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# GEMS/Food-EURO
# Second Workshop
# on
# Reliable Evaluation of Low-Level Contamination of Food

Report on a Workshop in the Frame
of GEMS/Food-EURO

**Kulmbach, Federal Republic of Germany, 26 - 27 May 1995**
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## ABSTRACT

Within the WHO European Programme for Monitoring and Assessment of Dietary Exposure to Potentially Hazardous Substances (GEMS/Food - EURO), measures are undertaken to assure the reliability and comparability of data handled in this Programme. During the collation of contamination data on various food items and diets, there are always some analytical results which will be reported as non-detectable (ND), i.e. the analytical result is below the limit of detection (LOD), or nonquantifiable (NQ), i.e. the analytical result is below the limit of quantification (LOQ). Such qualitative results must be combined with quantified (numerical) data expressed as numerical, statistical figures such as median and $90^{th}$ percentile.
The workshop discussed various calculation methods and agreed that the present unsatisfactory situation could be improved by applying easy to use mathematical or graphical extrapolation models which will be made available to GEMS/Food-EURO participating National Contact Points.
The recommended procedure ensures the reliability and comparability of GEMS/Food-EURO data sets and results in a more realistic description of the contamination of food; the responsible authorities will be provided with sound information forming the basis of their decisions.

**CONTENTS**

## INTRODUCTION

1. Reliable evaluation of analytical results of measurements of substances in foods and diets is a prerequisite for the realistic estimation of food contamination. Within the WHO European Programme on Monitoring and Assessment of Dietary Exposure to Potentially this programme and to provide decision-makers in the Member States and the scientific community with sound information Hazardous Substances (GEMS/Food-EURO), measures are undertaken to assure the reliability and comparability of data handled in and a reliable evaluation of these data.

2. During the collation of contamination data on various food items and diets, there are generally some analytical results reported as **non-detectable (ND)** or **non-quantifiable (NQ).** Such qualitative results may be combined with quantified (numerical) data usually expressed as statistics, such as median or $90^{th}$ percentile, to assess the exposure of populations to potentially hazardous substances such as heavy metals, pesticides, industrial chemicals, mycotoxins, veterinary drug residues and radionuclides.

3. In March 1994, WHO organized an international workshop to discuss current methods for evaluating data on low level contamination of food. In particular the workshop addressed the problem of combining quantified and non-quantified analytical data. This workshop reached a number of conclusions that were published by WHO in March 1995. In particular the workshop recommended that "WHO/EURO should explore together with Member States the further development of methods to describe the statistical distribution of analytical data where a large fraction of the data are non-quantified. Similarly, methods for the mathematical analysis of these data should be explored". The purpose of this workshop was to take forward the evaluation of low-level contamination, using as building blocks the results of research and investigations carried out as a consequence of the recommendation from the first workshop.

4. The second workshop was organized jointly by the Bundesanstalt für Fleischforschung, Kulmbach Germany, and the European Centre for Environment and Health, Rome Division, of the Regional Office for Europe of the World Health Organization. Participants came from Finland, Germany, Poland and the United Kingdom. Professor Honikel was elected Chairman and Dr Sherlock served as Rapporteur. The list of participants is in Annex 1.

## DISCUSSION AND CONCLUSIONS

5. Prior to this workshop the participants received several background papers (see Annex II); these papers were presented at the workshop along with several ad hoc contributions. The aim was to produce general recommendations that might be applied to the interpretation of data on low level contamination whilst allowing the flexibility to continue to treat data containing a high proportion of non-quantified results. The long-term aim was to provide a means whereby there could be uniform reporting of data, particularly on concentrations of contaminants but also on intakes calculated from these concentrations, thus providing a fair means of comparing data from different Member States.

### Recommendation from previous workshop

6. The previous workshop made a number of recommendations about the requirements for the analysis of foods and the reporting of data; many of these recommendations were restatements of good practice. However, the workshop also recommended that in those cases where fewer than 50% of the samples were quantified "An upper bound and a lower bound should be reported. The upper bound is calculated by setting all non-detects to the limit of detection and all non-quantifiables (if not numerically) reported to the limit of quantification. The lower bound is calculated by setting all nondetects and all non-quantifiables to zero.". The true mean of the data will lie between the upper bound and the lower bound. Although the method is relatively crude, it does at least have the merit of simplicity. However, the range between the lower bound and the upper bound can be very large giving rise to considerable uncertainty in concentrations and intakes based on these concentrations.

Advances made since the previous workshop

7. The workshop considered two papers prepared for the meeting. The first paper, titled: "Evaluation of censored contamination data" was by Vlachonikolis and Marriott, which reported work supported by WHO. The second paper titled:

"Assessment of data sets containing considerable values below the detection limits" was by Hecht and Honikel of the Federal Centre for Meat Research.

8. Vlachonikolis and Marriott conclude that:

- A general description of the data, in the form of transformation, mean and standard deviation (or something equivalent) is desirable if it is not misleading.

- With the proportion of censored data greater than or equal to 50%, it is important that the appropriate transformation should be used, and that must be based on uncensored or lightly censored, data sets for the contaminant in question.

- Fitting by maximum likelihood is the best option, providing asymptotically efficient estimates (i.e. estimates with minimum variance for large sample sizes). Fitting using quantiles is computationally easier but entails some loss of efficiency with large, heavily censored samples.

9. Hecht and Honikel conclude that:

- Environmental pollutants are distributed log normally in biological systems, having a standard deviation of **about** 1 when the data are transformed by (natural) logarithm This is valid for most of the common environmental pollutants.

- In these cases it is possible to estimate nonquantifiable percentiles, especially the median from the quantifiable ones, by multiplying them with certain factors without making artificial or arbitrary assumptions on the limits of detection.

- Assuming that the logarithmic standard deviation is 1, then using LOD/2 for non-quantified data provides a good estimate of the mean when the proportion of non-quantified data is < about .70% and only one LOD or very similar LODs are in the data set.

10. Sherlock presented information at the meeting that indicated that concentration data for several food contaminants were approximately log normally distributed with a mean logarithmic standard deviation of **about** 1 but with a range of standard deviations from 0.4 to 1.7. For his data sets (which had 60% or less data censored), using LOD/2 for data reported as <LOD provided a reasonably effective estimate of the arithmetic mean regardless of the standard deviation. He estimated the logarithmic mean (median) and standard deviation using a graphical method that assumed the distributions were log normal. Arnold confirmed that he had also used the graphical method and found it a reasonable approximation.

11. Brüggemann and Kumpulainen presented a further method for the determination of **average** contents of trace elements in staple foods or special food items. (This method was not discussed in detail by the participants.) The main point of the method is to analyse one single representative sample of a country, when the concentration of the analyze is above the LOD of the analytical method used. This method was developed for a special investigation in Europe in the frame of a FAO research project during which representative samples were prepared for some European countries and analysed in Finland; it is applicable for many trace elements. An additional advantage is that its application would be cheaper particularly for developing countries because only one single, but highly qualified, laboratory of a country would be involved in the analysis and sample preparation. Later this year, the method will be published in *Zeitschrift für Lebensmitteluntersuchung und -forschung*: The status of trace elements in staple foods from the former Federal Republic of Germany.)

**Discussion of the problem**

12. The workshop considered that there would never be one solution applicable to all data sets containing non-quantified analytical results. In particular when the proportion of nonquantified or non-detected results is greater than about 80%, little more could be done than had already been recommended at the previous workshop: namely, producing an upper bound and a lower bound estimate for the mean. However, for intermediate cases where fewer than 80% of the data are non-quantified or non-detected, it was practicable to estimate statistics describing the concentration distribution for food contaminants. The workshop recommended the approaches summarized in Table 1. Application of these methods should facilitate the reliable estimation of

various statistics and thereby increase the validity of comparisons of concentration and intake data provided by various Member States.

13. The workshop accepted that other scientists reporting data may wish to use different approaches. However, the workshop saw merit in promoting the awareness of problems associated with the interpretation of data on low-level contamination and to this end recommended that WHO should inform the Codex Alimentarius Commission and its relevant subsidiary bodies of the recommendations of this workshop. Similarly the workshop recommended that WHO should approach the European Union, FAO, LAEA and other international bodies.

14. Data on the concentration of contaminants in food and on dietary intakes of contaminants reach GEMS/Food-EURO via National Contact Points. Various laboratories in each Member State provide data to the respective National Contact Point. The large number of laboratories providing data for GEMS/Food-EURO inevitably means that a wide range of limits of detection or quantification will be reported. This compounds the difficulty of interpreting the data and of making comparisons between different Member States. Matters would be simplified if National Contact Points encouraged participating laboratories to report data with more uniform detection or quantification limits. As a first step the workshop recommended that National Contact Points should attempt to ensure that limits of detection do not differ by more than a factor of 10 (similarly with limits of quantification). In addition, efforts should be made to encourage participating laboratories to use methods giving similar and ideally the same, limits of detection and quantification. The workshop accepted that this degree of uniformity would be difficult to achieve but was convinced it would be the right target to aim for.

**RECOMMENDATIONS**

1. Analyses should be conducted in accordance with Good Laboratory Practice (including the use of validated methods, suitable reference materials and external quality assurance).

2. Ideally the limit of quantification should be no more than one half of the expected median concentration (if measurements are being made to identify true concentrations or time trends rather than for compliance monitoring).

3. All results that lie between the limit of detection and the limit of quantification should be reported numerically.

4. The purpose for which the data were generated should be reported. Data sets that were generated for different purposes should be reported separately. Details of the sampling should be reported.

5. According to national needs, monitoring should be directed to appropriate dietary staples and such other foods which are likely to be the main sources of intake. It is advised that the majority of the analytical effort should target those foods, including drinking water where relevant, contributing the first 85% of the total dietary intake of the contaminant.

6. To estimate low-level contamination the following quantities should be reported:

a) The number of samples analysed.
b) The number of laboratories reporting data.
c) The number of samples below the limit(s) of detection.
d) The range of the limits of detection in the data set.
e) The number of samples below the limit(s) of quantification but above the limit(s) of detection.
f) The range of the limits of quantification in the data set.
g) The lowest quantified result.
h) The minimum and maximum reported values (recognising that the maximum value ‘in particular will depend upon the number of samples).
i) mean, median and other statistics should be reported using the guidance in Table 1.

7. Caution must be exercised in the statistical interpretation of data on specific substances, such as pesticides, veterinary drugs and mycotoxins, that may be absent from food samples. For example, some lettuce may contain a specific fungicide whilst others may not. The presence of a proportion of 'true' zero concentrations in an otherwise well defined concentration distribution could distort the statistical interpretation of the data.

8. It is usually the case that, when many laboratories report data to a co-ordinating centre, the different data sets have different limits of detection and quantification. Co-ordinatingcentres should attempt to ensure that limits of detection do not differ by more than a factor of 10 (similarly with limits of quantification). Efforts should be made to encourage participating laboratories to use methods giving similar, and ideally the same, limits of detection and quantification.

9. Where appropriate, WHO should continue to assist Member States in the handling of raw data and in the interpretation and evaluation of monitoring results.

10. WHO should inform the Codex Alimentarius Commission and its relevant subsidiary bodies, such as CCFAC, CCPR, CCRVDF and CCMAS, of the recommendations of this workshop to promote the development of an international consensus on the evaluation of low-level concentration.

11. The WHO should issue guidance in the form of a manual or on a computer disc or both to assist the National Contact Points in the application of these recommendations. There should be simple step-by-step guidance showing in detail how to apply the recommendations in Table 1, in particular for the methods described in footnotes 1, 2 and 3 in Table1.

12. Consideration should be given to supporting further development of methods for the evaluation of low-level contamination.

13. The WHO should approach the European Union, FAO, LAEA and other international bodies to:

- to inform them of the outcome of this workshop; and
- to encourage them to consider promoting the recommendations at 1 to 12 above.

Table 1

| **Proportion of results < LOD** | **Simple estimate of mean** | **Estimation of statistics mean, median, standard dev.,etc.** |
|---|---|---|
| none, all quantified | true mean | full description should be provided |
| ≤60 % | using LOD/2 for all results less than LOD[1] | use methods in references [2] and [3] or graphical methods [4],[5] |
| > 60 but ≤80 % and with at least 25 results quantified | produce two estimates using 0 and LOD for all the results less than LOD 1,6 | use methods in reference 2 and 3 or graphical methods 4,5 **:use with caution** if the total number of measurements is< 100 |
| > 80 % | produce two estimates using 0 and LOD for all the results less than LOD 1,6 | none practicable. |

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1 Provided the data distribution is not highly skewed, this approximation is effective, if only one LOD exists in the data set or the LODs are not very different.

2 Vlachonikolis I.G. & Marriott FHC: "Evaluation of censored contamination data", *Journal of Food Additives and Contaminants 12:*637-44 (1995)

3 Hecht H. & Honikel K.O. "Assessment of data sets containing considerable values below the detection limits", Z. *Lebensm. Unters. Forsch., 201(6):592-7 (1995)*

4 Plot data on log-probability paper and produce best estimates of median and standard deviation, and thus arithmetic mean. See for details:

- Brittan Y. & Vlachonikolis I.G. "The impact of residual disability from illness and injury on the distribution of household income: A log normal approach" Centre for Socio-Legal Studies, Working paper No. 9., 1981
- Aitchison, J. & Brown, J.A.C. ,"The log normal distribution" Cambridge, Cambridge University Press, 1969

5 If different LODs are in the data set, use only the quantified results above the highest LOD.

6 This method produces an upper and a lower bound. This upper bound is produced by setting all non detectable results to LOD and all non quantified results (if not numerically reported) to LOQ. The lower bound is calculated by setting all non-detectable results and all nonquantifiable results to zero.

# Annex I

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# Annex 2
# Papers presented during the workshop

1) Vlachonikolis I.G. & Marriott F.H.C.
"Evaluation of censored contamination data",
*Journal of Food Additives and Contaminants 12:*637-44 (1995)

2) Hecht H. & Honikel K.O.
"Assessment of data sets containing considerable values below the detection limits",
*Z. Lebensm. Unters. Forsch., 201(6):592-7 (1995)*