Table 4. Summary of Control Procedures Appropriate for Different Numbers of Control Observations

No. control observations	Control rules for: Individual analytical runs	Control rules for: Consecutive analytical runs
1	1_{2s}	4_{1s}
2	$1_{3s}/2_{2s}/R_{4s}$	$4_{1s}/10_{\bar{x}}$
3	$1_{3s}/(2\text{ of }3)_{2s}/R_{4s}$	$9_{\bar{x}}$
4	$1_{3s}/2_{2s}/R_{4s}/4_{1s}$	$8_{\bar{x}}$
4–10	Mean/range	Trend analysis (*16*)
4–20	Mean/chi-square	Trend analysis (*16*)

is very large, it would be better to substitute the chi-square test for the range test (*3*).

Note: Reviewer A.H. recommends that mean and range control procedures be considered when it is desired to obtain very tight control of an analytical method. Experiences with their use in the Lipid Reference Laboratories has been very positive. The authors' only reservation is the difficulty in applying these procedures, mainly due to the data calculations. This, of course, will not be a limitation when implemented in laboratory computer systems, microprocessor-controlled instrument systems, or micro-computers.

Mean and range, or mean and chi-square procedures, have greater statistical power when N is large and also permit the probability for false rejection to be set to a specified level. However, when N is kept low because of practical and economic reasons, the statistical power of all the procedures will be relatively low. Mandel and Nanni (*13*) prefer using the mean and range of replicates rather than treating individual observations, because the assumption of a gaussian error distribution is less tenuous. This theoretical consideration must be weighed against the practical difficulties of implementing mean and range procedures in the high-production workload of clinical laboratories. Control decisions cannot be made directly from the raw control observations, but must wait until the calculations are performed. The calculations, though not difficult, are a little more time consuming, particularly when several analytes are being measured simultaneously by multi-channel analyzers.

There also is difficulty in combining control observations when they are obtained on control materials of different concentration, such as the commonly used low-abnormal, normal, and high-abnormal materials. Unless these observations on different materials are combined, the full statistical power available from the total number of control observations will not be realized. Combining these data requires some way of normalizing the raw observations, perhaps in the manner suggested by Larsen et al. (*14*). By comparison, combining data is very simple with the control procedure recommended here. The control data are normalized by determining by how many standard deviations an observation differs from the mean for that control material. To combine results on different control materials, one needs only to count the number of observations exceeding certain limits on the control charts for the individual materials. It would, of course, be possible to combine observations that are not simply individual values or measurements, thus this approach may be useful for combining results from mean and range control procedures when two or more control materials are being analyzed.

One limitation to the application of this multi-rule Shewhart procedure may be present practices in the rounding of analytical results. Direct-readout instruments often round an analytical result to the least significant digit based on the clinical usefulness of the result. This rounding may obliterate any difference between 1*s* and 2*s* limits or 2*s* and 3*s* limits. This is sometimes the case for analytes such as albumin, urea nitrogen, CO_2, creatinine, potassium, chloride, and calcium.[4] The limitation can be overcome by obtaining an extra significant digit in the readout of results. It is important for instrument manufacturers to consider the use of the data for quality-control purposes before rounding the results for clinical significance.

Another limitation may be the application of these control rules to data from more than one analytical run (across runs). The purpose in using data from consecutive runs is to increase the number of control observations and the corresponding power for error detection. Error conditions that continue from run to run will more likely be detected by pooling the control data from the individual runs. This requires that control data from previous runs be available in a form that is convenient for inspection. If this is not practical, then some of the control rules can be eliminated. The $10_{\bar{x}}$ rule should be eliminated first, because it requires the most data and contributes the least to error detection. The 4_{1s} rule is not as difficult to apply, requiring only the previous run when applied across materials. Application within a single material is more difficult, thus the use of a rule within materials may be eliminated prior to elimination of its use across materials. In considering the use of rules across runs, it should be remembered that the R_{4s} rule is *not* intended for use across runs, only within a single run.

We think the multi-rule Shewhart control procedure is useful and practical. It has the advantages of ease of implementation and use, a low probability for false rejection, and the effective combining of results from materials of different concentrations, yielding an improved capability for error detection. Mean and range procedures, as well as cusum procedures, may be theoretically more satisfying, but they have not demonstrated their practicality in clinical laboratories. Cusum procedures, though well known, are seldom used. Mean and range procedures, as introduced in clinical laboratories by Levey and Jennings (*2*), were quickly modified by Henry and Segalove (*15*) to use with individual observations. Of the procedures that have been tried, it is the control chart for individual observations that has most influenced the practice of quality control in clinical chemistry. This must attest to the practicality of the approach. Our effort here has been to define more carefully how this approach can be successfully used.

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