
The Relationship of Blood- and Urine-Boron to Boron Exposure in Borax-Workers and the Usefulness of Urine-Boron as an Exposure Marker

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Daily dietary-boron intake and on-the-job inspired boron were compared with blood- and urine-boron concentrations in workers engaged in packaging and shipping borax. Fourteen workers handling borax at jobs of low, medium, and high dust exposures were sampled throughout full shifts for 5 consecutive days each. Airborne borax concentrations ranged from means of 3.3 mg/m³ to 18 mg/m³, measured gravimetrically. End-of-shift mean blood-boron concentrations ranged from 0.11 to 0.26 µg/g; end-of-shift mean urine concentrations ranged from 3.16 to 10.72 µg/mg creatinine. Creatinine measures were used to adjust for differences in urine-specific gravity such that 1 ml of urine contains approximately 1 mg creatinine. There was no progressive increase in end-of-shift blood- or urine-boron concentrations across the days of the week. Urine testing done at the end of the work shift gave a somewhat better estimate of borate exposure than did blood testing, was sampled more easily, and was analytically less difficult to perform. Personal air samplers of two types were used: one, the 37-mm closed-face, two-piece cassette to estimate total dust and the other, the Institute of Occupational Medicine (IOM) sampler to estimate inspirable particulate mass. Under the conditions of this study, the IOM air sampler more nearly estimated human exposure as measured by blood- and urine-boron levels than did the sampler that measured total dust. The highest mean blood- and urine-boron levels in the workers were approximately an order of magnitude lower than blood and urine values found by others in dogs during feeding studies conducted as part of reproductive toxicity studies at the no-observed-adverse-effect level (NOAEL). The mean dietary intake of the workers was 1.35 mg boron/day, close to the 1.521 mg boron/day reported recently for the standard U.S. diet. Total estimated boron intake, which is diet plus environmental exposure, had for the high-borax dust exposure group a mean daily boron intake of 27.90 mg/day or, based on the body weights of the subjects, 0.38 mg boron/kg/day. These subjects had a mean blood-boron level of 0.26 µg boron/g blood, a factor of 10 lower than found in the dog or rat at NOAEL exposure levels. — Environ Health Perspect 102(Suppl 7):133–137 (1994)

Key words: borax, boron, exposure, blood, urine, air sampling

Introduction

This study examined the relationship between work exposure to borax dust and blood- and urine-boron levels to determine whether biologic monitoring would be possible, and to compare daily intake levels in workers exposed to boron to those reported from toxicologic studies in experimental animals. A related objective of this study was the evaluation of methods for measuring dust exposure.

Boron is present in inorganic borates such as borax and boric acid that are used

widely in industry and commerce. It is also an essential element for healthy plant growth and consequently is present in the daily diet. Boric acid has been shown to be readily absorbed from the human gastrointestinal tract (1). It is likely that the other water-soluble inorganic borates provide boron in a form that is readily absorbed through mucosal membranes. Its presence in the body is most likely in the form of a salt or acid, as indicated in William G. Woods' presentation in the symposium, "Introduction to the Element and Its Compounds" (2).

Rationale

Weir and Fisher (2) found that borax and boric acids have similar toxicity when dose is calculated as boron. This, plus the difficulty of chemically analyzing different borate species in biologic fluids, provides the rationale for calculating dose and tissue levels in terms of boron. The analysis of boron at low concentrations in tissue can

be quite precise as pointed out by Robert F. Moseman at the symposium (4).

Methods

Samples Used

Because the characteristics of samples of airborne dust collected by air samplers depend upon the aerodynamics of the sampler used, two types of personal air samplers were used. The first was a 37-mm closed-face cassette containing a 5-micrometer pore size polyvinyl chloride (PVC) filter, calibrated to represent the American Conference of Governmental Industrial Hygienists (ACGIH)-defined total dust; the second sampler was an Institute of Occupational Medicine, Edinburgh (IOM), sampling head designed to collect the inspirable particulate mass as recommended by the ACGIH Committee for Particle Size-Selective Sampling in the Workplace (5). This article uses the term total dust to designate the fraction of a

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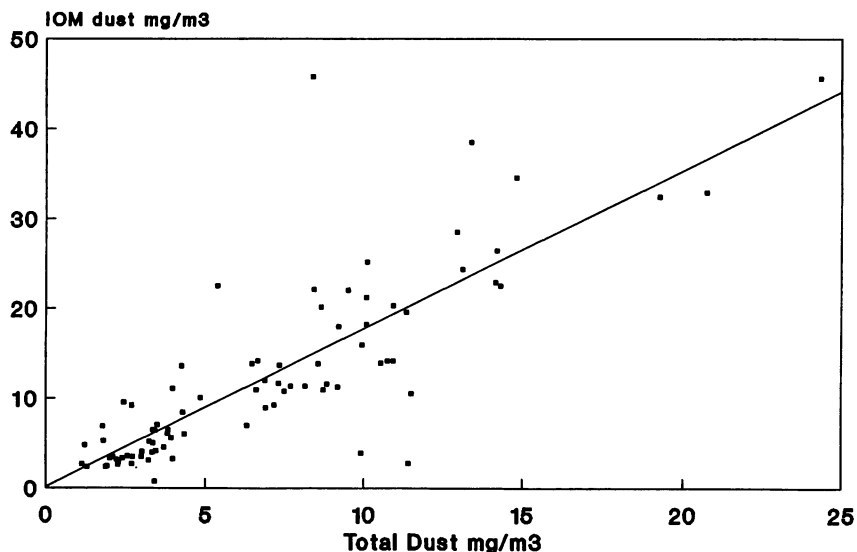


Figure 1. IOM dust versus total dust where $IOM = 0.14 + 1.76(TD)$, $r = 0.82$, and $p < 0.001$. Abbreviations: IOM, Institute of Occupational Medicine; TD, total dust.

polydispersed dust cloud captured by the 37-mm closed-face sampler. Both air samplers were used simultaneously during all sampling periods.

Work Area Studied

The work area studied, the same as that described by Wegman et al. (6), was a borax packaging and shipping facility of a major borax and boric acid production plant. The term borax, as used in this study refers to any one or mixtures of three hydration states of sodium tetraborate: $Na_2B_4O_7$, $Na_2B_4O_7 \cdot 5H_2O$, or $Na_2B_4O_7 \cdot 10H_2O$ —our analytical method was unable to differentiate between these three species adequately. Male workers in good health were selected from areas with high-, medium- or low-borax dust exposures, as judged by the industrial hygienist. Four workers were from the low-, five from the medium-, and five from the high-exposure area. Daily airborne boron exposures of each subject were measured throughout the entire work shift for 5 days of a work week. Particle size distribution was measured once for each worker, using a Marple Personal Cascade Impactor (Anderson Samplers, Atlanta, GA).

Dietary Monitoring

In addition, boron content of food and drink ingested during the 2 days prior to and each day during the test work week was measured. Subjects were instructed by a dietitian in the keeping of a dietary record. They were given prepared food

(Healthy Choice, Con Agra Frozen Foods, Omaha, NE), beverages, including bottled water, for the 7-day period beginning the Saturday prior to the measured work week and ending with the noon meal on the following Friday. Aliquots of any ingested food or drink not provided by the dietitian were required to be returned by the subject to the study team and were measured for boron content. Although constrained to eat the diet provided by the study or to return to the dietitian samples of consumed food and drink not provided by the study, subjects were not limited in the amount consumed. Analysis of boron in food and drink samples was done according to the method of Hunt and Shuler (7).

Sampling Techniques and Results

Blood and urine samples were obtained on Monday morning prior to the beginning of the work week, Monday afternoon at the end of the first day of work, at the end of work on Thursday, and at the end of work on Friday. End-of-shift urine and blood spot samples were selected as representative of the immediately preceding borax-exposure workshift because of the relatively short biological half-life for boron, approximately 21 hr (8). It also was thought that an end-of-shift spot sample would be the most practical sample for future biologic monitoring.

Mean TWA dust concentrations of borax for the low-, medium-, and high-exposure categories as measured by the total dust sampler were 2.76 (SD 0.86), 7.54 (SD 5.31), and 9.86 (SD 4.29) mg/m^3 , respectively; as measured by the

IOM sampler, they were 3.38 (SD 1.18), 12.62 (SD 9.17), and 17.98 (SD 11.37) mg/m^3 , respectively. The relationship between dust concentration values obtained by the two air-sampling methods is shown in Figure 1. This relationship is described by the equation

$$IOM \text{ mg/m}^3 = 0.14 + 1.76(TD) \text{ mg/m}^3, \\ r = .82, p < .001 \quad [1]$$

The particle-size distribution ranged from a mean of 20.7 μm for the high-exposure category to 16.8 μm for the low- and 16.7 for the medium-exposure categories. These rather large mean particle sizes probably account for much of the difference in sampling results from the two air samplers.

Boron air concentrations were calculated using analyses of boron content in borax settled-dust samples from horizontal surfaces at each worker's job site, and gravimetric measures of the worker's air-borne borax dust concentration. The mean percent boron in the settled-dust samples was 14.3; the range was 11.8 to 15.2, which indicates a relatively pure borax dust uncontaminated with dusts from other sources. The assumption was made that the percentage of boron in the settled-dust samples would be a good approximation of the percentage of boron in the air-borne dust.

Calculated boron air concentrations and estimates of on-the-job inhaled air volumes based on minutes-worked-per-shift and a 20.8 l/min respiratory minute volume (10 $m^3/8$ -hr shift) were used to calculate the amount of boron inhaled on the job for each subject. It was assumed that all inhaled particles were retained and ultimately absorbed into the systemic circulation. This retention assumption is probably not unrealistic; because of the large size of the dust particles in the work areas, the majority of the inspired particulate mass would have impacted on surfaces of the upper respiratory tree and either would have been absorbed directly through mucous membranes or swallowed where absorption would have occurred. Any error in the assumption would lead to an overestimation of the inhaled boron dose and thus be conservative from the standpoint of risk analysis.

Mean-inspired boron for the low-, medium-, and high-exposure categories based on IOM sampler results were 4.70 (SD 1.69), 16.18 (SD 11.64), and 24.77 (SD 15.35) mg boron/day, respectively. Those based on total dust (TD) sampler results

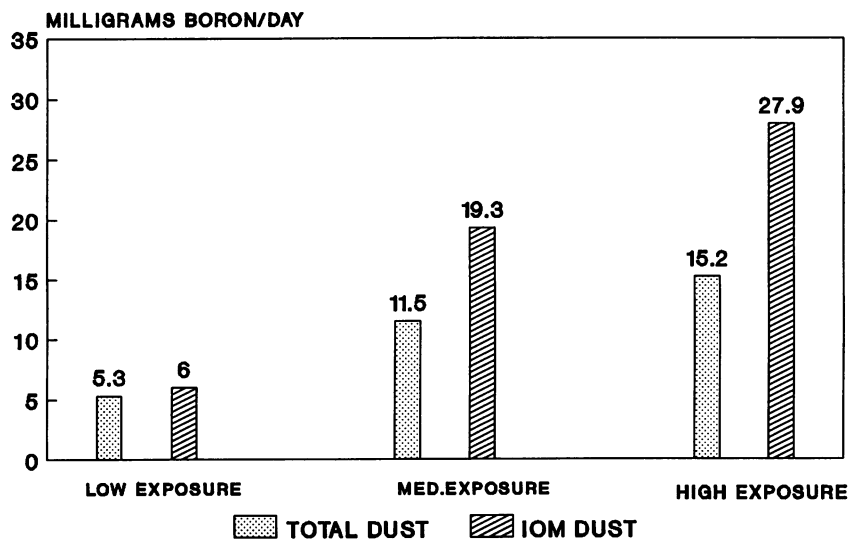


Figure 2. Total boron: mean diet plus work-dust exposure category and air sampler. Abbreviations: IOM, Institute of Occupational Medicine.

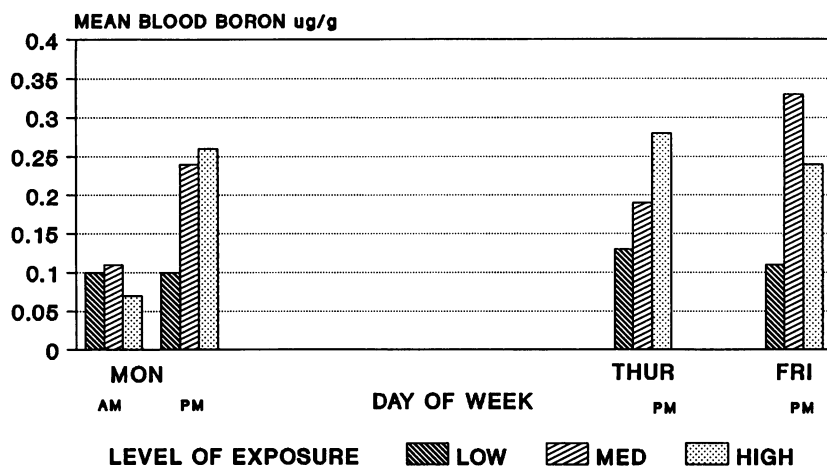


Figure 3. Mean boron levels ($\mu\text{g/g}$) by day of week and dust exposure category.

were 3.84 (SD 1.24), 9.67 (SD 6.72), and 13.60 (SD 5.76) mg boron/day, respectively.

Mean daily dietary boron intake for each worker was measured at 1.35 (SD 0.72) mg boron/day, without a statistically significant difference between exposure groups. The value 1.35 mg boron/day is not greatly different from the standard U.S. dietary boron content (9). Total daily boron intake calculated for each individual, including the measured dietary contribution and the calculated intake by inspiration, is shown by exposure-group mean in Figure 2. The high-exposure category mean total intake was 27.9 mg boron/day.

Boron levels for blood samples obtained on the Monday morning prior to the first

work shift of the week averaged 0.09 μg boron/g blood. There were no significant differences among the three exposure categories. Postshift boron values for blood samples drawn on the sampling days, Monday, Thursday, and Friday, were not different from the Monday morning preshift samples for the low-exposure category. For the medium- and high-exposure categories, later blood values were significantly higher than the Monday morning values, but there were no consistent differences between medium- and high-exposure groups for any sampling day. The relationships of blood boron to exposure categories and to points of time when blood was sampled are shown in Figure 3. The mean

Table 1. Human blood- and urine-boron, without work exposure.

Reference	Blood, $\mu\text{g/ml}$	Urine, $\mu\text{g/ml}$
Imbus (13)	0.10 (0.04–0.36)	0.70 (0.04–6.60)
Abou-Shakra (14)	0.06 (0.01–0.17)	0.75 (0.15–2.98)
Clarke (15)	0.03	–
Minoia (16)	–	1.80 (0.47–7.80)

postshift blood-boron concentration for the high-exposure category workers was 0.26 $\mu\text{g/g}$ which is within the range of normal values reported for nonoccupationally exposed working adults (Table 1).

Figure 4 presents the results of urine-boron measurements at preshift and postshift sampling times. Preshift, Monday morning values had a mean of 2.75 μg boron/mg creatinine without significant differences among exposure-category groups. Only the high-exposure category showed postshift boron excretion elevations that were statistically significant. These postshift values averaged 10.72 μg boron/mg creatinine with the highest daily average, 11.91 μg boron/mg creatinine on Monday afternoon. These values are slightly above the range of values reported for nonoccupationally exposed workers and 7 to 10 times their mean values assuming that normally 1 ml of urine contains 1 mg creatinine (Table 1).

The postshift blood- and urine-boron concentrations did not increase across the days of the work week, indicating that at the levels of exposure experienced by these workers (up to a mean of 27.9 mg boron/day or 0.38 mg boron/kg/day) there was no evidence of boron accumulation. Our observations that progressive accumulation does not occur are consistent with the experimental work at much higher doses in which animals that were fed diets containing up to 1575-ppm boron (67.9 mg boron/kg/day) did not demonstrate progressive increases in tissue levels once a plateau had been reached following the first day of dosing (10).

When boron intake over the period of the work shift and biologic measures of absorption at the end of the shift were treated as continuous variables, a series of bivariate models was obtained (Table 2). Comparison of the various models for blood- and urine-boron concentrations yields similar overall patterns. The r^2 column, which is a measure of the proportion of variance in the blood or urine accounted for by each model, indicates that measures of boron in the breakfast and the food consumed during the work shift did not contribute to the predictive power of the mea-

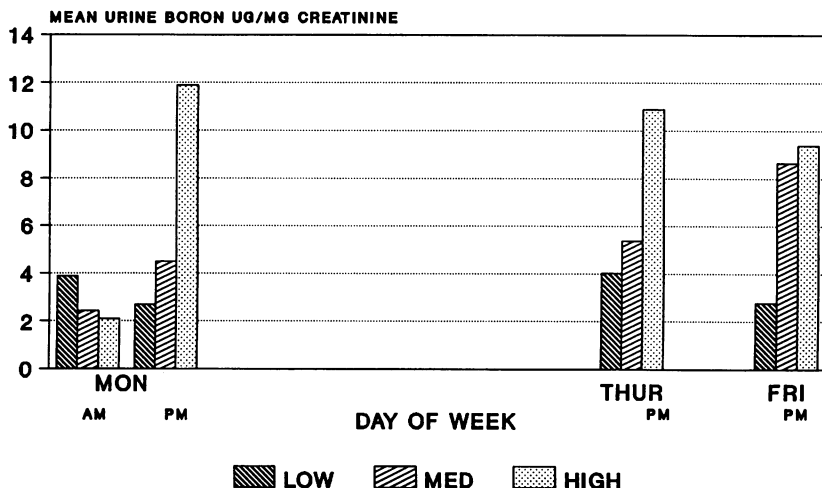


Figure 4. Urine-boron levels (µg / mg creatinine) by day of week and exposure category.

Table 2. Relation of boron intake (mg / shift) to blood and urine levels.^a

Independent variables	Intercept	Slope	Variance, r ²	Probability, p
For blood-boron, µg / g				
IOM, air and diet	0.070	0.008	0.74	0.001
IOM, air alone	0.073	0.008	0.77	0.001
Diet alone	0.236	(0.056)	0.05	0.460
TD, air and diet	0.052	0.015	0.52	0.003
TD, air alone	0.066	0.015	0.49	0.002
For urine-boron, µg / g creatinine				
IOM, air and diet	0.267	0.462	0.85	0.001
IOM, air alone	0.600	0.460	0.85	0.001
Diet alone	7.871	(0.160)	0.00	0.967
TD, air and diet	(0.327)	0.816	0.52	0.002
TD, air alone	0.571	0.806	0.49	0.002

Abbreviations: IOM, Institute of Occupational Medicine; TD, total dust. ^a Postshift blood- and urine-boron.

Table 3. Boron dose and blood- and urine-boron concentrations of workers compared to animals at the NOAEL for reproductive toxicity.

	Male worker (this study)	Dog fertility	Rat developmental
Dose, mg boron/ kg / day	0.38	8.75 (2)	13.70 ^a (9)
Urine, µg boron/ ml	10.72 ^b	180.00 (8)	— ^c
Blood, µg boron/ g	0.26	2.50–3.50 (8)	2.50–3.00 ^d

Abbreviations: NOAEL, no-observed-adverse-effect level. ^a Value approaches NOAEL. ^b µg boron/ mg creatinine. ^c No data. ^d Unpublished data, see text.

sured inhaled borax. The relative uniformity of the boron content of the assigned diets and the higher proportion of total boron absorption resulting from air exposure may account for the apparent lack of dietary effect.

Results and Discussion

It is clear from these bivariate models that the use of air-sample data based on the IOM air sampler to estimate boron intake accounted for more of the variance in the blood- and urine-boron concentrations

than data based on the total dust sampler. This observation leads to the conclusion that measures representing inspirable particulate mass rather than total dust more accurately estimate human dust exposure where the dust is of large particle size and the effect of concern is a systemic one.

The relationship between the workers' boron exposure and boron intake in animal chronic feeding studies can be looked at by comparing animals at the no-observed-adverse-effect level (NOAEL) with the high-exposure category workers. Because

boron's effects on fertility and fetal development appear to occur at lower dose levels than other toxic effects, the comparison was made with animal studies of reproductive effects.

Table 3 provides worker boron exposure and related end-of-shift blood- and urine-boron concentrations, together with reproductive NOAEL dietary boron levels for the dog (8), and the probably close-to-NOAEL level for the rat (9), along with their related blood- and urine-boron concentrations. [Data are sparse, and the rat blood-boron level at the 13.7-mg/ boron/kg/day dietary intake level comes not from the developmental toxicity study of Heindel et al. (9) but from a separate pilot study (Robert E. Chapin, unpublished data)]. Because there appear to be species differences between boron intake and resulting blood-boron levels, with man having a relatively higher blood-boron level for a given boron intake, comparisons of results of exposure across species should be based on blood-boron levels rather than on estimates of boron intake. Thus, under the conditions of this study, high-exposure category workers with a calculated mean daily boron intake of 27.9 mg boron (0.38 mg boron/kg/day) had a mean blood-boron level (0.26 µg boron/g blood) that was a factor of 10 lower than the dog and rat at NOAEL exposure levels (Table 3).

Conclusion

The findings of this study can be summarized: a linear relationship described by $IOM = 0.14 + 1.76(TD)$ exists between the two dust samplers used under the concentration and particle size distribution conditions of this study. The IOM sampler results are measurably better for predicting boron absorption as indicated by blood- and urine-boron levels than are results based on the total dust sampler, as indicated by the r² values. Equations for prediction of blood- and urine-boron concentrations are:

$$Blood-boron (\mu g / g) = 0.07 + 0.008(mg \text{ boron inhaled / shift}) \quad [2]$$

$$Urine-boron(\mu g / mg \text{ creat}) = 0.6 + 0.46(mg \text{ boron inhaled / shift}) \quad [3]$$

Borax mean air exposures of 17.98 mg/m³ measured for the high-exposure workers together with dietary boron resulted in an estimated absorption of 0.38 mg boron/kg/day. At this level there was no progressive accumulation across the work week.

REFERENCES

1. Jansen JA, Schou JS, Aggerbeck B. Gastrointestinal absorption and in vitro release of boric acid from water-emulsifying ointments. *Food Chem Toxicol* 22:49-53 (1984).
2. Woods WG. An introduction to boron: history, sources, uses, and chemistry. *Environ Health Perspect* 102(Suppl 7):13-11 (1994).
3. Weir RJ, Fisher RS. Toxicologic studies on borax and boric acid. *Toxicol Appl Pharmacol* 23:351-364 (1972).
4. Moseman RF. Chemical disposition of boron in animals and humans. *Environ Health Perspect* 102(Suppl 7):113-117 (1994).
5. Particle size-selective sampling in the workplace. In: Report of the ACGIH Technical Committee on Air Sampling Procedures. Cincinnati, Ohio: American Conference of Governmental Industrial Hygienists, 1985.
6. Wegman DH, Eisen EA, Hu X, Woskie SR, Smith RG, Garabrant DH. Acute and chronic respiratory effects of sodium borate particulate exposures. *Environ Health Perspect* 102(Suppl 7): 119-128 (1994).
7. Hunt CD, Shuler TR. Open-vessel, wet-ash, low-temperature digestion of biological materials for inductively coupled argon plasma spectroscopy (ICAP) analysis of boron and other elements. *J Micronutrient Anal* 6:161-174 (1989).
8. Jansen JA, Andersen J, Schou JS. Boric acid single dose pharmacokinetics after intravenous administration to man. *Arch Toxicol* 55:64-67 (1984).
9. Iyengar GV, Clarke WB, Downing RG, Tanner JT. Lithium in biological and dietary materials. *Trace Elem Anal Chem Med Biol, Proc Int Workshop*, 5: 267-269 (1988).
10. Ku WW, Chapin RE, Moseman RF, Brink RE, Pierce KD, Adams KY. Tissue disposition of boron in male Fischer rats. *Toxicol Appl Pharmacol* 111:145-151 (1991).
11. Weir RJ, Fisher RS. Archived material, volume 5 of the full study report from toxicologic studies on borax and boric acid. Los Angeles: U.S. Borax and Chemical Corporation, 1972.
12. Heindel JJ, Price CJ, Field EA, Marr MC, Myers CB, Morrissey RE, Schwetz BA. Developmental toxicity of boric acid in mice and rats. *Fundam Appl Toxicol* 18:266-277 (1992).
13. Imbus HR, Cholak J, Miller LH, Sterling T. Boron, cadmium, chromium and nickel in blood and urine. *Arch Environ Health* 6:112-121 (1963).
14. Abou-Shakra FR, Havercroft JM, Ward NI. Lithium and boron in biological tissues and fluids. *Trace Elem Med* 6:142-146 (1989).
15. Clarke WB, Koekebakker M, Barr RD, Downing RG, Fleming RF. Analysis of ultratrace lithium and boron by neutron activation and mass-spectrometric measurement of ^3He and ^4He . *Appl Radiat Isot* 38:735-743 (1987).
16. Minoia C, Sabbioni E, Apostoli P, Pietra R, Pozzoli L, Gallorini M, Nicolaou G, Alessio L, Capodaglio E. Trace element reference values in tissues from inhabitants of the European Community. I. A study of 46 elements in urine, blood, and serum of Italian subjects. *Sci Total Environ* 95:89-105 (1990).