SRM's and Verification of Commercial Standards

To the Editor:

It was somewhat disturbing to read the letter from Drs. Edith Zak Helman, J. M. Reingold, and I. O. Gleason, which appeared in Clin. Chem. 17, 1144 (1971). In their fifth paragraph the authors raised the question of the verification of commercial reference materials. While it is true that primary Standard Reference Materials (SRM's) do not exist for all the analyses reported in their Table 1, nevertheless it is also true that the NBS, through its Office of Standard Reference Materials, has now certified and issued primary SRM's for several of the analyses listed, thereby making verification of commercial standards possible.

Of the substances listed in Table 1, NBS now has available SRM's for calcium, glucose, uric acid, cholesterol, and bilirubin (plus nine others). Within the next year or so additional SRM's to cover most of the substances analyzed by automatic means will be issued. A brochure may be had on request that lists all the clinical SRM's now currently available.

In addition to producing and certifying clinical SRM's, NBS is involved in a program with the professional societies for the development of referee methods of analysis. Within the next few months NBS will publish the first-A referee methods for the determination of calcium in serum.

I fully agree with the suggestion stated in the last paragraph that an all-out effort by the National Committee for Clinical Laboratory Standards, the Standards Committees of the AACC, the College of American Pathologists, and pertinent government agencies should lay out an intensive program to develop referee methods as quickly as this can be done.

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Normal Ranges for Serum Creatine Phosphokinase

To the Editor:

The suggested normal range for the creatine phosphokinase (CPK) test on the recorder chart paper for the SMA 12/60 (Technicon Instruments Corp., Tarrytown, N. Y. 10591) was recently changed from 0–110 to 25–145 mU/ml; without explanation. Inasmuch as we are unaware of how normal values are established for the SMA 12/60, we thought it useful to document the newly suggested normal range, with use of the SMA 12/60 and Technicon reference controls and reagents. Such documentation is offered here.

We had found the normal range indicated by Technicon (0–110 mU/ml) to be overly restrictive; an inordinately high percentage of values exceeded the upper limits of normal. This discrepancy was particularly noticeable with results obtained on sera from our first-year medical students—about a quarter of them exceeded 110 mU/ml. Accordingly, we investigated the normal range: (a) a histogram was constructed from CPK values obtained on more than 1,000 hospital patients (Figure 1; only one value was plotted per patient), and (b) values obtained by the Technicon SMA 12/60 were compared with those by the Rosalki method (1), with use of 139 sera having a wide range of CPK activity (Figure 2).

Clearly, CPK values are skewed toward the higher values; the median is 60–70 mU/ml and the upper limit is near 160 mU/ml. The inexactitude in setting the upper limit of normal is a reflection of the considerable overlap or the frequent inability of CPK values to distinguish normal persons from abnormal, a failure variously attributed to muscle exertion, needle puncture, administration of drugs, stress, and other nonpathologic situations.

We do not condone use of data from hospital patients for determination of normal values; however, we think it can be used to invalidate a previously given normal range if the difference is sufficiently great. In some recent publi-
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Sugestions patients' test values are used to estimate "normal ranges" and "limits of precision" (2) and such values are used both for normal ranges and quality control in the averages-of-normals procedure (3, 4).

For comparison of results by the Rosalki method and by the Technicon SMA 12/60 method, we assayed 139 sera from hospital patients within 1 h. Figure 2 shows the scatter diagram; the regression line, calculated by the method of least squares, is y = 11.30 + 2.86x; the coefficient of correlation is 0.87. The normal range for the Rosalki method is 5–50 mU/ml for males and 5–30 mU/ml for females (1), corresponding to 26–97 and 26–154 mU/ml, respectively, by the SMA 12/60 method. A single, best normal range representation of the CPK determination with the SMA 12/60, without distinguishing between the sexes, would reduce to 26–154 mU/ml. This finding, bolstered by the results of the frequency studies in which the upper limit of normal was found to be approximately 160 mU/ml, confirms the recently suggested normal range of 25–145 mU/ml for the Technicon SMA 12/60 CPK determination.

References

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LABORATORY REPORT #2

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