

QUALITY ASSURANCE IN CHEMICAL PATHOLOGY

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A properly organised and conducted external quality assurance programme (QAP) can be an important source of information and support for pathologists, scientists and technicians.

The term quality assurance was introduced to distinguish it from internal quality control. **Internal quality control** checks on the quality of analytical procedures in real time. That is, it is the check on whether analyses being currently performed are precise and accurate and can be released to the clinicians.

External QAP is the quality control of the internal quality control. Hence the term quality assurance.

The elements that are considered essential for a good external QAP are listed in Table 1. This opinion is the result of over twenty years experience in organising external QAPs by a number of dedicated fellows and members of the Royal College of Pathologists of Australasia (RCPA) and The Australian Association of Clinical Biochemists (AACB).

Profession Base for a QAP

Although a number of QAPs are available from commercial firms, it is in the professions' best interest to organise the programme for itself. In this way the QAP can be responsive to the needs of the participants. Analytical problem areas can be highlighted and the profession take action both investigative and educational to improve the situation. This **control** of the QAP and responsiveness is important if the profession is to control its own destiny.

Human Material

All of the early QAPs as with quality control materials, were not based on human serum. This has led to a number of problems with various analytical techniques especially enzymes and those involving antibodies eg. drugs and proteins.

The material for the Australian programme has been developed in cooperation with the Commonwealth Serum Laboratory (C.S.L.) of Melbourne, Australia. It is entirely human

based. Additional amounts of enzymes and proteins of human origin are added to achieve **high** values. The enzymes are **extracted** from human tissue by C.S.L. The material should be tested for Hepatitis B and HIV before it is used.

Target Values

It has been the policy to assign target values for the various analyses in the various preparations ever since the Australian programme has been producing its own material. We have found that consensus means may be misleading. For instance a new method with a significant bias became available on a popular piece of equipment and the consensus mean shifted away from the true value.

Target values are assigned to the analyses when each new pool of material is manufactured. At the moment this is carried out once a

TABLE 1
ELEMENTS OF AN EXTERNAL QAP

1. Profession based
2. Human material for analysis
3. Target values
4. Allowable limits
5. Regular analysis
6. Sufficient number of different concentration levels
7. Easily read presentation of statistics
8. End of cycle summaries
9. Easily available ad hoc statistics
10. Special interest groups
11. Confidentiality

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year. In brief, selected laboratories take part in this assignment process, using any international **reference** material that is available for calibration etc.

The **consensus mean** is always a good check on the target values. A difference between target values and consensus means is nearly always explained by the bias of poor methods.

Allowable Limits

It is our opinion that the expression of variation between laboratories in terms of standard deviation (SD.) is not only theoretically incorrect but has limited use.

The method for indicating precision in the Australian programme is by the use of "Allowable Limits". These are set by the organisers in accordance with current state of the art. Originally they were set very wide but as the overall performance of laboratories has improved we have been able to progressively narrow the limits.

Difficulties with using the S.D. is exemplified by the following. In a method where there is poor interlaboratory correlation there will be a large S.D. which will hide an individual laboratory's poor precision. On the other hand there is such good interlaboratory correlation with potassium that a laboratory may be 0.2 mmol/l away from the target value (or consensus mean) and be outside the 2 S.D. limit.

Regular Analysis

Samples for the QAP should be analysed at such frequency that the results can check on internal quality control. The frequency should also be such that when a problem is detected, then the laboratory should not have to wait too long after correcting the fault to have the next check with the external QAP. The ideal is about once a fortnight.

Number of Concentration Levels

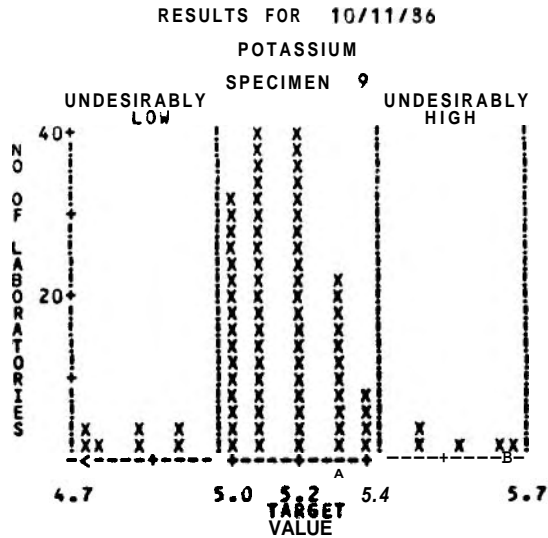
The range of values should have a span that is consistent with clinical realism and analytical capability. The range needs to be much wider than the reference range and should span the very low to the very high. There is a limit so that the high should not be such that the sample needs dilution to be measured.

The number of different levels used in the Australian programme is eleven. This allows a good check in linearity over the whole range.

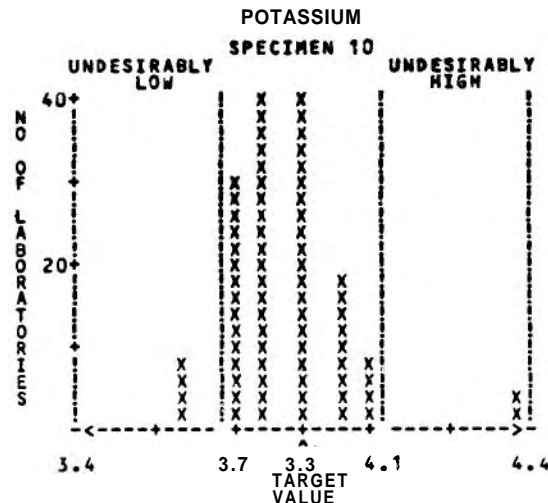
Presentation of Statistics

The results of the programme are read by busy people. The essential information should be presented in an easily readable graphical form with the necessary numerical **information** printed below for closer attention if required (Fig. 1).

A progressive graphical representation of the performance in each analysis is **useful** for laboratory directors to quickly determine



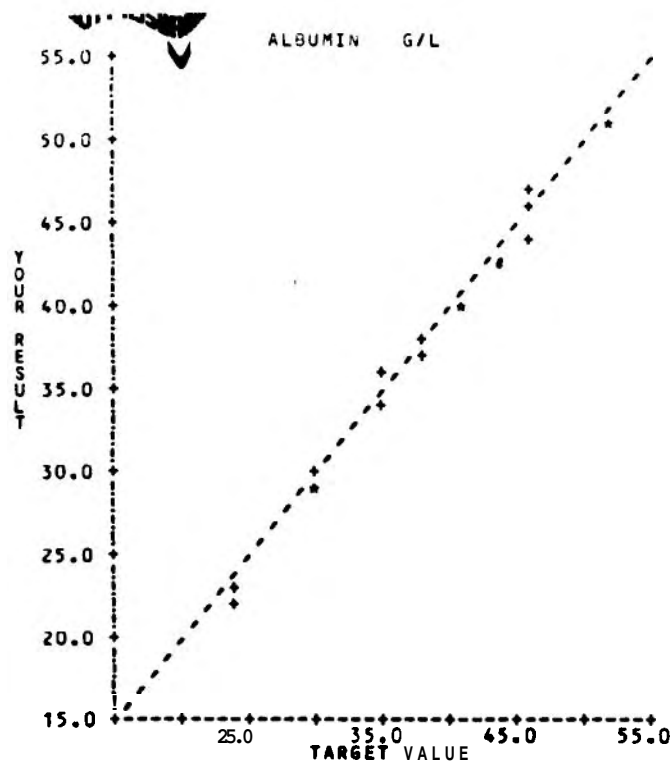
OVERALL MEAN = 5.1 MMOL/L
YOUR RESULT (^) = 5.3 MMOL/L



OVERALL MEAN = 3.3 MMOL/L
YOUR RESULT (^) = 3.3 MMOL/L

YOUR METHOD = CDNE
ELECTRODE = INDIRECT

FIG. 1: Results for potassium for one particular fortnightly return.



0 OUT OF 16 RESULTS OUTSIDE THE PERFORMANCE LIMITS

IMPRECISION

(.67) (.89) (1.25) (2.32)
 BEST-----20%-----50%-----90%-----
 YOUR S.D. (^) = 0.89
 YOUR METHOD S.D. = 1.21

INACCURACY

	TARGET VALUE	YOUR METHOD MEDIAN	YOUR CALC. VALUE
LOW VALUE	25.0	25.3	24.6
HIGH VALUE	50.0	49.5	50.1

(.02) (.61) (1.17) (2.83)
 BEST-----20%-----50%-----90%-----
 YOUR BIAS (^) = 0.23
 YOUR METHOD BIAS = 1.11

YOUR CORRELATION = 0.991

YOUR METHOD : 3CG - SUCCINATE

FIG. 2: End of cycle report of albumin for an individual laboratory.

ALBUMIN G/L			
IMPRECISION			
METHOD	NO. OF PARTICIPANTS	S.D.	
BROMOCRESOL PURPLE	13	1.16	
YOUR METHOD >>>	127	1.21	
aC6 - UNSPECIFIED BUFFER	11	1.30	
BCG - LACTATE	10	1.34	
BCG - CITRATE	48	1.36	
BCG - ACETATE	3	1.85	
HABA	1	8.88	

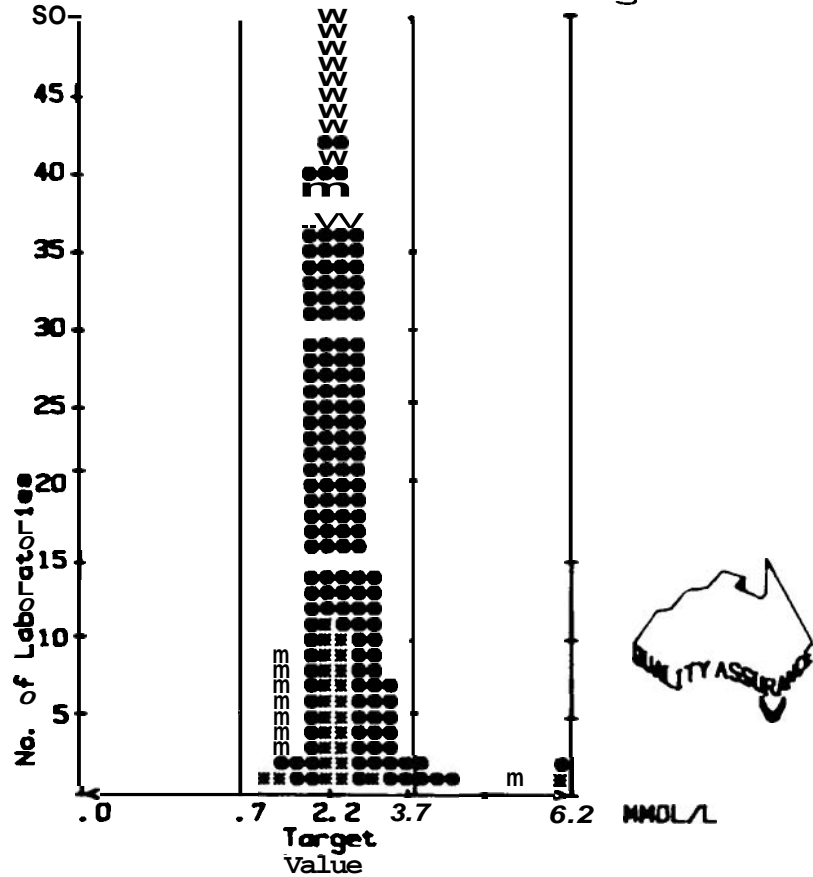
INACCURACY			
METHOD (TARGET VALUES)	AVERAGE BIAS	LOW VALUE 25.00	HIGH VALUE 50.0
BCG - LACTATE	0.9	26.2	49.4
YOUR METHOD >>>	1.1	25.3	49.5
BCC - UNSPECIFIED QUIER	1.2	25.7	49.4
BCG - CITRATE	1.4	26.0	49.7
BROMOCRESOL PURPLE	1.4	26.1	50.4
BC6 - ACETATE	1.5	25.6	52.4
HABA	56	24.9	39.3

LINEARITY	
METHOD	CORRELATXOW
BROMOCRESOL PURPLE	0.986
YOUR METHOD >>>	0.981
BC6 - UNSPECIFIED BUFFER	0.980
BCG - CITRATE	0.978
BCG - LACTATE	0.976
BCG - ACETATE	0.965
HABA	0.264

FIG.3: End of cycle report for albumin showing comparison of methods.

UREA CYCLE.10 Samples 10&11

Method Code : d-e-
 UREASE: Rate Boehringer



Total Number of Results = 437 Undesirable Results
 Mean = 2.35 Low = 0 0%

S. D. = 0.26 High = 7 2%

26 Outliers (> 3 SD) Removed Total = 7 2%

25 Results in this Subclassification
 Mean = 2.60
 S. D. = 1.55

Significantly ($p < 0.01$) Higher Than the Overall Mean

FIG. 4: Comparison of reagents within one method.

whether there is an improvement or deterioration in performance.

End of Cycle Summaries

Once enough data points have been collected, summary information can be presented on precision and accuracy (or bias) (Fig. 2). At this time there is sufficient information to also present comparisons between methods, instruments and reagents (Fig. 3). The purpose of this is to assist directors of laboratories that are using an **analytical** system that is performing poorly in choosing a better system.

Ad Hoc Statistics

The data base can be used to produce information that may be useful in problem solving eg. how does a particular reagent perform in comparison with all other methods. Fig. 4 represents a comparison between the **urease** rate method using a particular manufacturer's reagent with **all** other methods for measuring urea.

Special Interest Groups

Provision should be made for summary information to be made available (with the

individual participants' consent) to special interest groups. These groups may be administrative in nature viz all laboratories funded by a particular branch of government; or they may be related to users of various instruments viz **SMAC, Hitachi, TDX** or **Cobas Bio** users. The instrument groups are organised and run by members of the profession and not the instrument manufacturer or distributor.

Confidentiality

It has been traditional for **all** results to be confidential. If a government authority requires results of the programme for accreditation then it must ask each individual laboratory and not the organisers of the programme. The code relating the number to the name of the laboratory is held by the **chairman** of the organising committee. Those responsible for the day to day running of the programme do not have access to this information.

In the early days a participant took confidentiality very seriously. In recent times, perhaps in association with improved performance, many participants are fairly relaxed about the need for confidentiality.