



**REPORT ON AN INFORMAL CONSULTATION  
ON QUALITY ASSURANCE OF SOLID PHASE CHEMISTRY TESTS**

Geneva, 10-11 October 1994

**1. INTRODUCTION**

The term "Solid phase chemistry tests" comprises a variety of analytical test systems that are used by health laboratories for the diagnosis and monitoring of diseases. The term indicates that the reagents necessary for an analysis are bound to a solid phase ("carrier"), thus attributing specific properties to the material that have consequences on the mode of utilization of the test in the laboratory, the organization of laboratory work, their application in other environments and the training of personnel using this technology.

Solid phase test systems are not a new technology. In fact such test systems were already mentioned in Roman literature, and today they have found increasing interest worldwide because of the simplicity in their use.

The research and development of solid phase chemistry tests is rapidly expanding and simple test systems were developed that opened ways for better epidemiological surveillance and patient monitoring by facilitating laboratory investigations in the field and nearer to the patient.

The design of solid phase chemistry tests varies from very simple devices that are even provided to lay people for self-diagnosis and self-monitoring, to more sophisticated equipment that is used by hospital laboratories.

The simplicity of use makes solid phase chemistry tests an attractive tool for laboratory investigations. However, results of solid phase chemistry tests may differ from results obtained by classical procedures. The differences observed have led to concern as to whether solid phase chemistry tests can be recommended for use by laboratories in developing countries or by health professionals who have little experience in quality control of laboratory testing.

An informal consultation was held at WHO headquarters, Geneva, 10-11 October 1994, to assess the development of solid phase chemistry test systems and to provide guidance on the quality control for investigations using this technology. The consultation was chaired by Dr A. Vassault, Hôpital Necker, Paris, France assisted by Professor W. Appel, St. Vincentius-Krankenhaus, Karlsruhe, Germany as rapporteur.

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## 2. SITUATION ANALYSIS

The worldwide use of solid phase chemistry tests is rapidly expanding. Information provided by companies shows that the placements of solid phase analyzer systems have doubled between 1991 and 1993. Although the majority of instruments were placed in laboratories of developed countries, in relative terms in developing countries the placement of such instruments is considerably higher than that of conventional instruments. In fact some commercially available solid phase chemistry systems are mainly provided to laboratories in developing countries. Altogether about 100 000 solid phase chemistry analysers are distributed all over the world, about 20% of which are located in developing countries, whereas less than 10% of the total expenditure for laboratory devices and consumables worldwide is spent in developing countries, thus indicating that this technology attracts considerable attention in the third world.

Over half a million portable glucose meters for measurement near to the patient and for self-testing were distributed in 1992 worldwide and the total figure for such instruments being used is estimated to be more than three million. The majority of instruments were distributed to the peripheral health care level, i.e., to physicians and veterinarians, pharmacies and lay people. The number of instruments distributed may vary considerably from country to country and this is for various reasons:

1. The presence or absence of a reimbursement system for laboratory services. In countries that have a well developed health insurance system that covers the expenses for laboratory analysis, testing by others than medical professionals is not well appreciated.
2. The prevalence of certain diseases that make the use of periodical laboratory investigations pertinent for controlling and monitoring patients.
3. The country's infrastructure and economical development. Laboratories in countries in Latin America, the Western Pacific and Eastern Mediterranean regions are more attracted by solid phase chemistry test systems.

In Iran solid phase chemistry tests are used for urine analysis, blood glucose, microalbumin and serum cholesterol. The test systems for urine are both imported and locally produced. The tests are evaluated by the National Reference Laboratory. If a test system does not fulfil the requirements for testing a specified analyte, the whole lot is rejected and a recommendation is issued to all laboratories in the country not to use the reagents of the lot. It has happened that imported test strips had to be rejected although the strips were approved by the governmental administration of the country where the reagent was produced. Presently discussions are held between manufacturers, clinicians and the national authorities to develop guidelines for licensing.

Commercially available control materials were used in Iran for quality control. Unfortunately, their reference ranges for analytes as indicated by the manufacturers were too broad to be practical for quality control both for wet chemistry and solid phase chemistry tests.

In Latin America since their introduction in 1975, solid phase chemistry test systems for urine analysis have replaced traditional methods. Solid phase chemistry tests for blood testing were introduced

in 1978 for bedside testing ("near to the patient"). Recently more sophisticated solid phase test systems for drug testing were developed. For these tests South America has the greatest demand worldwide.

In Mexico, more sophisticated solid phase chemistry test systems were introduced in 1993. They are receiving increasing attention because of the simplicity in their use, which compensates for their costs. Differences of results were found between different solid phase chemistry test systems. The main problem in the use of both simple and more sophisticated solid phase chemistry test systems is related to quality control. Training of laboratory personnel using this technology was found to be a key element. Training should be provided by the manufacturer when the equipment is installed. After the installation, laboratory managers should be responsible for training to insure the long term effect of the education.

The Western Pacific region comprises a number of countries with remarkable differences in size, population, social structure and state of development.

Solid phase chemistry test systems are widely used in the Region by different levels of laboratories, but particularly by satellite laboratories, used all over the region, for both simple and more sophisticated systems. Often solid phase chemistry tests are used by untrained personnel, who consequently have problems with calibration, quality control and maintenance. These problems are found both in less developed and highly developed countries of the region. Usually quality control is not done, and a universally applicable control reagent does not exist. A network of "mentor laboratories" has been set up to train people using solid phase chemistry tests and to support peripheral laboratories and individual users through the provision of technical information.

In France the implementation of a legal decision in 1978 mandates the participation of each registered health laboratory in a quality assurance scheme. There are 4600 laboratories (85% private and 15% public health laboratories) in the national quality assurance scheme.

Eight percent of laboratories are using more sophisticated solid phase chemistry systems in France, and this number is continuously increasing. Portable glucometers are used to a large extent in hospitals and out patient services. The responsibility for quality control remains with the laboratory and laboratory investigations using devices for self-testing are not reimbursed by the health insurance. International reference materials and reference procedures are considered as most important and are the main tool for the evaluation of solid phase chemistry tests and fully automated laboratory diagnostic systems. A recent survey revealed that more than 50% of the self-testing devices are providing results that are out of the acceptable range when compared with standard laboratory methods.

Programmes for laboratory external quality assessment were established at national and regional level. In the south-west of France a telecommunication dialogue system was set up in 1985, where each participant can enter the results of weekly blind measurement from his/her own laboratory and call up the results of other participants in the survey. He/she can also compare his/her own results with the reference values. Since 1989 the dialogue system was expanded to more sophisticated on-line solid phase chemistry systems. The French south-west on-line external quality assessment scheme makes it possible to assess the performance of a laboratory in real time, whereas other external quality assessment schemes only allow for a retrospective analysis.

In Germany, laboratory proficiency surveillance has existed for many years but it was not until 1988 that regulatory measures made it obligatory for all laboratories. The terms of reference apply to liquid and solid phase chemistry test systems and include internal quality control and proficiency surveys. The proficiency surveys include 47 analytes in liquid phase and 30 analytes in solid phase. The laboratories are obliged to keep their quality control records at least for five years. Special legislation concerning proficiency surveillance for practitioners has been passed. At present this is being revised and simplified.

### **3. ASSESSMENT OF TECHNOLOGY**

Disposable non-instrumental solid phase chemistry systems, e.g., urine test strips have been used for many years. The dip stick analysis developed rapidly after AMES Company introduced these sticks for urine analysis in 1944. In the meantime this technology has received considerable attention outside the medical laboratory and a rapidly expanding market has included private practitioners, centres for preventive medicine, supermarkets and individual citizens. In light of the increasing importance of such tests in health care, the European Union (EU) is developing a recommendation for "in vitro devices for self-testing" in the EU directive "in vitro diagnostic medical devices".

The preparation and use of monoclonal antibodies and non-radioactive markers, such as coloured particles and enzymes, the activity of which can be measured by colorimetry has initiated the development of simple immunoassays in a test strip format. These tests strips can produce quantitative and qualitative results. The application of antibody coated particles, such as latex, carbon and colloidal gold that migrate on a membrane and concentrate in a region of the strip where another antibody was permanently fixed, has led to the development of simple discardable test systems based on the principle of immuno-chromatography. Such tests were developed for a broad range of analytes including human gonadotropic hormone, luteinizing hormone, occult blood, microalbumin, myoglobin, drugs, antigens of infectious agents, such as chlamydia, streptococci, hepatitis B virus, salmonellae and antibodies against rubella, heliobacter, mycobacterium tuberculosis and HIV.

More sophisticated solid phase chemistry test systems are mainly used for quantitative analysis based on a principle using multilayers on the solid phase support. In such a device the chemical reagents are placed close to each other but still kept separate on the solid phase support. This arrangement requires a suitable matrix, in which the reagents can be kept in a dry form for stabilization and where they are immediately reconstituted for diffusion after the specimen for investigation has been added.

### **4. QUALITY CONTROL AND COST EFFECTIVENESS**

Conventional automated laboratory analyzers, and particularly those of the older generation, are susceptible to drifting while being used for measurement. This forces the laboratory to frequently recalibrate the system. Solid phase chemistry systems do not need such frequent recalibration. Thus, the precision of measurement with solid phase chemistry systems was found to be considerably improved. Calibration is only required when a new lot of reagent is used for measurement. The accuracy of measurement must be evaluated when an instrument is installed and then periodically during proficiency surveillance cycles.

An analysis of the effectiveness of solid phase chemistry tests is not easy. At first glance the costs for reagents seem to exceed the costs for conventional test systems. However, a more realistic estimation ought to take into account all factors that contribute to the expenses of laboratory investigation, such as the qualification of the personnel making such investigations, the requirements for sampling and specimen transport, the costs for calibrators and quality control of equipment, the time for investigation, and the availability of the test. The costs for calibration and quality control were found to be about 1% of total costs for solid phase chemistry reagents, whereas they are 10% to 15% for reagents used with conventional systems.

## 5. FUTURE TRENDS

In the view of the participants, solid phase chemistry testing is a major area of development which will considerably influence the work and organization of laboratory services and particularly small laboratories. More solid phase chemistry test systems will be available for a variety of immunological tests and also for DNA analysis based on the amplification technology (such as the polymer chain reaction, PCR). Today, research and development focuses on tests that do not require any instrumentation. These tests may open new ways for the surveillance of communicable diseases and drug monitoring. They are made for health professionals who are not working in the laboratory, and also for lay people. Typically investigations with such devices are simple to make while providing a rapid result. Therefore, the use of such test systems in developing countries in the future should not be underestimated.

## RECOMMENDATIONS

The participants agreed to make the following recommendations:

Users of clinical laboratory tests need to be trained how to make the investigations and to be able to interpret the results properly. Quality assurance of these tests is also important. Solid phase chemistry tests are particularly suitable for use in developing countries where training and education is not easily accomplished. There is therefore a need to reemphasize the principles of quality assurance to remind users of their importance.

1. Industry is encouraged to look into all possibilities of developing solid phase test systems that are affordable and meet medical requirements in developing countries.
2. There is a need for international guidelines on the proper use of solid phase chemistry tests.
3. It is the responsibility of those who provide and diffuse solid phase chemistry tests to train and update the users including non-laboratory professionals on the appropriate use of this technology. Training should be provided not only by manufacturers, but also by laboratory training institutions and other professionals working with this technology.
4. In principle there exist no differences between the quality control of liquid phase and solid phase test systems. Therefore quality assessment of solid phase test systems should be an integral part of External Quality Assessment Schemes.
5. The same quality assurance measures that must be used in a laboratory also apply to other environments.
6. Analytical methods based on solid phase principles should be related to analytical methods of higher metrological order for the determination of analytes in fresh human samples.
7. There is a need for the development of quality control materials suitable for quality assessment of both liquid and solid phase test systems.
8. Humidity may cause special problems for the storage and performance of solid phase chemistry test systems. Therefore strict measures for the control of humidity during storage and utilization are recommended. Manufacturers are encouraged to use adequate protective packaging and provide clear instructions to users about the effect of humidity and the appropriate handling of the reagents.

These recommendations apply equally to devices for use in extra-laboratory situations by non-laboratory personnel.

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