I. INTRODUCTION

A. What is quality control?

"Quality control" is a term used originally in industry to describe a modern method of testing a product, during and after its manufacture, to determine if it confirms to previously established specifications. A certain minimum number of samples from each batch of the products examined and the test results are compared with the official specifications. If these control samples are found to be satisfactory, the whole batch is classified as acceptable; but if they do not meet the specifications, the batch is held for further testing or is rejected (Tonks, 1970).

This industrial method of testing can be applied to any process which is repetitive, and is very useful in analytical laboratories, control the accuracy and precision of analyses which are being carried out regularly and for which specifications have been established. The products are the results from various analytical procedures, and the specifications are the allowable limits of error or the statistical limits. The control samples are specimens similar in nature to the test samples but of known composition, or are accurately prepared pure solutions (similar to standards). These samples are introduced at regular intervals into the general work flow (Bowers, et al., 1967)

This industrial method has been applied to use in clinical chemistry laboratory. The purpose of quality control of analytical testing is to ensure the reliability of each measurement performed on a patient sample. There are two requirements for quality control interpretations (1) the results, which lead to decisions regarding the reliability of the analytical data, and (2) the quality control decisions, which related to the medical purposes for which the analyses are being done (Kaplan and Pesce, 1984).

There is no quality control system that is the best. Each laboratory should determine and use the quality control tools that meet its needs.

B. Essential of quality control in clinical laboratory.

In clinical laboratory, quality control process provides reliable data on the composition of specimens obtained from patients, as an aid to the diagnosis and treatment of disease. As the field of clinical chemistry has developed, there has been a corresponding increase in the number of tests requested per patient. Many hospitals are now performing chemical tests

on almost all admission and there is greater use of the "profile" tests for diagnostic purposes. The net results are that the chemistry laboratories are faced with an ever-increasing workload. As more chemical data are generated there is a greater need for effective quality control program in the laboratory (Tietz, 1987).

Each day appropriate volumes of control samples sufficient for the daily estimations are provided for each technician for each method being run that day. These samples are then analysed by the official methods, being included among the regular specimens near the beginning of each run. They must not be given any special attention or treatment, or be analysed separately from the other specimens. The instrument readings and the results obtained for them must be recorded in the bench books or computers along with the results for the patient's specimens, in the correct sequence as analysed; and also on the appropriate record forms (Tonks, 1970).

The analytical techniques carried out in a clinical laboratory are often complex and even the simpler ones contain many possible sources of error. It cannot be expected that absolute reproducibility or accuracy will ever be attained by any laboratory. It becomes necessary, therefore, to determine if the results of analyses are good enough to meet the needs of the medical practitioners and their patients. Unless the precision and accuracy are known, the physician cannot make full use of the results; and unless a certain standard of performance is realized, "normal values" can have no significance (Tonks, 1970).

During the past few years clinical chemists and pathologists have become increasingly aware of the lack of agreement seen in assays performed by different laboratories. Thus, the data produced in many laboratories are not as accurate and precise as may be desired (Tietz, 1987).

C. Method of quality control in clinical laboratory.

All clinical laboratories require an adequate quality control program. This program must be concerned not only with the control of precision, but also with the selection of proper methods and the assessment of the accuracy of these methods.

Periodically and regularly, control samples having widely divergent concentrations should be analysed in order to test accuracy and precision at high and low levels.

The specifications or control limits ofcourse are very important since they establish the level of quality. They must not be too severe

(resulting in too high proportion of rejected values, some of which may be clinically acceptable), or too lenient (resulting in the acceptance of some values which should have been rejected). The number of specimens analysed in one run may be small (perhaps only one) or very large (perhaps 60 for a manual method or 400 for an automated one). At least one "known" and one "unknown" control sample should be included near the beginning of each run, and if the number of specimens is large, for example greater than 60, at least one of the same control samples should analysed near the end of the run (Tonks, 1970).

Also, as part of a comprehensive quality control program, at least one calibrating standard should be included among every 10 specimens in the run. Even when only ONE unknown specimen is being analysed, a control sample and a calibrating standard should be analysed along with it.

A good quality control system will measure precision, and quickly detect any change in precision. It will also detect a significant loss of accuracy, but cannot, by itself, measure the accuracy of a method. The basic aim must be to have at least 95% of the results conform to the established specifications, that is, have percentage errors less than the allowable limits of error or the control limits of $\pm$ 2 C.V. (coefficient of variation).

In the past 25 years, and particularly in the last decade, several studies of the quality of clinical laboratory work have been conducted. These have indicated that there is a definite need for an improvement in the quality of work performed by clinical laboratories (Tonks, 1970).

There are many reasons for variations in laboratory results and for the occurrence of systematic and random errors such as poor methods (systematic and random errors), inaccurate standards and calibration graphs (systematic errors) impure chemicals and improperly prepared reagents (systematic errors) and individual variations in techniques and occasional mistakes in technique or calculations (random errors), etc.

D. Quality control materials in clinical chemistry laboratory.

Control sample is either compound or solution, etc., which has one or more accurately known characteristics and which is used for the purpose of verifying the accuracy and precision of measurements of these characteristic(s) in unknown similar objects by being treated in the same manner as the unknowns. For example, a serum of known composition

may be used as a control to verify that a certain component is being determined properly in a series of unknown serum samples; the control is analysed in exactly the same manner as the unknown samples and the result obtained for the control is compared with its true known values. It is important, as with the standard but even more so, that the control should be similar in composition and form to the patients' specimens. A control should not be used to calculate the values of the unknown samples, that is, it should not be used as a standard (Tonks, 1970).

The type of quality control material used in the laboratory is based on the laboratory's needs. The majority of decision making, that is, the daily bench-level work of medical technologists, involves the question of whether a particular set of patient analyses is valid. The quality control material is analyzed along with patients' specimens, therefore, large amounts (liters) of control material are need. There are currently several ways in which a laboratory can obtain sufficient quantities of quality control material. These are (1) frozen pooled specimen, (2) lyophilized pool material, and (3) liquid pools.

The cost of control material and the qualities, clarity, stability, and lyophilization error are compared in Table 1 (Kaplan and Pesce, 1984).

The following statements relate to all quality control serum pools. First, all pooled serum material should be free of hepatitis B antigen. In Thailand, HIV infection is highly prevalence, therefore, HIV infected serum should be excluded. Second, all control material requires refrigerator or freezer space for storage of a 1- to 2- year supply. One would prefer to change control lots only once a year, which is the present practice in most laboratories.

Table 1. Comparison of quality control materials.

Criteria	Frozen	Lyophilized	Liquid
Cost	Low	High	High
Clarity	Clear	Turbid	Clear
Stability	12 months	18 to 24 months	18 to 24 months
Lyophilization error	Absent	Present	Absent

Several different types of control samples are available to the clinical chemistry laboratory. Some have been lyophilized (freeze-dried) and must therefore be reconstituted before use; whereas others are already in liquid form, containing preservatives. Some have stated values, obtained either by calculations based on the weighing of added

components, or by actual analysis; these values may be in either normal or abnormal ranges. But other useful samples do not have values provided with them, that is, they are unassayed. While most attention has been given to serum controls, spinal fluid and urine controls are now commercially available. Each laboratory supervisor must make his own decision as to the type or types best suited for his own program.

It is essential that the control samples be stable or capable of being preserved for long periods. As a general rule, they should be similar in nature and composition to the patients' specimen. And it should be possible to introduce them at the start of the analytical procedures so that they will go through every step.

However, since it is at the boundaries of the normal range that the greatest accuracy and precision is required, when only one lot is being used this should have values in or near the normal range, except in those cases where the normal values are very low (e.g., for serum bilirubin and acid phosphatase).

The concentration of the components in locally-prepared serum pools must be determined by repeated analysis. It is recommended that at least 20 determinations should be carried out on 10 different days by the official method, and the mean value of these estimations should be used as the correct value or target value for the control serum (Tonks, 1970).

E. Why is quality control material needed in clinical chemistry laboratory?

In routine and research clinical chemistry, quality control materials are needed in quality management system. Quality management in clinical laboratory consists of internal quality control (IQC) and external quality assessment (EQA) (Browning, et al., 1986). Internal quality control (IQC) is the use of quality control materials, are analysed in the same way as specimens, for detect precision and accuracy of the system. External quality assessment (EQA) is program for compare analytical results between laboratories by using the same quality control materials and check efficiency or standard of system. Data on the analytes of specimens are useful for accreditation of laboratory or organization.

F. Problems in using control materials in monitoring precision in clinical chemistry.

The long-term precision of routine tests performed in clinical chemistry laboratory and interlaboratory quality control surveys can be obtained by measuring of the constituents of interest in a stable control material. Various forms of materials intended for this use are commercially available. The experience with freeze-frozen serum (Uldall, et al., 1989) and liquid serum (Premachandra, et al., 1987) for using as internal quality control has been limiting in local area. Lyophilized preparations are suitable for most organizations in using as a proficiency control materials for external quality assessment (EQA) as well as internal quality control (IQC).

Lyophilized process is commonly used to prepare freezed-dried serum in order to extend their shelf life. The procedure of lyophilization increases turbidity of the reconstituted serum because lipid constituent become insoluble (Oncley, et al., 1950). This in turn increases the absorbance of the material throughout most of the visible measurement (Atwood and Marshall, 1973), for which a blank may be needed to subtract. Several methods for amending this turbidity have been reported (Burstein and Samaiele, 1955) and are summarized in literature review.