.

Robin Felder, Ph.D.
The University of Virginia, Department of Pathology, Medical Automation Research Center (MARC). Dr. Felder is the Director of the MARC, Chairman of the Association for Laboratory Automation, and Chairman of EuroLabAutomation

Dr. Felder discussed the need for complete laboratory reorganization to meet the efficiency needs of the next century. He suggested that laboratories should focus on a combined approach that focuses on core laboratory automation and expansion of point-of-care diagnostics. Economic incentives will drive laboratories toward point-of-care with esoteric testing concentrated in the core laboratory. Dr. Felder showed data produced in the MARC resulting from several internal projects that demonstrated that the cost of point-of-care testing was much lower than the same tests performed in the core laboratory.

Core laboratories can benefit from automated workcells that perform specific duties. Dr. Felder described several robotic systems that the MARC has engineered in the last year. The first project he described was the creation of a workcell for coagulation analysis. Organon Teknika (Boxtel, The Netherlands) has funded the creation of the coagAutoLink robotic device that performs pre-analytical processing for the MDA 180 coagulation analyzer. Dr. Felder described the creation of the robotic system as well as data from the clinical trials. The coagAutoLink was able to reduce the time required to processes coagulation specimens by providing more consistent and error free sample handling.

David Bullock
Wolfson EQA Laboratory, United Kingdom

Dr. Bullock described the purpose of external quality assessment (EQA) for automated systems and how they can help us look at automation performance. EQA is similar to proficiency testing as it is called in the USA. As laboratories consolidate, they will have to deal with new needs in quality assessment. There is a need to harmonize the practice of quality and to integrate it with reporting. For example, immunoassay is being combined with chemistry and thus quality assessment products must be compatible with these consolidated systems. EQA reporting is moving rapidly to email data entry and web based data return to the user. Laboratories will be soon spending more time in data interpretation instead of the mechanics of data reporting. As the automated laboratory evolves there will be less technologist involvement in looking at specific data points. Instead technologists will be more concerned with interpreting the meaning of laboratory data for health providers.

Automated laboratories tend to have more realistic testing since the specimens are put in with the clinical specimens and run through the automated system. There is great debate as to whether EQA specimens should be run manually on backup analyzers or put through the automated laboratory setup. The best scheme for risk management might be to alternate manual methods and automated methods since this gives an accurate picture of total laboratory variability. When two immunoassay systems were recently compared, there was a significant variability in one vendor's system. For example, vendor A had as high as 20% while the other vendor had a variability of less than 7%. Thus, EQA is necessary to not only provide high quality patient data, but also as a method to monitor the quality of vendors.

There was a general agreement that automation reduces all over error in the laboratory as long as one approaches the problem with "intelligent effort." Bullock ended with a statement that the most comprehensive QC web site can be found at www.westguard.com.

Pierangelo Bonini
St. Rafaele Hospital, Milano, Italy

Integrating clinical laboratory and pharmacy in the hospital system: What does it mean.

Recent news in Italy showed that there were some injured patients resulting from

mixing up pharmaceutical delivery to patients. Thus patient misidentification is not only an Italian problem, but a worldwide problem. Dr. Bonini suggested that we are not creating the technologies necessary to protect patients from medical errors. Transfusion errors are in the range of 1 in 12,000 units transfused. ABO incompatibility occurs in 1 out of 6,000 transfusions. Adverse drug effects approx 10% of patients in the hospital resulting in 1.7 to 2.2 more days in the hospital with an increase in over $2,000 per patient. The risk of death in a hospital is increased almost 2 times as a result of misidentification. Medication errors occur 2-14% in hospitals (Leape et al. JAMA 21, 1994, pp1851-1857). Specimen mix-ups in laboratory occur in about 1 out of 300 specimens (Clinical Laboratory News). Errors result from explosive growth in biomedical disciplines, shortening patients stays, and fewer nursing staff. An ideal ID system should have strict connection between blood drawing and preparation of tubes, have good patient identifiers, fail safe transfer of ID, have absolutely no change in codes, reduction in amount of information to transfer to allow for redundancy, and be totally confidential.

Dr. Sanna and Bonini have developed the Smart Cart™ that is equipped with a bar code reader, computer, and label printer and applier. The Smart Cart will produce a Vacutainer tube equipped with a bar code with patient ID, data (personal, clinical) caregiver ID, sample ID request ID, drawing time and date, test list, as well as other user definable information. There is both a linear bar code for the instrument and a two dimensional code to encrypt high density information.

Alberto Sanna Ph.D.
St. Rafaelle Hospital, Milano, Italy

Alberto specializes in patient safety and security in labeling as well as patient confidentiality. His talk focused on a kiosk product to bring laboratory services closer to the patient. The EC Directive (95/46/EC) on the protection of individuals with regard to the processing of personal data is now a regulation for all EC countries. The intent is to avoid improper disclosure of healthcare information. Security is maintained by authentication, integrity, confidentiality, and non-repudiation. Authentication is defined as verifying that the purported sender is actually the sender. Integrity is ensuring that data is sent and received without alteration (detectable or undetectable). Some data alteration is not necessarily malicious. Confidentiality is such that only the intended receiver was able to gain access to the data even after archival storage of the information.

Non-repudiation is the property of the receiver being able to prove that the sender did, in fact, send the data despite the fact that the sender may later decide that they didn't send the data.

Confidentiality, and integrity is maintained by cryptography. The current methods use keys or passwords to encrypt or decrypt. The keys can be identical for encryption and decryption or different. The data goes through a Hash algorithm to digest the information then it is digitally keyed using a secret key. The result is a signed and encrypted document. If someone receives this document, the information can be deciphered using a public key. If the public key opens it, then if only verifies that the document is non-reputable, and perfect when it arrives. If you only use the public key, then you have the essence of a digital envelope. This means that who ever gets it shows that it was not altered when you opened it but does not prevent someone from intercepting and reading the document. An encrypted document is perfect for providing summons.

Sanna's Kiosk is designed for individuals to get perfect data. For example, the lab sends lab data through the Internet. How are you sure that the data has not been altered to result in patient errors. In the laboratory the tech or doc gets data from the LIS and then enters it into the Intranet. The Lab doctor adds a private key signature and sends it back into the database. The public key is then used to encrypt before sending. Someone equipped with the right password can then retrieve the data that has been essentially "signed" by the doctor. Kiosks are then located in pharmacies, accessible by patients through ATM like locations, in the waiting room of doctor's offices, or in their place of work. This concept is perfect for small practitioners to deliver secure data to their patients at home via the Internet and assure confidentiality.

In the future, the data must be formatted in a standard format to allow reuse in other

healthcare computer systems.

Bruce Elder
Global Healthcare Industry Manager, Sun Microsystem, Inc. bruce.elder@sun.com
Network services in health "towards better outcomes"

Mr. Elder started with a quote that "Everything which can be invented, has been invented." U.S. Patent Official, 1897 as a contrast to the present rate of new technology development. He explains that SUN feels that employees loose 20% of their relevant computer skills each year since technology is moving so fast. Mr. Elder also showed the following quote, "Any sufficiently advanced technology is indistinguishable from magic," from AC Clarke. Network bandwidth has been doubling every 6 months. This rate is 1000 faster than the increase in speed of computer processors. This is causing the computer industry to evolve from a hardware industry to a service industry. Almost any service you can imagine will soon be available through the net, even hospital administration. The increase in bandwidth is causing a self perpetuating cycle of useful service driving increased demand for services driving increased need for bandwidth driving more useful services.

The evolution of technologies will inevitably take the following steps. Common language (JAVA) driving component architecture (appliances) driving specialized components evolving to multicomponent systems (distributed object systems) that will begin communicating and coordinating (using JINI software), such as appliances that introduce each other. Eventually these systems will be aware of their context (what they are and what they are intended to do) and the network will become the computer. These systems will eventually become self-aware systems.

How is this relevant to healthcare? Healthcare costs are increasing which results in decreases access and decreases quality. To change this cycle you must change the economic incentives (this was the intent of managed care). For example, only give a fixed fee per disease. You can realign the health enterprise. For example, have centers that focus on only one procedure such as Coronary Arterical Bypass. This creates problems with access by indigent and complicated cases. The third method is to improve the use of resources. Currently administration controls 20% of costs by regulating the source of supplies and infrastructure. Clinicians control approximately 80% of medical costs. However, patients control 100% of costs since they have the option of selecting a health treatment or not. Network services could make medicine relevant by making it highly personalized and customized, timely (presented at the point-of-decision), easy (require no effort), and trusted (highly available, high quality, and with a positive source (brand)).

Building eHealth services one needs communication and connectivity with good content that can be translated into knowledge. All this should be easily charged to the patient (in new ways) and Web accessible. Thus medicine will be an online web service. Mr. Elder showed a case history of a case that the insurance company did not know what to do with the patient. At least 70% of cases in the investigative medical exam were incorrect in making a diagnosis. Computers with built in algorithms are making at least a 26% better diagnosis. For example, recent studies that examined the reduction in case load for insurance companies results in 50% reduction in risk for heart disease, and 70% reduction in risk for pre-natal diagnosis.

Mr. Elder showed a sobering statistic that there were 250 new health dot com companies in the USA in the last 6 month.

Dr. Alain Truchaud
Institut de Biologie, Nantes, France

Dr. Truchaud opened the session by explaining that automation is dependant on the environment of the laboratory. One must study the workflow, simulation of merging activities, and the architecture of the building before automation can be initiated. In brainstorming sessions one must consider the best arrangement of analytical area, distribution of services and point of care testing. These ideas must be integrated into a plan that incorporates the needs of all those who depend on laboratory services as well

as those who work in the laboratory.

Marek H. Dominiczak, co-editor Clinical Chemistry and Laboratory Medicine and Consultant and Honorary Clinical Senior Lecturer at the University of Glasgow. mhdlb@clinmed.gla.ac.uk
Management Skills in the Laboratory

Dr. Dominiczak explained that managers of laboratories have many tasks that they must take care of. Many laboratory activities are managerial in nature. Often, managers forget the human part of laboratory management. Dr. Dominiczak suggested that laboratories set up non-hierarchical teams where everyone contributes, learns, and eventually leads according to their expertise. Within sections, a non-hierarchical structure allows technical supervisors to serve at a similar level as senior scientists in problem solving. Consolidation is important to managers since it implies a new working structure that involves expanding the skills of the staff to accommodate the need to serve in many areas of the laboratory. The range of services of the laboratory can be maintained despite the need to reduce the labor component. However, humans are naturally resistant to change. One has to prepare to avoid a tribal war, entrenchment of individual empires, and failure to join the team effort.

Dr. Dominiczak shared two case histories from Oklahoma. Consolidation of the University Hospitals at Oklahoma cost over $100,000 but saved over 1 million dollars per year. Mayo Clinic required over 12 months to cross train the staff but realized significant savings.

Dr. Martti Syrjala
Project Leader for Laboratory Automation, Helsinki University Central Laboratory
Implementing new automation in an old laboratory: The Clids project in Helsinki University Central Hospital

Dr. Syrjala works in a 1500 bed hospital with 647,439 outpatient visits each year. The hospital is a component of the largest hospital consolidation in the history of Finland. The laboratory employs a relatively large number of technologists (400 people) since the laboratory tasks are spread all over town. About 3.5 million tests are performed each year. Their automated core laboratory performs about 44% of the testing for their many hospitals in Helsinki. Automation was considered in the early 1990s as a result of an economic depression, the need for new instrumentation, and the need for building renovation. They used a 14-station pneumatic tube solution to connect all the buildings within one square kilometer in order to send up to 48 specimens at a time. They adopted step-by-step total laboratory automation. Stage 1 involved pre-analytical automation, stage 2 involved analytical automation and stage 3 was the connection of the first two stages.

Personnel teams were assembled and charged with planning the laboratory. Lab technicians, physicians, clinical chemists and the lab engineer were involved. They invited a member of the vendor's staff to join the team. Dr. Syrjala described the significant mental walls that existed to the adoption of automation.

An online analysis tool was employed call Power Play that allowed one to examine retroactively the effect of automation implementation. After the installation of automation in their laboratory, they measured an reduction in data reporting rate by one hour and 10 minutes. At this point they report 25% of their workload by 10:0 AM. The requests for proposals were sent out in Q2/1996 and a detailed project plan was done in late 1997. The contract was complete by Q3, 1997. The first installations were done in Q4/1977. Q1 1998 the centrifugation and transportation was working. LabSystems in Q1, 1999 acquired CLIDS automation, which delayed the project so that it will not be completed until Q4 1999. However, they will have their equipment replaced with production models sometime this year.

The costs were approximately 3.1 million Euros or 35% in renovation (the renovation breakdown was 8% planning, 4% supervision, 30% construction, 35% plumbing and temperature control, 33% misc.), 24% sample handling, 26% instrument costs, and 14%

automation. Currently there are 50 less employees in the laboratory before the automation. However, not all of the 50 employees were reduced by the automation. Before automation the average number of tests reported per working hour was 7. After automation was installed they are now turning out over 47 tests per paid working hour.

The CLIDS system is complemented with wireless palmtop computer equipped with windows CE and bar code reader. One can obtain work lists, sample time, phlebotomist and remarks.

Alain Truchaud, Ph.D.
Institute de Biologie, Nantes, France.
Pluridisciplinary Approach in Laboratory Design

Dr. Truchaud described the plans of their group to renovate their hospital laboratory. They carefully planned to consolidate certain analytical activities such as the pre-analytical and the automated laboratory services. Esoteric testing was grouped according to discipline such as electrophoresis, immunofixation and autoimmune. Microtiter assays and immunoassays were consolidated, as were all flow based methods. They also grouped tests that require less than 3-hour turnaround and in a separate area those tests that could tolerate more than 3 hours turnaround. Space for human relaxation and education was also programmed into the space.

As with any automation project, responsibility has to be assigned to laboratory personnel that maximize the quality of the service to customers. For example each member of the team must participate in personnel training, cost containment, quality improvement. Ideally, personnel should improve the image of the laboratory by providing service to the clinical practitioner and training of the medical team.

Dr. Richard G. Jones
Senior Lecturer in Pathology at Leeds

Simulation is a computer tool that can be used for laboratory management planning in addition to its traditional role as a planner for computer control tools. Simulation models are conceptual descriptions of the known world that are executed in a computer system to make predictions about the future. Simulation tools have the advantages that it allows one to compress time and run a process that would normally take hours, days, weeks, months, and even years in just a matter of a few minutes. Insight can be gained about how to design a process. Anticipated rewards can also be determined. Simulation can be done with tools as simple as a spreadsheet or complex software tools that use discrete-event simulation languages. These complex software tools allow one to solve particularly complex problems involving many different processes operating at the same time involving many different people or tools.

Dr. Jones demonstrated the use of the ProModel package to evaluate a pharmacy efficiency. One can use the cartoon mode to visualize the activities that take place in the pharmacy, for example, processing orders and everyone taking a lunch break. After running the model, then a statistical package can evaluate the efficiency of the process. Dr. Jones suggested that laboratory directors hire the services of a consultant to create, run, and evaluate the model in their own laboratories due to the complexity of this field.

Doug Hirst
Biochemist at the Bradford Royal Infirmary, United Kingdom

Mr. Hirst created a spreadsheet based simulation tool to evaluate the workflow in two different laboratories. For example, one laboratory moved aliquots onto a group of instruments simultaneously.

Another laboratory used a linear system of moving the same specimen from station to station in a linear fashion. Input data was put into the model and evaluated using simple statistical analyses with bar graph output for data visualization. Residuals, or specimens that are waiting for access to laboratory resources can be monitored using this spreadsheet simulation tool. His model took about a month to build not counting the time for thinking about how to solve the problem.

Dr. Andreas Schuele
Franhofer Institute

Dr. Schuele uses simulation for similar problems as demonstrated by Mr. Hirst. Lab planning strategies gain more credibility following the use of a validated simulation model. Impediments to efficiency can be examined such as excessively long analysis times, queues in front of processing devices, and transportation bottlenecks. Three laboratories were examined including the Regensberg Hospital in Germany. In one case Dr. Schuele determined the optimal flow through a robot workcell equipped with a specimen input device, a centrifuge, and a variety of analyzers.

The model can include additional complexity of simulating the control of the system by process control software architecture. His presentation included the live demonstration of the model running and determining the optimal workcell organization for a variety of specimen arrival rates. The model required about two man months to gather the data.

J. Senervirate, Central Manchester Healthcare NHS Trust, United Kingdom.

Use of computer simulation to support reorganization planning of the Manchester Royal Infirmary

The Central Manchester Healthcare laboratory was equipped with the Hitachi 747 and 911 chemistry analyzers. Hematology was performed on the Sysmex SE 9500 and coagulation from Instrumentation Laboratories. The laboratory is facing financial pressures and pressure to increase efficiency. Mathematical models were developed to optimize the design and selection of automation using Simlab. To prepare for simulation, data was collected, workflow evaluated, and specific details gathered for each workplace characteristics and workload profiles. The output from Simlab included turnaround times, equipment productivity, queue length and other efficiency measures. A file containing data for 1785 orders, 32 workplaces, 29 staff positions, 24 different tubes routes and 78 tests was used for input data.

Model 1 was created which was calibrated against real data. Other models were created that included less tangible data such as telephone interruptions (overhead factors). The model produced graphical output of orders produced per minute. The highest peaks on the graph were indicative of the most productive models. They realized tangible data that could be used to design their next laboratory system and make purchases without the fear of excess overcapacity or insufficient capacity.

Tim Reynolds
Queens Hospital, UK
Work Order Communications: Pros and Cons

The British Government has provided a six-step plan for the implementation for information technology in hospitals. This 6 level plan starts with the definition of a simple clinical administrative data system at level one and spans the breadth of technologies up to full multimedia and telematic capabilities at level 6. Very few hospitals are even at level 4 in which there is seamless communication between the HIS and LIS. Mobile terminals have all the facilities of a field terminal and can be used at the bedside. Tasks that can be accomplished include admission to order supplies as well as lab order entry. The order entry system starts with a request for patient identification. Subsequent screens ask for the test which is to be ordered. One can also request esoteric requests such as psychiatric services and lung function tests. Order sets are automatically orderable as well as priority status.

Once you have logged on, the system automatically adds a digital signature of the user. The advantages are that the requests are fully legible, however, individuals using the system still make ordering mistakes. Tests already ordered can be viewed to reduce duplicate orders. The system prints bar coded labels, however some individuals circumvent the system by printing labels and then using them a day later. Order entry facilitates the laboratory flow since all the tubes have been already entered in the computer when it arrives in the laboratory. A major advantage is that the person making the request is fully accountable for the ordering event. A decision was made to allow the nurses to place test orders.

The system cost is about 4 million dollars for a 500 bed hospital. The high costs arise due to the need for PCs on all wards. Furthermore, the hospital information system network infrastructure has to be upgraded and maintained to support the continuous use of this system. More laboratory testing resulted from installation of the system since it was easier to order tests and it was also difficult to delete unwanted tests.

Simon Maasz
Quirepace Ltd., United Kingdom
Airtube Technology: Theory

Quirepace's largest installation involved the installation of 4.5 Km of tubes with over 20,000 carrier movements per week over 600 kilometers per day. Most samples can be delivered in 3-5 minutes in a well-designed tube system and virtually all specimens are delivered in less than 10 minutes. One of the difficulties with tube systems is that one has to walk to the ward station to make or received a delivery. The basic questions that must be addressed before buying a tube system include deciding the size and type of the items to transported, the working practices of the staff that will use it, and how fast the samples have to be delivered. For example, emergency samples are usually transported once at a time. Outpatient specimens are usually batched and the carriers sent every 10 minutes. Ward samples are usually batched into patient groups or specimen types.

Despite the fact that the best way to send samples are by type to the laboratory station that has to process them, humans basically place all tubes in one carrier. Therefore, the company usually creates a single station in the laboratory that requires tube sorting once they have arrived.

A tube diverter or interchange can make 120 transactions per hour. A graph was shown that predicts the probability of carriers queuing based on the percentage of capacity what is used. Once you increase the use above 60% starts to create significant backup in the system. Less than 30% use is a waste of money. Data from real sites demonstrate that virtually 98% of the tubes are sent when the system is below 60% capacity. A linear coupler provides 30 carriers in temporary storage and handles 500 carriers per hour and connects 10 independent systems. The use of a coupling system essentially hides the carriers if there is excess use of the system. Instead of carriers waiting on the bench for access to the system, they go into the automated coupler that feeds them into the tube at the appropriate time.

Wim Malcontent
MMC, The Netherlands
From Patient to Analyzer

Radio identification chips can be used to code patient demographics onto a blood specimen prior to transportation to the laboratory. The basic information that can be encoded by radio waves is basic identification, what tests are necessary, the phlebotomist, and the time. Other information that can be encoded are the pre-analytical steps that are required by the tube prior to analysis. For example, hematology tubes can be encoded to indicate to the reading system that centrifugation would not be necessary. Radio identification chips eliminate the mechanical complexities of printing paper labels. They use a passive tag with 8 kbytes of capacity. The writing cycles are limited to 100,000 cycles. The data is preserved for over 10 years on a chip. The system is totally paperless (including the label) and has all the advantages of a high density bar code system. There is more safety in this system since the code cannot be damaged or defaced. Additionally, additional information can be added to the code at any time. Time and motion studies have demonstrated that the RFID can be read much faster than bar code system.

Jonathan Kay
John Radcliffe Hospital, Oxford
Handheld computers with radio networks: Mobile laboratory access for clinical users

Providing instant information to physicians is a critical point in improving the efficiency

of medicine. Junior doctors are more mobile than senior staff and thus need to carry their computing power with them. Dr. Kay described the features that will be necessary for desirable and functional portable computers. The current "organizers" such as the early palm pilots, are not suitable for carrying large amounts of information or live web browsing. An ideal current technology is the Nokia clamshell telephone. Standards are needed that can be applied for developing the display of data that is necessary for medical practice. The Oxford Clinical Intranet project is focused on the computerized record, support and advisory information for physicians, and contextual links. The use of HTML and frames with JAVA script is probably the best choice given today's volatile computer market. One needs to provide certain data immediately to the physician, however, it is not immediately evident how this can be accomplished using today's technology. Keyboard containing pagers are excellent for this purpose, but there is some hesitation with having physicians carrying too many devices at once.

Sarath Krishnaswamy
Abbott Laboratories MediSense

Precision PcX is their latest bedside glucose product. The handheld nature of the device places constraints on the amount of data handling hardware and software into the device. Abbott is finding that data management systems are becoming the market driver for the sales of glucose systems. Therefore they have developed the Precision Net data management system that was co-released with their new analyzer product. The portability and need for graphics drove the need for enhanced microprocessor capabilities. The system provides real time data transfer through the hospital network. They also had to consider design features that prevented inadvertent removal from the hospital. The use of common user interface schemes such as Windows™ like interfaces should be used to avoid the need for training. Placing the instrument into a holder transfers data. This "drop and go" approach to data transfer uploads data and charges the battery. Gaining access to network jacks has necessitated piggybacking onto a local PC.

The architecture was created that had an independent communication layer with interface tools, network monitoring and instrument communication protocols. This layer communicates with the database. This architecture retains flexibility for future expansion. The instrument output data follows ASTM 1381 standards so that any group can accept instrument output. However, the need for network support has increased dramatically. Thus they are using systems that are remotely supportable and support a variety of protocols such as COM/DCOM, DHCP, and HTTP. They have also adopted the HL7 standard for data handling and XML.

"Monitors" who will have access to system maintenance software control the system. The system security provides the opportunity to lock the meters if QC is out of range, if the user is not qualified, if the incorrect lot of reagents is being used, or if the system appears to be malfunctioning. Report formats may be generated so that custom reports can be generated on demand.

Sean Field
Global Marketing and Business Development for Information Management, AVL Scientific

Data management functions will drive the growth of the point-of-care testing. Enterprise Analysis Corporation (EAC, Stamford, CT) provided data to Mr. Field that indicated that POC testing will grow from 25% in 1998 to 45% in 2008. This is potentially 12% growth in the industry. Data management is supposed to help with the fact that QC and maintenance is not getting done, typographical errors are introduced into data transcriptions, many lab tests are never logged, and unqualified users are performing testing. Providing high quality reports to physicians is another benefit of POC testing data management systems. EAC showed that in over 200 hospitals 15% of test results were being entered manually into the LIS, and another 15% were entered electronically. An astonishing number shown by EAC was that 70% of data was not being collected.

AVL proposes that an open POC data manager should not be vendor specific but have an open architecture to allow connection of all instruments on the market. There will

be significant efficiency gains that will result from instantaneous data management by the laboratory at any point in the hospital. The AVL product provides remote lockout for error conditions, remote setup of QC ranges and user authorization, and also a list of pending tests can be displayed.

Mike Campanelli
Bayer Diagnostics, USA

Mr. Campanelli explained that process control minimizes the negative impact of automation on the laboratory operation. Bayer has created a process control system to control the Advia LabCell system. The process controller has a routing layer that allows test order data from the HIS to route tubes to the proper area in the automated system. For example, decisions have to be made as to whether the tubes should be centrifuged, decapped, recapped, or aliquotted. Furthermore, there are communication issues with the instruments and the LIS. The process controller they have developed connects the Advia 1650 chemistry system, Centaur 240, Immuno 1, Clinitek Atlas (urine chemistry), Advia 120 (H1, H2, and H3) hematology instruments, and any automation friendly instrument that follows the NCCLS standard. Bayer uses HL7 version 2.3 for communication with either FTP or sockets via TCP/IP. Other standard protocols are also available.

The process control software deals with work orders, and add-on tests. All database functions are expected to stay in the laboratory LIS. LabCell process control will route specimens to an instrument based on ordered tests. It will manage communications between the LIS and LabCell as well as repeats, reflex, change orders, and add-on tests. Specimens in question are routed to a special holding area. Many instruments allow samples to be placed directly on the instrument in the case of super stats. Samples that are still in the system can be retrieved automatically by the robot or manually from a storage pick list. Finally, system validation should take place in the laboratory information system, LIS.

The Bayer process control software architecture is one of the more advanced systems on the market.

Jan Lindemans
University of Rotterdam Hospital

The University of Rotterdam Hospital processes more than 1000 specimens per day with 60% routine and 30% STAT and 10% superstat. Their laboratory contained 2 Chem 1 chemistry analyzers, and three immunochemistry systems in the addition to one immunoassay homogeneous system. The impetus for automation was that they were scheduled to replace their analyzers. Furthermore, 18 of 130 FTEs were to be reassigned to other tasks. They were hoping to get all STAT and possibly all tests reported within an hour. They also wanted to be able to take any sample matrix into the laboratory, either serum or plasma. Naturally, they wanted to accommodate backup and reflex testing.

Like most laboratories adopting laboratory automation possibilities, they started with a workflow analysis. Once equipped with quantitative data, they were able to better match their needs with the available hardware on the market. One major issue they faced was the interfacing of the main process controller with their existing LIS system. They quantitated the number of tests per day in order to determine which tests would have to be accommodated on the chemistry systems. They decided on two routine Hitachi 917 analyzers performing 4100 tests per day and one specialty 917 doing 1000 tests per day.

The chronology of the project was as follows: March 6th approval, August 10 delivery, August 20 end of installation, August 25 start the validation, and September 13 regular production. Thus, about one month transpired between delivery and full production. The system was not designed to accommodate allergy, protein electrophoresis and other esoteric tests. The system was not installed with a centrifuge because the laboratory spends much time doing paperwork on each specimen. Therefore, the centrifugation can be done while paperwork is being processed. If they move to bedside labeling, then centrifugation may become an option.

The rate of the system is 165/hr. They load 4 batches of 80 specimens every ten minutes and recorded the time results were reported. They also tested the system with

one H917 was shut down. They discovered that 98% of their results were reported in less than an hour. An average turnaround time was 40 minutes. When one H917 was turned off, the total turn around time rose to 2 hours with an average of one hour. Therefore the throughput under normal operation was 248 samples per hour with an average time for 32 minutes. Limited operation with one H917 turned off caused a shift in turnaround time of 133 samples/hour. When the system was put in real operation after all the testing they realized that turnaround time rose to as high as 3 hours for some samples. This rise was due to increases in pre-analytical time. Similarly, serum creatinine times were measured and they found that a significant number were reported in 2-3 hours due to pre-analytical variability. Thus, overall, they showed an overall improvement in turnaround time.

The disadvantages of CLAS (and any unidirectional TLA) are that the reruns have to be brought back to the beginning of the system and get in the queue with the latest specimens. Reagent management is demanding since the system uses reagents rapidly. Technical training is rather difficult for the system, so laboratories should train specialty operators. Host communication is a significant challenge for any laboratory automation system. It took almost two months to establish the connection since their LIS was only capable of handling 30 requests at a time.

Karl Lackner
Clinical Hospital of the University of Regensburg, Germany

The University of Regensburg hospital is a 900-bed hospital with 54 technicians in the laboratory. These 54 technologists perform a wide range of specialty tests so they wanted to shift technologists from routine testing to esoteric testing. They also wanted to decrease the turnaround time for a majority of their tests. They test about 2500-3000 tests per day with 40% priority (5% super STAT, 40% less than 1 hr, 55% less than 2 hrs) and 60% routine. Approximately 10% do not have any priority so they can be shifted to the next days work. They selected the Bayer LabCell laboratory automation system that includes a process controller, sorter and loading/storage device. However, the centrifugation and aliquotting device is not yet completed. The system was set up with an immuno 1, 2 Advia 120s, and two Advia 1650 chemistry systems.

Samples arrive in the laboratory using via a telelift system. The samples are bar coded in the wards so they can be quickly loaded on the conveyor system. Currently, sample data is bulk downloaded to the process controller. This is dynamic download is preferable to the query mode because it does not slow down the LIS processor. However, one looses the minute-to-minute control of specimen analysis and disposition. Super stats are added by hand since the system is just not fast enough to handle them. As long as a specimen is in the system somewhere, then it can be retrieved for reanalysis.

Dr. John Souverijn
University of Leiden, The Netherlands

The University of Leiden was the first hospital in Europe to install a total laboratory automation system. Their hospital consists of 870 beds with 23 thousand inpatients per year and 227 thousand outpatients. They analyze 1300 samples per day consisting of 630 clotted blood, 180 urines, 460 whole blood specimens (60 analyzed after centrifugation) and 30 send out specimens. Therefore they analyze over 10,000 samples per day.

The CLAS that they purchased will centrifuge, decap, sort, recap, and stock. They have installed 2 Hitachi 747s and one Hitachi 911 analyzer. They developed a Megaserver computer that interfaced between their LIS (Molis and Labzis) and to their Main CLAS Controller. They removed their Molis system and connected the Labzis directly to their Megaserver. This streamlined the computer operation for the system.

Non-standard specimens (e.g. small samples) are poured into a cup that is placed into the top of a regular test tube. 60 specimens put through the system in 50 minutes. If you add another 60 samples for a total of 12 minutes then you get the results in 70 minutes. It is roughly 60 samples in 60 minutes. The delays beyond these numbers are due to loading the system, deciding on what to do with repeats, validating the results, replenishing short samples, removing clots, addressing clerical errors, and replenishing reagents. Stat tests can be placed in front of 60 samples or bypass the centrifuge and put

them later in the system. The last option is to put the samples directly into the analyzer. However, this embodiment of the CLAS does not make this an easy task. The overall sample flow demonstrated that all specimens can be analyzed in less than two hours. During peak demand, only 10% of the specimens are completed in less than one hour. The slowest part of the system is the sampling at the 911 analyzer since it takes 6-9 seconds for each operation. Other bottlenecks are located in the specimen transportation system.

They have not calculated payback on the system. However, they have been able to reduce the number of technologists by 4 in the routine processing area of the laboratory. They feel that the CLAS provides many of the improvements that were anticipated when they purchased the system.

Dr. Roger Ekins
University College London, UK
Microarray Technologies: Present Applications and Future Possibilities

Dr. Ekins indicated that he has been involved in the development of immunoassay since the early 1950s. He developed a radioimmunoassay for thyroxin about the time that Yallow developed the immunoassay for insulin for which she received the Nobel Prize. The slope of the dose response curve as well as the sensitivity of the measurement determines the sensitivity of a system. The curves of B/F vs antibody concentration shows that the slope of the line become shallower with decreasing antibody concentration. This apparently seems to yield lower sensitivity, however this is a fallacy. It is important to measure the fractional occupancy of binding sites. If you measure the filled sites you are using a non-competitive system. If you measure the antigen then you are non-competitive and this is indeed the more sensitive method. For example if you plot the log of molecules/mL vs log Kab on the x axis you can demonstrate that you can measure 1000 molecules. Radioactivity will not get down this far since 125I yields 1 event per/sec/7.5 E6 labeled molecules. You need a new label. Fluorescent labels have the highest specific activity. Fluorescent molecules give many events per molecule.

An immunoassay developed by Boehringer Mannheim before their acquisition by Roche called Microspot was designed to label the binding ab and use a labeled secondary antibody. They found that an affinity constant of $K = 10^{10}$ to 10^{12} L/M for the antibody will give you sensitivities to 10^3 molecules. The diameter of the spot should be as small as possible in order to reduce background and increase the sensitivity.

Dr. Gill Webb
BioMerieux
DNA Chips for Mycobacteria: Identification and resistance detection

Microbiology labs are accustomed to the 2-4 days necessary to culture bacteria for their identification by sight or chemical methods. Molecular diagnostics represents a more elegant and potentially less expensive method for the identification of bacteria. Molecular methods are ideal where specimen preparation is difficult or the time between diagnosis and treatment is critical. Micobacterium tuberculosis identification can take up to two weeks under conventional methods. Molecular methods can reduce this time to a matter of hours. DNA chip technology from Affimetrix can be useful for tuberculosis diagnosis. Antisense to 16s ribosomal RNA sequences in mycobacterium tuberculosis were placed on the Affimetrix chip. The rpoB and katG gene were also studied since they have been shown to be the basis for resistance to drugs. These chips showed a high correlation with disease in the patients studied. Resistance was tested on 16 samples. A fully automated system is in development with Gen-Probe, Affimetrix, and bioMerieux for the use for virus and other pathogenic organisms.

Kevin Hazen, Ph.D
The University of Virginia, Charlottesville, Virginia, USA
Overview of Automation of Microbiology

There is a general increase in the number of organisms that cause disease in the

population. Simultaneously, there is an increase in resistance to antibiotics. Thus more esoteric and broader testing will be required in the near future. Dr. Hazen described the motivation and the many steps required for automation of the clinical microbiology laboratory. A number of vendors have automated various aspects of the steps of growing and identifying organisms. Blood culture instruments have existed for over several years such as the BacTec 500, and many laboratories are using them with great success. Spiral Biotec has produced a system for streaking agar plates. The Becton Dickinson (Sparks, Maryland, USA) has released the Probe TecET system that is a DNA based system.

Dr. Hazen provided us a general overview of this rapidly expanding and exciting field.

Some images from the conference