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New tools for laboratory design and management

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The clinical laboratory is changing from a place of activity based on sample analysis to an in vitro diagnostic network. To convince our team, partners, and administrators, we need new comprehensive tools to define a strategy with limited risk of failure or conflicts. Specific quality goals should be established before choosing automated tools for sample handling, analytical systems, laboratory information systems, communication systems, or advanced technologies. A system approach maps and simplifies the process, based more on a functional study than on classical disciplines. A customer–supplier approach establishes the requirements between partners either inside or outside the laboratory. The quality system must be a management tool, linking samples, tasks, information, and documents. Quantitative simulation modeling explores different automation alternatives and their impact on laboratory workflow. Finally, integration of results in interactive semirealistic simulation tools for laboratory design or reengineering can be used as communications tools to involve laboratory professionals in the change of their practice.

The clinical laboratory is changing from a place of activity based on sample analysis to an in vitro diagnostic network. This evolution is due to technological advances, a cost containment policy, and the implementation of systemic approach methods for Total Quality Management (TQM)[1] *[1]*. To face this evolution, the design of laboratories and the work of laboratory professionals must change rapidly. Technological tools are available in all the activities of the clinical laboratory, but we also need new management tools, not instruments but new methods and approaches used to convince our team, partners, and administrators to define a strategy with limited risk of failure or conflicts by crossing the frontiers between jobs and disciplines. We propose here the synthesis of our European experience in laboratory engineering. Our methods were applied to various private or hospital laboratories of various sizes, and in a specialized laboratory for clinical research in the pharmaceutical industry.

from sample analysis to in vitro diagnostic (ivd) service network

Traditionally, clinical laboratory activity could be defined as a qualitative or quantitative determination of an analyte or a cell in a patient sample; analytical systems, data processing, quality control, and good know-how were necessary to perform sample analysis. Nowadays, all the steps from sample collection to the reporting of the test results to the practitioner and the patient are included in quality assurance. These steps can be presented as a quality loop, presented on Fig. 1: The patient sample must be collected in the right container inside or outside the laboratory, according to the doctor's prescription and according to any physiological variations or drug interferences. Samples must then be transported to the laboratory without damage, avoiding mechanical, thermal, or delay problems. By accepting one sample, the clinical laboratory assumes that this sample is identical to the one collected from the patient. The clinical laboratory produces validated results, and passes them on with a minimal delay to the prescribing doctor and patient with some eventual service assistance in the interpretation of the results.

This is particularly relevant as many laboratories are merging to face cost containment, thus amplifying sample handling, automation, and information processing. This enlargement of the responsibility of the clinical laboratory induces the reorganization of the clinical laboratory process, as is the case in many other activities.

strategy to reengineer laboratory process

Considering robotic or conveyor belt technologies that were transferred from manufacturing processes to IVD activities, often discussed as the future of the clinical laboratory in Japan or in the US, we will make some comments and develop our European approach.

In industry, manufacturing processes are often assem-

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[1] Nonstandard abbreviations: TQM, Total Quality Management; IVD, in vitro diagnostics; and LIS, laboratory information systems.

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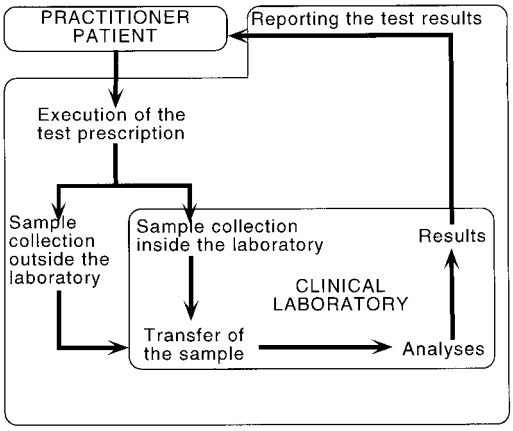

Fig. 1. Quality loop of clinical laboratory activities.

bly line processes, starting from raw materials to get a final product after various operating steps. The clinical laboratory process includes different samples from one patient, and different levels of investigations involving various automated or manual methods, used in a deductive reasoning: It is a disassembly process *[2]*.

If we consider a large clinical laboratory covering all disciplines and most analyte determinations, we propose the concept of Technopole: a global structure including the management of various analytical systems and know-hows, with various logistical functions to support the IVD network.

Considering the management of the analytical systems and know-hows, presented on Fig. 2, after sample sorting and preparation, we have a first level of investigation performed either by automated systems, which are often closed or dedicated to a group of assays (biochemistry profiles, cell counting, coagulation testing, immunoassays, etc.), or by methods with a low level of automation as in bacteriology or parasitology. We emphasize that so-called "full automated laboratories" *[3]* cover only the first part of this level of investigation.

Because of technological advances allowing the run of

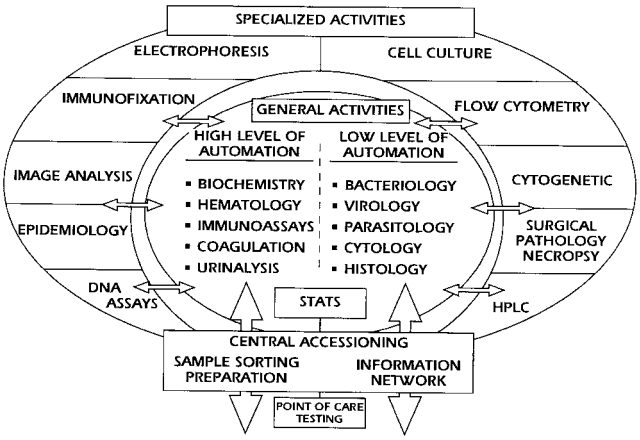

Fig. 2. Management of analytical tools and know-how in the IVD network.

stat samples on the same analytical systems as nonurgent samples, stat runs performed in the core laboratory are considered more as a personalized "fast testing service" than as a dedicated workstation. Point-of-care testing and decentralized stat labs are subcontractors of the core laboratory, their activity is under the control of the quality-assurance department of the laboratory, and they are connected to the information network.

At the second level, analyses are performed by various disciplines in specialized workcells including either some sophisticated equipment (flow cytometry; separative methods such as chromatography, electrophoresis, or image analysis) or activities requiring a controlled environment such as cell culture or DNA assays. Note that most of these specialized activities may be used by research and development activities in biotechnologies, bioproduction activities such as cell or gene therapy.

These analytical activities must be supported by logistical and engineering activities, presented in Fig. 3. In addition to secretaryship, documentation unit, purchasing office, washing unit, reagent preparation, and data processing, we emphasize some new activities:

1) Sample bank: Owing to various reasons like regulations, long-term monitoring of diseases, caution against medicolegal problems, and validation of new analytical methods, we store an increasing amount of samples. This storage in classical freezers is expensive, space consuming, and jeopardizes the quality of the samples in case of breakdown. We consider that a computerized sample bank with straws stored in liquid nitrogen will become a logistical activity shared by all the laboratories of the technical platform.

2) Quality assurance, as an independent and multidisciplinary department, concerns all the steps of the quality loop from sample collection to results reporting. In addition to the implementation of quality documents, the quality-assurance department is also responsible for the metrological aspects of the laboratory (control of pipettes, weighing scales, spectrophotometers, etc.).

3) Evaluation: New technologies must be evaluated and implemented with standardized protocols to cover technical, medical, and economical aspects in unbiased comparative evaluations involving laboratory technicians. Technical aspects include comparisons between configurations (analytical instruments + computers + environment). The required level of performance is defined in the specifications and checked when the new technology is implemented.

4) Management and strategy to build partnerships with external partners in industry, other laboratories, research and development programs, etc.

Logistical activities are performed by a part of the laboratory personnel obtained from the productivity benefits of a global management and automation programs of all the laboratories. They do not require high annual budgets, but save much money by common decisions based on a common methodology. These new activities

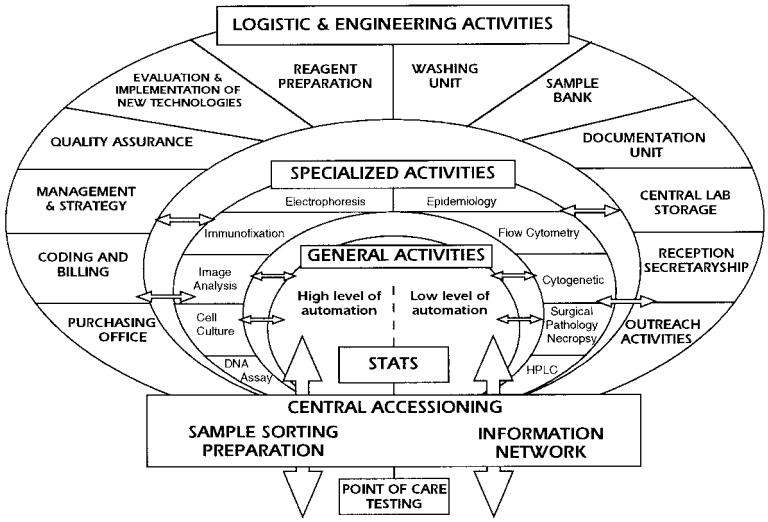

Fig. 3. Logistical and engineering activities in the IVD network.

imply a complete change of methods and work environment for concerned laboratory personnel.

INTEGRATION OF TECHNOLOGIES

In 1987, Burtis reviewed the evolution from analytical instruments to analytical systems *[4]*, and our profession succeeded in adapting new technologies to daily work because a good basis of standardization in analytical methods was already existing, directed towards the quality of the results.

Nearly 10 years later, the same author described in a review *[5]* how the technological revolution affects the way clinical laboratories are organized, staffed, equipped, and operated. The only way to adapt ourselves to this new challenge is to be able to rethink our profession with a global quality-assurance approach issued from our analytical know-how, applied to any technology used in the IVD network, and directed towards the patient.

Automated sample handling. Specific quality goals should be established between laboratory professionals before choosing automated systems: avoid mistakes requiring a new sample collection; reduce sample volume, secure identification and tracking all along the process, preservation; decrease sample handling, locate and contain biohazard *[6]*; decrease human labor, number of tubes, and paperwork.

Then, these quality goals may be applied to various steps of sample handling: sample transportation, centrifugation, detection, and aliquoting: (*a*) Sample transportation devices: controlled access to the samples, protection against breakage and leakage, separation between samples and documents, easy decontamination, thermal stability, tracking and traceability, time limit; (*b*) automated centrifuges: traceability (rotor, speed, duration, and temperature), biosafety (isolated area, closed covers for centrifugation baskets to avoid aerosols), automated detection of a possible breakage of tubes before further robotic handling, easy decontamination *[7]*; (*c*) sample detection: volume, clots, hyperlipemia, hemolysis, and hyperbilirubinemia; (*d*) sample aliquoting: ability to use different sizes of secondary tubes, checking of identification before aliquoting, no carryover by tips or fluidic device, compatibility with sample storage.

Automated analytical systems. (*a*) Sample loading: final control relating to the status of the sample to be analyzed in a specific workstation (volume, clots, hyperlipemia, hemolysis, and hyperbilirubinemia), a possible false identification, and medical and biological history of the patient. We prefer to keep automated sample handling under human control, as is the case in automated workstations, so-called islands of automation. (*b*) TQM of the workstation, including the instrument (operating procedures and associated records) and environment (stock of reagents and controls, room temperature and humidity).

Laboratory information systems (LIS). Most of these systems were designed mainly to manage patient identification and data collection from analytical systems; the next generation should integrate quality documents and edit quality records. Results should be presented in an attractive synthetic report enriched with the added value of a collective validation by a network of experts of the clinical laboratory, reinforced by using expert systems *[8]*.

Communication systems. The combination of digital and communication technologies has resulted in the possibility of interconnecting computers at the same or remote site *[5]*. These networks are very useful to get scientific information and exchange it with our colleagues around the world. Concerning information about the patients, it is now very easy to send instantaneously a complete file of results anywhere, but we must consider different questions carefully: (*a*) Reliability: Are we sure that the results were received? At the right place? (*b*) Confidentiality: Is

the access to transmitted results limited to the authorized person(s)? (*c*) Ethics: What kind of information should we transmit by a given communication system? In which cases should we transmit a letter or prefer a direct contact with the patient?

Advanced technologies. Rapid advances in measurement technologies *[5]* are always fascinating for the clinical chemist, but the transfer from research and development to IVD activities requires evaluation and standardization:

1) Evaluation: In the past, when we moved from chemical to enzymatic determinations or from flame photometry to ion-selective electrodes, groups of clinical chemists designed adapted evaluation protocols that allowed the organization of comparative evaluations to get a consensus on technical specifications *[9]*. Today, we have to design evaluation protocols for robots applied to sample handling, using the quality goals and requirements of our profession.

2) Metrology: From various industries, we learned that the good reliability of a manufacturing process is greatly helped by a perfect control and traceability of environmental factors such as temperature and humidity. In clinical chemistry, the more we are able to reach a low detection limit in analyte determination, the more environmental factors will interfere with the results: temperature and humidity in laboratories, and also cooling or warming devices, electromagnetic fields, atmospheric pollution, and carryover by laboratory personnel, dust, etc. Besides scientific upgrading, we will be able to transfer new technologies from research and development to our daily work only if we control the environment and flows in our laboratories. Modern standardization will include classical analytical factors and environmental factors.

change requirements and proposals to achieve the change

Integration of the analytical activities of the clinical laboratory in a global IVD network implies many changes:

1) The clinical laboratory is no more an entity in itself, and we must cross the frontiers between jobs, upgrade our knowledge, or find new skilled people. We propose the customer–supplier approach.

2) Computers are now completely integrated in our daily work for information processing. Samples are more transported than in the past, sometimes on long distances when collected externally, but also inside the laboratory (internal organization frequently includes different analytical sites). We must find a way to link samples (objects including a patient specimen, a container with a cap, and an identification label), information (sample status at different steps of sample processing, clinical and administrative information, results), and the tasks to be performed with associated documents and human added value. We will propose a method to manage and use the quality system.

2) Automation: To answer financial restraint, the laboratory manager must be sure of his decision: Quantitative simulations allow exploration of different alternatives and comparison of their impact on laboratory workflow. We will review some commercialized tools in this domain.

3) To help the integration of new practices and of existing and future new technologies under the frame of TQM, we have to redesign the laboratory with a flexible architecture optimizing movements of people, samples, and consumables. We developed an interactive semirealistic simulation approach.

customer–supplier approach

The modern relationship between clinical laboratory professionals and industry is not limited to a negotiation about prices but includes many other aspects like the quality and performance of the products according to specific needs, delivery respecting given days and hours, maintenance of instruments, etc. This relationship may be summarized by Fig. 4a: The supplier (with a know-how) and the customer (with needs) must establish a dialogue to specify the requirements of both sides in a written contract.

We extended this approach to the internal or external relations of the clinical laboratory because it allows a discussion between people of different professional cultures in a common language: A first example is sample collection (Fig. 4b): Because the quality of the results depends on the sample collection and transport, the sample collector, the "supplier" with a know-how in sample collection and in direct contact with the patient, must discuss with the clinical laboratory scientist, the "customer" with needs concerning sample integrity and correct identification, ways to fix the requirements of sample collection, how to transmit information, and sample transportation. A second example is the negotiation between the clinical laboratory, the "supplier" of results, and the medical practitioner, the "customer" with needs corresponding to a specific clinical activity (Fig. 4c). They must agree with each other to establish some objective criteria for results validation, some possible assistance in interpretation, acceptable delays, and how to report results.

management and use of the quality system

A quality-assurance system involves the implementation of three levels of quality documents: (*a*) organizational documents (upper level): general procedures; (*b*) operational documents (intermediate level): operating procedures; (*c*) trace documents (lower level): records.

First, the general procedures describe the organization of a sector of activity by answering the general questions of who does what, and eventually where and when. They also answer the question of how in a general way and by referring to some operating procedures. As the general procedures describe an organization, they are organizational documents.

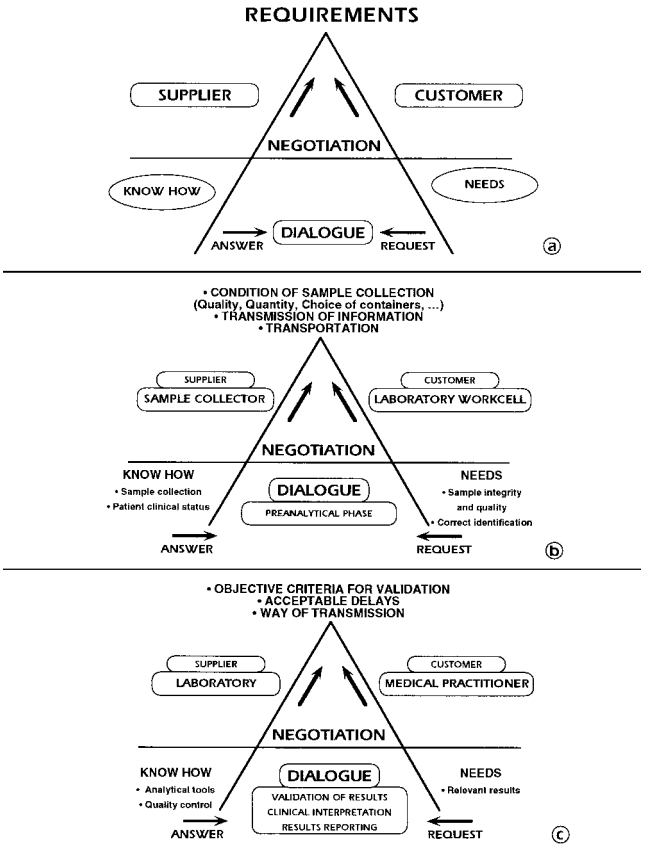

Fig. 4. Customer–supplier relationship in the IVD network: (*a*) general diagram; (*b*) application to sample collection; (*c*) application to results reporting.

The operating procedures are the documents that contain the instructions of work and enable the operator to achieve a given task. For this reason, they must be operational documents and available at the workstation where they are required. The operating procedures sometimes refer to the completion of records that correspond to the last level of quality documents.

The records are the documents that allow the traceability of the operations done by an operator. They include checklists of periodic maintenance completed by the operator, tables for the management of reagent lots, and the results of certain tests such as results of calibrations, quality controls, patient analyses, etc. These documents are the record of what happened on a certain date and constitute the memory of the laboratory as they allow the analysis of the cause of an error or a dysfunction. They may also be used, for instance, to find patient analyses done with a defective reagent lot.

Integration of the quality system in the daily work of the clinical laboratory. The quality system of the clinical laboratory must be more than an answer for the inspection of the laboratory, more than quality documents that are never opened by the end user at the workcell. The quality system must be designed by following the daily work of the laboratory personnel, with different levels of utilization depending on the experience of a given technician or secretary.

During a previous experiment in simulation modeling of the activity of clinical laboratories, we tested various methods and found that the only comprehensive methods for end users were flowcharts or flow diagrams used by Godolphin et al. to describe a process *[10]*. With a maximum of five symbols, we were able to describe all the steps of any processes in all disciplines.

Attached to this leading flowchart, which can be fixed on the cover of the log book of a workcell, we present the detailed documents that are necessary for implementing a given step of the process, and the traceability records. These documents are contained inside the log book.

Example of quality documents concerning a workcell around an automated analytical system. These documents are presented in Fig. 5: On the left, the work sequence emphasizes the steps where decisions must be taken and eventually recorded by the operator. In the middle, corresponding operating procedures explain the technical tasks but also try to anticipate the problems and the solutions for these problems; some operating procedures are general (biosafety, results reporting, waste disposal), but most of them are specific to the workcell. On the right are the records that certify that the daily work was performed in accordance with the quality system. By using this method, we found that it was possible to link information and samples to the tasks to be performed with a fast access to different levels of operating procedures and associated records, depending on the events and the skill of the operator. This approach is also a good basis to study the added value of the laboratory personnel before initiating an automation project.

Nowadays, commercialized LIS are able to handle only quality-control results but not quality-assurance documents. Quality-assurance documents can be managed electronically by using custom databases or hypertext documents.

QUANTITATIVE SIMULATION TOOLS

Clinical laboratory management requires a system approach including many aspects other than the analysis: total turnaround time from sample collection to issuing the result to the clinician, cost containment, biosafety, and regulations.

More than analytical speed, sample handling is one of the major problems in clinical laboratories, involving many manual processing steps. To reengineer sample handling, different steps should be followed: map the process, measure the performance, model, show the results through simulation tools, simplify and redesign, get the consensus *[10]*.

To answer financial restraint, the laboratory manager must be sure of his decision: Quantitative simulation tools allow exploration of different alternatives in laboratory

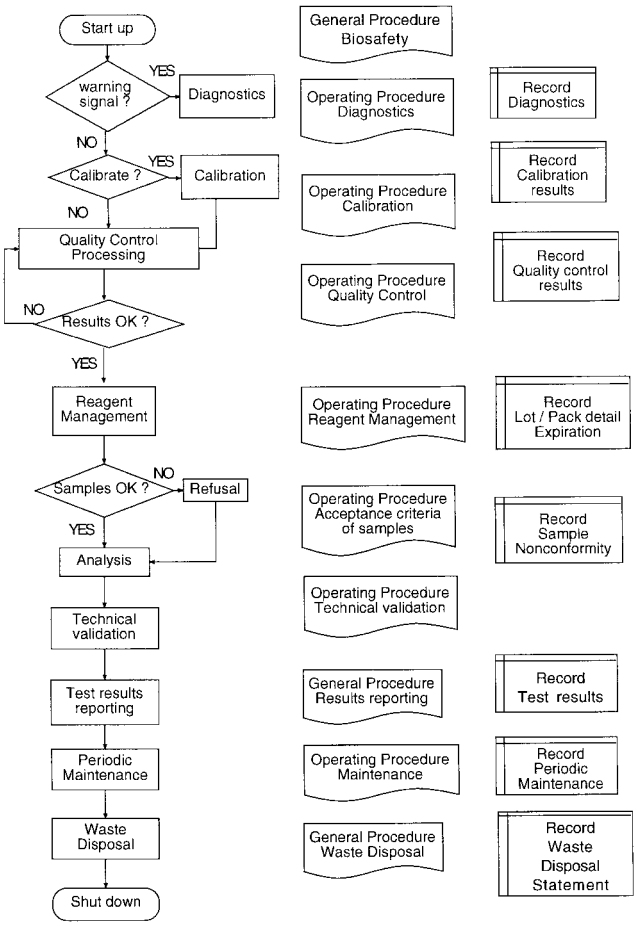

Fig. 5. Associated operating procedures and records at the workcell.

automation and compare their impact on laboratory workflow. *[11, 12]*. These tools are computation tools, useful to determine if one or two analytical systems are needed, the number of operators at different times of the day, the impact of a modification, or a breakdown at one step of the overall process. The results of these simulations are often given in Tables; only some expensive softwares like Witness (AT&T) or Siman (Systems Modeling) show real-time animation with moving shapes symbolizing the process; they cannot be used to communicate with laboratory personnel about a new organization of the laboratory.

INTERACTIVE SEMIREALISTIC SIMULATION APPROACH

Modeling and computing laboratory workflow is only half of the way. As nobody likes change and everybody is afraid of being out of work, the personnel must be involved in laboratory engineering.

To improve biosafety, the laboratory should be organized and designed in a way that makes the implementation of biosafety and waste management operating procedures by laboratory personnel easy and fast, thus improving their overall productivity.

We developed in our laboratory an interactive semirealistic simulation approach to get feedback from personnel and make them feel confident in the project.

The first step is to distinguish inside the laboratory between different areas with various levels of eventual biohazard and fix the rules according to the specific practice of the laboratory team. Then we prepared a first schematic drawing of the laboratory with the different areas on the computer, and we simulated the flows. During a meeting with the team, on request, we can show and animate the flows of different categories of people (technicians, administrative staff, manufacturers, patients), samples (collected in or outside the laboratory), waste, and consumables. We can combine the different flows, demonstrate unacceptable overlapping in the existing organization, and discuss improvements with the laboratory team.

In Fig. 6 we present an example concerning the flow of people in a project of a 500 m^2 laboratory with two floors. The first draft is presented in Fig. 6a: Reception, waiting room, and sample collection rooms for outpatients are located on the upper floor. Secretariat, laboratories, changing rooms, restroom, and waste storage are located downstairs. Biohazardous zones are colored in gray.

One can click on any of the three icons: people, samples, and consumables. For our example, we clicked on people. At the base of the screen (Fig. 6b), different categories of people are presented with different colors (technicians, red; administration, yellow; patients, purple; messengers, blue; suppliers, green). Each category may be activated separately by clicking on the corresponding icon. On the selected screen presented here, all the flows are figured in colored lines corresponding to the different categories, and shapes of technicians (red) and administrative personnel (yellow) are moving along red and yellow lines.

On this screen, it is obvious that, upstairs, patients and messengers bringing samples from outpatients to the laboratory are mixed at the reception; downstairs, everybody is circulating through the same corridor, and administrative people have to cross a biohazardous zone.

From a first meeting, we changed the design of the laboratory to get the draft presented in Fig. 6c, including also improvements in the flow of samples and consumables. Concerning the people, messengers enter downstairs and deliver the samples to a technical reception and sorting area; the biohazardous zone is completely separated from the administrative area.

The advantage of this method is the involvement of laboratory personnel in a new practice: The project becomes *their* project. Such a simulation also helps to improve the dialogue with decision makers and architects, by justifying specific requests of the laboratory.

CONCLUSION

To change from a place of activity based on sample analysis to an in vitro diagnostic network, the laboratory

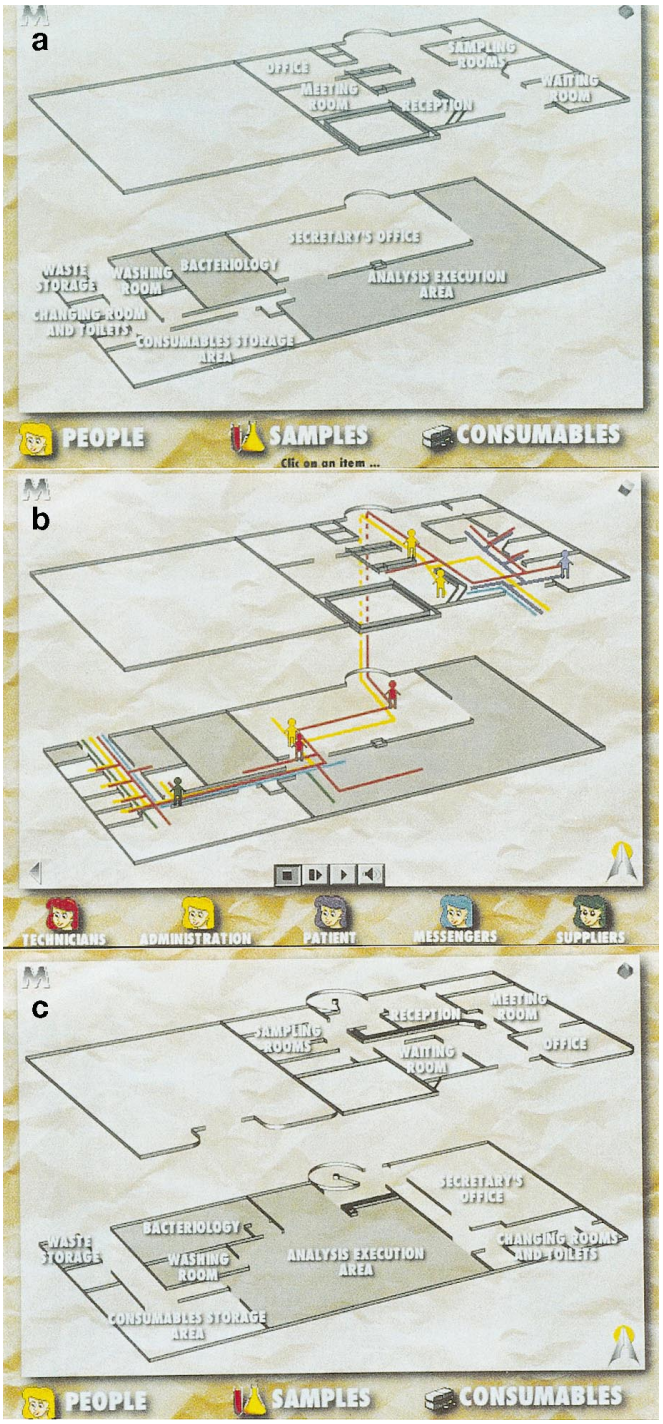

Fig. 6. Interactive semirealistic simulation for laboratory design: (*a*) first draft, main screen; (*b*) first draft, "people" flow; (*c*) revised draft.

process must be reengineered in a system approach, including analytical systems, know-how, and logistical functions. Various levels of investigations, from highly automated systems to manual specialized methods, should be used in deductive reasoning to solve the individual enigma of a patient case. New technologies, including communication technologies, should be evaluated from a clinical laboratory point of view, and specifications should be established. The IVD network implies a network of expertises and the ability to set up feasible requirements with a customer–supplier approach. The quality system must be the frame of the management, and also a practical assistance to the daily work. To improve laboratory organization and productivity, we need computation tools to make the good decisions, but we also need multimedia interactive methods to involve the team in their changing practice.

The question today for laboratory professionals is, "To be or not to be in the future of the IVD network." The only way to adapt ourselves is to use new management methods to reengineer our profession and select emerging technologies with a global quality-assurance approach issued from our analytical know-how, directed towards the patient.

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