Quality-Control Considerations with the Du Pont Automatic Clinical Analyzer (ACA)

Gloria Welt Sage

I describe an approach to quality-control of results produced by a discrete analyzer, the Du Pont ACA.

A comprehensive quality-assurance program is required in order to achieve and maintain a high level of reliability in the clinical laboratory. In most manual and automatic clinical procedures, a reference standard or series of reference standards is used to establish a slope or standard curve, and controls are also included with samples from patients. The consistency of the mean value of the controls and the standard deviation of the control values about the mean are used to assess the accuracy and precision of the procedure. Quality-control charts of the Levey-Jennings type (1) are usually drawn, which enable one to detect problems with reagents, standards and instruments, as well as with the controls themselves.

In applying these quality-control methods to instruments such as the Automatic Clinical Analyzer (ACA; Du Pont Co., Wilmington, Del. 19888), one is confronted with operational differences that demand a different approach to quality-control.

With the ACA, standards are not measured with each group of patients' specimens; instead, for each reagent-pack lot one establishes that there is a linear relation between the instrumental readout and the corresponding assayed values. To establish this relation one might assay three concentrations of reference standard in triplicate and make slope and intercept adjustments on the instrument until one achieves as close agreement as desired, which will vary with the particular clinical assay.

Two critical features should be stressed: (a) A three-point calibration curve is determined once for each pack lot, not daily with each group of samples; and (b) the closeness with which instrumental readout and reference-standard values agree is deliberately determined by the person establishing the curve, and is verified by triplicate assay of each of three reference standards. The effect of these points on the Levey-Jennings quality-control charts is apparent. Within a reagent-pack lot, the mean for the controls will be determined in part by how closely the instrumental and "true" values correspond.

The standard deviation is a measure of functional variability in the instrument as well as of intra-pack lot variation of reagent packets. (It should be mentioned, for the benefit of those unfamiliar with the ACA, that certain instrumental checks and adjustments are performed daily, to ensure proper functioning of the sampling and photometric systems.) When one changes to a new reagent pack lot, one readjusts the instrument as mentioned above. Because of practical limitations in the calibration procedure, new mean values for the controls will be established. The shift in the mean might be considerable, but in all cases it should be within acceptable limits. Accumulation of the new control data with that of the old pack lot, may increase the standard deviation if there is a measurable shift in the means. Hence the standard deviation may no longer be as sensitive an indicator of the precision of the procedure as it could be. To monitor the precision independent of the expected systematic variation between lots of reagent packs, one should use the following formula for the variance, \( S^2 \).
**Table 1. Summary of Four-Month Quality-Control Data for Four Procedures on the Du Pont ACA**

<table>
<thead>
<tr>
<th>Procedure:</th>
<th>Total protein</th>
<th>Albumin</th>
<th>Creatinine</th>
<th>BUN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control:</td>
<td>Normal</td>
<td>Abnormal</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td><em>X</em></td>
<td>6.89</td>
<td>5.67</td>
<td>4.06</td>
<td>2.90</td>
</tr>
<tr>
<td><em>S</em></td>
<td>0.097</td>
<td>0.106</td>
<td>0.066</td>
<td>0.045</td>
</tr>
<tr>
<td><em>S</em></td>
<td>0.111</td>
<td>0.121</td>
<td>0.096</td>
<td>0.072</td>
</tr>
</tbody>
</table>

Range of _X_ = 6.81-6.93 5.57-5.69 3.97-4.14 2.85-2.97 1.26-1.29 5.08-5.19 13.50-13.99 55.96-58.31

No. pack lots tested 3 3 5 5 5 5 5 5

* _X_ is the control mean for the ith pack lot, _X_ the cumulative mean, _S_ the standard deviation, and _S_ the cumulative standard deviation based on equation 1.

\[
S^2 = \frac{\sum \sum X_{ij}^2 - \left(\sum X_{ij}\right)^2}{\sum (n_i - 1) - m}
\]

\[
S_T^2 = \frac{\sum (n_i - 1)S_i^2}{\sum (n_i - 1)}
\]

where _X_{ij} is the jth of a set of _n_ measurements made with use of the ith of _m_ pack lots. The variance with the ith pack lot is _S_^2. In this way the variation is determined with respect to the mean of the particular pack lot. Only with respect to the pack lot mean can the Levey-Jennings chart be expected to have its usual statistical distribution.

On the basis of the limits impressed on the calibration curve, one can choose limits for the control mean between pack lots. By adding ±2 SD (from equation 1) to these limits, the inter-pack lot warnings limits can be identified.

Figure 1 shows Levey-Jennings plots for both a normal and abnormal control for albumin on the ACA. The plot covers a four-month period and includes five changes in pack lot. The intra-lot means and warning limits, _X_ and _X_ ± 2SD, are indicated as well as the cumulative mean and warning limits _X_ and _X_ ± 2SD.

Table 1 summarizes the quality-control for four tests on the ACA. The difference between _S_ and _S_T are substantial in some cases. Figure 2 is a flowchart that indicates the action to be taken in analyzing the quality-control charts on instruments such as the ACA.

With the increasing popularity of group quality-control programs, individualized treatment of data to obtain intra-pack lot standard deviations involves an additional effort and frequently a duplication of work, but in this case an awareness of these problems and some extra analysis are warranted.

**Reference**