External Quality Assessment of Assays of Lead in Blood

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The operation and results of the United Kingdom External Quality Assessment Scheme for Lead in Blood, which currently has about 140 participants within and outside the U.K. are described. The choice of specimens, scheme design, and scoring of performance are discussed, as is the validity of the consensus values used as a basis for the scoring. There has been a continued improvement in performance as assessed by this program, some of which appears to have been stimulated by the introduction of Variance Index scoring. The relative performance of the methods for assaying lead in blood is also examined.

The assay of lead in blood is important in diagnosing patients with suspected toxicity, detecting excessive industrial or environmental exposure, and monitoring the cases found by such testing or screening procedures. Its reliability in all these situations, particularly with the increasing emphasis in the U.K. on blood lead values in occupational health enforcement (1), obviously requires that the results produced in all laboratories must be both precise (reproducible) and accurate (free from bias). Otherwise, incorrect clinical decisions might be made and data from multicenter studies could be misinterpreted. Despite this, the literature contains few reports of interlaboratory surveys, and even fewer of regular external quality-assessment schemes; the scanty data that have been published indicate that the situation is not satisfactory.

Berlin and his colleagues (2, 3) have carried out surveys in Europe of lead, mercury, and cadmium assays with blood and urine specimens. In 1972 the results for blood lead determined in 22 laboratories ranged from 0.7 to 4.1 μmol/L (median of 2.4 μmol/L); a larger continuing study (62 participants) in 1974 showed a between-laboratory CV of 43% at a median of 1.1 μmol/L (range 0.5–4.2 μmol/L). In Scandinavia, Paulev et al. (4) reported CVs of about 12 and 17% at lead concentrations of 1.0 and 2.9 μmol/L among five participants in 1977. The Centers for Disease Control in the U.S., which has carried out surveys at about three-monthly intervals since 1974 as part of a proficiency testing program, reported a similar performance in 1979 (5), with typical CVs of 22% for lead at 2.5 μmol/L. In addition, the most commonly used methods were shown, as expected, to be positively biased (in comparison with a definitive method) at low lead concentrations and negatively biased at high concentrations; mean results were accurate around 2.0 μmol/L. More recently Saltzman (6) has collated data for 1979–1983 from three schemes in North America, yielding CVs of 10, 13, and 19% for 25, 54, and 237 laboratories at mean lead concentrations around 2.5 μmol/L.

After several years' experience with the U.K. External Quality Assessment Scheme (UKEQAS) for General Clinical Chemistry (formerly the National Quality Control Scheme) at Birmingham (7, 8), our two laboratories initiated jointly a similar national scheme for lead in blood.4 Distribution of specimens commenced in 1973, and the scheme has since been extended to include participants outside the U.K. Here we describe the history and operation of the scheme, present some of the results obtained, and comment on the current state of the art.

Materials and Methods

Specimen Selection and Preparation

At the inception of the scheme, human blood was chosen as the specimen. Specimens are prepared at the Health and Safety Executive Occupational Medicine and Hygiene Laboratories (HSE), which arranged with a local hospital to provide one unit of blood every two weeks to meet the requirements of the scheme. The blood is given by volunteer donors who understand the purpose for which it is to be used.

The blood is collected into an acid-washed bottle with diopotassium EDTA as anticoagulant (final concentration 1.5 g/L); this is preferred to heparin to ensure that clotting does not occur during the hemolysis stage of specimen preparation. Samples are screened for hepatitis B surface antigen and (since December 1985) for antibody to human T-cell lymphotropic virus, type III.

Homogeneous material is produced by sonicating the blood at 4°C with an instrument delivering 80 W. Full hemolysis, verified by microscopic inspection, is obtained with three 45-s bursts of energy. A measured volume is then transferred to a dispensing vessel with a magnetic stirrer and controller, which provides contra-rotatory mixing. To the blood is added, over a 60-s period with constant mixing, an aqueous solution of lead and cadmium nitrates prepared from 1000 μg/L "Spectrosol" stock solutions (BDH Ltd., Poole, Dorset, U.K.); mixing is continued for 2 h. The amounts of lead and cadmium added currently range from zero to 4.0 μmol/L (800 μg/L) and 180 nmol/L (20 μg/L), respectively; thus, the final concentrations in the specimens cover the range of values commonly associated with environmental and occupational exposure.

Aliquots (2 mL) are then dispensed into 5-mL screw-cap glass bottles previously determined to be free from contamination by lead or cadmium. These specimens are then packed in polystyrene containers and boxed, and the package is sterilized by gamma irradiation from a 60Co source

4 Nonstandard abbreviations: UKEQAS, U.K. External Quality Assessment Scheme; HSE, Health and Safety Executive Occupational Medicine and Hygiene Laboratories; EQA, external quality assessment; VIS, Variance Index Score; MRVIS, Mean Running Variance Index Score; BIS, Bias Index Score; MRBIS, Mean Running Bias Index Score; SDBIS, standard deviation of the Bias Index Score.
(Isotron, Reading, Berks., U.K.) for about 12 h (total dose, 2.5 Mrad). The prepared material is then dispatched to Birmingham for distribution to the participating laboratories.

This procedure has remained essentially unchanged throughout the operation of the scheme. Initial studies (unpublished data) demonstrated the homogeneity of the specimens and their stability. Stability for three months at 4 °C and during a week's transit at 30 °C has meant that there should be no contribution to the variation in results from the specimens themselves.

**Operation of the Scheme**

The operation of this scheme owes much to experience derived from the UKEQAS for General Clinical Chemistry (7, 8), which is also organized from the Wolfson Research Laboratories in Birmingham, U.K. In addition, because many facilities are shared by the two schemes, the designs are constrained to be compatible.

**Frequency of distribution.** Although the frequent distribution of multiple specimens facilitates the rapid collection of a large amount of data to provide a comprehensive assessment of participants' performance (9), external quality assessment (EQA) is intended to complement rather than replace internal quality control. It has therefore been proposed that EQA surveys should be sufficiently infrequent to avoid confusion between these two aspects of quality assurance (10, 11). Thus the frequency of distribution for each scheme must be chosen in the light of the requirements for the analyte(s) involved and the facilities available.

Blood lead is determined relatively infrequently in many laboratories; this, with the postal delays consequent on the inclusion of overseas participants, suggested a two- to four-week frequency. A biweekly frequency distribution of a single specimen was selected to agree with the UKEQAS for General Clinical Chemistry program, to provide a continuous service from which reports would reflect performance as near to current as was feasible. This frequency was also compatible with the specimen-production capacity of HSE, each distribution being prepared from one unit of donated whole blood.

**Cycle time and operating schedule.** To prevent confusion between successive distributions in an EQA scheme, the cycle time (i.e., the period from receipt of specimens by participants to receipt of reports) should be shorter than the interval between distributions. This design has been modified, however, to allow a reasonable time for overseas participants to receive and analyze their specimens.

After receipt in Birmingham by rail from HSE, specimens are distributed to participants. Each is accompanied by a results document bearing the laboratory's code number, the specimen number, and the date by which results must be received by the organizing laboratory. Specimens are normally mailed (by first class or air mail) on the Tuesday of week 1. Participants receive and assay the specimen during weeks 1 and 2, and return the completed results documents to arrive before the closing date, 09:00 h on the Tuesday of week 3. Many overseas participants telephone, telegraph, or telex their results to ensure inclusion. Participants are instructed to assay the specimen as if it were a routine clinical specimen; thus, only a single result is reported.

Results, in μmol/L or μg/dl, are entered into a computer (PDP 11/44; Digital Equipment Corp., Maynard, MA 01754) and, after conversion if necessary to μmol/L by the computer, the results are analyzed statistically and scored as described below. Reports are then generated for dispatch to participants on the Wednesday of week 3, again by first class or air mail.

The cycle time is thus 16 days for U.K. participants, somewhat more variable for those overseas. The overlap between distributions has produced very few difficulties, both specimens and results documents being clearly identified by the distribution number.

**Data Processing**

The routine processing is described above, and therefore only the report formats and scoring system are described here.

**Report format.** Initially, only limited data-processing facilities were available and reports were photocopies of a general computer printout, as for the UKEQAS (7). These showed the results returned by all participants (identified by laboratory code number only) with the overall mean, SD, and CV, and the same parameters recalculated after exclusion of results lying more than 3 SD from the untrimmed mean. A histogram and a table giving the same (recalculated) information for each method group were also provided. Later, to provide incentive towards improvement of performance, a scoring system based on Variance Index (see below) and similar to that used in the UKEQAS (7, 8, 12) was introduced. Participants receive graphs (Figure 1) showing how their performance has changed over approximately the preceding two years.

With improved computing facilities, provision of individual reports incorporating Variance Index information for each participant became feasible in 1979. The current format (Figure 2; a separate sheet gives a histogram of results) provides the same information as before, but the only individual result shown is the participant's own. The Variance Index Score (VIS; see below) attributable to this result is given, as is the laboratory's current Mean Running VIS (MRVIS). The average MRVIS for all participants provides a comparison with other laboratories' performance. Definitions of the Variance Index parameters used in the report are on the back of the report.

**Variance Index scoring system.** Variance Index scoring was introduced into the UKEQAS to provide participants with a single number reflecting the overall performance of their laboratory for the analytes involved (7, 8). Though some participants initially found it difficult to interpret, it is now well-accepted. Its influence has been evidenced by a continued improvement in average performance since its introduction, whereas little progress had been noted over the preceding three years (7). Similar effects have been seen in other schemes (12).

Variance Index scoring was introduced into this scheme in 1979, coincident with a change to molar SI units and the introduction of individual reports. An MRVIS is calculated from 10 individual VISs, i.e., covering a period of about five to six months, as follows (12):

\[
\text{Variance Index} = \left[ \left( \frac{1}{n} \sum (x_i - \bar{x})^2 \right)^{\frac{1}{2}} \right] \cdot 100 \cdot 100/CCV
\]

where \( x = \) participant's result

\( \bar{x} = \) recalculated overall mean

\( CCV = \) chosen coefficient of variation (15% for lead)

If Variance Index < 400, VIS = Variance Index. If Variance Index > 400, VIS = 400; i.e., the maximum VIS is 400.

MRVIS = the arithmetic mean of the 10 most recent VISs obtained by the participant
**U.K. EXTERNAL QUALITY ASSESSMENT SCHEME**

FOR GENERAL CLINICAL CHEMISTRY

Wolfson Research Labs., Queen Elizabeth Medical Centre, Birmingham B15 2TH, U.K. (Tel. 021-472-1311 Ext. 172)

MATERIAL DISTRIBUTED SPECIMEN 254

DISTRIBUTED HUMAN BLOOD

LEAD

<table>
<thead>
<tr>
<th>NO. OF RESULTS</th>
<th>MEAN (UMOL/L)</th>
<th>STANDARD DEVIATION (UMOL/L)</th>
<th>COEFFICIENT OF VARIATION (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL RESULTS</td>
<td>70</td>
<td>2.38</td>
<td>0.20</td>
</tr>
<tr>
<td>RECALCULATED, EXCLUDING VALUES LYTING MORE THAN 3.0 S.D. FROM THE MEAN</td>
<td>69</td>
<td>2.39</td>
<td>0.16</td>
</tr>
<tr>
<td>RECALCULATED RESULTS ACCORDING TO METHODS USED, EXCLUDING VALUES LYTING MORE THAN 3.0 S.D. FROM THE METHODS MEAN :</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATOMIC ABSORPTION - DELVES CUP</td>
<td>8</td>
<td>2.62</td>
<td>0.11</td>
</tr>
<tr>
<td>ATOMIC ABSORPTION - FLAMELESS ATOMIC ABSORPTION</td>
<td>52</td>
<td>2.39</td>
<td>0.17</td>
</tr>
<tr>
<td>ATOMIC ABSORPTION - OTHER</td>
<td>5</td>
<td>2.41</td>
<td>0.07</td>
</tr>
<tr>
<td>MANUAL DITHIZONE</td>
<td>1</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td>ELECTROCHEMICAL</td>
<td>1</td>
<td>3.00</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE**

YOUR RESULT : 2.47
YOUR VIS : 24
YOUR MRVIS : 25
AVERAGE MRVIS : 47

CADMIUM ADDED TO THIS SPECIMEN = 73 NMOL/L

**N.B.1** RESULTS RETURNED IN UC/ML CONVERTED BY DIVIDING BY 20.72 (LEAD) OR MULTIPLYING BY 88.95 (CADMIUM).

Fig. 2. Current format (1979 onwards) of report for a participating laboratory

The influence of analyte concentration is minimised by using the percentage deviation from the consensus value (see Figure 3). VISs for different analytes can also be combined by using appropriate chosen coefficients of variation determined from the relative state of the art (8); the choice of CCV for a single analyte such as blood lead is less critical, although comparability with VISs from other schemes is desirable.

Although both bias and imprecision contribute to the MRVIS, it is possible to derive analogous indices by retaining the signs of the VISs to give Bias Index Scores (BISs). The MRBIS is then the mean of the 10 most recent BISs, and the SDBIS is their standard deviation (12). The MRBIS is an indicator of relative bias and the SDBIS of consistency of bias, which may be equated with intralaboratory precision when the specimens have the same matrix composition.

**Results**

Reproducibility and Recovery of Consensus Values

Between 1980 and 1982, 11 pairs of duplicate specimens and four pairs of specimens with or without added lead were
distributed. Each pair, unknown to participants, constituted consecutive distributions in the scheme. Statistical analyses of the overall means (recalculated after exclusion of results lying more than 3 SD from the initial mean) are shown in Table 1. The maximum difference between duplicate specimens was 0.13 μmol/L (at 2.5 μmol/L). The unsupplemented specimens in the analytical recovery studies had lead concentrations <1 μmol/L, and the distributions of results were skewed to higher values. The recoveries were therefore also calculated on the basis of the medians for these specimens (Table 1).

Laboratory Performance

The relationships between lead concentration and interlaboratory CVs (recalculated after exclusion of values lying more than 3 SD from the initial mean) in 1973–1974, 1978, and 1983 are shown in Figure 3. The number of participants contributing increased over this period from an initial 35, but remained constant at around 40 from 1974 to 1978. Changes in laboratory performance since 1978 may also be assessed by examination of participants’ scores. Figure 4 shows changes in the average MRVIS for all laboratories since the introduction of Variance Index scoring into the scheme in 1979, during which period the number of participants increased from 50 to 120.

The influence of factors affecting the performance of individual participants was assessed in 1981, when the average MRVIS was 62. Details of laboratory workload and circumstances were requested for classification as clinical, environmental, and (or) occupational if the source(s) formed a major (>40%) component of blood lead assay workload.

Table 1. Reproducibility and Recovery (1980–82) of Trimmed Means Derived from 47–91 Results (Average 66)

<table>
<thead>
<tr>
<th>CV of mean, %</th>
<th>Mean lead concn, μmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproducibility (n = 11 pairs)</td>
<td>Average</td>
</tr>
<tr>
<td>Added lead, μmol/L</td>
<td>1.2</td>
</tr>
<tr>
<td>Recovery (n = 4 pairs)</td>
<td>Average</td>
</tr>
<tr>
<td>Based on mean</td>
<td>1.26–2.75</td>
</tr>
<tr>
<td>Based on median</td>
<td>1.26–2.75</td>
</tr>
</tbody>
</table>

*Trimmed mean for both specimens.

**Median of untrimmed results for unsupplemented specimen only.

Fig. 3. Relationships between interlaboratory CVs (recalculated after exclusion of results >3 SD from the untrimmed mean) and mean blood lead concentration in 1973–1974 (X), 1979 (O), and 1983 (□).

Laboratories were also classified as health service (hospital and university clinical laboratories), industrial (companies monitoring their own employees), or other (governmental, university nonclinical, and commercial laboratories). The average MRVISs in 1981 for these classifications are given in Table 2, together with the associated SDs. Laboratory workload was also classified according to annual workload (tests/year) and according to average batch frequency (interval between batches), both of which were used to compare MRVIS (Table 3).

Method Performance

Interlaboratory agreement in an EQA scheme also provides an assessment of methods, and the average CVs (after outlier exclusion) for specimens distributed in 1978 and 1983 are shown in Table 4 for each of the method groups and subgroups. An alternative assessment may be derived from Variance Index parameters, and Table 4 also gives the average MRVIS, MRBIS, and SDBS (see above) at December 1983 for the method groups and subgroups.

Table 2. Performance (1981) of Participants Classified According to Principal Component(s) of Workload and Laboratory Type

<table>
<thead>
<tr>
<th>Type of laboratory:</th>
<th>MRVIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source of workload:</td>
<td>n</td>
</tr>
<tr>
<td>Clinical</td>
<td>26</td>
</tr>
<tr>
<td>Environmental</td>
<td>14</td>
</tr>
<tr>
<td>Occupational</td>
<td>49</td>
</tr>
<tr>
<td>Type of laboratory:</td>
<td>n</td>
</tr>
<tr>
<td>Health service</td>
<td>42</td>
</tr>
<tr>
<td>Industrial</td>
<td>20</td>
</tr>
<tr>
<td>Other</td>
<td>27</td>
</tr>
<tr>
<td>All participants</td>
<td>89</td>
</tr>
</tbody>
</table>

*Governmental, university nonclinical, and commercial laboratories.

Table 3. Performance (1981) of Participants Classified According to Annual Blood Lead Assay Workload (1980) and Interval between Batches

<table>
<thead>
<tr>
<th>No. of laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRVIS 0–80</td>
</tr>
<tr>
<td>Annual workload, tests/year</td>
</tr>
<tr>
<td>&gt;1000</td>
</tr>
<tr>
<td>Average batch interval</td>
</tr>
<tr>
<td>1 day–1 week</td>
</tr>
</tbody>
</table>
Discussion

Friberg and Vahter (13) endorse the need in blood lead and cadmium assay for continual application of quality assurance, in terms of both internal quality control and external quality assessment, to ensure consistent reporting of reliable results. The objective of an EQA scheme is to stimulate improved interlaboratory concordance of results through provision of objective data on participants’ performance. For this to be successful we believe there must be frequent distributions of reliable specimens, with prompt generation of informative and intelligible reports including a scoring system based on valid target values. The UKEQAS for Lead in Blood has endeavored to fulfill these criteria.

Distributions at two-weekly intervals have been maintained for over 10 years, with an increasing number of participants. The specimen preparation procedure has been validated, and its adequacy is supported by the fact that many participants with good performance consistently obtain results close to the consensus mean value. In addition, these means are reproducible (Table 1). Thus, the observed spread of results between laboratories does not appear to be related to any variability in the specimens themselves.

The report format has been refined as developments in our computer facilities have enabled advances. Reports contain the information needed for participants to assess their performance, while remaining comprehensible. Our experience in other schemes indicates that simplicity is essential, since it is often those participants who have least time, motivation, or ability to devote to report interpretation who most need to take corrective action.

Variance Index scoring was likewise incorporated when facilities became available, the number of participants returning results justified its introduction, and dependence of between-laboratory variation on lead concentration was minimal (Figure 3). The rapid improvement in average performance after the introduction of VISs and MRVISes into participants’ reports (Figure 4) indicates the usefulness of such scoring in providing a laboratory with an objective ongoing assessment of its performance over the last five to six months (10 specimens), confirming experience in other schemes (7, 12). The MRVIS appears to provide a more sensitive means of assessing changes in performance, integrated over some period (sufficiently long to give a robust and stable score, but short enough to respond quickly to changes in performance), than does simple inspection of a laboratory’s results in conjunction with histograms and means. Consideration of the algebraic signs of VISs (i.e., BISes) can also facilitate discrimination between bias and imprecision (12), although the MRBIS and SDBIS have not been routinely introduced into reports for this scheme. Currently, participants are advised to investigate problems by graphing the relationship between their results and the overall mean.

The overall mean, irrespective of method, is used as the designated (target) value for assessment of performance. The specimens distributed are based on whole human blood, as are the clinical specimens assayed, so any matrix effects might therefore be expected to be similar. No participants have provided data to refute this hypothesis, although no formal studies have been carried out to prove it. Furthermore, because several of the method groups are small, the use of method means, as in the UKEQAS for General Clinical Chemistry (8), could lead to problems of variability of the mean due to a low number of results. Recovery of added lead appears satisfactory (Table 1), though it was neither feasible nor economic to obtain comparative results by isotope dilution/mass spectrometry on a regular basis, and a single analysis on one specimen would be of little value.

The scheme is well-accepted by participants, testified to by the growing numbers of laboratories outside the U.K. We believe that all laboratories within the U.K. assaying lead in blood participate, and the scheme is now reaching the total number of participants that can be accommodated with specimens prepared from a single donation of blood.

Laboratory Performance

The performance of most laboratories continues to improve, although an MRVIS <25 probably represents a minimum that is difficult to improve upon. In general, each participant should aim for an MRVIS <33, with a score <67 (currently attained by 84% of both U.K. and overseas participants) being considered generally satisfactory.

Within the U.K., a system for surveillance of performance in UKEQASs in clinical chemistry by a National Quality Assurance Advisory Panel, consisting of nominees of the four professional organizations relevant to the discipline, has been developed (14). This Advisory Panel has confidential access to data on the performance of participants in the U.K. (identified only by their laboratory code numbers) and offers advice and assistance, on a confidential basis, where a participant’s performance appears to give cause for concern (currently at an MRVIS >80 for blood lead assay). For those laboratories carrying out blood lead assays on occupationally exposed workers under the Control of Lead at Work Regulations (1) there is also an informal requirement for the disclosure of their laboratory code number, with joint surveillance by the Chairman of the Advisory Panel and the Deputy Director Medical Services (Pathology) of the Occupational Medicine and Hygiene Laboratories of the Health and Safety Executive; such laboratories must maintain an MRVIS <80. The Advisory Panel was constituted in 1977, monitoring performance for blood lead assay since 1979, and the joint surveillance came into effect in 1982 with the implementation of the Control of Lead at Work Regulations.

Table 4. Blood Lead Performance by Method, Assessed by the Average Interlaboratory CV for 1978 and 1983 and by the Average MRVIS, MRBIS, and SDBIS at Distribution 210 (December 1983)

<table>
<thead>
<tr>
<th>Method</th>
<th>1978 CV</th>
<th>1983 CV</th>
<th>MRVIS</th>
<th>1983 MRVIS</th>
<th>MRBIS</th>
<th>SDBIS</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delves cup</td>
<td>7.7</td>
<td>6.6</td>
<td>5.1</td>
<td>5.6</td>
<td>4.8</td>
<td>3.6</td>
<td>25</td>
</tr>
<tr>
<td>Flameless atomic absorption</td>
<td>10.2</td>
<td>10.2</td>
<td>8.9</td>
<td>9.2</td>
<td>9.2</td>
<td>8.9</td>
<td>65</td>
</tr>
<tr>
<td>With acid digestion</td>
<td>16.2</td>
<td>16.2</td>
<td>16.2</td>
<td>16.2</td>
<td>16.2</td>
<td>16.2</td>
<td>5</td>
</tr>
<tr>
<td>With extraction</td>
<td>10.9</td>
<td>10.9</td>
<td>10.9</td>
<td>10.9</td>
<td>10.9</td>
<td>10.9</td>
<td>3</td>
</tr>
<tr>
<td>With neither</td>
<td>8.7</td>
<td>8.7</td>
<td>8.7</td>
<td>8.7</td>
<td>8.7</td>
<td>8.7</td>
<td>51</td>
</tr>
<tr>
<td>Punched disc</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>4</td>
</tr>
<tr>
<td>Other (flame) atomic absorption</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>11</td>
</tr>
<tr>
<td>Dithizone</td>
<td>17.8</td>
<td>17.8</td>
<td>17.8</td>
<td>17.8</td>
<td>17.8</td>
<td>17.8</td>
<td>2</td>
</tr>
<tr>
<td>Anodic stripping</td>
<td>7.7</td>
<td>7.7</td>
<td>7.7</td>
<td>7.7</td>
<td>7.7</td>
<td>7.7</td>
<td>6</td>
</tr>
<tr>
<td>Voltammetry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other methods</td>
<td>—</td>
<td>—</td>
<td>51</td>
<td>51</td>
<td>51</td>
<td>51</td>
<td>2</td>
</tr>
<tr>
<td>All participants</td>
<td>12.2</td>
<td>12.2</td>
<td>12.2</td>
<td>12.2</td>
<td>12.2</td>
<td>12.2</td>
<td>2</td>
</tr>
</tbody>
</table>

CV, coefficient of variation; %, percentage; n, number of participants.
Between-laboratory variability is now about half that in 1979, and the average MRVIS for all participants continues to fall (Figure 4). The improvement is not explicable by changes in the lead concentrations surveyed because the main change has been a reduction in the number of specimens with lead content >4.0 μmol/L (Figure 3). The very slight tendency to lower CVs for specimens with higher lead concentrations shown in Figure 3 agrees with Saltzman's data analysis (6). The data presented by Saltzman, however, show little evidence of improvements in interlaboratory agreement, and the interlaboratory CVs he quotes should yield average VISs of 67, 87, and 127 for the three schemes studied (6). The performance data quoted by Friberg and Vahter (13) for the monitoring phase of an environmental survey for 10 laboratories that had undergone a training program, with an estimated average MRVIS around 50 (range 20–80), are more in accord with our findings.

There was indeed a tendency in our scheme for those laboratories carrying out the assay predominantly for environmental monitoring purposes to have better performance than the clinical (p <0.01; by Student's t-test) or occupational monitoring (p <0.02) participants (Table 2). This might be associated with the lower lead concentrations involved and the more stringent performance criteria within which they work. The only significant difference within the classification according to laboratory type was between industrial and other laboratories (p <0.05).

There was no simple relationship between either workload indicator and the MRVIS, though Table 3 demonstrates a definite association, such that a much greater proportion of the laboratories that carried out fewer assays or assayed batches infrequently had higher MRVISs (p <0.001 in both cases; χ² test). More detailed examination suggested that, although good performance was attained by some laboratories carrying out as few as 50 assays a year, an interval between assay batches greater than two weeks was associated with an MRVIS >80 (the current U.K. criterion of unsatisfactory performance) in five of six cases. In addition, there appeared to be an effect of inappropriately low batch size: two laboratories with an MRVIS >80 carried out the assay either daily or every two days but had workloads below 500 tests/year.

Method Performance

The performance of the types of method used by participants may be assessed by examining reproducibility and recovery data, as described for the overall consensus values. Such an examination in 1980, based on two pairs of duplicate specimens and two pairs with or without added lead, suggested a slight negative bias (about −5%) for the Delves cup method group and similar reproducibility for all three atomic absorption groups; the conclusions were the same whether the method group meant or the results for the individual laboratories in the groups were considered. The dithizone group, however, gave poor recovery (77%) of added lead, and the reproducibility of their results was 2.5 times worse than for the atomic absorption groups. Though one of the five participating laboratories using the dithizone method had apparently satisfactory performance, the average MRVIS for this group was 90 (average 65 for atomic absorption users). Dithizone users were therefore advised to examine their performance, given the unreliability of the method in some laboratories.

Between-laboratory agreement in 1978 appeared to be best for the more automated procedures (Delves cup and flameless atomic absorption), but by 1983 much of the difference between method groups had disappeared as overall performance improved (Table 4). Variance Index parameters yield a more sensitive and more robust assessment of trends in performance, and the average MRVIS data in Table 4 confirm this conclusion.

The average SDBISs in Table 4 show that precision is the primary problem in flameless atomic absorption with acid digestion or extraction, and suggest that it may also be a factor in the dithizone and flame atomic absorption groups. With regard to bias, the only groups with average MRBISs of 15 or greater are flameless atomic absorption with acid digestion or extraction, dithizone, and other methods (Table 4). These indicate biases of −5%, +2%, and +5%, respectively, from the overall mean, though the latter two groups each consist of two participants only. The bias of −2% for the anodic stripping voltammetry group relative to the Delves cup and flameless atomic absorption groups (Table 4) is in general agreement with Saltzman's estimate of −2.7% (6).

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