

# Calculating the uncertainty in lead concentration for *in vivo* bone lead x-ray fluorescence

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## Abstract

A revised mathematical treatment of the calibration line intercept has been published for *in vivo* bone lead measurements using <sup>109</sup>Cd-based K-shell x-ray fluorescence. The revised calibration line treatment prompts changes, presented herein, to the method for calculating the measurement uncertainty.

## 1. Introduction

Lead (Pb) is a ubiquitous toxin that has several health effects on humans. Monitoring of lead exposure is usually performed via measuring lead in whole blood, but the biological residence time of lead in blood is approximately 36 days (Rabinowitz *et al* 1976). The majority of the human body burden of lead does not reside in blood but in the skeleton (Barry and Mossman 1970, Barry 1975, 1981), wherein the biological residence time is of the order of years (Rabinowitz *et al* 1976, Gerhardsson *et al* 1993, Chettle 1995, Börjesson *et al* 1997, Brito *et al* 2000). Lead in bone is thus a measure of long-term lead exposure (Somervaille *et al* 1988).

The *in vivo* measurement of lead in bone using K-shell x-ray fluorescence (XRF) is a well-established (Ahlgren *et al* 1976) but still developing technique (Todd *et al* 2001a, 2001b, Chettle and McNeill 2002). The present paper applies only to the method wherein the 88.034 keV  $\gamma$ -rays from <sup>109</sup>Cd are used to fluoresce the K-shell x-rays of lead. Usually the  $K_{\alpha_1}$  and  $K_{\alpha_2}$  peaks are used to derive an estimate of either the amplitude or the area of the  $K_{\alpha_1}$ . Similarly, the  $K_{\beta_1}$  is estimated from the  $K_{\beta_1}$  and  $K_{\beta_3}$  peaks. These estimates are then used to calculate the *in vivo* lead concentration. The <sup>109</sup>Cd  $\gamma$ -rays can also undergo coherent scatter primarily off the calcium, phosphorous and oxygen atoms in the bone, giving rise to a peak of coherently scattered photons in the spectrum of scattered radiation. In the <sup>109</sup>Cd-based KXRF method, the ratios of the x-ray peak signals (areas or amplitudes),  $x_i$ , to the coherent peak signal, *coh*, are treated as the measurement system responses (Somervaille *et al* 1985, Todd 2000c). The use of these ratios renders the responses independent of several factors,

principally the source-to-skin distance, overlying tissue thickness, bone shape, bone size, bone orientation and minor subject movement (Chettle *et al* 1991).

Lead-doped, hydrated plaster-of-Paris ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) phantoms are used for calibration. From these, the responses (from each x-ray,  $i$ ) from an *in vivo* subject can be converted into estimates of the *in vivo* lead concentration,  $[\text{Pb}]_i$  (an expression for which follows), which are then combined into a single, inverse-variance-weighted-mean estimate of the concentration,  $[\text{Pb}]_\mu$ , where

$$[\text{Pb}]_\mu = \frac{\sum_{i=1}^n \frac{[\text{Pb}]_i}{\sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}. \quad (1)$$

The uncertainty in  $[\text{Pb}]_\mu$ ,  $\sigma_{[\text{Pb}]_\mu}$ , is given by

$$\sigma_{[\text{Pb}]_\mu}^2 = \left( \sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2} \right)^{-1}.$$

The coherent scatter normalization introduces the need for a matrix ‘correction’ that takes into account the different coherent scattering cross sections of the phantom and the human (*in vivo* bone) matrices (Somervaille *et al* 1985, Todd 2000c). The coherent correction factor,  $k$ , is the ratio of the coherent scattering cross sections for the two matrices.  $k$  is a function of energy and angle but, for purposes of this discussion, can be considered to be a constant. The matrix correction yields *in vivo* results that have units of  $\mu\text{g}$  of lead per gram of bone mineral (hereafter  $\mu\text{g g}^{-1}$ ).

Formulae for  $[\text{Pb}]_i$  and the uncertainty therein,  $\sigma_{[\text{Pb}]_i}$  (the latter derived from a variance propagation approach), were in use for several years before first being published (Gordon *et al* 1994). Typographical errors in the published paper were reported (Todd 2000a, 2000b). In the original method (Gordon *et al* 1994), the phantom calibration line intercept,  $C_i$ , is always subtracted from the *in vivo* response:

$$[\text{Pb}]_i = \frac{k \frac{x_i}{coh} - C_i}{m_i}$$

where  $m_i$  is the slope of the calibration line obtained from phantoms for x-ray  $i$ .

Since then, a description of the physical origins of  $C_i$  has been reported (Todd 2000d). In brief,  $C_i$  can arise from one or more sources: trace-level lead contamination of the plaster of Paris, plaster-of-Paris impurities other than lead, external lead contamination of the phantoms and/or measurement system from environmental sources, contaminating lead signal(s) from non-phantom items (e.g. chairs, floor tiles, lead paint on walls) and any ‘offset’ in the peak extraction program that results in overestimation of small, but non-zero peak sizes. These different potential sources of  $C_i$  suggest different handling of  $C_i$ , and it was therefore proposed (Todd 2000d) that the treatment of  $C_i$  be modified to take into account the source of  $C_i$ : (a) to stop measurements (i.e. produce no result) if  $C_i$  is significantly less than zero (because an error in the measurement process is indicated thereby); (b) to calculate the calibration line passing through the origin if  $C_i$  is not significantly different from zero; and (c) to calculate the calibration line with a non-zero intercept only when  $C_i$  is significantly greater than zero. For (a), no calculation of  $[\text{Pb}]_i$  should be performed; for (b) and (c), it was proposed that, in contrast to the original method,  $C_i$  not be subtracted from the *in vivo* signal, giving

$$[\text{Pb}]_i = \frac{k \frac{x_i}{coh}}{m_i}. \quad (2)$$

In 2001, a ‘correction’ was published (Kondrashov and Rothenberg 2001) to the method wherein the intercept was always subtracted (Gordon *et al* 1994). The correction is valid if

the intercept continues to be taken into account. However, as indicated above, advocated previously and reiterated recently (Todd 2000a, 2000b, 2000d, Todd *et al* 2002), the use of equation (2) is normally to be preferred because it reduces the possibility of bias in the estimate of lead concentration.

The revised treatment of  $C_i$  (Todd 2000d) affects the calculation of  $\sigma_{[\text{Pb}]_i}^2$ , formulae for which were not presented with the revised treatment of  $C_i$  and are therefore presented here.

## 2. Methods

### 2.1. The uncertainty in $[\text{Pb}]_i$ , $\sigma_{[\text{Pb}]_i}$ , for the revised treatment of $C_i$

To calculate  $\sigma_{[\text{Pb}]_i}^2$  for equation (2), we start from the generalized formula for the variance in  $Y = f(X_i)$  (wherein  $X_i$  is a generalized argument and not an x-ray size,  $x_i$ ):

$$\sigma_Y^2 = \sum_{i=1}^n \left( \frac{\partial Y}{\partial X_i} \right)^2 \sigma_{X_i}^2 + \sum_{\substack{i=1 \\ i \neq j}}^n 2 \left( \frac{\partial Y}{\partial X_i} \right) \left( \frac{\partial Y}{\partial X_j} \right) \sigma_{X_i X_j}^2 \quad (3)$$

for

$$[\text{Pb}]_i = \frac{k \frac{x_i}{coh}}{m_i}, \quad \frac{\partial [\text{Pb}]_i}{\partial x_i} = \frac{k}{m_i coh}, \quad \frac{\partial [\text{Pb}]_i}{\partial coh} = -\frac{kx_i}{m_i coh^2}$$

and

$$\frac{\partial [\text{Pb}]_i}{\partial m_i} = \frac{-kx_i}{m_i^2 coh}.$$

The covariances between  $x_i$ ,  $coh$  and  $m_i$  are all assumed to be zero (Gordon *et al* 1994, Todd 2000a, 2000b):

$$\sigma_{x_i coh}^2 = \sigma_{x_i m_i}^2 = \sigma_{m_i coh}^2 = 0$$

whereupon

$$\begin{aligned} \sigma_{[\text{Pb}]_i}^2 &= \left( \frac{k}{m_i coh} \right)^2 \sigma_{x_i}^2 + \left( \frac{kx_i}{m_i coh^2} \right)^2 \sigma_{coh}^2 + \left( \frac{kx_i}{m_i^2 coh} \right)^2 \sigma_{m_i}^2 \\ &= \left( \frac{k}{m_i coh} \right)^2 \left( \sigma_{x_i}^2 + \frac{x_i^2 \sigma_{coh}^2}{coh^2} + \frac{x_i^2 \sigma_{m_i}^2}{m_i^2} \right). \end{aligned} \quad (4)$$

For the 'high' and 'low' bone lead *in vivo* subjects of Gordon *et al*, the values of  $\sigma_{[\text{Pb}]_i}$ , derived from equation (4), are shown in tables 1 and 2 respectively. For interest only, tables 1 and 2 also show the  $\sigma_{[\text{Pb}]_i}$  reported by Gordon *et al*, which differ by only a small amount ( $-0.03$  to  $0.33 \mu\text{g g}^{-1}$ ) from those obtained using the revised treatment of  $C_i$ .

### 2.2. The covariance between individual estimates of concentration, $\sigma_{[\text{Pb}]_i [\text{Pb}]_j}^2$

There is a covariance between  $[\text{Pb}]_i$  and  $[\text{Pb}]_j$ ,  $\sigma_{[\text{Pb}]_i [\text{Pb}]_j}^2$ , that arises because both  $[\text{Pb}]_i$  and  $[\text{Pb}]_j$  depend on the same  $coh$  and which contributes to  $\sigma_{[\text{Pb}]_\mu}^2$ . To calculate the magnitude of this contribution, we start from a general expression that allows for a statistically independent coherent peak signal,  $coh_i$ , for each x-ray:

$$[\text{Pb}]_\mu = \frac{\sum_{i=1}^n \frac{[\text{Pb}]_i}{\sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}} = \frac{\sum_{i=1}^n \frac{kx_i}{m_i coh_i \sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}.$$

**Table 1.** Estimates of  $\sigma_{[\text{Pb}]_i}$  for Gordon *et al* (subject B).

Parameter	Peak				
	Coherent	$\alpha_1$	$\alpha_2$	$\beta_1$	$\beta_3$
Amplitude ( $x_i$ for x-rays)	2523	421.5	313.9	81.29	34.61
Amplitude uncertainty ( $\sigma_{x_i}$ for x-rays)	15.16	24.81	38.52	7.399	7.532
Slope ( $m_i$ )		0.003 22	0.001 87	0.000 671	0.000 367
Slope variance ( $\sigma_{m_i}^2$ )		$1.07 \times 10^{-9}$	$8.45 \times 10^{-10}$	$6.34 \times 10^{-11}$	$8.89 \times 10^{-11}$
Intercept ( $C_i$ )		0.0184	0.0134	0.004 19	0.0014
Intercept variance ( $\sigma_{C_i}^2$ )		$5.06 \times 10^{-6}$	0.000 004	$3 \times 10^{-7}$	$4.21 \times 10^{-7}$
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i>		4.551	12.001	6.461	12.054
$\sigma_{[\text{Pb}]_i}$ from modified treatment of $C_i$		4.547	12.030	6.449	11.963
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i> overestimates $\sigma_{[\text{Pb}]_i}$ from the modified treatment by ( $\mu\text{g g}^{-1}$ )		0.004	-0.028	0.013	0.091
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i> overestimates $\sigma_{[\text{Pb}]_i}$ from the modified treatment by (%)		0.1	-0.2	0.2	0.8

**Table 2.** Estimates of  $\sigma_{[\text{Pb}]_i}$  for Gordon *et al* (subject C).

Parameter	Peak				
	Coherent	$\alpha_1$	$\alpha_2$	$\beta_1$	$\beta_3$
Amplitude ( $x_i$ for x-rays)	3436	31.74	85.46	9.106	6.438
Amplitude uncertainty ( $\sigma_{x_i}$ for x-rays)	17.69	29.96	50.07	8.102	8.442
Slope ( $m_i$ )		0.003 22	0.001 87	0.000 671	0.000 367
Slope variance ( $\sigma_{m_i}^2$ )		$1.07 \times 10^{-9}$	$8.45 \times 10^{-10}$	$6.34 \times 10^{-11}$	$8.89 \times 10^{-11}$
Intercept ( $C_i$ )		0.0184	0.0134	0.004 19	0.0014
Intercept variance ( $\sigma_{C_i}^2$ )		$5.06 \times 10^{-6}$	0.000 004	$3 \times 10^{-7}$	$4.21 \times 10^{-7}$
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i>		4.090	11.473	5.273	10.102
$\sigma_{[\text{Pb}]_i}$ from modified treatment of $C_i$		3.954	11.382	5.131	9.776
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i> overestimates $\sigma_{[\text{Pb}]_i}$ from the modified treatment by ( $\mu\text{g g}^{-1}$ )		0.136	0.092	0.142	0.326
$\sigma_{[\text{Pb}]_i}$ from Gordon <i>et al</i> overestimates $\sigma_{[\text{Pb}]_i}$ from the modified treatment by (%)		3.4	0.8	2.8	3.3

Applying the same generalized formula for the variance (equation (3)) (wherein the  $\sigma_{[\text{Pb}]_i}^2$  are the weighting factors and can be considered constants for the purposes of this argument), we obtain:

$$\sigma_{[\text{Pb}]_\mu}^2 = \sum_{i=1}^n \left( \frac{\partial[\text{Pb}]_\mu}{\partial x_i} \right)^2 \sigma_{x_i}^2 + \left( \frac{\partial[\text{Pb}]_\mu}{\partial m_i} \right)^2 \sigma_{m_i}^2 + \left( \frac{\partial[\text{Pb}]_\mu}{\partial \text{coh}_i} \right)^2 \sigma_{\text{coh}_i}^2$$

for which we need the partial differentials:

$$\frac{\partial[\text{Pb}]_\mu}{\partial x_i} = \frac{\sum_{i=1}^n \frac{k}{m_i \text{coh}_i \sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}$$

$$\frac{\partial[\text{Pb}]_\mu}{\partial m_i} = \frac{\sum_{i=1}^n \frac{-k x_i}{m_i^2 \text{coh}_i \sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}$$

and

$$\frac{\partial[\text{Pb}]_{\mu}}{\partial \text{coh}_i} = \frac{\sum_{i=1}^n \frac{-kx_i}{m_i \text{coh}_i^2 \sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}$$

giving

$$\sigma_{[\text{Pb}]_{\mu}}^2 = \frac{1}{\left(\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}\right)^2} \left[ \sum_{i=1}^n \frac{k^2 \sigma_{x_i}^2}{m_i^2 \text{coh}_i^2 \sigma_{[\text{Pb}]_i}^4} + \frac{k^2 x_i^2 \sigma_{m_i}^2}{m_i^4 \text{coh}_i^2 \sigma_{[\text{Pb}]_i}^4} + \frac{k^2 x_i^2 \sigma_{\text{coh}_i}^2}{m_i^2 \text{coh}_i^4 \sigma_{[\text{Pb}]_i}^4} \right].$$

If all the  $\text{coh}_i$  are equal (i.e. the same single, coherent peak), then

$$\frac{\partial[\text{Pb}]_{\mu}}{\partial \text{coh}} = \frac{\sum_{i=1}^n \frac{-kx_i}{m_i \text{coh}^2 \sigma_{[\text{Pb}]_i}^2}}{\sum_{i=1}^n \frac{1}{\sigma_{[\text{Pb}]_i}^2}}$$

which gives an expression for  $\sigma_{[\text{Pb}]_{\mu}}^2$  that contains both diagonal and non-diagonal elements:

$$\sigma_{[\text{Pb}]_{\mu}}^2 = \frac{1}{\left(\sum_{i=1}^n \sigma_{[\text{Pb}]_i}^2\right)^2} \left[ \sum_{i=1}^n \left( \frac{k^2 \sigma_{x_i}^2}{m_i^2 \text{coh}^2 \sigma_{[\text{Pb}]_i}^4} + \frac{k^2 x_i^2 \sigma_{m_i}^2}{m_i^4 \text{coh}^2 \sigma_{[\text{Pb}]_i}^4} + \frac{k^2 x_i^2 \sigma_{\text{coh}}^2}{m_i^2 \text{coh}^4 \sigma_{[\text{Pb}]_i}^4} \right) + \sum_{\substack{i=1 \\ j=1 \\ i \neq j}}^n \frac{2k^2 x_i x_j \sigma_{\text{coh}}^2}{m_i m_j \text{coh}^4 \sigma_{[\text{Pb}]_i}^2 \sigma_{[\text{Pb}]_j}^2} \right]. \quad (5)$$

The contribution to the measurement uncertainty arising from  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$  is therefore

$$\frac{1}{\left(\sum_{i=1}^n \sigma_{[\text{Pb}]_i}^2\right)^2} \left[ \frac{2k^2}{\text{coh}^4} \sum_{\substack{i=1 \\ j=1 \\ i \neq j}}^n \frac{x_i x_j \sigma_{\text{coh}}^2}{m_i m_j \sigma_{[\text{Pb}]_i}^2 \sigma_{[\text{Pb}]_j}^2} \right].$$

It should be noted that the above term differs from the term given by Gordon *et al* (their equation (10)) by a factor of  $2/(\sum_{i=1}^n \sigma_{[\text{Pb}]_i}^2)^2$ , a typographical error in Gordon *et al* that has not previously been reported. It should also be noted that Todd's 'guess' of how the covariance term of Gordon *et al* was arrived at (Todd 2000a, 2000b) is incorrect.

### 2.3. The effect of the revised treatment of $C_i$ on $[\text{Pb}]_{\mu}$ and $\sigma_{[\text{Pb}]_{\mu}}$

Table 3 shows that  $\sigma_{[\text{Pb}]_{\mu}}$  for the revised treatment of  $C_i$  (i.e. calculated from equation (5)) differs from that reported by Gordon *et al* by between 0.005 and 0.088  $\mu\text{g g}^{-1}$ : far less than the measurement uncertainty itself (3.404 and 2.885  $\mu\text{g g}^{-1}$  for subjects B and C, respectively).

The effect of the modified treatment of  $C_i$  on  $[\text{Pb}]_{\mu}$  can be larger and, for the calibration lines of Gordon *et al*, is greater than the measurement uncertainty. Of course, the effect of the modified treatment of  $C_i$  depends on the magnitude of  $C_i$  and can be zero if  $C_i$  for a particular phantom calibration line is zero.

If, as is usual, only the  $K_{\alpha_1}$  and  $K_{\beta_1}$  are used to estimate the *in vivo* lead concentration, the effect of the modified treatment of  $C_i$  is diminished for the calibration lines of Gordon *et al* (table 3 also shows  $[\text{Pb}]_{\mu}$  and  $\sigma_{[\text{Pb}]_{\mu}}$  calculated from only these two peaks), and  $[\text{Pb}]_{\mu}$  for the modified treatment of  $C_i$  no longer differs from that of Gordon *et al* by more than  $\sigma_{[\text{Pb}]_{\mu}}$ .

**Table 3.** Lead concentrations and the uncertainties therein calculated using three different methods for two *in vivo* subjects.

Method	Subject B	Subject C
Calculating $[\text{Pb}]_{\mu}$ using $K_{\alpha 2}$ , $K_{\alpha 1}$ , $K_{\beta 1}$ and $K_{\beta 3}$		
$[\text{Pb}]_{\mu} \pm \sigma_{[\text{Pb}]_{\mu}}$ from Gordon <i>et al</i> , excluding $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$	$65.7 \pm 3.408$	$-2.5 \pm 2.972$ (99.998%)
$[\text{Pb}]_{\mu} \pm \sigma_{[\text{Pb}]_{\mu}}$ from Gordon <i>et al</i> , including $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$	$65.7 \pm 3.417$	$-2.5 \pm 2.972$ (100%)
$[\text{Pb}]_{\mu} \pm \sigma_{[\text{Pb}]_{\mu}}$ for modified treatment of $C_i$ , excluding $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$	$74.2 \pm 3.404$	$6.0 \pm 2.885$ (99.996%)
$[\text{Pb}]_{\mu} \pm \sigma_{[\text{Pb}]_{\mu}}$ for modified treatment of $C_i$ , including $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$	$74.2 \pm 3.421$	$6.0 \pm 2.885$ (100%)
Calculating $[\text{Pb}]_{\mu}$ using $K_{\alpha 1}$ and $K_{\beta 1}$ only		
$[\text{Pb}]_{\mu} \pm \sigma_{[\text{Pb}]_{\mu}}$ for modified treatment of $C_i$	$65.3 \pm 3.721$	$-3.9 \pm 3.232$

Strictly speaking, calculations based on the sizes of two peaks should be performed on data obtained when only those two peaks are fitted (the calculations in table 3 are based on sizes obtained by fitting all four peaks). The results shown in table 3 were therefore checked against those obtained from combining the  $\alpha$  and  $\beta$  peak sizes and the calibration lines from Gordon *et al* (neither is this, itself, the same as fitting only two peaks but the outcome should be similar). The  $[\text{Pb}]_{\mu}$  and  $\sigma_{[\text{Pb}]_{\mu}}$  obtained from this calculation were  $74.511 \pm 3.416 \mu\text{g g}^{-1}$  for subject B ( $\pm 3.403 \mu\text{g g}^{-1}$  without the contribution from  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$ ; a contribution of 0.38% to  $\sigma_{[\text{Pb}]_{\mu}}$ ) and  $5.985 \pm 2.895 \mu\text{g g}^{-1}$  for subject C ( $\pm 2.895$  [99.997%]  $\mu\text{g g}^{-1}$  without the contribution from  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$ ). These values for  $[\text{Pb}]_{\mu}$  and  $\sigma_{[\text{Pb}]_{\mu}}$  are reassuringly consistent with those given in table 3 for the calculations based on two (of the four fitted) peaks.

Table 3 also shows, for the convenience of the reader, the effect of the covariance between individual estimates of concentration,  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$ , both for the original data of Gordon *et al* and for the revised treatment presented herein. Table 3 shows that the effect of  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$  is small, both for the treatment of Gordon *et al* (wherein  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$  increases  $\sigma_{[\text{Pb}]_{\mu}}$  by 0.26% for subject B and by 0.002% for subject C) and for the modified treatment of  $C_i$  (wherein  $\sigma_{[\text{Pb}]_i[\text{Pb}]_j}^2$  increases  $\sigma_{[\text{Pb}]_{\mu}}$  by 0.5% for subject B and by 0.004% for subject C).

#### 2.4. Further work

A comparison between the standard deviation of repeated measurements and the average value of  $\sigma_{[\text{Pb}]_{\mu}}$  (Todd *et al* 2000) showed that the latter underestimated the former, often significantly. The differences may arise from contributions to the uncertainty that are not accounted for in the formulae for the uncertainty from, for example, short-term and long-term reproducibility. Further work is in progress to identify the importance of such components. The differences between the standard deviation of repeated measurements and the uncertainty derived from counting statistics and calibration are substantially greater, and therefore substantially more important, than the effect of the formulae presented here. The revised formulae are nevertheless necessary for a consistent method.

### 3. Conclusion

Formulae for the uncertainty in the predicted lead concentration derived from bone lead x-ray fluorescence spectra are presented for a previously published revised treatment of the calibration line intercept. The revised treatment, although appropriate, has little effect on the calculated uncertainty but can have a larger effect on the calculated concentration. Further work is required to determine sources of measurement uncertainty not reflected in the formulation.

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