Development of reference limits within the scope of biological effect monitoring. Interpersonal and intrapersonal variation

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SUMMARY

The first part of this thesis concerns the detection of abnormally increased or decreased values of haematological and clinical chemical parameters of a single worker during Biological Effect Monitoring (BEM).

BEM is considered to be a method by which probable non-adverse effects can be identified in order to lead to corrective actions. A practical difficulty is to discriminate accidental fluctuations of successive values for a single worker from non-adverse effects presented by means of e.g. one or more increased/decreased value(s). Utilising conventional cross-sectional-based reference values has been discussed. Due to interpersonal and intrapersonal variations, cross-sectional reference values for some blood constituents are insensitive in identifying significant mild stages of deviating test results for a single worker. Personal reference values would enable better results.

In this thesis the mean value and the standard deviation value (sd) of a series of values derived from a single worker have been stated to represent, in principle, the set point concentration of homoeostatic regulation and, respectively, the extent of fluctuations allowed by the homoeostatic mechanism of the blood parameter involved.
The difference in personal mean values among persons indicates the interpersonal variance, whereas the personal sd represents the intrapersonal variance.

Based on the definition of an early impairment by the WHO, a change in a personal mean value and/or personal sd value may indicate signals of possibly impaired regulatory mechanisms and could be seen as a non-adverse effect.

Because, as a response to internal (natural tendency) and external (workload, lifestyle) stimuli, achieving and maintaining homoeostasis are dynamic processes, the point in time of observation in order to assess a personal mean value and sd could be essential for the importance of the interpretation of physiological functions.

For calculating reference limits two statistical procedures are more or less available. However, one procedure lacks information about the *interpersonal* variance of the blood constituent of a reference population, while the other lacks information about the *intrapersonal* variance of the blood constituent of a reference population.

The aim of this study is to find reference values which take into account the interpersonal and intrapersonal variances of a reference population.
The second part concerns a field study. For two years monthly sampling took place of haematological and clinical chemical data provided by 188 blue-collar workers at a large Dutch steel company. These employees were categorised in advance according to age, work schedule, occupational energy expenditure and medical history. During the blood sampling period assessments were attempted concerning drinking and smoking habits, non-work related energy expenditure and psychological stress.

The results concerning interpersonal and intrapersonal variation indicate utilisation of personal reference values, whereas the impact of factors possibly influencing personal mean values and sd, although statistically significantly present, was rather too weak to play a role in occupational health practise. Time dependencies (personal slopes) are present for most blood parameters and must be taken into account in developing reference limits. Personal autocorrelation coefficients are mostly low and not relevant if the period between two measurements is not shorter than three months.

In the third part a new procedure for following possible changes in the values of haematological and clinical chemical parameters of a single person during a period of time was proposed.

This procedure takes into account not only the current values of a blood parameter of a single worker but also information of interpersonal and intrapersonal variations of the blood parameters involved in a reference population.
By applying this procedure to the values of Haemoglobin (Hb) for the 188 workers in the field study, reference values for Hb were estimated. By applying this procedure again to the values of Hb of another population of 74 workers and referring to the estimated reference values of Hb, the utility of the procedure was demonstrated.

The general discussion indicates that the practical limitations for early detection of health impairment in workers by means of BEM, even according to the newly proposed procedure of following the course of a blood constituent, are still very questionable: there is little knowledge about the area of “natural” variations and non-adverse effects due to workload, the practical utilisation of statistical procedures in the field of BEM, and the usefulness of reference values in making decisions during BEM to take corrective actions.