# The Italian external quality assessment scheme for trace element analysis in body fluids

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**Summary**. - We describe the operative procedures of the Italian external quality assessment scheme (EQAS) for the determination of trace elements in body fluids. The aims of the scheme are both the education of participants and the continuous development and optimization of procedures for collaborative EQA trials. Participation is free of charge. Interlaboratory exercises for EQA are organised every three or four months for the determination of cadmium and lead in blood; aluminium, copper, selenium and zinc in serum; chromium and nickel in urine. Freeze-dried control materials are prepared in the laboratory from animal blood or human urine. In each trial, each participant receives from six to eight samples, chosen from among the pools selected for that occasion using a randomised strategy and including unknown duplicate specimens. Laboratory performances are evaluated on the basis of proximity to target values, differences in results for duplicate samples and comparison with established acceptability limits. The development of dedicated software for the bidirectional transmission of data between the organising centre and the peripheral laboratory gives the participants the chance to verify immediately the quality of their results and take action without delay, if needed.

*Key words*: blood, urine, external quality assessment, trace element, Italy.

**Riassunto** (*Il programma italiano di valutazione esterna della qualità nella determinazione degli elementi in traccia nei fluidi biologici*). - Vengono descritte le operazioni del programma italiano di valutazione esterna della qualità (VEQ) nella determinazione degli elementi in traccia nei fluidi biologici. Gli scopi del programma sono sia l'educazione dei partecipanti, sia il continuo sviluppo e ottimizzazione delle procedure adottate per esercizi collaborativi di VEQ. La partecipazione al programma è completamente gratuita. Il programma consiste in esercizi periodici interlaboratoriali per la VEQ nelle determinazioni di: cadmio e piombo nel sangue; alluminio, rame, selenio e zinco nel siero; cromo e nichel nelle urine. Materiali di controllo liofilizzati sono preparati in laboratorio da sangue animale e urine umane. In ogni esercizio, ogni partecipante riceve un gruppo di campioni di controllo (da sei a otto) scelti tra quelli selezionati per la distribuzione in base a una strategia randomizzata che include duplicati non noti. Le prestazioni analitiche dei laboratori sono valutate in base all'accordo con il valore atteso, le differenze tra i risultati ottenuti per campioni duplicati e il confronto con limiti di accettabilità predefiniti. Lo sviluppo di un software dedicato per la trasmissione telematica di dati tra il centro organizzatore e il laboratorio periferico permette ai partecipanti di valutare le proprie prestazioni in tempo reale e di attuare immediatamente misure correttive, se necessario.

*Parole chiave:* sangue, urine, elementi in traccia, valutazione esterna di qualità, Italia.

## Introduction

The Italian external quality assessment scheme (EQAS) for trace elements in body fluids, known in Italy as "Progetto METOS", (toxic metal project) started in 1983 with a scheme for the determination of lead and cadmium in blood. The programme was promoted on a voluntary basis by a working party of the Italian National Institute for Health (Istituto Superiore di Sanità, ISS), to warrant the comparability of results obtained in multicentre programmes for the biological monitoring of the general European population against the risk of saturnism [1-4]. The scheme was based on the use of common internal quality control samples and participation in periodical exercises for EQA (external quality assessment). This first initiative provided Italian laboratories with the means to assess their performances and stimulated the development of a philosophy of quality. Since then, additional schemes for other elements and matrices of interest for the participants have been developed within the framework of the "Progetto METOS", which now includes three matrices and seven analytes [5-9].

The Italian EQAS, which will be described in detail here, focused on: the production of safe, low-cost control materials, covering the concentrations of interest; the implementation of strategies of sample distribution that minimise the chances of control samples being identified; the development of an "on-line" system for the bidirectional transmission of data for a more effective use of EQA.

## Organization of the scheme

The aims of the programme are:

- continuous development and optimization of procedures for EQA;

- evaluation of the quality of the analytical performance provided by Italian laboratories in the determination of trace elements;

- provision to laboratories of objective means to assess the reliability of their results in comparison with those of others, thus promoting the maintenance and improvement of analytical performance through the periodical monitoring of analytical procedures, identification of the sources of error and replacement of inadequate methods and obsolete instrumentation;

- provision of professional advice, to educate the operators and promote the philosophy of quality assurance.

The Italian EQAS includes schemes for the analysis of: lead and cadmium in blood; aluminium, copper, selenium and zinc in serum; nickel and chromium in urine. The choice of new schemes to be implemented is made on the basis of periodic surveys of the laboratories' requirements and their workload for specific analytes and matrices. All control materials used in the scheme are prepared at ISS, from animal blood and human urine. Interlaboratory comparisons for EQA are organised every three or four months. Participation is voluntary, free of charge and open to national and foreign laboratories operating in the field. Full anonymity is granted to all participants, identified by means of code numbers and the analytical method. Since the Italian EQAS is purely educational, no measures are taken against poor performers, but advice is available on request. However, the dispatch of samples is discontinued to laboratories who fail to provide results for more than two trials.

As an educational measure, two batches of control samples with known concentration (medium-low and medium-high level) were initially provided to participants in EQAS for the determination of aluminium, cadmium and lead, to be used for internal quality control. However, the increased workload and costs due to the introduction of schemes for other elements and matrices made it no longer possible to provide such samples.

## Preparation of control samples

### Choice and treatment of starting material: blood, serum, urine

Control materials are prepared in the laboratory from cow blood, cow and horse serum, (purchased from Zootecnica "Il Gabbiano", Casole d'Elsa, Siena, Italy) or human urine. Animal blood is preferred to human blood because of larger availability, lower cost and higher safety of manipulation. For blood lead determination, we have shown that the analytical performance assessed on control samples based on cow blood did not differ from that on fresh human blood samples [10, 11].

Cow blood is collected using $K_2EDTA$ (1.5 mg/ml) as an anticoagulant, frozen at -80 °C, thawed and centrifuged to obtain an homogeneous material. Serum based control samples are prepared from cow or horse serum. Endogenous levels of Cu and Zn are reduced by separation of caeruloplasmin and zinc on activated sepharose [12]. Human urine is collected from healthy volunteers who had no known exposure to nickel or chromium, deep-frozen to increase sedimentation and then thawed and centrifuged. Gentamycin (20 mg/l) is added to all materials to avoid bacterial growth and improve conservation.

### Choice of concentration levels

All control materials used in the Italian EQAS, with one exception, are intended for single-element determination, to avoid contamination due to repeated sampling from the same tube. Therefore, batches of control samples are prepared separately for each element/matrix pair. Only copper and zinc are determined in the same serum sample, because the required sample preparation is more demanding and most laboratories determine both elements.

Control materials are prepared for aluminium, cadmium, chromium, lead and nickel at concentration levels covering both environmental and clinical or occupational exposure. The concentrations of control materials for copper, selenium and zinc analysis include low and high levels occurring in pathological conditions. Different concentration levels are generally obtained by addition of salts of the elements with two exceptions. Control samples for copper determination are spiked with different amounts of caeruloplasmin, available as a separate fraction after the elution of horse serum from activated sepharose. This method provides control materials with a composition as similar as possible to that of real samples, where approximately 95% of copper is bound to caeruloplasmin. For a similar reason, control materials with different selenium concentrations are obtained by mixing serum pools with high and low selenium content (horse/cow serum) in different ratios.

Six to twelve pools at different concentrations are prepared for each element/matrix once a year. Table 1 reports the ranges of concentrations for the control materials prepared for each element/matrix during 1994 and 1995.

### Distribution and storage

Each pool is divided in plastic vials, deep frozen, lyophilised and stored at +4 °C. The volume of control samples depend on the element/matrix pair and volume required for analysis. At present, we use aliquots of 2 ml

for control samples intended for Al, Cd, Pb and Se determination; 4 ml for Cr, Cu and Zn; 10 ml for Ni. Homogeneity and accuracy of the preparations are tested by analysing 5% of the samples of each batch.

## Strategy for the distribution of control samples to participants

Six to eight samples, including some as unknown duplicates, are distributed to the participants in each trial. To avoid identification of samples and exchange of information between different centres, for each occasion of testing, the pools to be distributed are selected from those available. The samples for each laboratory are then individually chosen among the selected pools and given randomly generated reference codes. The whole procedure is carried out by a computer programme, which creates additional records in a database, for the storage of all the relevant information and the input of results. Finally, the same computer programme prints: a) a list of the samples and their reference codes assigned to each laboratory (to be used during the distribution of samples); b) the sample labels with the reference codes and the data sheets for reporting results. In this way, the chances of transcription errors are minimised.

## Flow of information from and to laboratories: results and reports

Results are returned within four weeks, by fax, surface or electronic mail. The software controlling the on-line transfer of laboratory results (INFOMETOS) has been especially developed for this application and is provided to all participants on request. Users have access via modem to their electronic data-sheet (Fig. 1, a) for the on-line transmission of their results to the organising centre. After user's approval, individual results are added to the database and cannot be further modified. Users are then allowed on-line access to "expected values" (i.e. results of preliminary analyses carried out in the organisers' laboratory by atomic absorption spectrometry) (Fig. 1, b).

The overall results returned are elaborated at the end of each trial, without any exclusion. The statistics calculated are reported in Table 2. If at least three replicate specimens were included in the set of samples received by the laboratory, the intra-laboratory precision is estimated as pooled standard deviation of the replicate results (PSD), i.e.:

$$PSD = \sqrt{(\Sigma d_i{}^2/2n)},$$

where $d_i$ is the difference between the two replicate results and n is the number of analysed pairs.

**Table 1.** - Ranges of concentrations for the control materials prepared for each element/matrix during 1994 and 1995

| Matrix | Element | Range of concentrations (µg/l) |
|--------|---------|-------------------------------|
| Blood | Cd | 1.3 - 4.4 |
| | Pb | 21 - 570 |
| Serum | Al | 9 - 205 |
| | Cu | 500 - 1500 |
| | Zn | 450 - 1450 |
| | Se | 25 - 140 |
| Urine | Cr | 0.8 - 13.8 |
| | Ni | 1.3 - 14.2 |

The median of the results of all laboratories is taken as target value, if there is a good agreement with the "expected values" and the recovery of the amount of metal added. In the Authors' experience, the agreement between the median and the values obtained in the preliminary analyses is generally good. However, discrepancies occur when the number of participants with relevant experience and satisfying performance is limited. In this case, the values obtained by the organisers are used as target values.

The linear regression between the laboratory results (y) and target values (x) is calculated for the samples analysed in each trial, to help participants to investigate the sources of error.

Participants receive a report which shows the results provided by all participants, statistics and indices of their performance. This report is sent with the next group of samples, about four weeks later.

A flow chart of the organization of the Italian EQAS is reported in Fig. 2.

### Indices of laboratory performances

Indices of laboratory performances include for each sample: the rank of the laboratory within the group of participants (absolute and normalised rank); the deviation from expected values and z-scores; the deviation from the median of all results and its comparison with established acceptability limits. For each element and matrix, the maximum acceptable deviation has been defined for two concentrations (low and high), taking into account both analytical capabilities and clinical needs. Acceptability limits at any other concentration

*(a)*

INFOMETOS　　　　　　　　External quality assessment　　　　　　　19-12-95

| Control code - PB1/038/038/PB |
| --- |
| Date of receipt ...................................... : |
| Date of analysis.................................... : |
| Method code ........................................ : |

| Code | Result (μg/l) | No. | (Ex. Val.) | Code | Result (μg/l) | No. | (Ex. Val.) |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 60 - | - 1.000 | - | - | 56 - | - 1.000 | - | - |
| 52 - | - 1.000 | - | - | 69 - | - 1.000 | - | - |
| 96 - | - 1.000 | - | - | 57 - | - 1.000 | - | - |
| 66 - | - 1.000 | - | - | 88 - | - 1.000 | - | - |
| - | - 1.000 | | | - | - 1.000 | | |
| - | - 1.000 | | | - | - 1.000 | | |

Notes ............ :

*(b)*

INFOMETOS　　　　　　　　External quality assessment　　　　　　　19-12-95

| Control code - PB1/038/038/PB |
| --- |
| Date of receipt ................................... : 22-06-95 |
| Date of analysis ................................ : 17-07-95 |
| Method code ....................................... :　　08 |

| Code | Result (μg/l) | No. | (Ex. Val.) | Code | Result (μg/l) | No. | (Ex. Val.) |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 60 - | 64.000 | 56 | 53.000 | 56 - | 189.000 | 82 | 185.0000 |
| 52 - | 211.000 | 58 | 212.000 | 69 - | 544.000 | 54 | 525.000 |
| 96 - | 102.000 | 57 | 96.000 | 57 - | 286.000 | 84 | 289.000 |
| 66 - | 287.000 | 84 | 289.000 | 88 - | 192.000 | 82 | 185.000 |
| - | - 1.000 | | | - | - 1.000 | | |
| - | - 1.000 | | | - | - 1.000 | | |

Notes ............ :

**Fig. 1.** - INFOMETOS electronic data-sheet for the input of data by the user *(a)* and after results have been registered into the database *(b)*. No: number of results received from participants at the connection time; Ex. Val.: expected values.

**Table 2.** - Information provided in the report to participants
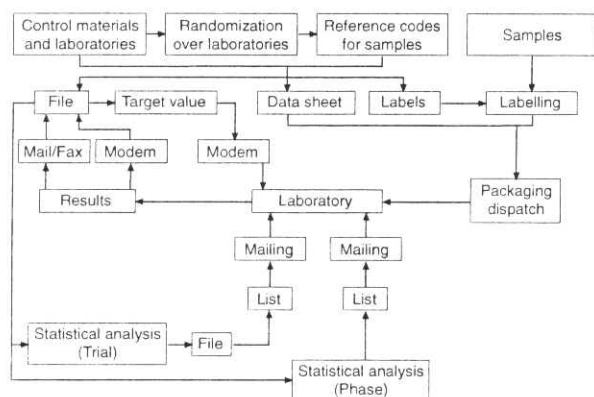
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*Intralaboratory precision* (when available)
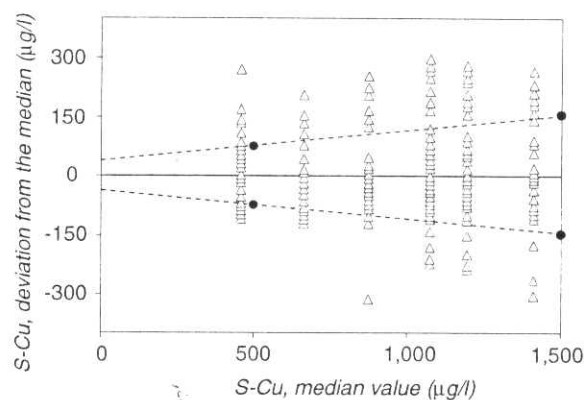Pooled standard deviation

*Linear regression*
All laboratory results for the samples analysed in the trial (y)
All correspondent "target values" (x)
Intercept, slope and determination coefficient of the resultant linear regression

*For each analysed sample*
Laboratory result
Result rank and normalised rank
Number of results (no exclusion)
Mean
Standard deviation (SD)
Maximum and minimum reported values
Median
Skewness and ratio between the skewness and its standard error
Kurtosis and ratio between the kurtosis and its standard error
"Expected value"
"Expected SD"
Z-score
Q-score
Maximum acceptable deviation from the median
Deviation from the median of the laboratory result
Percent deviation from the median of the laboratory result
Results obtained by all participants analysing the same sample
Absolute deviations from the median obtained by all the other participants analysing the same sample
Absolute deviation from the median of the laboratory result
Median of the absolute deviations from the median (MAD)
Rank and normalised rank of the laboratory deviation from the median

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**Fig. 3.** - Acceptability limits for serum copper determination over the range of concentrations of interest and example of the distribution of the deviations from the median of the results obtained by the participants in an EQA exercise (deviations exceeding ± 300 µg/l not plotted).

**Table 3.** - Maximum acceptable deviations to the target values established for various elements at low and high concentrations, for the definition of the acceptability limits over the range of concentrations

| Matrix/element | Concentration (µg/l) | Acceptable bias (µg/l) |
|---|---|---|
| Blood Pb | 100 | ± 20 (20%) |
|  | 800 | ± 80 (10%) |
| Blood Cd | 1 | ± 0.6 (60%) |
|  | 15 | ± 1.5 (10%) |
| Serum Al | 10 | ± 3 (30%) |
|  | 120 | ± 12 (10%) |
| Serum Cu, Zn | 500 | ± 75 (15%) |
|  | 1500 | ± 150 (10%) |
| Serum Se | 30 | ± 6 (20%) |
|  | 120 | ± 12 (10%) |
| Urine Cr, Ni | 1 | ± 0.6 (60%) |
|  | 10 | ± 1.5 (15%) |



**Fig. 2.** - Flow chart of the organization of the Italian EQAS.

can be obtained by linear regression. An example of this criterion is reported in Fig. 3 for serum copper and the maximum acceptable deviations chosen for all elements included in this scheme are given in Table 3. Results which fail to meet acceptability criteria are clearly marked in the report issued at the end of each trial.

**Table 4.** - Participants and average compliance (1995) in the Italian EQAS for each element/matrix and number of analyses reported for the same analyte in 1994

| Matrix/element | Participants | Compliance (%) | Analyses/year |
|---|---|---|---|
| Blood Pb | 93 | 94.6 | 63333 |
| Blood Cd | 48 | 89.6 | 6481 |
| Serum Al | 58 | 93.1 | 19013 |
| Serum Cn | 50 | 98.0 | 12180 |
| Serum Zn | 47 | 95.7 | 6533 |
| Serum Se | 15 | 80.0 | 1319 |
| Urine Cr | 37 | 97.3 | 14675 |
| Urine Ni | 32 | 93.8 | 5433 |

**Table 5.** - Global performances of laboratories during the last phase (three trials carried out between mid 1994 and mid 1995) in the various schemes in terms of average absolute deviation from the mean (DEVm) and dispersion of the results (average inter-laboratory coefficient of variation, CV%)

| Matrix/element | Average concentration of the control samples ($\mu g/l$) | DEVm ($\mu g/l$) | Average CV (%) |
|---|---|---|---|
| Blood Cd | 2.8 | 0.9 | 34 |
| Blood Pb | 188 | 33 | 18 |
| Serum Al | 95 | 18 | 18 |
| Serum Cu | 980 | 173 | 19 |
| Serum Zn | 920 | 200 | 21 |
| Serum Se | 80 | 13 | 16 |
| Urine Cr | 5.7 | 1.8 | 31 |
| Urine Ni | 7.6 | 2.8 | 36 |

Z-scores are calculated as: z-score = $|(x_i - X_e)/SD_e|$, where $x_i$ is the laboratory result, $X_e$ is the "expected value" and $SD_e$ is the "expected standard deviation", i.e. the SD taken as a goal for the group of participants and defined as half of the corresponding acceptable deviation for the same concentration (Table 3). This choice provides consistency between the two methods of evaluation of performance.

The overall performances of the laboratories are evaluated once a year, taking into account the percentage of acceptable results provided by each centre. Laboratories are then classified according to the percentage of acceptable results as "good performers", i.e. with 80-100% of acceptable results; "acceptable performers", i.e. with 50-79% of acceptable results and "poor performers", i.e. laboratories with less than 50% of acceptable results.
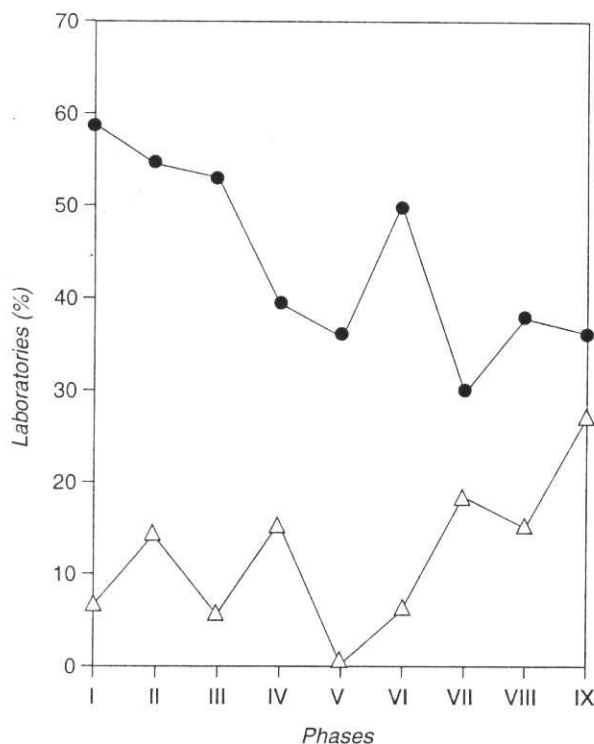
Fig. 4. - Trend observed over the years (1985-1995) for the percentage of "good" (triangles) and "poor" (circles) performers in serum aluminium analysis.



**Fig. 5.** - Different types of error, occurring in 4 laboratories for serum aluminium determination, as highlighted by the linear regression between their results (y) and the target values (x). Good performance (thick solid line, diamonds), mixed error (dotted line, grey squares), proportional error (dashed line, circles) and constant error (thin solid line, black triangles).

## Results

### Participants

At present, more than 100 laboratories voluntarily take part in the operation of the Italian EQAS, taking into account all schemes. Although some have dropped out, the large majority participate regularly in the EQA exercises and the compliance is satisfactory. Table 4 reports the number of participants for each element/matrix, the average compliance in 1995 and the workload reported by the participants for each element/matrix. Participants include local prevention units, i.e. "Presidi Multizonali di Prevenzione" (51%), commercial laboratories (18%), hospital (15%), university and research laboratories (14%).

Participants use the methods of their choice. Analytical techniques include flame and electrothermal atomic absorption spectrometry, inductively coupled plasma atomic emission spectrometry, inductively coupled plasma mass spectrometry and colorimetry.

### Global performances

An overall view of the performances of the Italian laboratories in trace element analysis during the latest phase (three exercises, carried out between mid 1994 and mid 1995) is given in Table 5, in terms of dispersion of the results, i.e. the average coefficient of variation (CV%),
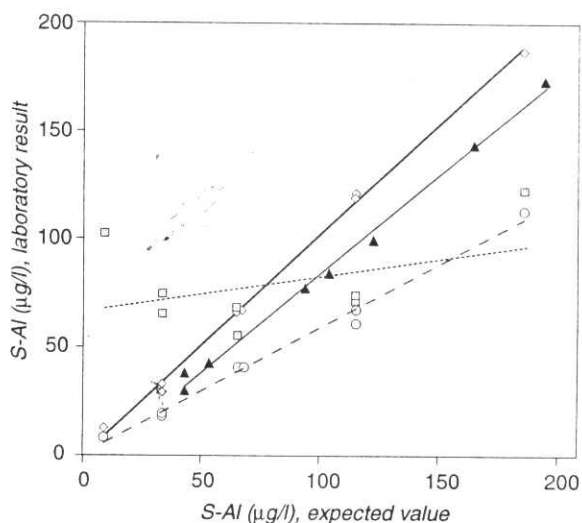
and global inaccuracy, i.e. the average absolute deviation from the mean, calculated as the square root of the mean of the variances observed for each sample. In this evaluation, both variances and CV% were obtained after exclusion of data exceeding the interval: mean ± 3 SD. Also, data obtained on samples at very low concentration, such as unspiked bovine blood for Cd and Pb analysis, were not included, because analytical imprecision increases sharply for concentrations close to detection limits and these data will not be representative of the global performance of the participants.

Positive trends have been observed over the years, in terms of increasing percentages of "good performers" and decreasing percentages of "poor performers", although the inclusion of new laboratories caused the worsening of the global performances on some occasions. An example is given in Fig. 4 for serum aluminium. For the newer schemes, however, not enough data have yet been collected to allow trends to be estimated. For these schemes, preliminary results on the distribution of results among classes of z-scores are shown in Table 6.

## Discussion

The Italian EQAS for trace elements in body fluids is well known and accepted by Italian laboratories operating in the field. The procedures adopted allow participants to evaluate critically their performance over the whole range of concentrations of interest and, as a result, to modify or substitute inadequate analytical procedures and to update equipment. As an example, we report in Fig. 5

**Table 6.** - Distribution (frequency %) of the results according to classes of z-scores in subsequent trials of the EQAS for: Cr and Ni in urine; Se, Cu and Zn in serum

| Analyte | Trial | Classes of z-score | | | |
| | | $\|z\| \leq 2$ (%) | $2 < \|z\| \leq 3$ (%) | $\|z\| > 3$ (%) | Total (%) |
| --- | --- | --- | --- | --- | --- |
| Cr | 001 | 59.4 | 13.2 | 27.4 | 100 |
| | 002 | 64.6 | 6.1 | 29.3 | 100 |
| | 003 | 71.4 | 12.9 | 15.8 | 100 |
| Ni | 001 | 45.9 | 14.4 | 39.8 | 100 |
| | 002 | 39.9 | 10.7 | 49.4 | 100 |
| | 003 | 52.2 | 15.3 | 32.5 | 100 |
| Se | 001 | 58.3 | 10.4 | 31.3 | 100 |
| | 002 | 71.6 | 14.8 | 13.6 | 100 |
| Cu | 001 | 60.5 | 15.6 | 23.9 | 100 |
| | 002 | 57.3 | 21.5 | 21.2 | 100 |
| Zn | 001 | 42.4 | 20.8 | 36.9 | 100 |
| | 002 | 49.8 | 17.5 | 32.7 | 100 |

the performances of 4 laboratories for the determination of Al in serum over a range of concentration. The regression lines obtained between laboratory values (y) and target values (x) highlighted the presence of different types of error in the four cases.

In this scheme, we focused on the optimisation of the cost/benefit ratio with the development of: safe, low cost control materials, covering the whole range of concentrations of interest; optimised procedures of sample distribution which minimise the possibility of samples being identified; development of procedures for the on-line transmission of data, to reduce the chances of transcription errors and allow a more effective use of EQA.

Over the years we were able to demonstrate that control samples from animal blood were reliable and commutable with patient samples, as laboratories showed comparable performance in the analysis of control samples from cow blood and fresh human samples [10, 11]. The randomised procedures developed for the distribution of samples allowed us to obtain an unbiased evaluation of the laboratory performance [7].

Although positive trends have been observed for most analytes, some problems still remain. Due to the scheme being voluntary, participation is limited to centres who are also more aware of quality issues and no information is available about the quality of results achieved in centres who do not participate in this scheme. Another problem is that, after more than ten years of activity of the schemes for blood lead and serum aluminium, some laboratories behave as persistent poor performers and do not appear to have benefited from participation in EQAS. Further initiatives would be necessary to implement quality assurance within the laboratory in the field of occupational and environmental medicine, which may include compulsory participation in EQAS in order to achieve accreditation. However, these actions involve other bodies than the organisers of this EQAS.

The delay between the analysis of specimens for EQA and the return of results may compromise the identification of the sources of error occurring at the time when the analyses were carried out. Even worse, failure to early recognise the problems arising in the laboratory may have caused all results provided by the laboratory, in the meantime, to be biased. For this reason, we focused on the development of dedicated software for on-line transmission of EQAS results and direct access to "expected values" by the operators. The procedure

developed is user-friendly and gives the participants a unique chance to rapidly obtain information on their performance and take appropriate measures if needed.

The transmission of results by modem is becoming increasingly used and will be the system of choice in the near future. The development of on-line systems for EQA is especially important in view of the possibility of EQAS for rare analyses to be carried out at European level.

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**Appendix** - Summary of the scheme

| | |
|---|---|
| **Country** | Italy. |
| **Name of scheme** | METOS. |
| **Status of scheme** | National but open to foreign participants. Voluntary.<br>Run by Department of Clinical Biochemistry, National Institute of Health<br>*Aims*: continuous development and optimization of procedures for EQA; assessment of analytical performance provided by Italian laboratories; improvement of analytical performance and education of operators.<br>*Participants:* more than 100 laboratories, including local prevention units (51%), commercial (18%), hospital (15%), university and research laboratories (14%). |
| **Scheme description** | *Control materials:* lyophilised, single-element samples (except for Cu/Zn), in plastic vials; prepared at the ISS from cow blood, cow/horse serum and human urine; different concentrations obtained by: addition of caeruloplasmin (serum Cu); pooling serum samples with high and low selenium content (serum Se); addition of known amounts of analytes (all other analytes);<br>*Target value:* median of the results of all laboratories or values obtained by the organisers in the preliminary analyses ("expected values").<br>*Internal quality control samples:* initially included in the programme but not more available to participants.<br>*Organization of EQA exercises:* EQA exercises organised every three/four months: for each analyte/matrix six to eight samples, including some as unknown duplicates, are sent to each participant. The samples assigned to each laboratory are randomly selected among the pools available and given reference codes using a computerised procedure, to avoid identification and exchange of information. Results returned within 30 days by fax, post or modem.<br>*Elaboration of results:* median and parametric statistics for each sample. Linear regression between laboratory results (y) and target values (x).<br>*Criteria for evaluation of laboratory performance:* rank of the laboratory within the group of participants (absolute and normalised rank); deviation from expected values, q-scores and z-scores; deviation from the median and its comparison with established acceptability limits. Overall performances of laboratories evaluated once a year, from the percentage of acceptable results: 80-100%, "good performers"; 50-79%, "acceptable performers"; less than 50%, "poor performers".<br>*Measures taken against poor performers:* none.<br>*Advice and training:* available on request.<br>*Financial support:* from the own resources of ISS; participation is free of charge. |
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| **Analytes and matrices covered** | Aluminium, copper, selenium, zinc in serum.<br>Lead and cadmium in whole blood.<br>Chromium and nickel in urine. |