



Bioassays in workers exposed to long time random intakes

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ARTICLE INFO

Keywords:

Internal dosimetry
Biokinetic models
Bioassay evaluation
ICRP
Simulation
Uncertainties

ABSTRACT

Workers who are occupationally exposed to radioactive aerosols are usually subjected to periodic controls of internal contamination by performing bioassays (whole body or partial body monitoring and measurement of excreta samples). The intakes are also estimated by using Static Air Samples (SAS). These measurements are used to estimate the radioactive intakes of the workers. A typical assumption is the workers are chronically (constant) exposed for long periods of time. However, the intakes are random and there are also periods without any exposure (weekends, holidays, etc.). The method presented here considers both facts. Simulations help to choose the most appropriate method of evaluation to minimize the statistical uncertainties in the intake. It has been applied to evaluate workers exposed to UO₂ aerosols for a long time (30 years or more for most of them) in the same working area (sintering). Results of measurements of uranium in urine and daily intakes (from SAS) of these workers have been used. For this evaluation, the new Occupational Intakes of Radionuclides (OIR) biokinetic models of the International Commission on Radiological Protection (ICRP) for uranium have been solved. For some workers the evaluation gives a significant deviation between the intake estimated from urine samples and the intake estimated using the SAS values, supporting the idea that the physiological standard parameters of the reference worker are not always applicable. The computations have been implemented in the BIOKMOD code.

1. Introduction

Workers who are occupationally exposed to the incorporation of radioactive aerosols (e.g., in nuclear fuel factories using uranium and/or plutonium) are normally subjected to periodic controls of internal contamination by performing bioassays (whole body or partial body monitoring and measurement of excreta samples). In addition, a monitoring of the environmental concentration of activity in the air is carried out in the working areas, using Static Air Samplers (SAS) or Personal Air Samplers (PAS). SAS are usually used as a control method to ensure that certain activity concentration levels are not exceeded in the workplace.

The total amount of activity incorporated by the worker (intake in Bq) and the Committed Effective Dose E(50) (Sv) associated with the internal exposure at the workplace, are obtained from the interpretation of *in vitro* monitoring data (activity concentration in urine and feces) and/or *in vivo* measurement data (retained activity in the lungs, thyroid, whole body, ... at the time of measurement). This evaluation requires biokinetic models describing the distribution of radionuclides in the body and usually assumes a reference worker. Typical Intake scenarios

to consider are (1) acute intake at the time of an incident, (2) acute intake in the middle of the monitoring interval of the routine monitoring program or (3) chronic constant intakes. In this last case it is usually assumed that the worker is chronically exposed for long periods of time (at least since the last bioassay was carried out), while periods without exposure (weekends, holidays, etc.) are not usually considered for dose assessment.

Nevertheless, the real situations are much more complex: the daily intakes, as it will be shown in this work, are far from being constant, and the characteristics of each worker can substantially influence the estimation of the intake. In addition, the effect of considering that the intakes are random was analyzed to check the impact on the evaluation of the incorporated activity from monitoring data. The method presented here allows to reduce the uncertainties attributable to the random nature of the intakes. The information provided by the SAS can help the evaluator to make a more realistic use of the date and time associated to bioassay data for dose assessments.

BIOKMOD software (Sánchez-León 2007) (<http://oed.usal.es/webMathematica/Biokmod/>) has been updated with the new

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<https://doi.org/10.1016/j.apradiso.2021.110057>

Received 27 July 2021; Received in revised form 4 November 2021; Accepted 2 December 2021

Available online 4 December 2021

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Occupational Intakes of Radionuclides (OIR) models of Co, Cs, I and U (ICRP, 2015; ICRP, 2016; ICRP, 2017; ICRP, 2019) published by the International Commission on Radiological Protection (ICRP). The new version of this code allows the estimation of the intake using thousands of daily intakes (the complete working life of a worker can be included). It has been developed using the Wolfram Language (Sánchez-León, 2017).

Real cases of occupational internal exposures of uranium oxides (mainly UO₂) aerosols are evaluated in this publication. Bioassay data and SAS data are available from workers exposed to low enriched uranium during the fabrication of nuclear fuel elements of nuclear power plants at the Juzbado Plant of ENUSA in Salamanca, Spain.

Uranium is both radiologically and chemically toxic. Most regulatory bodies agree in a higher concern on the chemical toxicity when uranium content in the kidneys is above 3 µg g⁻¹ (retrospective approach) and on the radiological hazard when the annual effective dose is above 6 mSv (ISO, 2015).

2. Mathematical description of the evaluation method

In this section, the mathematical criteria to estimate the incorporations of workers exposed to the inhalation of radioactive isotopes are described.

The main issue is to know the value of the daily intake b (Bq) from monitoring data. In some nuclear facilities there are Static Air Samplers (SAS) that suck the air from the work area and deposit the aerosols in filters that are measured to estimate the daily intake of each worker (López-Fidalgo J. and Sánchez-León G, 2005). However, several studies (e.g., Puncher et al, 2007) have shown that SAS can be unrepresentative of the real incorporations of workers. Also, individual monitoring programs based on bioassay methods (body radioactivity counters and/or analysis of urine and feces) can be used to estimate the intake.

For the assessment of the intake by means of bioassay data, the ICRP reference bioassay retention $r_f(t)$ and excretion $r_e(t)$ functions are needed. These functions describe the distribution of the radionuclide in the body, depending on time t after the intake: (i) $r_f(t)$ represents the predicted activity of a radionuclide retained in the body, organ, or tissue at a time t , after a single intake of 1 Bq at $t = 0$ and (ii) $r_e(t)$ represents the predicted activity of a radionuclide in a 24-h excreta sample (urine or fecal) at a time t , after a single intake of 1 Bq at $t = 0$. From now on, the response function $r(t)$ will denote both $r_f(t)$ or $r_e(t)$ depending on the type of bioassay.

The $r(t)$ expression can be obtained solving mathematically the appropriate biokinetic model. In the ICRP series of OIR publications (ICRP, 2015; ICRP, 2016; ICRP, 2017; ICRP, 2019) the biokinetic models are described for most of radionuclides considering the pathway of intake and other factors (chemical form, particle size defined by the AMAD for radioactive aerosols, and other parameters). A set of tabulated values for $r(t)$ can be found in the OIR Data Viewer (ICRP 2019), but it is more useful to use mathematical expression of $r(t)$, which can be obtained from BIOKMOD (<http://oed.usal.es/webMathematica/Biokmod/>), developed by one of the authors. The last version of this code includes some of the OIR models (Co, Cs, I, U). Also, the BIOKMOD user can build and solve any other model included in the ICRP publications. On the other hand, the equations described in this section have also been included.

2.1. Multiple daily intakes

Each working day (wd) j , a worker is exposed to an intake b_j (being b_j the total intake along the shift in Bq d⁻¹). The total intake during a period of T days will be: $B(\text{Bq}) = \sum_j b_j(\text{Bq})$.

In case of multiple daily intakes $\{b_1, b_2, \dots, b_j\}$ the predicted retention or excretion of the worker after a time t (usually in days) after the first intake occurred, considering that t only takes integers values (this is only a practical consideration, but it is not a mathematical requirement),

will be:

$$R_M(t) = b_1 r(t) + b_2 r(t-1) + \dots + b_j r(1) = \sum_{j=1}^t b_j r(t-j+1) \quad (1)$$

2.2. Multiple constant intakes

The general approach when evaluating internal doses is to assume the total intake B happens during the period T with a constant rate B/T then the retention or excretion can be expressed as:

$$R_C(t) = \left\{ \begin{array}{l} \frac{B}{T} \int_0^t r(t) dt \text{ for } 0 < t \leq T \text{ and } \frac{B}{T} \int_{t-T}^t r(t) dt \text{ for } t > T \end{array} \right\} \quad (2)$$

A more realistic approach (López-Fidalgo J, Sánchez-León G. 2019) is to consider the interval T divided in subintervals $\{T_0, \dots, T_b, \dots, T_n\}$, and within each subinterval T_i a total intake B_i occurs (the average daily input, \bar{b}_i , will be B_i/T_i).

If k intervals are assumed $(s_1, T_1), (s_2, s_2 + T_2), \dots, (s_k, s_k + T_k)$, with continuous intakes b_i during the period from s_i to $s_i + T_i$ with $i = 1, 2, \dots, k$, then the observed quantity $R_{MC}(t)$ defined either as retained activity (in an organ, a tissue or the body) or excreted activity (urine or fecal), at time t (being $t = 0$ the moment when the first intake began), can be represented as:

$$R_{MC}(t) = \hat{b}_1 R_{C1}(t) + \hat{b}_2 R_{C2}(t) \dots + \hat{b}_k R_{Ck}(t) = \sum_{i=1}^k \hat{b}_i R_{Ci}(t) \quad (3)$$

Where

$$R_{Ci}(t) = \begin{cases} 0 & t \leq s_i \\ \int_{s_i}^{t-s_i} r(s) ds & s_i < t < s_i + T_i \\ 0 & t \leq s_i \\ \int_{t-s_i-T_i}^{t-s_i} r(s) ds & t \geq s_i + T_i \end{cases}$$

A single intake \bar{b}_i can also be considered as a particular case of constant intake where b_i happens in an interval $T_i > 0$, then, the decay of b_i is given by $b_i r(t-s)$. This is useful when an accidental single intake b_i occurs.

2.3. Uncertainties

The individual daily intake b_j is usually a random variable with mean μ_b and variance σ_b^2 referred to working days. When considering many single inputs b_j , then it is shown (Sánchez-León, 2007; López-Fidalgo J. and Sánchez-León G, 2005) that the retention function $R(t)$ and the corresponding probability bands are given by:

$$R(t) = \mu_b \sum_{j=1}^t r(j) + z \sigma_b \sum_{j=1}^t r^2(j) \quad (4)$$

z is the 100 $(Y + 1)/2$ -quantile of the standard normal distribution.

It is important to point out that the intake occurs during the period T on working days $\{w_1, w_2, \dots, w_d, \dots, w_N\}$ being N the numbers of working days and M the number of natural days ($N \leq M$) of the period T . Considering only the working days the average and standard deviation are estimated by:

$$\mu_b = \frac{1}{N} \sum_{k=1}^N b_i \quad (5)$$

$$\sigma_b = \sqrt{\frac{1}{N-1} \sum_{k=1}^N (b_i - \mu_b)^2} \quad (6)$$

And the average of the period T considering the M natural days (nd):

$$\hat{b} = \frac{1}{M} \sum_{k=1}^N b_i \tag{7}$$

Then, the total intake B is:

$$B = \hat{b} M = \mu_b N$$

and

$$\hat{b} = \mu_b N / M \tag{8}$$

2.4. Estimation of the intake by fitting the bioassay data

Workers at risk of intakes of radionuclides in the workplace, when annual dose may be expected above 1 mSv, are included in individual monitoring programs defined by monitoring methods (*in vivo* measurements of activity in the body and *in vitro* analysis of excreta samples). The results of the activity excretion from urine or feces (Bq d⁻¹, Bq L⁻¹) or the activity content (Bq) in the body or in an organ or region, are represented by {*t*₁, *m*₁, *u*₁}, {*t*₂, *m*₂, *u*₂}, ...} being the experimental value of the measured *m*_{*i*} with uncertainty *u*_{*i*} taken at time *t*_{*i*}. These values can be used to estimate the intake quantities (Bq).

One method applied to estimate the quantity intakes *b*_{*i*} is the maximum likelihood method such as it is described in ISO 27048:2011 (ISO, 2011). Assuming that each measurement {*m*_{*i*}, *u*_{*i*}} is taken from a lognormal distribution with scattering factor of *SF*_{*i*}, then for the *n* measurements (Log; natural log):

$$\chi^2 = \sum_{i=1}^N \frac{(\text{Log}[b_i r(b_i)] - \text{Log}[m_i])^2}{\text{Log}(SF_i)} \tag{9}$$

Where:

$$SF_i = \exp \sqrt{\text{Log}(SF_{A_i})^2 + \text{Log}(SF_{B_i})^2}$$

Being:

$$\text{Log}(SF_{A_i}) = \frac{u_i}{m_i}$$

*SF*_{*B*}: Depending on type of bioassay (typically *SF*_{*B*} = 1.4 for measurements of ²³⁴Th in lungs, *SF*_{*B*} = 1.2 for ²³⁵U in lungs, *SF*_{*B*} = 1.7 for urine samples normalized to 24h excretion using creatinine content in the samples and *SF*_{*B*} = 3 in case of 24-h fecal samples).

In the case of multiple daily intakes where it is assumed an average daily intake *b*₁ during an interval *T*₁, *b*₂ during an interval *T*₂, ..., *b*_{*k*} during an interval *T*_{*k*}, *n* from eq. (9), can be derived to:

$$\text{Arg_Min}_{\{b_1, \dots, b_k\}} \left[\sum_{i=1}^N \left(\frac{\text{Log}[R_M(t_i, \{\tilde{b}_1, \dots, \tilde{b}_k\})] - \text{Log}[m_i]}{(u_i/m_i)^2 + \text{Log}[SF_B]^2} \right)^2 \right] \tag{10}$$

being:

(*b*₁, ..., *b*_{*k*}) the unknown intakes *b*₁, ..., *b*_{*k*} to be estimated and

$$R_M(t, \tilde{b}_1, \dots, \tilde{b}_k) \approx \tilde{b}_1(r(t) + r(t-1) + \dots) + \tilde{b}_2(r(t-j) + \dots + r(t-j-1)) + \dots + \tilde{b}_k(r(t-j-s) + \dots) \tag{11}$$

If the multiple constant intakes model is used then the intakes can be estimated by the bioassay data using equation (12) or the method described in López-Fidalgo J and Sánchez-León G, 2019.

$$\text{Arg_Min}_{\{b_1, \dots, b_k\}} \left[\sum_{i=1}^N \left(\frac{\text{Log}[R_{MC}(t_i, \{\tilde{b}_1, \dots, \tilde{b}_k\})] - \text{Log}[m_i]}{(u_i/m_i)^2 + \text{Log}[SF_B]^2} \right)^2 \right] \tag{12}$$

Where:

$$R_{MC}(t, \tilde{b}_1, \dots, \tilde{b}_k) = \tilde{b}_1 R_{C1}(t) + \tilde{b}_2 R_{C2}(t) \dots + \tilde{b}_k R_{Ck}(t) \tag{13}$$

Sometimes, when empirical information is available, weighting factors can be applied. For instance: if *b*₂ = *w*₁ *b*₁ then *b*₂ will be replaced by *w*₁ *b*₁. It can be very useful.

2.5. From the intake to the dose

The main purpose in radiological protection is to know the Committed Effective Dose E(50) Sv of internally exposed individuals. In case of internal exposure of a worker with an intake *B* (in Bq), estimated using some of the methods described before, the dose is simply assessed as follows:

$$E(50) \text{ (Sv)} = B(\text{Bq}) \times e(50) \text{ (Sv Bq}^{-1}) \tag{14}$$

being *e*(50) the committed effective dose coefficient provided by ICRP according to the intake scenario (pathway of intake, radionuclide that is incorporated, physical and chemical form of the aerosol). The most recent Dose coefficients from OIR “Occupational Intake of Radionuclides” models of ICRP can be obtained from OIR DataViewer (ICRP, 2019. Supplementary materials).

3. Workers exposed to irregular and random intakes. Bioassay selection

This section refers to workers chronically exposed to the intake of oxides (mainly UO₂) by inhalation. However, this methodology can be applied to any other cases of chronic exposure. The biokinetic model of uranium described in ICRP Publications 130 (ICRP 2015) and ICRP 137 (ICRP 2016) included in BIOKMOD will be used. The effect of considering the random nature of chronic aerosols intake will be evaluated. Simulations modelling random intakes and the bioassay data have been made to choose the most appropriate method of evaluation to minimize the uncertainties in the intake estimation

Two important innovations have been implemented in BIOKMOD to perform this analysis:

- a) A big number of multiple single intakes can be computed. It allows including of daily intakes of a worker as input data, which implies dealing with thousands of intakes. This permit considering periods without incorporation such as weekends, vacations, and sick leaves.
- b) Several intervals of constant intakes can be defined, and the user can decide the intervals when the intake conditions are similar, assigning weights for different intervals, based on SAS data.

The effect of a random incorporation considering three types of bioassay methods (Lung, Urine and Faecal excretion) in realist situations has been simulated (ANNEX I of Appendix A) to check the advantages and disadvantages of each measurement. The conclusions are the following:

The most suitable bioassay method for individual monitoring programs of workers occupationally exposed to UO₂ is the determination of uranium in urine samples (urine 24 h-excretion). A period of at least 24 h without exposure is recommended (López-Fidalgo and Sánchez-León, 2019) before starting the 24-h sample collection. This allows reducing the uncertainty due to the random intakes. Although the previous analysis refers to UO₂, the behavior of a rapid elimination fraction is present in the biokinetics of other uranium and plutonium compounds, so also in these cases urine measurements will usually be the most appropriate bioassay method to select. In the case of an accidental intake, according to the simulation, a combination of 24h-Urine excretion and Lung retention is recommended if the first 24 h Urine excretion analysis gives a value higher than 1 Bq of U d⁻¹.

4. Criteria to estimate the intake using 24-urine excretion samples

In this section the most appropriate statistical method to estimate the intake from the measurement of urine samples is evaluated. The optimal moments in which the samples should be collected was studied in a previous publication (López-Fidalgo and Sánchez-León, 2019; Rodríguez-Díaz and Sánchez León, 2019), focusing on the uncertainty of the measurements.

Now the focuses will be on the following choices: i) the time when the samples should be taken and ii) the mathematical method for fitting monitoring data of the urine samples.

Several exposure scenarios have been simulated with the following assumptions:

1. A reference worker is exposed 185 Bq per year of UO₂ of 4.2% enriched uranium aerosols of AMAD = 5 μm (it is equivalent to 1 mSv y⁻¹ as it is shown in ANNEX I of Appendix A) during 225 working days per year for a period of 10 year. Therefore, the average daily intake per year is: μ_b = 0.82222 BqU/wd and $\hat{b} = 0.50685$ BqU/nd (wd: working days, nd: natural days).
2. On exposure days wd the worker is exposed to a lognormal distribution of mean μ_b and standard deviation σ_b, being μ_b ≈ σ_b (based on real data from ENUSA Juzbado Fuel fabrication plant).

The 24 h urine sample is collected from the worker every 365 day, except the first year, when it is taken approximately 6 months after the start of the exposure. Regarding the collection of samples two situations are considered:

- Situation 1.- The worker has not been exposed 8 days before the sample is taken (typical situation if the urine sample is collected after vacations). The purpose of considering this option is that (Fig. I.2), the statistical uncertainty decreases after some days without exposure due to the random nature of the incorporations.
- Situation 2.- The worker has been exposed the days immediately before the sample collection.

With the above criteria, a set of 30 simulations were carried out.

For each simulation *k* the first step is to obtain the daily intakes for a period of 10 years according to “Situation 1” and “Situation 2” criteria, obtaining: *I_k*: {*b*₁, ..., *b_j*, ..., *b_n*}. Some of the *b_j* values may be 0, the ones corresponding to days without intakes (such as weekend or holidays). The working days are those with *b_j* ≠ 0, denoted *I_{W,k}*: {*b_{W,1}*, ..., *b_{W,j}*, ... *b_{W,n}*}. The average \hat{I}_k of *I_k* and $\hat{I}_{W,k}$ of *I_{W,k}* are calculated. Or course, \hat{I}_k and $\hat{I}_{W,k}$ values are very close to $\hat{b} = 0.50685$ Bq/nd and μ_b = 0.82222 Bq/wd.

The next step is to suppose that one sample is collected annually for a period of 10 years, the first one is taken approximately in the middle of the first year of work. To be precise in “Situation 1” the sample are taken the days: {*t*₁, ..., *t*₁₀} = {168, 168 + 365, ..., 168+9 × 365} and in “Situation 2”: {*t*₁, ..., *t*₁₀} = {159, 159 + 365, ..., 159+9 × 365}.

The daily urine excretions are calculated according to eq. (1) assuming multiple single intakes given by the *I_k* values. So, the activities in the urine samples *m_i* (in Bq d⁻¹ of U) the day *t_i* are obtained. The uncertainties of the measures *u_i* has been assumed to be 0.1 *m_i*. Then a list, denoted as *List1*, of 30 simulated sample values for “Situation 1”, and another list, *List2*, for “Situation 2” are obtained. That is: *List1*: {*List1*₁, ..., *List1*₃₀} being: *List1*₁ = {{*t*₁, *m*_{1,1}, *u*_{1,1}}, ..., {*t*₁₀, *m*_{10,1}, *u*_{10,1}}}, ..., *List1*₃₀ = {{*t*₁, *m*_{1,2}, *u*_{1,2}}, ..., {*t*₁₀, *m*_{10,30}, *u*_{10,30}}}, and *List2*: {*List2*₁, ..., *List2*₃₀} being: *List2*₁ = {{*t*₁, *m*_{1,1}, *u*_{1,1}}, ..., {*t*₁₀, *m*_{10,1}, *u*_{10,1}}}, ..., *List2*₃₀ = {{*t*₁, *m*_{1,2}, *u*_{1,2}}, ..., {*t*₁₀, *m*_{10,30}, *u*_{10,30}}}.

The next step is to estimate the average daily intake, denoted *s_k*, for the whole period (10 years) fitting the urine samples values simulated. Then we can compare the “true value” \hat{I}_k with *s_k*. The methods used to fit

the bioassay data and to calculate the chi-squared (eq. (9) and (10)). We try to find the best criterium to make the best estimation. With this goal we have defined the following scenarios:

- Scenario 1.- *List1* values are fitting assuming multiple single intakes obtaining the estimated average daily intake for each list, denoted by {*s1*₁, ..., *s1*₃₀}, and the corresponding chi-squared: {*X*²_{1,1}, ..., *X*²_{1,30}}
- Scenario 2.- *List1* values are fitting assuming multiple constant intake obtaining the estimated daily intake for each list, denoted by {*s2*₁, ..., *s2*₃₀}, and {*X*²_{2,1}, ..., *X*²_{2,30}}.
- Scenario 3.- *List1* values are fitting assuming a single constant intake obtaining the estimated daily intake for each list, denoted by {*s3*₁, ..., *s3*₃₀} and {*X*²_{3,1}, ..., *X*²_{3,30}}.
- Scenario 4.- *List2* values are fitting assuming multiple single intakes obtaining the estimated daily intake for each list, denoted by {*s4*₁, ..., *s4*₃₀} and {*X*²_{4,1}, ..., *X*²_{4,30}}.
- Scenario 5.- *List2* values are fitting assuming a single constant intake obtaining the estimated daily intake for each list, denoted by {*s5*₁, ..., *s5*₃₀} and {*X*²_{5,1}, ..., *X*²_{5,30}}.

To compare the scenarios the relative differences δ_{Sc,s} (Sc: scenario: {1, 2, 3, 4, 5} and s: simulation: {1, ..., 30}) between the average of daily intake obtained by fitting and the “true values” { \hat{I}_1 , ..., \hat{I}_{30} } have been computed. That is: Scenario Sc: { δ_{Sc,1} = (sSc₁ - \hat{I}_1)/ \hat{I}_1 , ..., δ_{Sc,1} = (sSc₃₀ - \hat{I}_{30})/ \hat{I}_{30} }

Then the mean <δ_{Sc}> of {δ_{Sc,1}, δ_{Sc,30}} and the standard deviation σ_{Sc} for each scenario Sc have been computed. From these data, the value 100 Max|δ_{Sc} ± σ_{Sc}| (that will be denoted ‘Deviation’) is obtained. Also, the average of the χ² of each scenario has been calculated. Table 1 shows the Deviations and the average of chi-squared χ² values.

The best option (the smallest Deviation and χ²) is scenario 1: The worker is not exposed some days before the sample is taken and the sample values are fitted assuming multiple single intakes. However, in “real world” sometimes the worker may have been exposed in the days immediately prior to the sample collection. Even in this case, the best method of estimating the intake is the multiple single intakes

5. Real cases of workers exposed to inhalation of UO₂ for a long time

This section compares real data of intakes in a small group of seven workers being long term exposed to inhalation of uranium oxides for which incorporation data based on SAS and urine samples are available. Most of these workers have spent more than 30 years working in the same area (sintering) exposed to similar exposure conditions (López et al., 2019; López M.A. et al, 2020).

The study covers the exposure period 1985–2019. Data are available for individual intakes based on SAS since 2000 and for urine samples since 2014. The data have been provided by ENUSA facility of Juzbado (Salamanca, Spain).

The daily intakes based on SAS for the period 2000–2018 (approx. 6000 days) have been analyzed. According to the observed data two periods are established: 2000–2013 and 2014–2019, because the improvements made in the working area in 2013 reduced the environmental uranium concentration.

In addition, bioassay data of uranium in 24 h urine samples are

Table 1
Comparison of the scenarios.

Scenario	Deviation	<χ ² >
1	4.6%	0.058
2	7.5%	0.100
3	15.9%	0.178
4	8.6%	0.390
5	16.6%	0.434

available since 2014. The urine samples values Bq d^{-1} of ^{234}U for each worker is represented in Fig. 1. It represents the net values with the urine background (0.565 Bq d^{-1} of ^{234}U) subtracted [The background data was provided by ENUSA]. Measured of ^{238}U and ^{235}U are available, but some of them are lower than the DL for this reason the measures of ^{234}U are only used. For U of an enrichment of 4.2%, wt. ^{235}U (84.95% ^{234}U in activity), the typical in Juzbado Plant, $1 \text{ Bq of } ^{234}\text{U} \approx 1.18 \text{ Bq of U}$.

Therefore, different reference times for the study have been considered:

T_0 : period since the start of exposure of the worker (around 1985 for most of worker) until 1999, for which data from the air samplers (SAS) are not available.

T_1 : period from 2000 to 2013, when daily incorporations of workers based on the SAS are available.

T_2 : period from 2014 to 2018 or 2019 (depending on the worker). The daily incorporations are available based on both, SAS and annual urine samples; this period is assumed to begin 180 days before the first sample is collected.

For each worker a list, *ListInt*, of pairs of numbers with the daily incorporations calculated from the SAS data is available: *ListInt*: $\{\{b_1, d_1\}, \dots, \{b_i, d_i\}, \dots\}$, where b_i is the activity incorporated by the worker on day d_i . The natural days in which the worker was not exposed, $b_i = 0$. The pairs $\{b_i, d_i\}$ where $b_i = 0$ are eliminated in *ListInt*, it means that only the working days (wd), d_{wd} , those where $b_i \neq 0$ are included. Then it is split into two sublists: *ListIntakeT1* for period T_1 and *ListIntakeT2* for period T_2 . From *ListIntakeT1* and *ListIntakeT2* the average of the daily inputs $\{\bar{b}_{wd1}, \bar{b}_{wd2}\}$ are computed. Hence a weighting factor defined as $rb_{wd} = \bar{b}_{wd1}/\bar{b}_{wd2}$ is calculated.

Also, for each worker a list (denoted *ListSample*) with the results of the 24h urine samples values is available: *ListSample*: $\{\{t_j, m_j, u_j\}, \dots, \{t_j, m_j, u_j\}, \dots\}$, where t_j is the day when the sample was collected, m_j is the measurement, and u_j the uncertainty of the measurement.

The next step is to estimate the intake of the worker using *ListSample*. The algorithm applied is described in ANNEX II (of Appendix A). It can be summarized as follows:

We have defined two parameters $bm1$ and $bm2$ to be found by fitting *ListSample*, being $bm1$ and $bm2$ the unknown daily intake averages referred to the working days in periods T_1 and T_2 respectively. In *ListIntakeT1* and *ListIntakeT2* the b_j values are replaced by $bm1$ and $bm2$, that if $b_j > 0$ then $b_j = bm1$ (in *ListIntakeT1*) or $b_j = bm2$ (in *ListIntakeT2*). We know from SAS that $rb_{wd} = \bar{b}_{nd1}/\bar{b}_{nd2}$, it is reasonable to assume that $bm1 \approx rb_{wd} bm2$. After these replacements *ListIntakeT1* and *ListIntakeT2* are joined. So, we produce a list with a pattern similar to:

Listfit $\{b_i, d_i\}$: $\{\{rb_{wd} bm2, 1\}, \dots, \{rb_{wd} bm2, k\}, \{bm2, k+1\}, \dots, \{bm2, k+n\}\}$

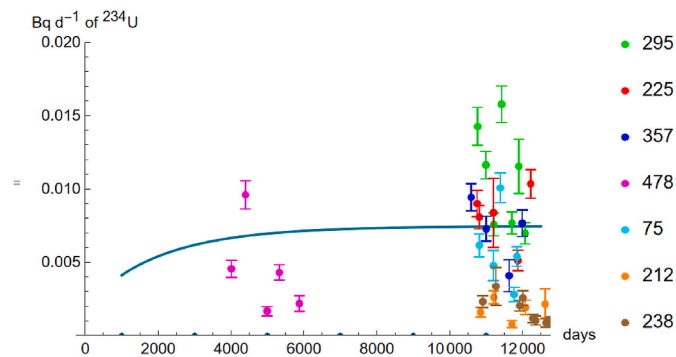


Fig. 1. Urine sample values for different workers (OX: days since the worker started to be exposed; OY represents the net values with the background (0.565 Bq d^{-1} of ^{234}U) subtracted.

Then, $bm2$ is estimated by fitting *Listfit* and *ListSample* using eq. (10). In fact, it is a particular case of eq. (10) with only one unknown ($bm2$).

The total intake B_1 and B_2 in the period T_1 and T_2 are $B_1 = N_{wd1} bm1$ and $B_2 = N_{wd2} bm2$, being N_{wd1} and N_{wd2} the numbers of working days in the periods T_1 and T_2 . Then eq. (14) can be used to calculate the Committed Effective Dose $E(50)$.

Remark: Note that the daily intake values from SAS (*ListInt*) have only been used to know the days when the worker was exposed and to compute a weighting factor rb_{wd} .

An example fitting the data of a worker (ANNEX II of Appendix A) is shown in Fig. 2.

It has been used to analyze several real cases of occupational internal exposures to uranium oxides. Specifically, as mentioned before, a group of long-term exposed workers was selected, most of them exposed for more than 30 years to similar exposure conditions. All of them have worked in the same area (sintering) doing the same work. Their daily incorporation data are available based on SAS measurements for the last 18 years, and on 24 h urine monitoring data for the last 5 years.

Two periods are considered for the study: T_1 (before 2014) and T_2 (from 2014 to the last available data for each worker). In most workers the daily intakes were appreciably higher before 2014 (It can be observed in Fig. 3, where the day 10 700 corresponds to the year 2014). Improvements were made to the ventilation system of the workplace in 2013 to reduce the uranium concentration in air.

Table 2 shows the total intake B_{SAS} (in Bq of U) of each worker for the period T_1+T_2 , when there are data on daily intakes by SAS, and for the same period the estimation of the total intake B_{URI} (in Bq of U) from the urine sample. Then, $B_{URI}/B_{SAS} = F$ is calculated.

6. Discussions, and conclusions

To assess the intakes of workers who have been exposed to inhalation of uranium oxide aerosols for a long time, usually constant daily incorporations are assumed. Individual monitoring programs for these workers are based on in vitro bioassay methods for routine. In case of accidental intakes, *in vivo* lung monitoring may also be carried out when available and suitable. The worker is not exposed every day at the workplace, and the incorporations vary from one day to another in a random way. A mathematical model was developed to deal with the intakes in a realistic way (random incorporations that only occur in working days). This approach has been implemented into the BIOKMOD code for the assessment of internal exposures of workers at risk of UO_2 inhalation, comparing different statistical fitting criteria to estimate the intakes from monitoring data. In this assessment, the OIR models (ICRP,

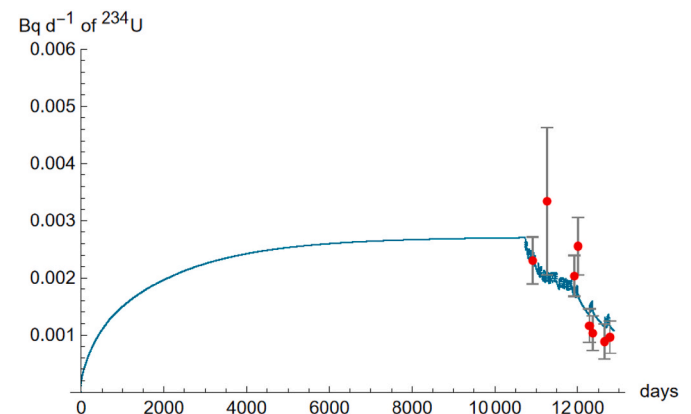


Fig. 2. Estimated daily urine excretion obtained by fitting compared with the urine sample values (red points). The scattered points in the last period is due to the days without intakes are considered. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

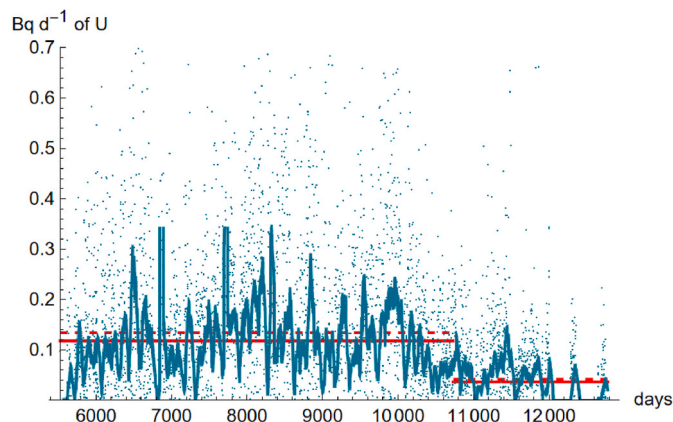


Fig. 3. The small points represent the daily intakes (using SAS) for the same worker of Fig. 2. The blue line is the moving average of the last 50 data. The red solid lines represent the daily intake average of the periods T1 and T2 estimated from SAS and the red dashed lines estimated from urine samples. Both lines are quite similar, however, in most workers the intakes estimated using urine samples are higher than the ones obtained from SAS. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 2

Total intake of the worker of each case of study, calculated using urine data and SAS.

Worker	t_i (days)	t_f (days)	Exposition ($^{\circ}$) (hours)	B_{SAS} (Bq of U)	B_{URI} (Bq of U)	$B_{URI}/$ B_{SAS} F
478	1	6327	20837	682	1425	2.09
225	5526	12374	21484	824	3108	3.77
295	5417	12266	22990	900	4275	4.75
357	5380	12056	22164	784	2657	3.39
75	5526	11849	20127	746	2190	2.94
212	5526	13185	15513	505	690	1.37
238	5526	12778	17949	689	784	1.13

^a Exposition time recorded by worker from t_i to t_f .

2015; ICRP, 2017) has been used, being implemented in the BIOKMOD (<http://oed.usal.es/webMathematica/Biokmod/>) as well. It has been checked that, under normal conditions, the most appropriate bioassay technique is the measurements of uranium in 24-h urine samples. However, the usual method of treating constant chronic incorporations may present great uncertainties, and a more realistic treatment may be more adequate to estimate the intakes.

In a group of workers, all of them working in the same area (sintering) during a long time, the intake has been calculated for each worker using the data based on SAS and fitting the urine samples to a multi single intake model (Table 2).

The existence of great uncertainties associated to the estimation of intakes when these estimations are based on the SAS data is already known. However, there is relevant information from SAS to be used when the intakes are assessed based on the results of the activity concentration of uranium in urine samples:

- The data of the daily incorporations from SAS allow to know which days the worker was exposed to intake of UO_2 .
- A weighting factor rb_{wd} for period T_1 with respect to period T_2 was calculated. It can be used to improve the estimation based in the urine samples

Although, for fitting purpose, two periods has been considered, the method developed is applicable to more complex situation considering more than two periods $\{T_1, T_2, \dots, T_k\}$ with different average daily

intakes $\{B_1/T_1, B_2/T_2, \dots, B_k/T_k\}$ to be estimated.

Although there may be an appreciable deviation in the intake with SAS values comparing with those obtained from the urine samples, given the very long time considered, it would be expected that the ratio between the total intake estimated from urine sample and from SAS values should be similar to all workers. However, this ratio is close to a value of 3 for most of them. This value is consistent with a previous study in which the SAS and PAS (personal air sample) measurements were compared for the same area for 6 months and it was obtained a ratio PAS/SAS around 3. It is assumed that the PAS is more representative of the real incorporation and especially in such long exposure times. The predicted urine excretion for UO_2 is 4 times lower in the ICRP 78 model than in the ICRP 137 (López M.A, 2020). This means that the deviation PAS/SAS could be considerably higher, about $PAS/SAS \approx 3 \times 4 = 12$.

However, there are two cases (Table 2, worker 238 and 212) where the values of uranium in urine are clearly lower than the rest, and the value of the ratio F (ratio of the intake estimated from SAS and the estimated from urine sample) is substantially different from the rest. An explanation may be that the workers present an abnormal background value, but even with a smaller background the values found in these samples are abnormally low. A better explanation may be related to physiological characteristics that may be far from the standard values of the reference worker used in the biokinetic model. In fact, the biokinetic model used to calculate uranium in urine involves several factors. To estimate the activity retained or excreted, the corresponding retention/excretion functions are needed. These functions are obtained from the compartmental model defined by ICRP. Therefore, it is a mathematical idealization of complex physiological processes which are available in ICRP Publications. These compartmental models include several transfer parameters that refer to a reference person (here those specific to the reference worker are used). The models are specific to each element and also depend on the route of intake (typically inhalation, ingestion, injection). It has common transfer parameters, other parameter models are specific of the chemical form of the material that is incorporated and, in the case of inhalation there are parameters associated with the physical form (usually associated with the aerodynamic diameter of aerosols, the AMAD), but the latter will affect all workers in the area. Several studies (Paquet et al 2016; Leggett and Harrison, 1995) show the difference in the parameters used in ICRP 137 (ICRP, 2017) to model UO_2 (Cited in ICRP 137 parr. 15.3.1.2).

In summary, for workers exposed to low concentrations of UO_2 , as it is usually the case in industry, the most convenient bioassay is the determination of uranium in urine. However, in these evaluations there may be workers who systematically present deviations with respect to the majority of workers exposed to similar conditions. Probably the main cause is that these workers present particular physiological conditions with factors far from those corresponding to the standard worker. In the event of an accident with a high risk of incorporation in these workers, more than one type of bioassay method should be applied. The computations have been implemented in the BIOKMOD code. Although the described method has been applied to workers exposed to the inhalation of UO_2 aerosols, it could be applied to other cases of chronic incorporation as well (e.g., workers exposed to chronic inhalation plutonium where incorporations are controlled using SAS or PAS and in vitro bioassay is performed too).

CRediT authorship contribution statement

María Antonia López: Writing – original draft, Writing – review & editing. **Montserrat Moraleda:** Writing – original draft. **Juan M. Rodríguez-Díaz:** Writing – review & editing, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

Acknowledgements

This research was funded by the Spanish Ministerio de Economía y Competitividad and Junta de Castilla y León (Projects 'MTM2016-80539-C2-2-R' and 'SA080P17', 'SA105P20'). The experimental data were provided by ENUSA.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.apradiso.2021.110057>.

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