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CHARACTERISTICS AND ATTRIBUTES OF INSTRUMENTS INTENDED FOR AUTOMATED ANALYSIS IN CLINICAL CHEMISTRY

(Recommendations 1982)

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CHARACTERISTICS AND ATTRIBUTES OF INSTRUMENTS INTENDED FOR AUTOMATED ANALYSIS IN CLINICAL CHEMISTRY

Instruments for automated analysis are needed in clinical chemistry to reduce manual work, increase the productivity of laboratory staff, improve the quality of results and, thereby, enhance the contribution of clinical chemistry to the improvement of patient care. Desirable characteristics of instruments intended for automated analysis in clinical chemistry are described in this document. The described attributes are most appropriate to instruments in which a biological fluid specimen such as blood, urine, cerebrospinal fluid or amniotic fluid is subjected to automated analysis. This document is not concerned with those measuring or detection instruments which are attached to a patient or with those instruments intended to process solid material such as faeces, calculi or material taken by biopsy. Many of the terms used are defined in the Glossary.

The document is based on a model of the processes in clinical chemistry analysis including information flow and material flow and includes: (i) specimen identification and presentation, (ii) sampling, (iii) preparation for measurement, (iv) measurement and calculation, (v) accuracy and precision, (vi) safety, (vii) environmental protection, (viii) protection of the instrument, (ix) identification of instrument defects, (x) instruction manual, (xi) general comments on instrument design, (xii) glossary.

PREFACE

Mechanized systems of analysis began to be used widely in clinical chemistry laboratories in the 1960s. Their introduction met a long felt need for increasing the output of such laboratories which in turn was due to the increased use of chemical analyses in the diagnosis and treatment of disease.

The design of suitable instruments required certain compromises in the analytical methods used and many clinical chemists were concerned that convenience in design of commercial instruments might determine the choice of methods.

In addition, instruments already in use had important defects, e.g. :
- they could not "read" specimen identifications,
- they required more serum than desirable,
- they were subject to drift and noise,
- their analytical data were imprecise or inaccurate with certain methods,
- they were unsuitable for emergency analyses,
- they led to contamination between specimens and/or samples.

Clinical chemists were anxious to express their views on such matters and state their requirements. This is the background of the present document.

Incorporating all the suggested attributes in one instrument is probably not feasible. Nevertheless, the Commission thought it important to describe the ideals which should be striven for by those designing and building such equipment. Also, the document may be useful to potential users.

The document has been shown to others and some have commented that it states the obvious but unattainable. The Commission has been comforted by the fact that, in the meantime, instruments involving many of the listed attributes that were at one time regarded as un-

attainable, have now been marketed. It is because of such developments in technology that the Commission has resisted writing minimum specifications for such factors as precision, volume of serum used, etc.

As a result of comment by other readers, it may not be superfluous to point out that many of the apparently simple statements in this document have far reaching implications and that these are worthy of careful consideration.

The glossary of terms is not meant to be complete but is a list of those terms used in the document which required formal definition.

1. INTRODUCTION

1.1 Instruments for automated analysis are needed in clinical chemistry to reduce manual work, increase the productivity of laboratory staff, improve the quality and availability of results and, thereby, enhance the contribution of clinical chemistry to the improvement of patient care.

1.2 Desirable characteristics of instruments intended for automated analysis in clinical chemistry are described in this document.

1.3 The described attributes are most appropriate to instruments in which a biological fluid specimen such as blood, urine, cerebrospinal fluid or amniotic fluid is subjected to automated analysis. This document is not concerned with those measuring or detection instruments which are attached to a patient or with those instruments intended to process solid material such as faeces, calculi or material taken by biopsy.

1.4 Many of the terms used are defined in the Glossary.

1.5 Although the term "patient" is used throughout this document, the term "individual" would be more appropriate when the processes described are concerned with the detection of pre-symptomatic disease.

2. PROCESSES INVOLVED IN CLINICAL CHEMICAL ANALYSIS

2.1 The diagram on the next page summarizes the processes in clinical chemical analysis. Those from specimen preparation to calculation of result are the province of the automated analytical instrument. The processes before specimen preparation and after calculation of results are envisaged as being external to the instrument. Both material and information must be transported through the instrument.

2.2 In clinical laboratory investigation the requesting procedures used are diverse and dependent upon local conditions and traditions. No instrument should be so rigid in design that it necessitates major alterations of these procedures. Therefore, the starting point of these recommendations is a specimen on which requests are made.

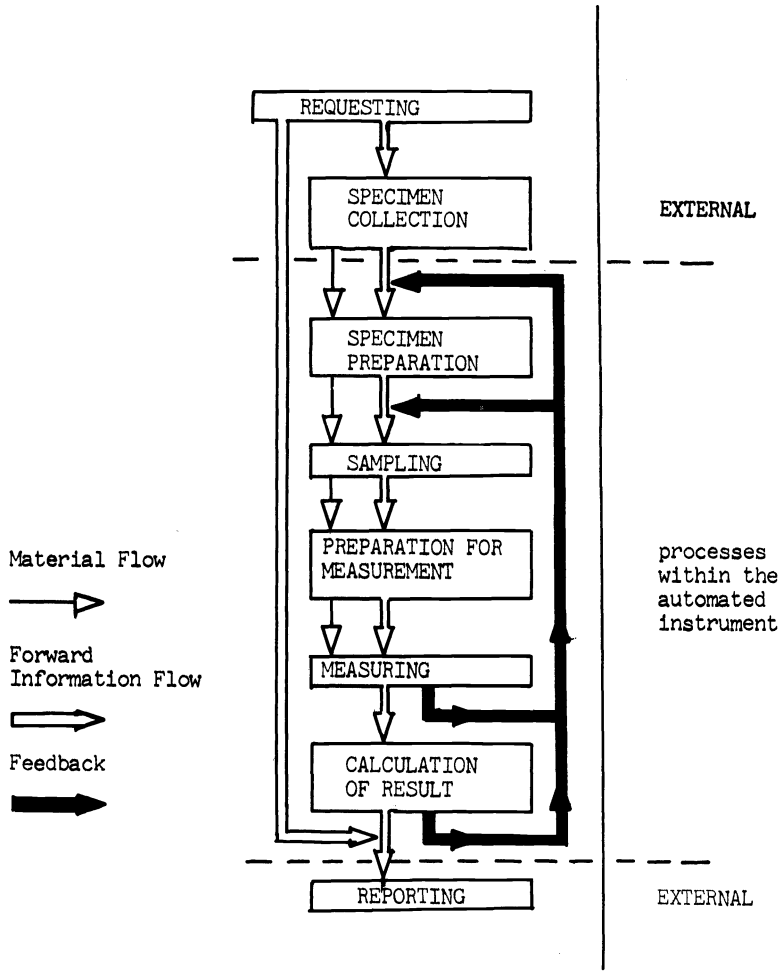
3. SPECIMEN IDENTIFICATION AND PRESENTATION

3.1 As described earlier in this document, several aspects of data handling such as patient identification at the time of specimen collection are external to the instrument. However, at the time of presentation of the specimen to the instrument the identification of the specimen must be unequivocal. The form and contents of this indentification should be the choice of the user (e.g. in its simplest form a laboratory accession number) and must be in human and instrument-readable form and physically linked to the specimen. If a particular result makes it necessary to perform further analyses, (see 4.3) additional information may have to be carried in the specimen identification.

3.2 Specimen preparation : Specimen preparation should be considered an integral part of the analytical process. Common preparation techniques include separation of blood plasma from cells, mixing of sediment or supernate, etc., as appropriate, according to the specimen specifications.

3.3 Status of specimen : Physical or chemical abnormalities of the specimen, e.g. hyperbilirubinaemia, haemolysis, and lipaemia, need to be detected and recorded and associated with the result that is produced. If the status of the specimen is such that the result would be invalid, analysis or the production of a report should be prevented. Such detection, discrimination or rejection should be automated and programmable for each determination.

3.4 Storage within the instrument : Between the presentation and sampling steps, the specimen should be stored under conditions which prevent changes in its composition. This includes storage prior to repeated determinations (see 4.3).



Summary of activities, information and material flow in clinical chemical analysis

4. SAMPLING

4.1 Sample size : The required volume of sample should be small and adjustable according to the analytical procedure. For a given determination, the same analytical procedure, and thus sample volume, should be used for specimens from infants and adults. However, collection procedures could be different for infants and adults. For example, the collection of blood from infants may involve skin puncture and for adults collection by venipuncture, but there would be a common analytical pathway.

The sample volume should be small enough to allow even multiple analyses on specimens from infants.

4.2 Selection of determinations : The instrument should be able to accept specimens of different biological fluids, from a loading zone of sufficient capacity to meet the laboratory's requirements. The instrument should be able to sample specimens (e.g. whole blood), or prepared specimens (e.g. plasma or serum). The instrument should perform only the tests requested and consume only the volume of sample required for those tests. However, an automated instrument could initiate repeated determination of the same quantity or determination of additional analytes with minimum use of specimen, reagents and instrument capacity, depending on the results obtained with the initially requested determinations.

4.3 Repeated determinations : Part of the specimen should be retained in the instrument so that determinations may be repeated, particularly if a reading was found to be

outside the predefined limits for the method. Identification of the sample must remain unequivocal.

4.4 Emergency determinations : At any time it should be possible for the instrument operator to interpose specimens, single or multiple, for emergency determinations. Again specimen identification should be unequivocal. By implication that the instrument can be used for emergency determinations it must be simple to operate, and have both short start-up and analysis times.

4.5 Contamination : Contamination resulting from contact between specimens, samples and/or reagents should not occur. The problem should be solved by physical instrument design and not by means of computation.

5. PREPARATION FOR MEASUREMENT

5.1 The automated instrument must at least be capable of performing generally accepted chemical or physical methods of analysis, currently used in clinical chemistry. Such instrument design implies the provision of a transport system for specimen and sample to the appropriate devices required for the analytical processes, e.g. addition of reagents, mixing, heating and separation of solutions. Such processes are followed by a detection or measuring step, e.g. for absorption, emission, fluorescence, electrode potential, conductivity, mass etc.

Poor analytical methods or sub-optimal conditions should not be used for the convenience of instrument design. The frequency of calibration of the instrument is dependent upon the stability of the instrumental, reagent and specimen factors involved in the analytical processes. Infrequent calibration is an important attribute of automated instruments, but provision for re-calibration at any time should be included. Each part of the analytical process, (e.g. the sampling and measuring steps) as well as the entire procedure, should be capable of being checked for such reliability factors as precision and accuracy. Variations occuring during preparation for measurement contribute to the overall variability, particularly when chemical reactions are involved without adequate control of such conditions as temperature, light and mixing. The control of these conditions is an essential aspect of instrument design.

5.2 Monitoring of functions : As many functions of the instrument as possible, starting with specimen handling, should be automated, (see glossary). When controlled variables such as transducer output or temperature exceed prescribed limits, or in the case of a mechanical or electrical dysfunction, an alarm system should operate. This system must stop the instrument in a way that avoids the production of erroneous results, damage to the instrument, loss of valid results and loss of specimens. It must provide informative error messages to the operator.

5.3 Noise and drift : The instrument should function essentially without electronic or chemical noise or drift. Full information concerning drift correction, when this took place, should be readily available to the operator.

5.4 Chemical reagents : The need for users to check reagents supplied by commercial sources or prepared in the own laboratory must be considered by manufacturers in the design of their instruments. If it is necessary for manufacturers to supply reagents for their instruments, composition and specifications of these reagents must be stated.

Drifts due to reagent deterioration should be prevented by the storage of reagents under conditions which ensure chemical stability. The minimum volume of a reagent required for correct operation of the instrument should be of the order of that required for a single determination, including any necessary calibration or control. In this way reagent consumption can be kept small when few analyses have to be performed.

5.5 Simulation of the analytical procedure : If feasible, all steps of a procedure should be specified to a degree that enables them to be carried out or simulated without resort to the particular instrument for programming and checking purposes.

6. MEASUREMENT AND CALCULATION

6.1 The instrument used in the measuring step of the analytical method should have defined characteristics and provide accurate and precise physical measurements of the component. It should be noted that some kinds of quantities (e.g. catalytic activity), have to be measured by definition under prescribed conditions.

Where appropriate facilities for independent physical measurement should be provided thus

avoiding repeated calibration. The signal, i.e. the output of the transducer, should be obtainable on request. The sensitivity of the transducer must be sufficient to allow accurate and precise results over the range of values expected.

6.2 Temperature control : Temperature variations during the whole process and especially the measurement should be controlled within narrow specified limits.

6.3 Output of results : The instrument output of results should be available in digital form and only meaningful figures reported. The result must be associated with the specimen identification, either directly or through a laboratory accession number. Also available to the operator should be messages concerning the state of the specimen. The same data should be in appropriate form for transmission to an external computer. However it should be possible to display data output even if the external computer is not functioning.

6.4 Output of reports : Results must be associated with specimen identification, patient specifications and requesting source before a report is produced. Absence of specimen specifications should not preclude obtaining a result in an emergency situation. Additional information such as quality control data, plausibility checks and reference values may be necessary for correct editing of a result. This may be accomplished either within the instrument or in an external data processing system.

The user should be able to specify the make-up, format and size of the report.

7. ACCURACY AND PRECISION

Frequently the accuracy, precision and specificity of present methods in clinical chemistry are inadequate and should be improved. Therefore no specific figures can be recommended but the introduction of new instruments should improve the situation and not compromise on accuracy, precision or specificity for instrument design convenience.

8. SAFETY

The instrument should not create safety hazards. Such hazards not only include the obvious ones such as acoustical, electrical, mechanical or chemical hazards but also the spread of infection from specimens.

9. ENVIRONMENTAL PROTECTION

The environment should not be endangered by the dispersal of waste from an instrument and this must be an important consideration in the design and use of the instrument.

10. PROTECTION OF THE INSTRUMENT

Instrument performance should not be affected by external factors such as electrical variations and interference, static electricity, light, alterations in ambient temperature and humidity, vibration and dust.

The materials used in, and the construction of the instrument, should not interact with chemicals and specimens in such a way as to affect the results. The instrument should be so designed that physical change, e.g. vibration and temperature, in one part of the instrument should not affect the correct function of any of its parts.

11. IDENTIFICATION OF INSTRUMENT DEFECTS

The instrument should include a defect detection system. The information provided by such systems should identify the parts requiring service or replacement. Manufacturers should strive to ensure that most defects can be repaired by the user. The manufacturer must make clear in the user's instruction manual which defects of the instrument can be corrected by the operator and must support such information with full documentation.

12. INSTRUCTION MANUAL

A comprehensive instruction manual must be provided. A useful guide to the contents is contained in NCCLS (1) document "ASI-1, preparation of manuals for installation, operation and repair of laboratory instruments".

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(1) NCCLS : abbreviation for National Committee for Clinical Laboratory Standards, 771 E. Lancaster Ave., Villanova, Pa. 19085 (USA)

13. AVAILABILITY OF DOCUMENTATION OF COMPUTER PROGRAMS

Rarely is the data handling system within analytical instruments satisfactory for all situations and software alterations are frequently necessary. The manufacturer should provide documentation of calculation steps and enough details of the computer programs for the user to make changes.

GENERAL COMMENTS ON INSTRUMENT DESIGN

Instrument designers should be aware of the shortage of bench and floor space in the majority of clinical laboratories. Thus, the space occupied must be as small as possible. The need for special services such as ventilation, drainage, gases, etc. should be kept to a minimum as their provision may be difficult in a hospital environment. Manufacturers should avoid the need for specially designed tubes, cups, racks, etc. As computers and instruments are commonly provided from different sources, manufacturers should follow international agreements on the standardization of interface design.

The placing of controls and displays has considerable importance in complex instruments and satisfactory ergonometric design is an essential attribute of any instrument. Equally important in such design is the possibility for the operators to maintain the instrument in a clean and efficient condition.

GLOSSARY

Some terms used in this document are defined here because their definitions in conventional dictionaries are ambiguous. Some definitions were already accepted by IUPAC Commissions, others were elaborated by the Commission on Automation. These definitions are intended to help the understanding of the document.

Accuracy : Agreement between the best estimate of a quantity and its true value.

Automate (adj. automated) : To replace human manipulative effort and facilities in the performance of a given process by mechanical and instrumental devices which are regulated by feed-back of information, so that the apparatus is self-monitoring or self-adjusting.

Drift : A non-random change in signal with time.

Instrument (noun) : A device used for observing, measuring or communicating the state of quality, which replaces, refines, extends or supplements human faculties.
Note 1 : An instrument may include one or more mechanisms involved in the performance of useful work.
Note 2 : The use of the word instrument as a verb is not recommended.

Mechanism : A combination of parts of which at least one is movable and capable of producing an effect.

Monitor (verb) : To observe continually a system.

Noise : The random fluctuations occurring in a signal that are inherent to the combination of instrument and method.

Patient identification : Patient name and unique personal identification number.

Patient specifications : All information, including patient identification, that relates to the patient and is pertinent to the correct interpretation of a result.

Precision : Agreement between replicate measurements.

Program (noun) : Means for instructing a device to perform action.

Program (verb) : To provide a set of instructions requiring a device to perform action.

Report : A combination of patient information, specimen information and a result. The report may contain interpretative data such as comparison of the observed quantity with reference values.

Result : The final value reported for a measured quantity after performing a measuring procedure including all sub-procedures and evaluations.

Sample : That appropriately representative part of a specimen which is used in the analytical procedure. It is usually an accurately measured amount.

Specimen : The material available for analysis.

Note : A specimen may be further defined, e.g. as "blood specimen", "serum specimen", to specify the kind of material.

Specimen identification : Patient identification and specimen specifications.

Specimen specifications : Nature of specimen, determinations requested, and all information specifically related to the specimen that is pertinent to the correct interpretation of a result.