

Guidance on Use of IMBA Software for DOE Safety Applications



**U.S. Department of Energy
Office of Environment, Safety and Health
1000 Independence Avenue, S.W.
Washington, D.C. 20585-2040**

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FOREWORD

This document provides guidance to U.S. Department of Energy internal dosimetrists in the use of the Integrated Modules for Bioassay Assessment (IMBA) computer codes for calculating dose to workers from intakes of radioactive materials. Information is provided herein that supplements information found in the IMBA documentation provided by the code developer. Comments and questions regarding this document should be addressed to:

Robert Loesch
EH-31/270CC
Office of Quality Assurance Programs
U.S. Department of Energy
1000 Independence Avenue, S.W.
Washington, D.C. 20585-0270
Phone (301) 903-4443
Email: robert.loesch@eh.doe.gov

CHANGE HISTORY

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Rev 1	Added footnote 25 in Section 5.7.2 Weights. Corrected $K_{xfer,tbB}$ and $K_{tba,bladder}$ in Attachment A.	12/07/2006

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EXECUTIVE SUMMARY

The development and maintenance of a collection, or toolbox, of high-use, U.S. Department of Energy (DOE) safety software quality assurance (SSQA)-compliant codes is one of the major improvement actions supported under DOE O 414.1C, *Quality Assurance*, and DOE G 414.1-4, *Safety Software Guide for Use with 10 CFR 830 Subpart A, Quality Assurance Requirements, and DOE O 414.1C Quality Assurance*. To evaluate Integrated Modules for Bioassay Assessment (IMBA) products for inclusion in the toolbox, a software-specific gap analysis¹ was performed. This gap analysis evaluated the SSQA attributes of the IMBA products against the work activities specified in DOE O 414.1C and DOE G 414.1-4. As discussed in the final report, IMBA Expert™ USDOE-Edition version 4.0.28, IMBA Professional Plus (IPP) version 4.0.28, and all future minor releases of IPP 4.0.x are recommended for inclusion in the DOE Safety Software Central Registry contingent upon the critical recommendations identified being implemented by the United Kingdom's Health Protection Agency (HPA) and the DOE Office of Environment, Safety and Health and are then reviewed by the DOE Central Registry program lead.

IMBA Expert™ DOE-Edition and IPP, which were developed by HPA, are computer codes used to evaluate bioassay data and calculate internal dose following occupational intakes of radioactive materials. IMBA Expert™ DOE-Edition was developed under contract to the DOE and at the end of 2006 will no longer be formally supported by HPA. IPP is a commercial derivative of IMBA Expert™ DOE-Edition and is the product that has been designated by HPA for continued development and support. HPA has provided a migration path from IMBA Expert™ DOE-Edition to IPP for all DOE licensees.

In the interim period before these changes are completed, the IMBA products are still considered useful assets in the support of safety-related calculations. This guidance report, which is applicable to both IMBA products, includes a discussion of the known limitations of IMBA and provides workarounds where possible. Guidance is also given on using certain features of IMBA that can be confusing to the user. This report is supplemental to and does not supersede the documentation supplied by HPA. While not ensuring correct application of IPP or IMBA Expert™ DOE-Edition in every instance, use of the information contained here will minimize potential user errors and further standardize the use of these products.

¹ *Gap Analysis for IMBA and DOE Safety Software Central Registry Recommendation*, DOE/EH-0711, August 2006.

1. Introduction

DOE O 414.1C, *Quality Assurance*, specifies required quality assurance activities in various areas including safety software. DOE G 414.1-4, *Safety Software Guide for Use with 10 CFR 830 Subpart A, Quality Assurance Requirements, and DOE O 414.1C Quality Assurance*, provides detailed guidance on how to implement the requirements of DOE O 414.1C for safety software. The development and maintenance of a collection, or toolbox, of high-use, U.S. Department of Energy (DOE) safety software quality assurance (SSQA)-compliant codes is one of the major improvement actions supported under DOE O 414.1C, *Quality Assurance*, and DOE G 414.1-4, *Safety Software Guide for Use with 10 CFR 830 Subpart A, Quality Assurance Requirements, and DOE O 414.1C Quality Assurance*. This collection of toolbox codes is referred to as the DOE Safety Software Central Registry.

Integrated Modules for Bioassay Analysis (IMBA) Expert™ USDOE-Edition version 4.0.28 and IMBA Professional Plus (IPP) version 4.0.28 were evaluated for inclusion in the DOE Safety Software Central Registry and documented in a gap analysis. The gap analysis² evaluated the SSQA attributes against the work activities specified in DOE O 414.1C and DOE G 414.1-4.

As part of the process of adding software to the Central Registry, software application guidance reports are issued. Guidance reports are intended to:

- point out specific limitations and weaknesses and provide instructions on informed use of the subject software despite the identified gaps and other vulnerabilities
- provide useful information supplemental to documentation provided by the IMBA developers

The five manuals³ and online help facility that are included with IMBA are generally regarded by users as providing excellent coverage and detail on most topics related to using IMBA. Nevertheless, there are some topics that are not covered in the documentation or could benefit from further discussion. A number of these topics are discussed in this report. While not ensuring correct application of IPP or IMBA Expert™ USDOE-Edition in every context, use of the information contained here should minimize potential user errors and further standardize the use of these products in DOE facilities.

² *Gap Analysis for IMBA and DOE Safety Software Central Registry Recommendation*, DOE/EH-0711, June 2006.

³ IMBA Expert™ USDOE-Edition and IPP each have five manuals that are listed in Section 7.

2. Description of the IMBA Codes

Starting in the mid 1980's, a number of computer codes for the evaluation of bioassay data and calculation of internal dose became commercially available. These codes, including but not limited to GENMOD, INDOS, REMEDY, and CINDY, were based on the models and methodology of the International Commission on Radiological Protection (ICRP) Publication 26 and the 30 series of reports. The ICRP published new, more complex, and comprehensive internal dosimetry models and methods starting in 1994 with the issuance of the ICRP Publication 66 *Human Respiratory Tract Model* (HRTM). A series of new systemic models thus were published shortly thereafter in ICRP publications 67, 68, 69, and 71, which will be referred to as the ICRP 6X/7X models. As of the mid 1990's, the computer codes listed above were unable to use the new HRTM and systemic models and were never upgraded to incorporate these models. To fill this gap, in 1997 British Nuclear Fuels, Westlakes Research Institute, and the United Kingdom (U.K.) National Radiological Protection Board (NRPB) started development of a computer code⁴ that would incorporate the new models. This code actually comprised a series of independent modules that did specific tasks and communicated with each other through input/output files. For this reason, the code was called Integrated Modules for Bioassay Analysis, or IMBA.

In 2001, the NRPB, whose functions were later absorbed into the U.K. Health Protection Agency (HPA), and ACJ & Associates started development of a user-friendly interface for the IMBA modules. This effort was funded in part by DOE, and in 2003 the first version of IMBA Expert™ USDOE-Edition (henceforth referred to as IMBA Expert™) was distributed to the following participating sites:

1. Office of Worker Protection Programs (EH-52) [now the Office of Quality Assurance Programs (EH-31)], DOE, Washington, D.C.
2. Pacific Northwest National Laboratory, Richland, WA
3. Savannah River Site, Aiken, SC
4. Los Alamos National Laboratory, Los Alamos, NM
5. Lawrence Livermore National Laboratory, Livermore, CA
6. BWXT Y-12 Plant, Oak Ridge, TN
7. Sandia National Laboratories, Albuquerque, NM

The final version of IMBA Expert™ (version 4.0.28) was delivered in 2004, and formal HPA support for the code will end on December 31, 2006. Other, customized IMBA products were developed for specific users, including the Canadian power reactor industry and for the US National Institutes of Occupational Safety and Health. In 2005, IPP was introduced. This IMBA product incorporated all of the functionality offered in the earlier IMBA products and was designated as the product that will be supported and enhanced in the future. At the issuance of this report, IPP remains the only commercially available software to evaluate bioassay data and calculate internal dose with the newer ICRP models. Licensees of IMBA Expert™ DOE-Edition were given the opportunity to upgrade to IPP for a nominal fee until the end of 2006. Unless stated otherwise, the guidance provided in this document applies to both IMBA Expert™ and IPP. A description of IMBA is summarized in Table 2-1.

⁴ Birchall, A., Jarvis, N.S., Peace, M.S., Riddell, A.E., Battersby W.P., *The IMBA Suite: Integrated Modules for Bioassay Analysis Radiation Protection Dosimetry* (79), Nos. 1-4, pp. 107-110, 1998.

Table 2-1. IMBA Summary Description

Type	Specific Information
Code Name	<ul style="list-style-type: none"> • IMBA Expert™ USDOE Version 4.0.28 • IMBA Professional Plus Version 4.0.28
Developing Organization and Sponsor	ACJ & Associates and HPA worked together on the development of IMBA Expert™. HPA has recently taken over complete responsibility for IPP.
Version of the Code	IMBA Expert™ DOE-Edition Version 4.0.28 and IPP Version 4.0.28
Software Platform/Portability	Microsoft® Windows
Coding and Computer	Visual Basic® Power Basic®
Technical Support	U.K. Health Protection Agency – Radiation Protection Division (HPA-RPD), Chilton, Didcot, Oxfordshire, OX11 0RQ U.K.
Code Procurement	HPA-RPD, Chilton, Didcot, Oxfordshire, OX11 0RQ U.K.
Documentation Supplied with Code Transmittal	Each product has its own set of documentation that consists of: <ul style="list-style-type: none"> • User's Manual • Appendix A - Technical Basis • Appendix B - Bioassay Quality Assurance • Appendix C - Dose Quality Assurance • Appendix D - Example Bioassay Cases
Nature of Problem	IMBA includes the capability to: assess an intake from bioassay measurement data, calculate bioassay quantities at different times after a specific intake, and calculate equivalent organ doses and effective dose from a single intake.
Restrictions or Limitations	IMBA does not implement independent kinetics for daughters of radionuclides like Th-232, which results in overestimates of dose (note that bioassay evaluation functions are not impacted by this limitation). The addition of new radionuclides into the IMBA library and the modification of existing biokinetic models is a rather involved process that cannot be done by the typical user. IMBA is also limited to 200 data points and 10 intakes.
Run Time	Execution time for an intake evaluation is typically under 1 minute.
Computer Hardware Requirements	No special hardware is required.
Computer Software Requirements	Windows® 98 through XP
Other Products Available	<ul style="list-style-type: none"> • IMBA Expert™ ORAU-Edition • IMBA Expert™ CANDU-Edition • IMBA Expert™ UK-Edition

3. Results of Gap Analysis

In DOE O 414.1C, *Quality Assurance*, and DOE G 414.1-4, *Safety Software Guide for Use with 10 CFR 830 Subpart A, Quality Assurance Requirements, and DOE O 414.1C Quality Assurance*, DOE has specified requirements essential for the development, deployment, and use of software that will successfully meet the identified needs. These requirements include steps or work activities including explicit statements of the design requirements of the software and its verification and validation (V&V). Areas where the software does not meet the requirements are referred to as gaps. The process of identifying gaps is a gap analysis. Thus, although a gap analysis considers V&V, it is far more comprehensive than a simple confirmation that the software generates correct answers.

Based on the outcome of the gap analysis, IMBA Expert™ USDOE-Edition version 4.0.28, IPP version 4.0.28, and all future minor releases of IPP 4.0.x were recommended for inclusion in the DOE Safety Software Central Registry contingent upon the critical recommendations identified in the analysis being implemented by HPA and subsequently reviewed and approved by the DOE Office of Environment, Safety and Health and the Central Registry program lead.

IMBA was evaluated in eleven work activities, three of which are of particular interest to the user and will be discussed further. The gap analysis report should be consulted for a complete discussion of all work activities. One of the most important aspects of a code to the user is whether or not it generates correct results. IMBA fully met the criteria of model validation/performance work activity, which is specific for software being considered as a toolbox code in the DOE Safety Software Central Registry. Through these criteria, the evaluation determined that IMBA products properly and correctly implement industry accepted scientific methods for solving internal dosimetry scenarios.

3.1 Verification and Validation

The V&V work activity was determined to be partially met, and the key testing sub-activities were identified as being robust, repeatable, and consistently implemented. These results indicate that a high-quality product is delivered to the DOE users.

3.2 Configuration Control

There were several issues related to configuration control that were identified in the software configuration management work activity. One of the most important issues is that it can be difficult for the user to determine if the most recent versions of code modules and data files are being used. The impact of this problem can be minimized to some extent by using the automatic update feature of IMBA, but there were some reports of this feature not functioning properly. One of the recommendations issued in the gap analysis was for HPA to provide a final service pack for IMBA Expert™ USDOE-Edition (V 4.0.28) directly to each licensed user to ensure that they all have the correct and latest software components. Users of IMBA Expert™ DOE-Edition should update to this final version. Users of IPP who cannot use the automatic update feature should frequently visit the HPA update site⁵ for the latest information on the code.

3.3 Tracking and Reporting of Software Defects

Issues related to software defect (“bug”) identification, tracking, and reporting were identified in the evaluation of the problem reporting and corrective action work activity. The most important issue brought out in the evaluation is that users are not necessarily notified of defects that are identified by

⁵ http://www.hpa.org.uk/radiation/publications/software/imbapro_plus/imbaupdates.htm

other users or of available fixes and potential workarounds. One of the recommendations issued in the gap analysis was for DOE to establish its own defect reporting and tracking system for IMBA Expert™ DOE-Edition to supplement the one provided by HPA⁶. Users are encouraged to participate and use this system when it becomes available.

⁶ http://www.eh.doe.gov/sqa/central_registry.htm

4. Software Limitations

IMBA has a number of design limitations that are summarized as follows:

- Although a relatively stable program, if IMBA crashes, a portion of the program is frequently left resident in memory. When this happens and the user attempts to restart IMBA, an error message is given stating that IMBA is already running. This limitation is discussed in Section 5.1.
- The number of bioassay data of any one type that may be evaluated at one time is limited to 200. This limit can be extended to 400 through the use of the user defined bioassay type and is discussed in Section 5.2.
- The number of intakes that can be evaluated at one time is 10.
- IMBA Expert™ DOE-Edition can evaluate intakes and resulting doses for 112 isotopes of 56 elements. These numbers cannot be readily changed by the user⁷. The practical implication of this limitation is that bioassay data for a radionuclide that is not in the IMBA library may be difficult or impossible to evaluate with IMBA.
- The algorithm used in IMBA cannot properly evaluate biokinetic models that have equal rate constants in a particular series of compartments. This limitation and a workaround are discussed in Section 5.4.
- Intakes of HTO cannot be directly evaluated with urine bioassay data. This limitation and a workaround are discussed in Section 5.5.
- The biological half-life of tritiated water (HTO) in the body is a parameter that is frequently required to be modified in order to adequately model HTO urine bioassay data. This parameter is not readily modified in IMBA by the user. This limitation and workarounds are discussed in Section 5.5.
- IMBA calculates doses from intakes of radioactive series like ²³²Th using shared kinetics, which means that the radioactive daughters are assumed to be metabolized like the parent. This can cause calculated doses from intakes of these materials to be overestimated. This limitation is discussed in Section 5.6.
- The IMBA update feature does not work with all computer configurations. Difficulties have been reported with firewalls, proxy servers, and some specific network configurations.

⁷ Add-ons are being planned for Summer/Fall 2006 to include all ICRP 38 nuclides.

5. Guidance

The five manuals and online help facility that are included with IMBA are generally regarded as providing excellent coverage and detail on most topics related to using IMBA. Nevertheless, there are some topics that are not covered in the documentation or could benefit from further discussion, which is provided in this section.

IMBA has a number of design limitations. Some of these limitations, along with suggested workarounds, are discussed in this section. No workarounds are offered for the following limitations:

- The number of intakes that can be evaluated at one time is 10.
- IMBA Expert™ DOE-Edition can evaluate intakes and resulting doses for 112 isotopes of 56 elements. These numbers cannot be readily changed by the user. The practical implication of this limitation is that bioassay data for a radionuclide that is not in the IMBA library may be difficult or impossible to evaluate with IMBA.

5.1 Crash and Recovery

IMBA is a relatively stable program that rarely crashes. However, if IMBA does crash, a portion of the program is frequently left resident in memory. When this happens and the user attempts to restart IMBA, an error message is given stating that IMBA is already running. In this situation, the Windows Task Manager/Applications tab should be used to terminate the version of IMBA left running by the crash before attempting to restart IMBA.

A side effect of starting IMBA while it is already running is that a new directory named IMBA x , where x can be a numerical value (1, 2, etc.), may be created. This phenomenon is related to multiple instances of IMBA running on a server. On single user installations, the user may safely delete the IMBA x folder.

5.2 Limitation on Number of Bioassay Results

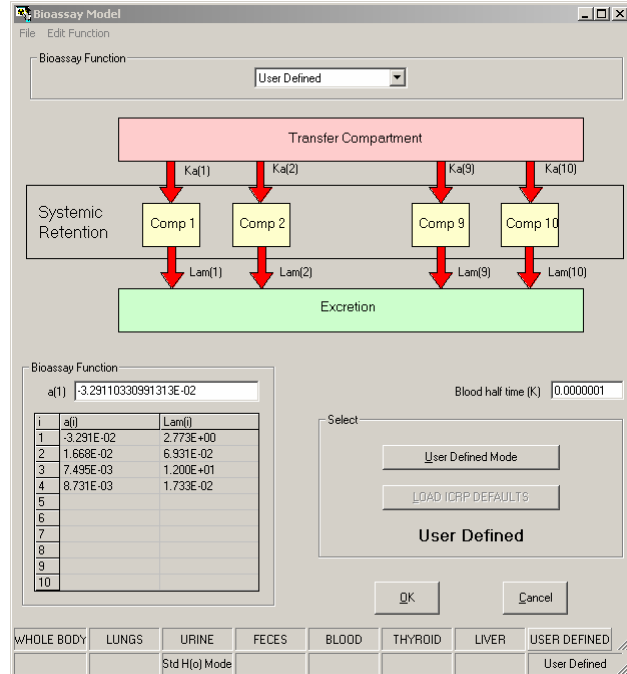
IMBA has an upper limit of 200 bioassay results of a particular type. For example, only 200 urine bioassay results can be entered in under the urine bioassay type. This limit can create difficulties for historical cases, where there may be hundreds of bioassay results collected over decades, and can be extended to 400 bioassay results by using the user defined bioassay type in addition to the urine bioassay type. This procedure is illustrated with an example where 365 urine bioassay data points for organically bound tritium (OBT) are evaluated.

- Select the radionuclide/biokinetic models, and using the data-entry tool, enter the 200 urine bioassay results in the usual fashion with *Urine* selected as the bioassay type.
- In the second bioassay quantity table select *User Defined* as the bioassay type, and using the data-entry tool enter the remaining 165 urine bioassay data points.

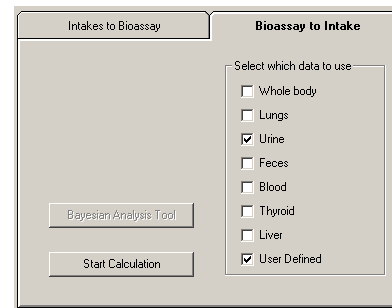
Specified Time (d)	Collection period (d)	Calculated Rate (Bq/d)	Measurement Time (d)
			1.000E+00
			2.000E+00
			3.000E+00
			4.000E+00
			5.000E+00
			6.000E+00
			7.000E+00
			8.000E+00

Specified Time (d)	N/A	Calculated Value (Bq)	Measurement Time (d)
			2.010E+02
			2.020E+02
			2.030E+02
			2.040E+02
			2.050E+02
			2.060E+02
			2.070E+02
			2.080E+02

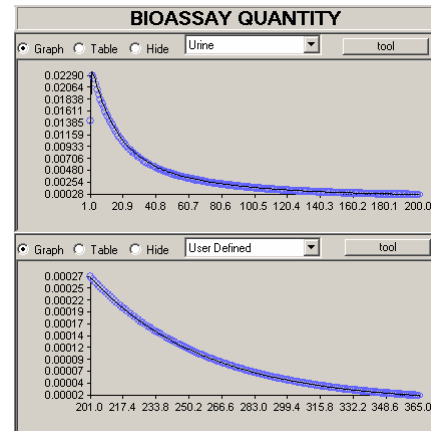
- In the Bioassay Model panel, select *User Defined* and enter in the same bioassay model used for urine. This model is the one displayed when *Urine* is selected for the bioassay function.



- In the Calculation panel, check both *Urine* and *User Defined* under Bioassay to Intake.



- Calculate the intake. Both the urine and user defined data will be used to calculate the intake of OBT. The predicted urinary excretion for days 1-200 will be in the Urine graph and the predicted urinary excretion for days 201-365 will be in the User Defined graph.



Because there is only one intake calculated from the two sets of data, dose is calculated in the normal fashion and no special actions are required.

5.3 Incremental Excreta Samples

Excreta samples (e.g., urine) must be entered into IMBA as incremental samples. The most familiar incremental excreta sample is probably the 24-hour urine sample, which represents all of the urine voided during a given 24-hour period. By convention, the incremental sampling period is specified by the time t in days that the sampling ends and the sampling period Δt in days. For example, if a 24-hour urine sample is collected at $t = 7$ days, this means that all of the urine voided from day 6 to day 7 was collected.

This is all rather straightforward until an incremental sample such as a 12-hour urine sample is to be entered. Assuming that a 12-hour urine sample collected at $t = 7$ days contains 1 Bq of an analyte, the sample, which represents all of the urine voided from day 6.5 to day 7, must be normalized to one day and entered into IMBA as 2 Bq/day at $t = 7$ days with a collection period of 0.5 days. The reason the observed excretion data must be normalized to a day (1 Bq/0.5 day = 2 Bq/day) is that predicted urinary excretion line cannot be smoothly drawn through the observed data points if there are different collection periods. However, note that the normalized excretion is indeed adjusted for the collection period when the calculations are performed, so the correct answer is obtained. This discussion applies to excreta data collected after either a chronic intake or an acute intake.

An important point here is that a urinary excretion rate of 2 Bq/day over 1 day...

Measurement Time (d)	Collection period (d)	Measurement Rate(Bq/d)	Data Type	Measurement Error	Error Distribution
1.000E+03	1.000E+00	2.000E+00	Real	6.000E-01	NORM

...and a urinary excretion date of 2 Bq/day over half a day...

Measurement Time (d)	Collection period (d)	Measurement Rate(Bq/d)	Data Type	Measurement Error	Error Distribution
1.000E+03	5.000E-01	2.000E+00	Real	6.000E-01	NORM

...will both result in the same intake if the urinary excretion rate is fairly constant over the specified day (e.g., for Type M ²³⁹Pu at 1000 days after an acute intake). On the other hand, if the urinary excretion rate is rapidly changing over the specified day, different intakes will result.

5.4 Equal Rate Constants

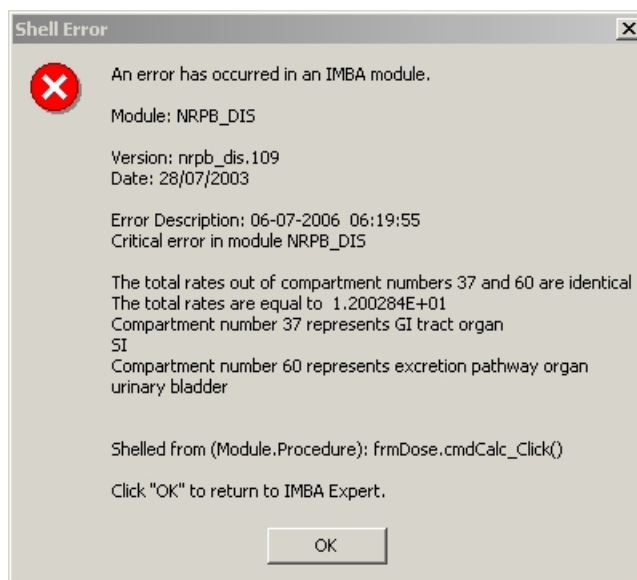
The organs and tissues of the body are modeled by the ICRP as a system of compartments between which the movement of materials is governed by first-order linear differential equations. Note that in this system, which is referred to as the biokinetic model, there is not necessarily a direct relationship between a compartment and an organ.

Two types of biokinetic models of particular interest are catenary and recycling models. In a catenary model, the material moves in one direction going from one compartment to the next (like the links in a chain). In a recycling model, material can leave a compartment and eventually loop back to the same compartment. Perhaps the most important algorithm in an internal dosimetry code is the one selected to solve the system of differential equations for the content of organs and tissues at specified times. This information is used to calculate intake retention functions, which are used to evaluate bioassay data, and to calculate the number of nuclear decays that take place over specified times, which are used to calculate the dose delivered to the organ. In general, the solutions to a catenary system are less challenging to obtain than are solutions to a recycling system.

The approach used in IMBA to calculate the retention of materials in an organ⁸ is somewhat unique. First, the compartments of the biokinetic model are defined and the contents of the compartments at a series of times are calculated using the matrix exponential algorithm. This algorithm can directly solve recycling models and catenary models that have compartments with identical rate constants (the importance of this will be discussed shortly). Then, a series of exponential terms are fit to the compartment contents to create a retention function for the compartment. The fit to the retention data is designed so that the retention calculated with this function is within +/- 1% of the exact solution. Note that fitting the retention data, which can be rather involved, is performed only once by the IMBA developers during the implementation of a particular biokinetic model.

Thus, whenever the content of an organ is needed, it is calculated with the retention function rather than solving the system of differential equations directly. The primary advantage of the computational approach used in IMBA is that recycling systems are represented as equivalent catenary systems that have simple algebraic solutions. This allows for faster, more robust solutions. Speed of computation was particularly important when the IMBA modules were originally developed in the early 1990's, but this has become less important over time as the computing power of personal computers has continued to increase. The primary disadvantage of the approach is that modification of existing biokinetic models or the addition of new ones is difficult.

One important characteristic of the computational approach used in IMBA is that the calculation will fail to produce an answer if the rate constants in a particular chain are not unique. In older versions of IMBA Expert™ DOE-Edition, the program would generate neither results nor errors. Newer versions of IMBA Expert™ DOE-Edition and IPP provide information like that shown below.



This situation has been reported by users for cases where the fraction (f_i) of material absorbed by the small intestine is equal to 0.5 (⁶⁵Zn in particular). This is not considered a significant issue because it results in a complete failure to calculate a retention fraction (as opposed to the calculation of an incorrect retention fraction). The problem also has a simple workaround (e.g., multiply f_i by a small factor such as 0.999).

⁸ James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert™ USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis*, page 79, April 2004.

5.5 Evaluation of Tritiated Water Intakes Using Urine Data

IMBA has systemic biokinetic models for organic tritium and inorganic tritium (water), which are described in *Appendix A*⁹. The two models have the same compartmental structure, which is shown in Figure 1. For inorganic tritium deposited in the transfer compartment

- 3% is transferred to the OBT where it is cleared with a 40-day half-life, and
- 97% is transferred to the water compartment where it is cleared with a 10-day half-life

These percentages are 50%/50% for organic tritium. IMBA has a default urine bioassay model for organic tritium (see Figure 2) that allows the evaluation of intakes of organic tritium using urine bioassay data. IMBA does not offer a default urine bioassay function for inorganic tritium, which makes it awkward to use urine bioassay data to evaluate intakes of inorganic tritium. This shortcoming can be easily rectified with the following procedure:

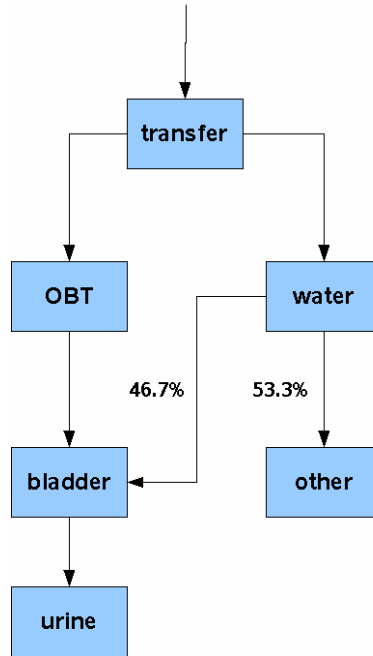
- Select the inorganic tritium model.
- Go to the Bioassay Model panel (shown in Figure 3).
- Select the *Urine* as the bioassay function.
- Select *User Defined* as the mode.
- Enter the coefficients and rate constants from the following table (see Attachment A).

A(i) Coefficient	Lam(i) Rate Constant
9.638985746E-03	1.200000000E+01
3.236795167E-02	6.931471806E-02
5.238864693E-04	1.732867951E-02
-4.253082389E-02	2.772588722E+00

- Enter 10^{-7} for the blood half-time.

⁹James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert™ USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis, Section A.7.1.11, April 2004.*

Figure 1. IMBA Compartmental Model for Organic and Inorganic Tritium



Urine bioassay data in units of activity per day can now be used to directly evaluate intakes of inorganic tritium.

Figure 2. IMBA Urine Bioassay Model for Organic Tritium

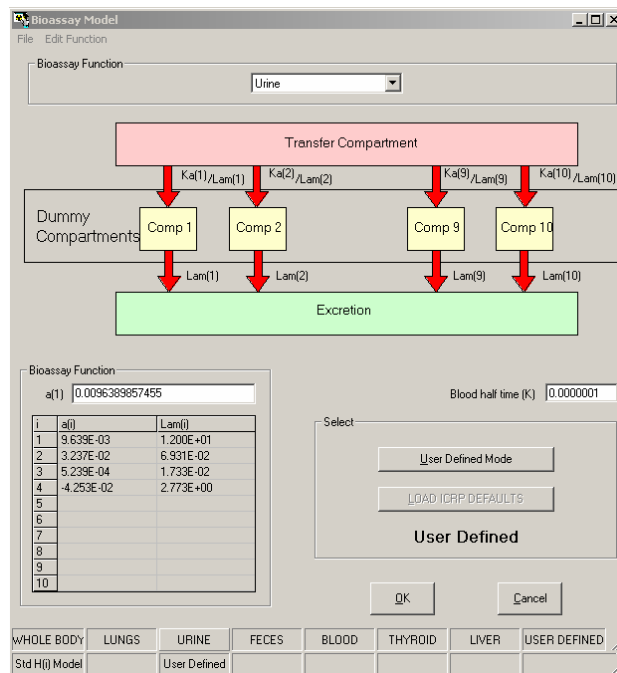
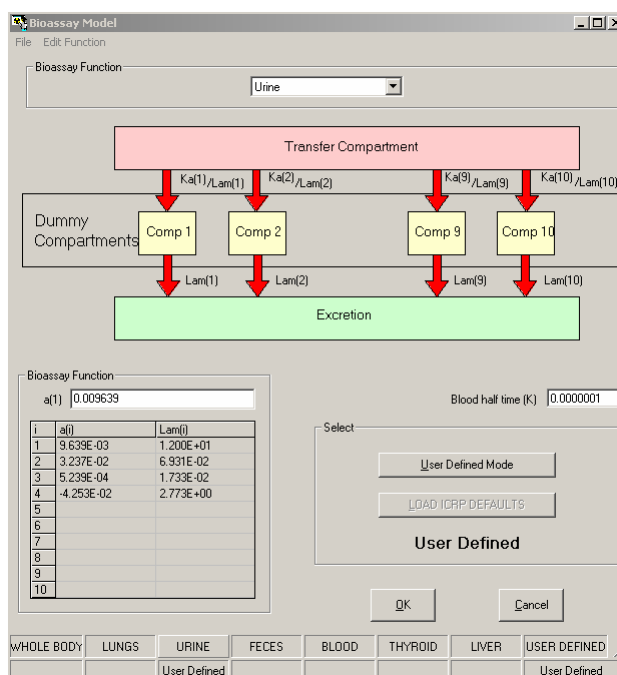


Figure 3. IMBA Urine Bioassay Model for Inorganic Tritium



The intake retention function calculated from this user defined urine bioassay function is the 24-hour incremental urinary excretion. If the same coefficients and rate constants are entered into a user defined bioassay function, the instantaneous urinary excretion rate in units of activity per day at time t will be produced. The instantaneous and incremental excretion functions are almost identical when the rate of change of the excretion is low (flat parts of the excretion curve) but can differ if the excretion rate is changing rapidly (steep parts of the excretion curve). No additional changes are required in IMBA in order to calculate the dose from intakes calculated with the instantaneous urinary excretion function.

The parameters originate as follows: The content of the urine compartment $q_u(t)$ at time t after an injection of inorganic tritium is given by a sum of four exponential terms with coefficients C and rate constants γ .

$$q_u(t) = \sum_{i=1}^4 C_i e^{\gamma_i t}$$

The coefficients and rate constants were calculated directly from the stable element inorganic tritium biokinetic model (see Attachment A). The instantaneous urinary excretion rate $e_u(t)$ is the derivative of the content function with respect to time

$$e_u(t) = \sum_{i=1}^4 \gamma_i C_i e^{\gamma_i t}$$

The $Lam(i)$ in the table is γ_i from this function and $a(i)$ is $\gamma_i C_i$.

Although this modification allows urine samples to be evaluated directly, there are still two remaining issues related to evaluating intakes of inorganic tritium:

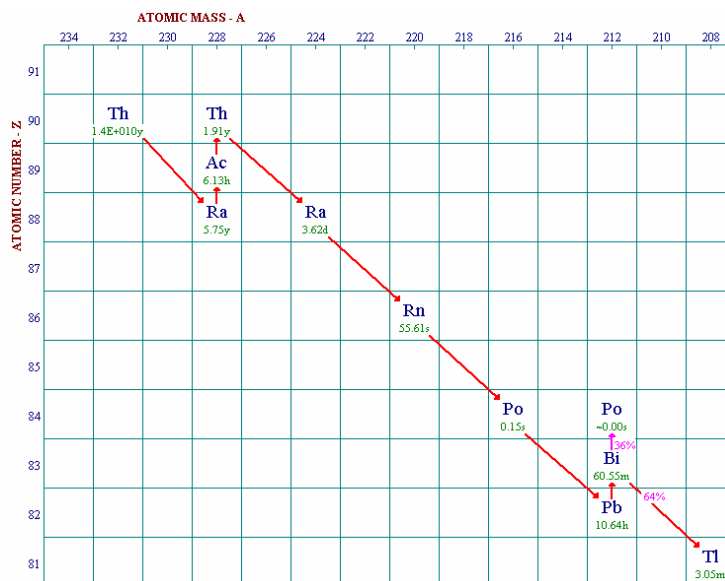
- The tritium in the urine samples must be expressed in units of activity per unit time (e.g., *Bq/day*) rather than concentration (e.g., *Bq/L*).
- The biological half-life of tritiated water in the body typically ranges anywhere from 6 days to 12 days, and this parameter is frequently modified to obtain better fits to the observed data. However, this half-life cannot be readily modified in IMBA.

For these reasons, alternate methods (other than IMBA) are frequently used to evaluate intakes of inorganic tritium. Good examples of such methods are given in *IDEAS/IAEA Intercomparison Exercise on Internal Dose Assessment*¹⁰ and in Annex VI of *IAEA Safety Report No. 37*¹¹.

5.6 Dose from Intakes of Thorium

As shown in Figure 4, ²³²Th is the long-lived parent of radioactive decay chain that includes 10 daughters that are themselves radioactive.

Figure 4. Thorium-232 Decay Series



Thus, following an intake of pure ²³²Th these radioactive daughters will begin to grow in and deliver dose to the organs and tissues of the body. The dose that is ultimately delivered by the daughters is strongly dependent on how they are assumed to be metabolized by the body. For example, ²³²Th that is inhaled will be transported and deposited in the body according to the thorium biokinetic model. When a ²³²Th atom decays to ²²⁸Ra, one can assume that

- the ²²⁸Ra will continue to follow the biokinetics of the ²³²Th parent (shared kinetics)

or

- the ²²⁸Ra will follow the biokinetics of radium after it is born (independent kinetics).

ICRP used shared kinetics in its Publication 30 models but uses independent kinetics for ²³²Th in its latest Publication 6X biokinetic and dosimetric models. The dose per unit intake of ²³²Th is significantly lower

¹⁰ IDEAS/IAEA Intercomparison Exercise on Internal Dose Assessment, SCK-CEN-BLG-1018, October 2005.

¹¹ IAEA Safety Report No. 37, Methods for Assessing Occupational Radiation Doses Due to Intakes of Radionuclides, 2004.

if one assumes independent kinetics rather than shared kinetics, which is one reason why the new intake-to-dose conversion factors are lower for ^{232}Th .

The algorithm used in IMBA to calculate the number of decays in an organ or tissue is limited to shared kinetics, (i.e., biokinetics of the daughters must match the parent). Thus, IMBA overestimates the dose per unit intake from radionuclides like ^{232}Th , whose daughter contributes a large fraction of the total dose¹². Note that radionuclides like $^{234,235,238}\text{U}$ are not impacted by this because the daughters do not contribute significant dose. Also, this does not impact the estimation of ^{232}Th intakes from ^{232}Th in the urine or whole body.

The workaround for this problem is to calculate the intake using IMBA and then apply appropriate published ICRP intake-to-dose conversion factors (DCF) that are based on independent kinetics. The intake-to-dose conversion factor (DCF) for inhalation of Type M and Type S ^{232}Th from the ICRP CD¹³ are given in the Tables 5-1 and 5-2. For example, if the Type M ^{232}Th intake was calculated with IMBA to be 100 Bq, the committed effective dose is as follows:

$$(100 \text{ Bq})(2.9\text{E-}5 \text{ Sv/Bq}) = 2.9\text{E-}3 \text{ Sv} = 0.29 \text{ rem.}$$

For comparison, the DCF calculated by IMBA using shared kinetics is 1.47E-4 Sv/Bq, which results in a dose of 1.47 rem in the above example. Thus, the use of shared kinetics within IMBA can result in an overestimation of the dose to ^{232}Th by about a factor of 5. The doses calculated with IMBA from intakes of ^{228}Th are also overestimated because of the use of shared kinetics. The DCF for inhalation of Type M and Type S ^{228}Th from the ICRP CD, which uses independent kinetics, are given in the Tables 5-3 and 5-4. Note that the use of effective dose from these tables may be restricted by Federal regulations that require the use of ICRP 26 tissue weighting factors (see discussion in Section 5.10).

¹² James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert™ USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis*, Section A.9.3.2.1, April 2004.

¹³ ICRP CD1: *Database of Dose Coefficient: Workers and Members of the Public*, ISBN: 0-08-043876-8, 2002.

Table 5-1. DCF (Sv/Bq) for Inhalation of Type M ²³²Th Aerosol

(DCF for inhalation of 5 micron ²³²Th particulate aerosol by an adult worker, absorption Type M, $f_1 = 0.0005$. Highest committed equivalent dose coefficient: Bone Surface, 1.5E-03 Sv/Bq)

Time after intake	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Adrenals	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.30E-06	3.80E-06	4.40E-06
Bladder Wall	3.00E-10	1.20E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Bone Surface	2.20E-08	2.70E-07	1.50E-06	2.80E-05	1.60E-04	3.30E-04	6.50E-04	9.40E-04	1.30E-03	1.50E-03
Brain	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.30E-06	3.80E-06	4.40E-06
Breast	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Oesophagus	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
St Wall	6.60E-10	1.50E-09	3.80E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
SI Wall	1.20E-09	2.10E-09	4.30E-09	4.80E-08	2.50E-07	5.40E-07	1.30E-06	2.30E-06	3.80E-06	4.40E-06
ULI Wall	4.40E-09	6.80E-09	9.20E-09	5.30E-08	2.60E-07	5.50E-07	1.40E-06	2.30E-06	3.90E-06	4.50E-06
LLI Wall	4.80E-09	1.80E-08	2.00E-08	6.50E-08	2.70E-07	5.80E-07	1.40E-06	2.40E-06	4.10E-06	4.60E-06
Colon	4.60E-09	1.20E-08	1.40E-08	5.80E-08	2.60E-07	5.60E-07	1.40E-06	2.30E-06	4.00E-06	4.50E-06
Kidneys	2.30E-09	2.50E-08	9.90E-08	8.10E-07	3.90E-06	7.20E-06	1.20E-05	1.60E-05	2.10E-05	2.30E-05
Liver	5.80E-10	5.40E-09	2.80E-08	5.20E-07	2.80E-06	5.60E-06	1.10E-05	1.50E-05	2.10E-05	2.30E-05
Muscle	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Ovaries	3.10E-10	2.10E-09	1.00E-08	2.00E-07	1.30E-06	2.80E-06	5.80E-06	8.50E-06	1.20E-05	1.30E-05
Pancreas	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Red Marrow	1.90E-09	2.20E-08	1.20E-07	2.30E-06	1.20E-05	2.00E-05	3.30E-05	4.20E-05	5.40E-05	5.70E-05
ET Airways	6.00E-08	4.10E-07	1.60E-06	9.00E-06	1.10E-05	1.10E-05	1.20E-05	1.30E-05	1.40E-05	1.50E-05
Lungs	4.30E-07	2.10E-06	6.20E-06	1.10E-05	1.20E-05	1.20E-05	1.30E-05	1.40E-05	1.50E-05	1.60E-05
Skin	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Spleen	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.30E-06	3.80E-06	4.40E-06
Testes	3.20E-10	2.10E-09	1.10E-08	2.00E-07	1.30E-06	2.80E-06	5.90E-06	8.60E-06	1.20E-05	1.30E-05
Thymus	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Thyroid	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Uterus	2.90E-10	1.10E-09	3.40E-09	4.70E-08	2.50E-07	5.40E-07	1.30E-06	2.20E-06	3.80E-06	4.40E-06
Remainder	3.60E-10	1.60E-09	5.20E-09	5.90E-08	2.90E-07	6.10E-07	1.40E-06	2.40E-06	4.00E-06	4.60E-06
Effective dose	5.30E-08	2.60E-07	7.80E-07	2.00E-06	5.00E-06	8.30E-06	1.40E-05	2.00E-05	2.70E-05	2.90E-05

Table 5-2. DCF (Sv/Bq) for Inhalation of Type S ²³²Th Aerosol

(DCF for inhalation of 5 micron ²³²Th particulate aerosol by an adult worker, absorption Type S, $f_1 = 0.0002$. Highest committed equivalent dose coefficient: Bone Surface, 1.4E-04 Sv/Bq)

Time after intake	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Adrenals	3.60E-12	1.50E-11	4.90E-11	1.10E-09	1.40E-08	4.00E-08	1.10E-07	2.00E-07	3.60E-07	4.10E-07
Bladder Wall	3.70E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.70E-08	1.10E-07	1.90E-07	3.50E-07	4.00E-07
Bone Surface	2.60E-10	3.50E-09	2.10E-08	6.30E-07	7.80E-06	2.20E-05	5.30E-05	8.40E-05	1.30E-04	1.40E-04
Brain	3.60E-12	1.50E-11	4.80E-11	1.10E-09	1.30E-08	3.70E-08	1.10E-07	2.00E-07	3.50E-07	4.00E-07
Breast	3.60E-12	1.50E-11	5.00E-11	1.20E-09	1.40E-08	4.00E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
Oesophagus	3.60E-12	1.50E-11	5.00E-11	1.20E-09	1.40E-08	4.00E-08	1.10E-07	2.00E-07	3.60E-07	4.10E-07
St Wall	3.90E-10	4.10E-10	4.50E-10	1.50E-09	1.40E-08	3.90E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
SI Wall	9.70E-10	1.00E-09	1.10E-09	2.10E-09	1.40E-08	3.90E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
ULI Wall	4.30E-09	6.00E-09	6.20E-09	7.50E-09	2.00E-08	4.70E-08	1.20E-07	2.10E-07	3.70E-07	4.30E-07
LLI Wall	4.80E-09	1.70E-08	1.80E-08	2.00E-08	3.50E-08	6.60E-08	1.50E-07	2.50E-07	4.20E-07	4.80E-07
Colon	4.50E-09	1.10E-08	1.10E-08	1.30E-08	2.60E-08	5.50E-08	1.30E-07	2.30E-07	3.90E-07	4.50E-07
Kidneys	2.80E-11	3.20E-10	1.40E-09	1.90E-08	1.90E-07	4.90E-07	1.10E-06	1.60E-06	2.20E-06	2.40E-06
Liver	7.10E-12	7.10E-11	4.00E-10	1.20E-08	1.50E-07	4.30E-07	1.00E-06	1.60E-06	2.30E-06	2.50E-06
Muscle	3.70E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.80E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
Ovaries	4.10E-12	2.80E-11	1.50E-10	4.40E-09	6.00E-08	1.80E-07	4.60E-07	7.50E-07	1.20E-06	1.30E-06
Pancreas	3.70E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.90E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
Red Marrow	2.30E-11	2.80E-10	1.70E-09	5.20E-08	5.90E-07	1.40E-06	3.00E-06	4.20E-06	5.70E-06	6.10E-06
ET Airways	6.60E-08	4.60E-07	1.90E-06	2.10E-05	7.40E-05	9.90E-05	1.00E-04	1.10E-04	1.10E-04	1.10E-04
Lungs	4.80E-07	2.40E-06	7.30E-06	1.60E-05	3.10E-05	4.50E-05	6.20E-05	7.00E-05	7.60E-05	7.70E-05
Skin	3.60E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.80E-08	1.10E-07	2.00E-07	3.50E-07	4.00E-07
Spleen	3.60E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.90E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
Testes	3.90E-12	2.80E-11	1.50E-10	4.50E-09	6.10E-08	1.80E-07	4.70E-07	7.60E-07	1.20E-06	1.30E-06
Thymus	3.60E-12	1.50E-11	5.00E-11	1.20E-09	1.40E-08	4.00E-08	1.10E-07	2.00E-07	3.60E-07	4.10E-07
Thyroid	3.60E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.80E-08	1.10E-07	2.00E-07	3.50E-07	4.10E-07
Uterus	3.70E-12	1.50E-11	4.90E-11	1.10E-09	1.30E-08	3.70E-08	1.10E-07	1.90E-07	3.50E-07	4.00E-07
Remainder	5.70E-11	2.70E-10	1.10E-09	1.20E-08	5.20E-08	9.20E-08	1.70E-07	2.60E-07	4.20E-07	4.80E-07
Effective dose	5.80E-08	2.90E-07	8.80E-07	2.00E-06	3.90E-06	5.80E-06	8.50E-06	1.00E-05	1.20E-05	1.20E-05

Table 5-3. DCF (Sv/Bq) for Inhalation of Type M ²²⁸Th Aerosol

(DCF for inhalation of 5 micron ²²⁸Th particulate aerosol by an adult worker, absorption Type M, $f_1 = 0.0005$. Highest committed equivalent dose coefficient: Bone Surface, 2.8E-04 Sv/Bq)

Time after intake	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Adrenals	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.60E-07	7.60E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Bladder Wall	4.90E-10	3.20E-09	1.50E-08	2.20E-07	6.60E-07	7.60E-07	7.80E-07	7.80E-07	7.80E-07	7.80E-07
Bone Surface	4.40E-08	7.70E-07	4.60E-06	7.50E-05	2.40E-04	2.70E-04	2.80E-04	2.80E-04	2.80E-04	2.80E-04
Brain	4.80E-10	3.10E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Breast	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Oesophagus	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
St Wall	1.00E-09	3.70E-09	1.60E-08	2.20E-07	6.60E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
SI Wall	1.90E-09	4.70E-09	1.70E-08	2.20E-07	6.60E-07	7.60E-07	7.70E-07	7.80E-07	7.80E-07	7.80E-07
ULI Wall	8.10E-09	1.60E-08	3.40E-08	3.20E-07	9.30E-07	1.10E-06	1.10E-06	1.10E-06	1.10E-06	1.10E-06
LLI Wall	9.70E-09	5.80E-08	8.60E-08	5.30E-07	1.50E-06	1.70E-06	1.70E-06	1.70E-06	1.70E-06	1.70E-06
Colon	8.80E-09	3.40E-08	5.60E-08	4.10E-07	1.20E-06	1.40E-06	1.40E-06	1.40E-06	1.40E-06	1.40E-06
Kidneys	3.90E-09	6.30E-08	2.90E-07	2.30E-06	6.30E-06	7.20E-06	7.30E-06	7.30E-06	7.30E-06	7.30E-06
Liver	1.00E-09	2.30E-08	2.00E-07	3.40E-06	9.90E-06	1.10E-05	1.20E-05	1.20E-05	1.20E-05	1.20E-05
Muscle	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Ovaries	5.60E-10	6.30E-09	3.60E-08	5.90E-07	1.90E-06	2.30E-06	2.30E-06	2.30E-06	2.30E-06	2.30E-06
Pancreas	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.60E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Red Marrow	3.80E-09	6.50E-08	3.90E-07	6.50E-06	1.90E-05	2.10E-05	2.20E-05	2.20E-05	2.20E-05	2.20E-05
ET Airways	3.00E-07	2.30E-06	1.00E-05	5.30E-05	5.80E-05	5.80E-05	5.80E-05	5.80E-05	5.80E-05	5.80E-05
Lungs	1.10E-06	1.40E-05	6.80E-05	1.20E-04	1.30E-04	1.30E-04	1.30E-04	1.30E-04	1.30E-04	1.30E-04
Skin	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Spleen	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.60E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Testes	5.50E-10	6.30E-09	3.60E-08	6.00E-07	1.90E-06	2.30E-06	2.40E-06	2.40E-06	2.40E-06	2.40E-06
Thymus	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Thyroid	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Uterus	4.80E-10	3.20E-09	1.50E-08	2.20E-07	6.50E-07	7.50E-07	7.70E-07	7.70E-07	7.70E-07	7.70E-07
Remainder	7.00E-10	4.90E-09	2.30E-08	2.70E-07	7.40E-07	8.50E-07	8.70E-07	8.70E-07	8.70E-07	8.70E-07
Effective dose	1.40E-07	1.70E-06	8.30E-06	1.70E-05	2.10E-05	2.20E-05	2.20E-05	2.20E-05	2.20E-05	2.20E-05

Table 5-4. DCF (Sv/Bq) for Inhalation of Type S ²²⁸Th Aerosol

(DCF for inhalation of 5 micron ²²⁸Th particulate aerosol by an adult worker, absorption Type S, $f_1 = 0.0002$. More than one organ/tissue has the same highest committed equivalent dose coefficient)

Time after intake	1 day	7 days	30 days	1 year	5 years	10 years	20 years	30 years	45 years	50 years
Adrenals	9.30E-12	8.20E-11	4.60E-10	6.70E-09	2.80E-08	3.60E-08	3.70E-08	3.70E-08	3.70E-08	3.70E-08
Bladder Wall	1.10E-11	8.20E-11	2.70E-10	5.00E-09	2.50E-08	3.20E-08	3.40E-08	3.40E-08	3.40E-08	3.40E-08
Bone Surface	8.30E-10	1.20E-08	6.70E-08	1.60E-06	8.80E-06	1.20E-05	1.20E-05	1.20E-05	1.20E-05	1.20E-05
Brain	9.00E-12	5.60E-11	2.50E-10	5.00E-09	2.50E-08	3.20E-08	3.40E-08	3.40E-08	3.40E-08	3.40E-08
Breast	9.00E-12	8.20E-11	4.70E-10	6.80E-09	2.80E-08	3.60E-08	3.70E-08	3.70E-08	3.70E-08	3.70E-08
Oesophagus	9.60E-12	9.00E-11	5.10E-10	7.20E-09	2.90E-08	3.60E-08	3.80E-08	3.80E-08	3.80E-08	3.80E-08
St Wall	5.60E-10	6.50E-10	1.00E-09	6.70E-09	2.80E-08	3.50E-08	3.60E-08	3.60E-08	3.60E-08	3.60E-08
SI Wall	1.50E-09	1.70E-09	2.10E-09	7.30E-09	2.80E-08	3.50E-08	3.60E-08	3.70E-08	3.70E-08	3.70E-08
ULI Wall	8.10E-09	1.30E-08	1.50E-08	2.40E-08	5.30E-08	6.30E-08	6.50E-08	6.50E-08	6.50E-08	6.50E-08
LLI Wall	9.60E-09	5.50E-08	6.00E-08	7.70E-08	1.20E-07	1.40E-07	1.40E-07	1.40E-07	1.40E-07	1.40E-07
Colon	8.70E-09	3.10E-08	3.40E-08	4.70E-08	8.20E-08	9.60E-08	9.70E-08	9.70E-08	9.70E-08	9.70E-08
Kidneys	5.90E-11	8.80E-10	4.20E-09	5.20E-08	2.40E-07	3.10E-07	3.20E-07	3.20E-07	3.20E-07	3.20E-07
Liver	1.90E-11	3.60E-10	3.00E-09	7.70E-08	3.80E-07	4.90E-07	5.10E-07	5.10E-07	5.10E-07	5.10E-07
Muscle	1.00E-11	7.50E-11	3.40E-10	5.70E-09	2.60E-08	3.40E-08	3.50E-08	3.50E-08	3.50E-08	3.50E-08
Ovaries	1.80E-11	1.80E-10	6.40E-10	1.30E-08	7.20E-08	9.70E-08	1.00E-07	1.00E-07	1.00E-07	1.00E-07
Pancreas	9.60E-12	7.60E-11	4.00E-10	6.20E-09	2.70E-08	3.50E-08	3.60E-08	3.60E-08	3.60E-08	3.60E-08
Red Marrow	7.70E-11	1.00E-09	5.80E-09	1.40E-07	7.20E-07	9.10E-07	9.40E-07	9.40E-07	9.40E-07	9.40E-07
ET Airways	3.10E-07	2.50E-06	1.20E-05	1.10E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04
Lungs	1.30E-06	1.60E-05	8.10E-05	1.80E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04	2.10E-04
Skin	9.00E-12	6.20E-11	2.80E-10	5.30E-09	2.60E-08	3.30E-08	3.40E-08	3.40E-08	3.40E-08	3.40E-08
Spleen	9.40E-12	7.70E-11	4.00E-10	6.20E-09	2.70E-08	3.50E-08	3.60E-08	3.60E-08	3.60E-08	3.60E-08
Testes	1.00E-11	1.00E-10	5.40E-10	1.30E-08	7.30E-08	9.80E-08	1.00E-07	1.00E-07	1.00E-07	1.00E-07
Thymus	9.60E-12	9.00E-11	5.10E-10	7.20E-09	2.90E-08	3.60E-08	3.80E-08	3.80E-08	3.80E-08	3.80E-08
Thyroid	9.10E-12	6.60E-11	3.30E-10	5.70E-09	2.60E-08	3.40E-08	3.50E-08	3.50E-08	3.50E-08	3.50E-08
Uterus	1.20E-11	8.60E-11	2.80E-10	5.00E-09	2.50E-08	3.20E-08	3.40E-08	3.40E-08	3.40E-08	3.40E-08
Remainder	2.00E-10	1.30E-09	6.40E-09	6.30E-08	1.30E-07	1.40E-07	1.50E-07	1.50E-07	1.50E-07	1.50E-07
Effective dose	1.50E-07	1.90E-06	9.70E-06	2.10E-05	2.50E-05	2.50E-05	2.50E-05	2.50E-05	2.50E-05	2.50E-05

5.7 A Discussion of Fitting Models to Data

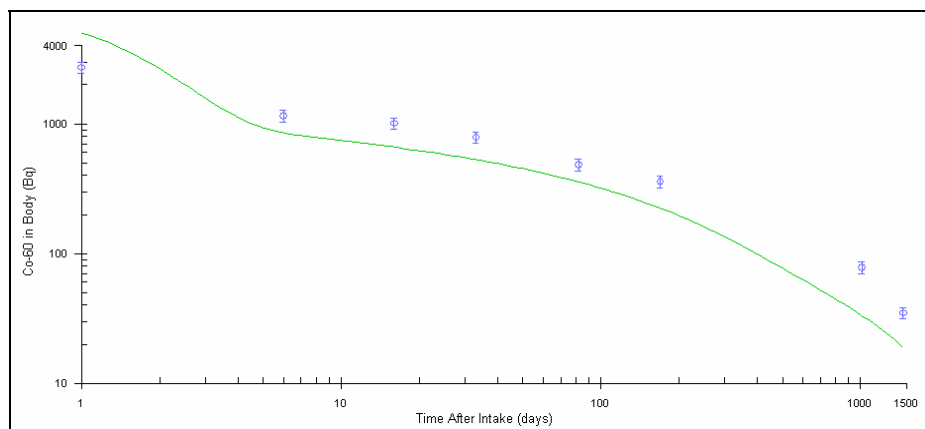
In the process of calculating dose from intakes of radioactive materials, possibly the most critical step is the fitting of a model to the observed bioassay data. This step is considered to be the most critical because it requires the highest degree of professional judgment. A discussion of fitting a model to the data and some useful tips are provided here to facilitate this step of the process.

An excellent discussion of the statistical fitting techniques available in IMBA for estimating intakes from bioassay data is provided in the technical documentation¹⁴. There are three fitting techniques¹⁵ available:

- least-squares (LS)
- maximum likelihood (ML)
- Bayesian

In addition, errors must be designated for the individual data points. A sample bioassay evaluation case for ⁶⁰Co whole body counts is presented in the IMBA documentation¹⁶. The initial fit to the data is shown in Figure 5. The solid line is the predicted body content and the points are the individual measurements, complete with estimated uncertainties.

Figure 5. Fit of Whole-Body Count Data to 5 μ m AMAD Type M ⁶⁰Co Model



In this example, an ML fit was used with individual errors taken to be 10% of the observed whole-body content (i.e., a uniform relative error with $k = 0.1$). The i^{th} weighted residual r_i for the observed body burden o_i and the predicted body burden e_i are defined as

$$r_i = w_i(o_i - e_i),$$

¹⁴ James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert™ USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis*, Sections A.10, A.11, and A.12, April 2004.

¹⁵ There is actually a fourth method that is not discussed in the documentation: a “fit by eye.” This is accomplished by manually entering the intake and observing the location of the predicted curve relative to the data. This process is repeated until the fit is pleasing to the eye.

¹⁶ James, A.C., *User Manual for IMBA Expert™ USDOE-Edition Version 3.2 Appendix D: Bioassay Example Cases*, Section D.2, March 2004.

where w_i is the weight, which is discussed below. As covered in *Appendix A*¹⁷, in the LS fit and ML fit (under the assumption of normally distributed errors) the best fit is obtained by minimizing the weighted residuals (see Equation A.42)

$$\sum_{i=1}^n \left[\frac{m_i - If(t_i)}{\sigma_i} \right]^2 = \sum_{i=1}^n \left[\frac{r_i}{\sigma_i} \right]^2 = \sum_{i=1}^n w_i [r_i]^2$$

where the weighting factor is given by

$$w_i = \frac{1}{\sigma_i^2}$$

In practice, w_i is the inverse square of whatever is put in the i^{th} row of the Measurement Error column in the bioassay data-entry screen. A portion of this screen for the ⁶⁰Co example is shown below.

Measurement Value(Bq)	Data Type	Measurement Error	Error Distribution
2.720E+03	Real	2.720E+02	NORM
1.150E+03	Real	1.150E+02	NORM
1.010E+03	Real	1.010E+02	NORM
7.900E+02	Real	7.900E+01	NORM
4.820E+02	Real	4.820E+01	NORM
3.580E+02	Real	3.580E+01	NORM
7.800E+01	Real	7.800E+00	NORM
3.500E+01	Real	3.500E+00	NORM

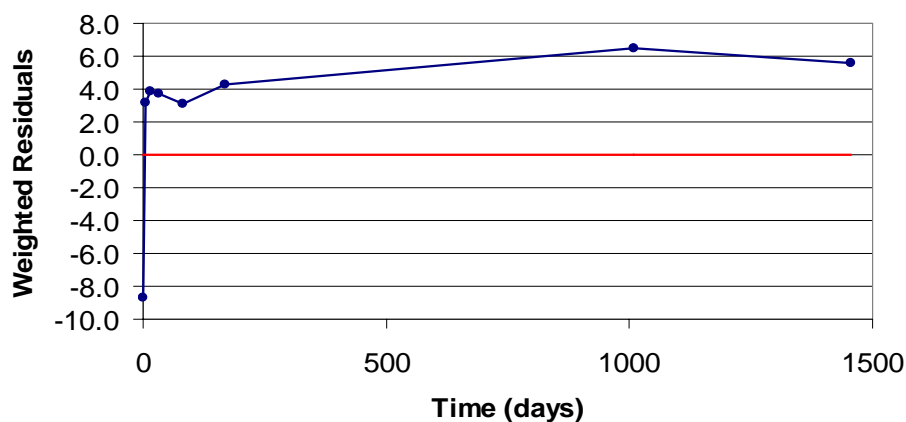
In this example, the measurement error is taken to be 10% of the observed measurement. Thus, the weighting factor is equal to the inverse of the square of 10% of the measurement. Note that the 10% factor is arbitrary. The same intake estimate will result from any percentage selected. The value of the weights on each datum relative to each other determines the fit. If a lognormal error distribution is selected, the measurement error is the geometric standard deviation (GSD). Again, the relative values of the GSD determine the fit. For example, the same intakes result from GSDs of 2 and 5.

Ideally, the data points to be randomly scattered on either side of the line of best fit. One of the best ways to judge this is a residuals plot¹⁸, where the residuals r are plotted versus the time t of the measurement. The residuals plot in Figure 6 clearly shows that most of the residuals are on one side of the zero line. This model shows significant lack of fit. The primary advantages of the residuals plot are that the scale is linear and the weighted differences between the observed and expected results are viewed.

¹⁷ James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert™ USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis*, Section A.10.1.1, April 2004.

¹⁸ Gunst and Mason, *Regression Analysis and its Application*, Chapter 7, New York: Marcel Dekker, 1980.

Figure 6. Weighted Residuals Plot for 5 μm AMAD Type M ^{60}Co Model



If different weights or a different fitting technique are used, the systematic difference between the data and the model will not be reduced. This would be apparent in the case of a single acute or chronic intake, where the overall shape of the predicted curve is entirely fixed by the chosen biokinetic model. The best estimate of the single parameter being estimated, the intake, is found by moving the curve up and down relative to the observed data. Thus, the systematic difference between the data and the model cannot be reduced by selecting a different fitting technique or weighting scheme. The fit will be poor because the wrong model will have been used.

However, close examination of the points on the line reveals that the curve does not fit the data because of the first point. If the first point could be ignored, the fit might be better. Using the excluded data type in IMBA¹⁹, the first point can be left out of the fit calculation. The result is shown in Figure 7. Note that the excluded point is in red whereas the included points are in blue. This is a much better fit, as shown in the residuals plot in Figure 8. To justify the discarding of the first point two arguments could be made: a deterministic argument identifying a reasonable cause for the first measurement to be flawed, or a statistical argument stating that the first count is an outlier and should not be treated the same as the other counts. Even with these two arguments, it still could be stated that there is no justification. Books are written on the subject of rejecting data. Ultimately, the decision to reject data is determined by professional judgment. Arbitrarily assigning the first point a very small weight in order to allow the curve to move up is less desirable than assigning the excluded data type to that point because in the former approach it may not be clear that the first point was discarded.

¹⁹ This is a very useful option in IMBA that allows one or more data points to be excluded from the fit while at the same time includes them in the plot. This is the “honest” way of excluding data because it is clear what has been done.

Figure 7. Fit of Whole-Body Count Data to 5 μm AMAD Type M Model Excluding First Point

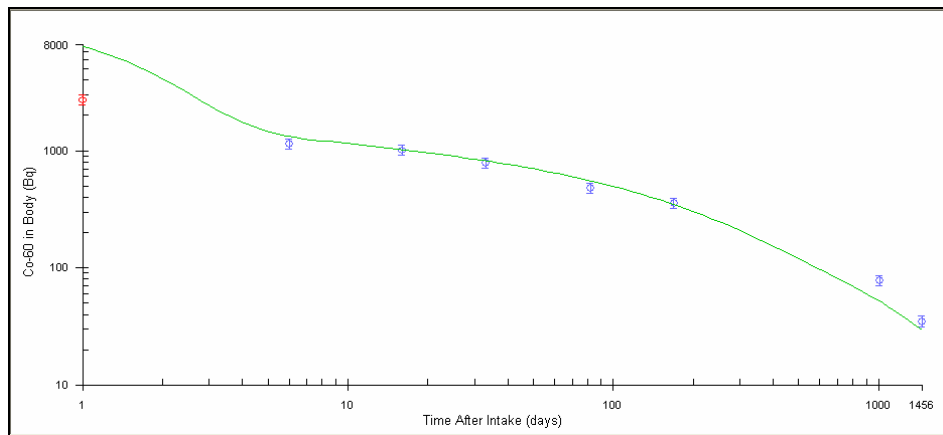
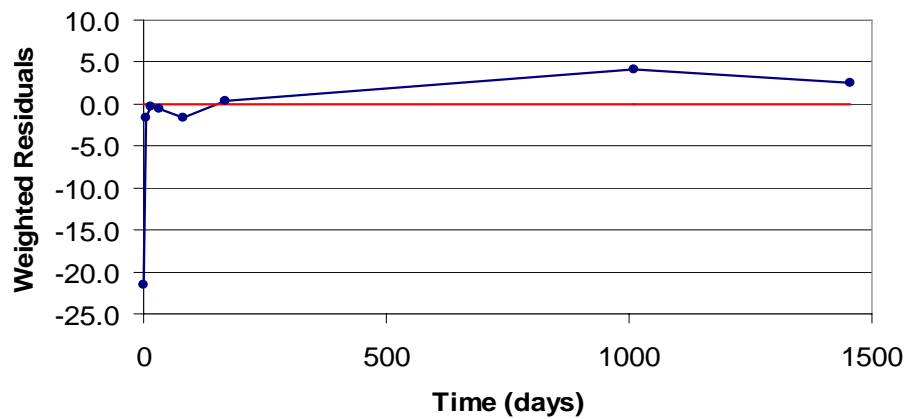


Figure 8. Weighted Residuals Plot for 5 μm AMAD Type M ^{60}Co Model Excluding the First Point



Rather than manipulate the data, modification of the biokinetic model will obtain a better fit. This approach was used in the example in *Appendix D*²⁰ when the AMAD of the inhaled aerosol was changed from 5 μm to 1 μm . The resulting fit is shown in Figure 9 and the residual plot in Figure 10.

²⁰ James, A.C., *User Manual for IMBA Expert™ USDOE-Edition Version 3.2 Appendix D: Bioassay Example Cases*, Section D.2, March 2004.

Figure 9. Fit of Whole-Body Count Data to 1 μm AMAD Type M ^{60}Co Model

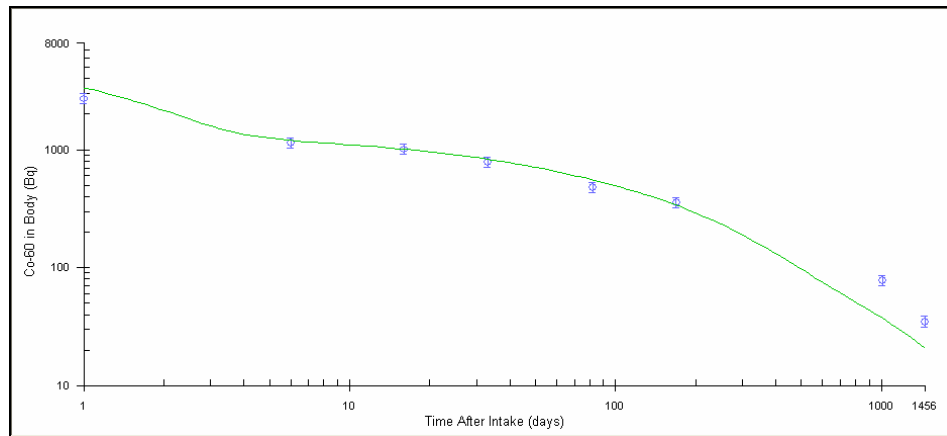
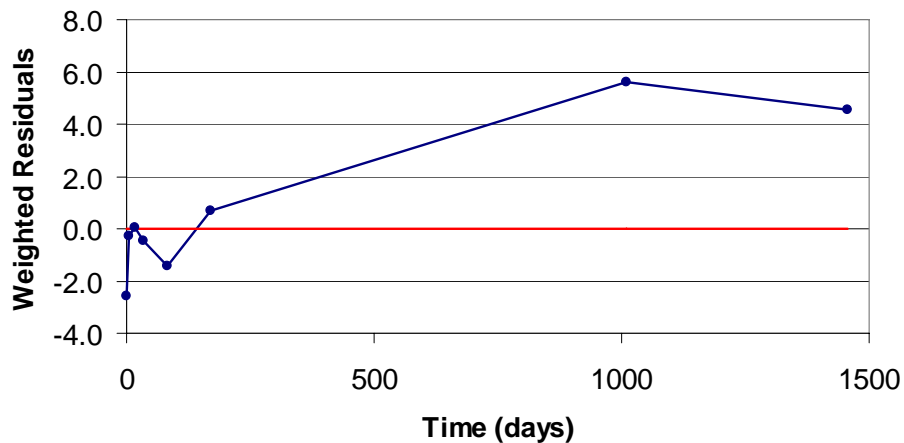


Figure 10. Weighted Residuals Plot for 1 μm AMAD Type M ^{60}Co Model



Although there is still some lack of fit with the last two measurements, the result is much better than that from the first attempt. An even better fit to the data, as shown in Figures 11 and 12, can be achieved by using a mixture of 1 μm Type M and Type S material. The proportions of Type M and Type S are selected by IMBA to create the best fit to the data. The fit is best because the curve is a linear combination of two curves (Type M and Type S) with different shapes. By changing the relative fractions of the two types the shape of the curve can be changed to better match the data.

Figure 11. Fit of Whole-Body Count Data to 1 μm AMAD Type M/S ^{60}Co Model

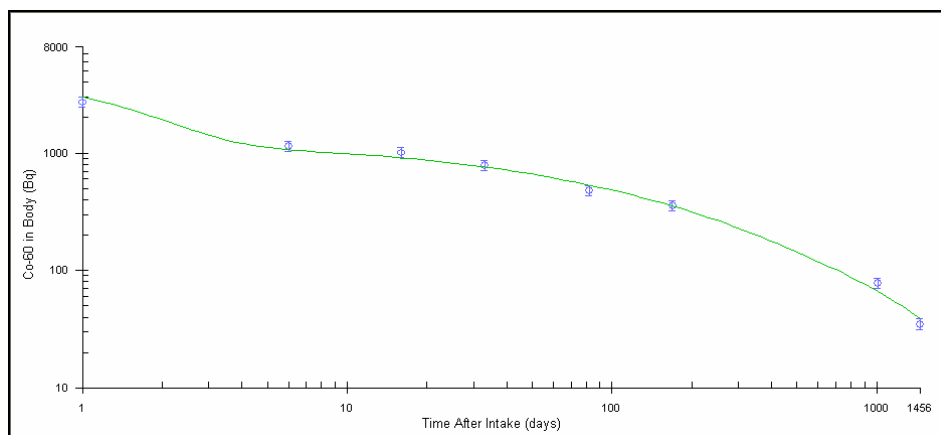
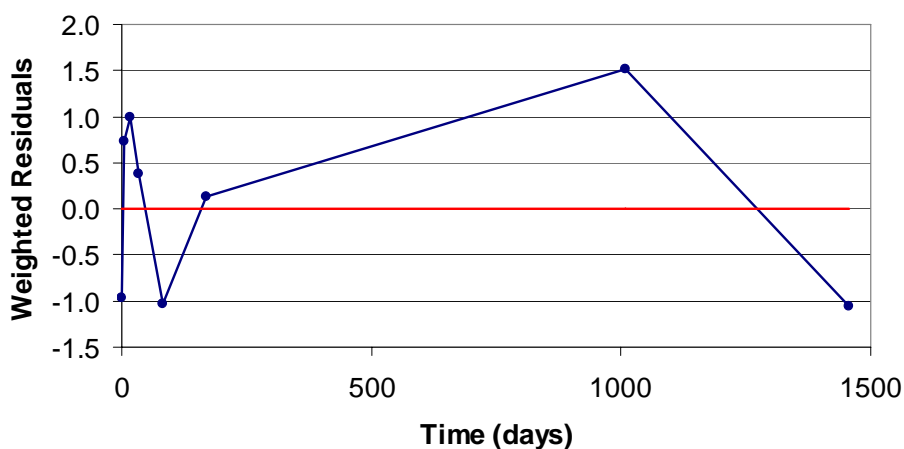


Figure 12. Weighted Residuals Plot for 1 μm AMAD Type M/S ^{60}Co Model



Regarding the question of how much the biokinetic models should be modified in the quest for a better fit, although somewhat arbitrary (because the models are not supported by an actual analysis of the aerosol), changes in aerosol AMAD and solubility type are fairly reasonable modifications. This is because the parameters correspond to characteristics of the inhaled material that may be expected to change in a predictable way, and these parameters were designed by the ICRP to be modified.

Further modifications that can be made to model parameters are rate constants in the respiratory tract and systemic models. Such modifications are frequently made with no justification other than the fact that they result in a better fit to the observed data. While a better fit is a necessary requirement for justifying a change in model parameters, it is not sufficient. In other words, just because the fit is better does not mean that the changes in the model reflect what is happening in the biological system.

Therefore, it is recommended that, when appropriate, efforts be made to corroborate changes made in the biokinetic models. For example, changes based on the analysis of different types of bioassay data like urine, feces, and in-vivo are more convincing than changes based on urine data alone. Another useful approach is to search the peer-reviewed literature to see if alternate models are available that are

applicable to the case at hand. Finally, the Principle of Parsimony²¹ should always be applied to all changes in biokinetic models (i.e., change the models as little as is necessary to achieve the desired result).

5.7.1 Fitting Methods

The LS fit and ML fit will give relatively the same estimate for a single intake from bioassay data all above the level of detection (LOD). Since IMBA does not support LS fit for multiple intakes or for less-than limit of detection (<LOD) data, in these situations the ML fit must be used. IMBA also offers a Bayesian fit, but to be useful a meaningful prior must be selected. In the ⁶⁰Co example given in *Appendix D*²², the prior would be the probability distribution of the intake given no bioassay data. In other words, if it were stated that a person just had an intake of ⁶⁰Co but supplied no data, the prior would be a best guess of the intake and its probability distribution.

The use of an inappropriate prior can lead to incorrect intake estimates. For example, in the ⁶⁰Co example the prior was a normal distribution with a mean of 2000 Bq and a standard deviation of 1500 Bq. If measured burdens are generated from a known intake of 9800 Bq of ⁶⁰Co and a Bayesian fit is performed with this prior, an intake of 9800 Bq will not be the result. In general, the ML fit is recommended as the default fitting method.

5.7.2 Weights

In general, the weighting factors should be selected to produce (to the greatest degree possible) a residuals plot in which the residuals are uniformly and randomly distributed about zero²³. The guidance on the selection of weighting factors (errors) provided in *Appendix A*²⁴ gives a good starting point.

The relative weights assigned to each datum are especially important if the data are very different in absolute magnitude. For example, consider the case of urine bioassay data and chest count data collected after an intake of insoluble plutonium. The chest count data (with results in 100's of nCi) will completely swamp the urine data (with results in fractions of pCi) and dominate the intake estimate unless the relative weights are carefully chosen. A similar situation frequently occurs when bioassay data collected shortly after an intake swamp smaller results collected at longer times after the intake.

In considering what weight to apply to a <LOD datum, the answer depends on the meaning of LOD and if it is acceptable for the predicted datum (the line of best fit) to be above the LOD for the datum in question. If the LOD is a modern, statistically based decision level like those defined in ANSI-13.30, then it is fairly probable that the true value of the datum could be above the LOD and yet still be reported as <LOD. In this case, it would be reasonable to assign the same weight to the <LOD datum as that assigned to a real datum of the same magnitude. On the other hand, if the LOD has been defined as a judgment-based upper plausible limit, then a predicted datum (line of best fit) above the <LOD datum

²¹ Also known as Occam's Razor. The basic idea is to choose the simplest explanation of a phenomenon (i.e., the one that requires the fewest leaps of logic or faith).

²² James, A.C., *User Manual for IMBA Expert*TM USDOE-Edition Version 3.2 Appendix D: Bioassay Example Cases, Section D.2, March 2004.

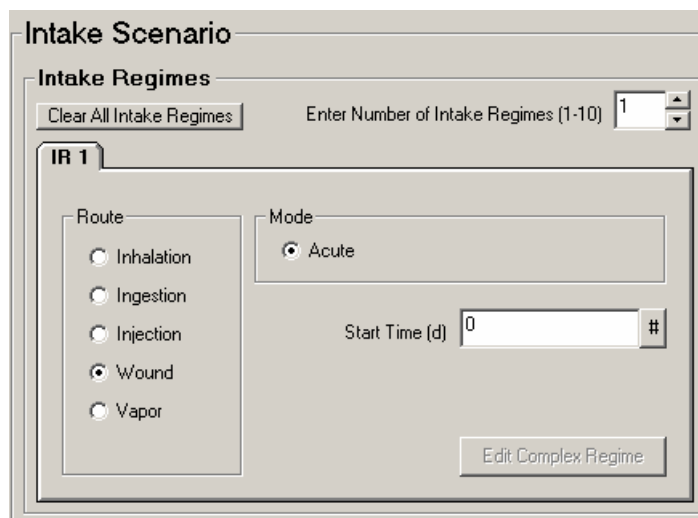
²³ Draper and Smith, *Applied Regression Analysis*, New York: Wiley, 1981.

²⁴ James, A.C., Birchall, A., Marsh, J.W., Puncher, M., *User Manual for IMBA Expert*TM USDOE-Edition (Phase II) Version 3.2, Appendix A: Technical Basis, Section A.10.3, April 2004.

would probably not be acceptable. In this situation, a relatively large weight (small standard deviation) should be used for the <LOD datum. This forces the line of best fit to be below the <LOD datum²⁵.

5.8 Modeling Intakes Through Wounds

IMBA provides an option to model an intake via a wound, as shown in the following screenshot:

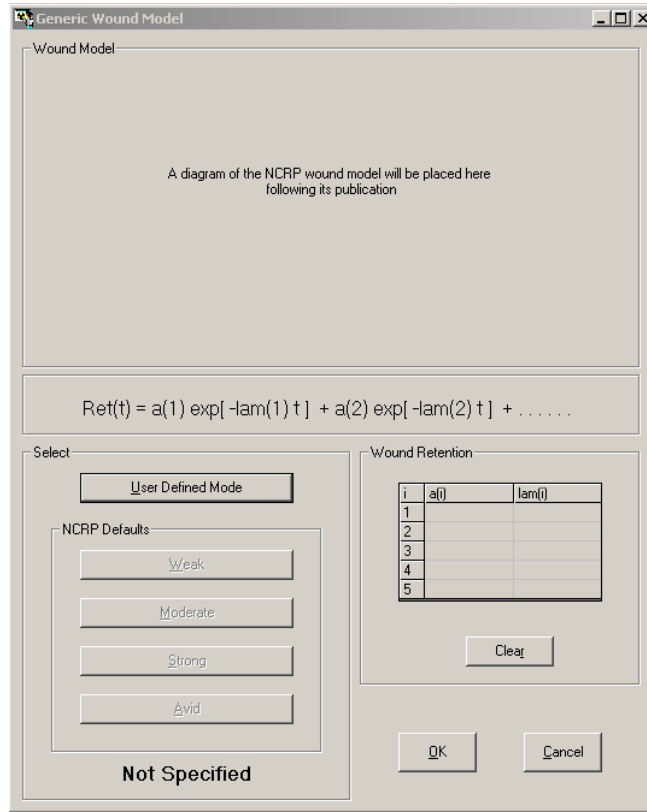


At this time, a default wound model is not implemented in IMBA because the ICRP has not recommended a model. However, the National Council on Radiological Protection (NCRP) is close to publishing a generic wound model²⁶ that can be used in IMBA. The intent to adopt this model becomes obvious when one opens the wound model panel, as shown in the next screenshot.

Until the NCRP model is implemented, intakes via a wound must be modeled with the *User Defined* mode. In this mode, the retention in the wound is expressed as a sum of up to five exponential terms. Note that each term has a coefficient and a rate constant and the sum of the coefficients must equal unity.

²⁵ IMBA Expert and IMBA Professional Plus have a minor bug in the routine that implements the <LOD fitting protocol. This bug prevents one from using this approach to force the line of best fit below the <LOD result if this result is significantly below the rest of the observed data. This is indeed a minor issue, and in fact one could argue that it was a design feature to prevent users from forcing the line of best fit too far from the majority of the observed data.

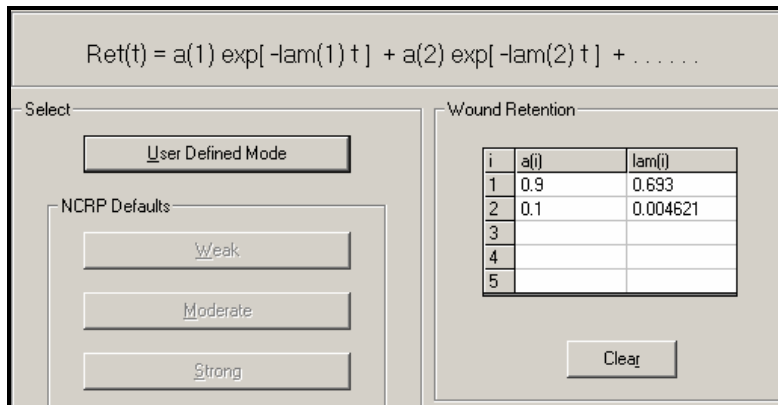
²⁶ Guilmette, R. A., and Durbin, P. W., *Scientific Basis for the Development of Biokinetic Models for Radionuclide-Contaminated Wounds* *Radiation Protection Dosimetry* (105) Nos. 1-4, pp. 213-218, 2003.



For example, assume that the wound exhibits a retention pattern consistent with two single-exponential compartments: one with a relatively short half-life, on the order of 1 day, and one with a relatively longer half-life, on the order of 150 days. The wound model would be

$$R_{wou}(t) = 0.9 e^{\frac{-\ln(2)}{1 \text{ day}} t} + 0.1 e^{\frac{-\ln(2)}{150 \text{ days}} t} \quad (1)$$

where $R_{wou}(t)$ is the fraction retention of the plutonium in the wound assuming no radioactive decay and t is the time since the wound occurred. These parameters are entered into the user-defined wound model of IMBA, as shown below.



When a radioactive material is introduced into the body via a wound, assuming there is no medical intervention, four things can happen:

- The material can be *absorbed* from the wound into the bloodstream.
- The material can be *transported* from the wound to the lymphatic system.
- The material can be *retained* in the tissue in the vicinity of the wound.
- The material can be *removed* from the wound to the environment by natural processes (e.g., when a scab falls off the wound).

This raises a subtle point about the IMBA wound model: according to the model, all of the material deposited in the wound will eventually be absorbed into the bloodstream. None is transported to the lymph nodes, removed from the wound, or retained indefinitely in the wound. This characteristic of the wound model becomes important when one is trying to reconcile in-vivo (wound-count) data and excretion (urine) data.

Material retained indefinitely in the wound can be modeled by assigning one compartment an extremely long translocation half-life, but in practice the fraction of the deposited material absorbed from the wound site into the bloodstream is the most important dosimetrically. This is because absorbed material will be metabolized as if it had been absorbed from the lung or gastrointestinal tract whereas material left at the wound site does not tend to irradiate critical organs. This also means that standard models (and IMBA) can be used to evaluate urinary excretion and to calculate the dose to the systemic organs following an uptake via a wound, but they cannot be used to calculate the dose to the wound site.

The excision of contaminated tissue from the wound site creates a discontinuity in the source term. For example, if 1 nCi of plutonium is deposited in a wound and the processes described above promptly begin to translocate it from the wound and a physician excises 0.5 nCi of plutonium from the wound a day later, there is a sudden reduction in the quantity of plutonium in the wound. This reduction is equivalent to a negative intake and can be difficult to model. One approach is to simply ignore the urinary excretion data prior to the excision and model the data observed afterwards. This often works well because excisions are usually performed within hours of a wound event.

The general approach to modeling urinary excretion data following a wound is to first use a single compartment with a short half-life to simulate a wound with instantaneous uptake to the blood. If the shape of the curve does not adequately fit the observed urinary excretion, the half-life of the short-lived compartment can be increased and a second or perhaps a third longer-lived compartment added. More than three compartments are seldom necessary to obtain an acceptable fit.

5.9 In-growth of ^{241}Am from ^{241}Pu

Americium-241 ($t_{1/2}=432$ years) is the radioactive daughter of ^{241}Pu ($t_{1/2} = 14.4$ years), which is a major component (on an activity basis) of weapons grade plutonium. Because ^{241}Am in the lungs is much easier to detect and quantify than are the plutonium isotopes present in weapons grade plutonium, ^{241}Am is frequently used as a tracer for in-vivo bioassay (chest counts) of weapons grade plutonium. However, the ratio of ^{241}Am to ^{241}Pu (and therefore the other plutonium isotopes) is not constant because of the different physical decay rates. IMBA offers a feature to account for this and neatly allow for the analysis of ^{241}Am chest count data.

To illustrate this feature, a set of benchmark chest count data²⁷ resulting from two acute inhalation intakes of the $^{241}\text{Pu}/^{241}\text{Am}$ five years apart (the first intake is on 0 day and the second intake is on day 1826) was entered in IMBA. The Pu/Am ratio was assumed to be 100:1 for both intakes. This data set was evaluated in IMBA with the following options selected in the *Advanced Fitting Options* tab.

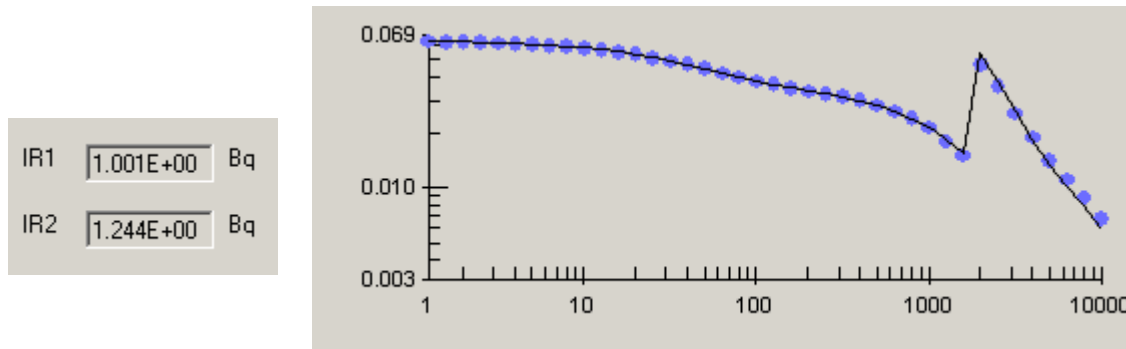
Ingrowth of indicator radionuclide

Allow ingrowth of Am-241 from Pu-241

Pu/Am ratio fixed at t=0

Pu/Am ratio fixed at start of each intake regime

The following wrong answers (both should be 1 Bq of ^{241}Am) resulted.



However, when the same data set was evaluated assuming that the Pu/Am ratio was fixed at the start of each intake...

Ingrowth of indicator radionuclide

Allow ingrowth of Am-241 from Pu-241

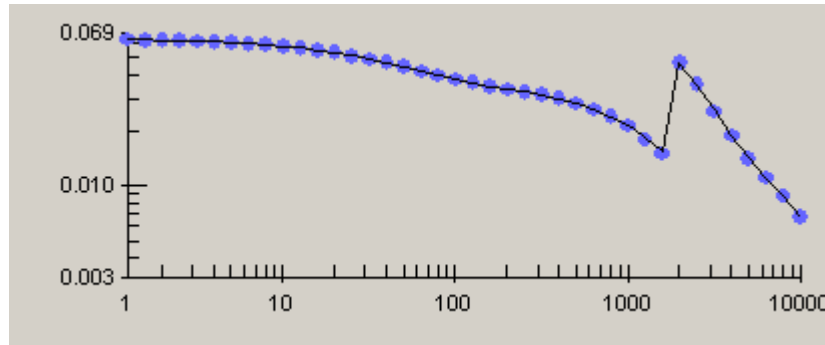
Pu/Am ratio fixed at t=0

Pu/Am ratio fixed at start of each intake regime

the right answers resulted.

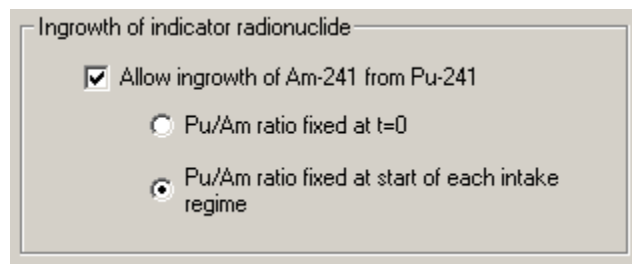
²⁷ The benchmark was calculated independently of IMBA.

IR1 9.980E-01 Bq
IR2 9.962E-01 Bq



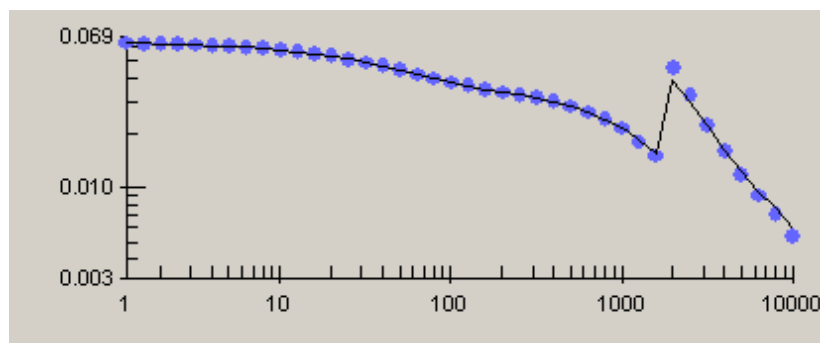
Thus, if the $^{241}\text{Pu}/^{241}\text{Am}$ ratio of the inhaled material is assumed to remain constant between intakes, the second option in the in-growth window should be selected.

To illustrate this feature further, a second set of benchmark chest count data for two acute inhalation intakes of the $^{241}\text{Pu}/^{241}\text{Am}$ five years apart (the second intake on day 1826) was entered into IMBA. The Pu/Am ratio was assumed to be 100:1 for the first intake and 46.19:1 for the second intake. In other words, the material inhaled at $t=1826$ days was the material inhaled at $t=0$ days physically decayed for 1826 days. The data set was evaluated in IMBA with the following options selected in the *Advanced Fitting Options* tab.

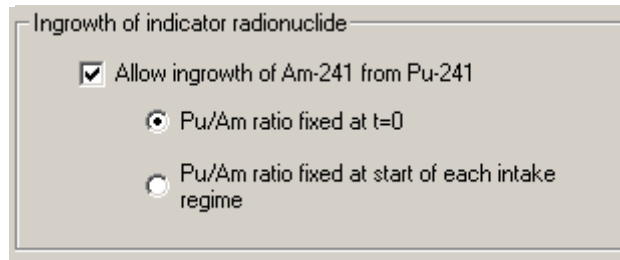


This is wrong (again, both intakes should be 1 Bq of ^{241}Am).

IR1 9.957E-01 Bq
IR2 7.665E-01 Bq

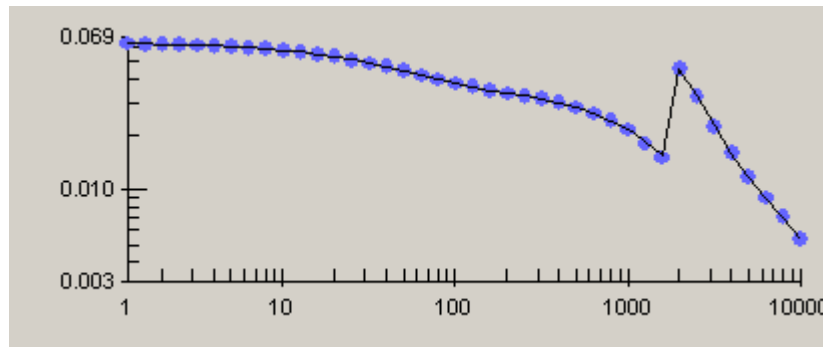


However, assuming that the Pu/Am ratio was fixed at $t=0$



gives the right answer.

IR1	9.980E-01	Bq
IR2	9.962E-01	Bq

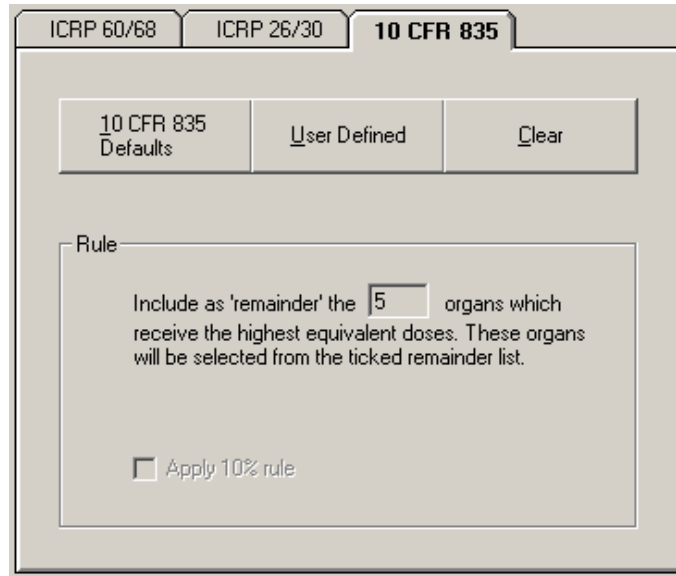


Thus, if the $^{241}Pu/^{241}Am$ ratio of the inhaled material is assumed to change as a result of physically decay between the intakes, the first option in the in-growth window should be selected.

5.10 Tissue Weighting Factors

The regulations given in Title 10 Code of Federal Regulations Part 835 (10 CFR 835) are relevant to the use of IMBA in facilities regulated by DOE. These regulations do not limit the various methodologies used in the assessment of internal dose with the exception of tissue weighting factors²⁸. In practice, this means that the internal dosimetrist may use the most technically accurate models and methods for evaluating bioassay data and assigning dose in a specific case, with the exception of the tissue weighting factors. These factors, which are specified in 10 CFR 835.2, are used to weight organ dose equivalents so that they can be summed to give a committed effective dose equivalent. As shown below, IMBA offers the option of selecting ICRP 60, ICRP 26, or 10 CFR 835 tissue weighting factors.

²⁸ *Guidance on the Revision of Internal Radiation Dose Estimates in Response to Updated Internal Dosimetry Methodologies*, U.S. DOE Office of Worker Protection Policy and Programs Radiological Control, Technical Position RCTP 2004-01.



The 10 CFR 835 tissue weighting factors should be used in IMBA for all occupational internal doses resulting from activities at facilities regulated by DOE²⁹.

5.11 Check for Updates

Both IMBA Expert™ DOE-Edition and IPP have a “Check for Updates” feature accessible under the Help menu. This feature compares the versions of the modules currently installed against the latest versions available and downloads and installs any newer versions.

While this update feature works in many cases, certain network configurations such as the existence of firewalls and proxy servers have caused difficulties. When IMBA has problems completing the update sequence, it can generate the following error message.



This error message’s statement that “At present there is no internet connection detected.” is misleading. Any failures for the update feature to complete successfully will cause this error to be generated, even with a valid internet connection.

²⁹ There are U.S. DOE regulated facilities that have requested and been granted exemptions to 10 CFR 835 that allows them to use ICRP 60 tissue weighting factors. This recommendation is not applicable to those facilities.

A manual update of IMBA can be performed by downloading the latest module versions into their appropriate directories as indicated on the IMBA update page:

http://www.hpa.org.uk/radiation/publications/software/imbapro_plus/imbaupdates.htm

Note: Users should be aware that only IMBA Expert™ USDOE Version 4.0.28 is approved as a software toolbox code. Any updates above this version are at the responsibility of the individual user.

6. Acronyms and Definitions

AMAD. Activity median aerodynamic diameter (AMAD) is the diameter of a unit density sphere with the same terminal settling velocity in air as that of the aerosol particle whose activity is the median for the entire aerosol.

Becquerel (Bq). The SI unit of radioactivity, which equals one (1) disintegration per second.

Committed Dose Equivalent ($H_{T,50}$). The dose equivalent calculated to be received by a tissue or organ over a 50-year period after the intake of a radionuclide into the body. It does not include contributions from radiation sources external to the body. Committed dose equivalent is expressed in units of rem (or *sievert*) (1 rem = 0.01 *sievert*).

Committed Effective Dose Equivalent (CEDE). In ICRP 30, the sum of the committed dose equivalents ($H_{T,50}$) over a fifty-year period to various organs or tissues in the body, each multiplied by the appropriate weighting factor (w_T) -- that is $H_{E,50} = \sum w_T H_{T,50}$. CEDE is applicable to exposure from internally deposited radionuclides.

Committed Equivalent Dose (CDE). The ICRP 6X/7X equivalent of CEDE.

DCF. Intake-to-dose conversion factor, which gives the committed dose per unit intake of radioactive material.

HPA. Health Protection Agency of the United Kingdom, which was created in April 2005 and absorbed the duties of the National Radiological Protection Board (NRPB) at that time.

Rem. The unit of dose equivalent or effective dose equivalent. The *rem* is numerically equal to the absorbed dose in rad multiplied by a quality factor, distribution factor, and any other necessary modifying factor (1 *rem* = 0.01 *sievert*).

Sievert (Sv). The SI unit of any of the quantities expressed as dose equivalent. The dose equivalent in *sievert* is equal to the absorbed dose in gray multiplied by the quality factor (1 Sv = 100 *rem*).

7. IMBA Manuals

User Manual for IMBA Expert™ USDOE-Edition Version 3.2, April 2004.

User Manual for IMBA Expert™ USDOE-Edition Version 3.2, Appendix A: Technical Basis, April 2004.

User Manual for IMBA Expert™ USDOE-Edition Version 3.2, Appendix B: Bioassay Quality Assurance, March 2004.

User Manual for IMBA Expert™ USDOE-Edition Version 3.2, Appendix C: Dose Quality Assurance, March 2004.

User Manual for IMBA Expert™ USDOE-Edition Version 3.2 Appendix D: Bioassay Example Cases, March 2004.

User Manual for IMBA Professional Plus, (Version 4.0), May 2005.

IMBA Professional Plus (Version 4.0) User Manual Appendix A: Technical Basis, August 2005.

IMBA Professional Plus (Version 4.0) User Manual Appendix B: Bioassay Quality Assurance, August 2005.

IMBA Professional Plus (Version 4.0) User Manual Appendix C: Dose Quality Assurance, August 2005.

IMBA Professional Plus (Version 4.0) User Manual, Appendix D: Example Bioassay Cases, August 2005.

Attachment A. Biokinetics of Tritiated Water

The parameters for the urinary excretion of HTO are calculated using the ICRP 68 biokinetic model. Implemented in Mathcad 2001i³⁰.

$$\text{TOL} \equiv 10^{-5}$$

$$\text{ORIGIN} \equiv 1$$

Define the compartments of the biokinetic model.

$$\text{xfer} \equiv 1$$

$$\text{bladder} \equiv 4$$

$$\text{tb}_A \equiv 2$$

$$\text{urine} \equiv 5$$

$$\text{tb}_B \equiv 3$$

$$\text{other} \equiv 6$$

Define transfer and total removal rate constants of the HTO model.

$$k_{\text{xfer, tb}_A} := 0.97 \cdot \frac{\ln(2)}{0.25 \cdot \text{day}}$$

$$k_{\text{tb}_A, \text{bladder}} := \frac{1.4}{3.0} \cdot \frac{\ln(2)}{10 \cdot \text{day}}$$

$$k_{\text{xfer, tb}_B} := 0.03 \cdot \frac{\ln(2)}{0.25 \cdot \text{day}}$$

$$k_{\text{tb}_A, \text{other}} := \frac{1.6}{3.0} \cdot \frac{\ln(2)}{10 \cdot \text{day}}$$

$$k_{\text{tb}_B, \text{bladder}} := \frac{\ln(2)}{40 \cdot \text{day}}$$

$$k_{\text{bladder, urine}} := 12 \cdot \text{day}^{-1}$$

³⁰ Mathsoft, Inc., Cambridge, MA.

$$k_{\text{xfer}, \text{xfer}} := -(k_{\text{xfer}, \text{tb}_A} + k_{\text{xfer}, \text{tb}_B})$$

$$k_{\text{bladder}, \text{bladder}} := -k_{\text{bladder}, \text{urine}}$$

$$k_{\text{tb}_A, \text{tb}_A} := -(k_{\text{tb}_A, \text{bladder}} + k_{\text{tb}_A, \text{other}})$$

$$k_{\text{urine}, \text{urine}} := 0$$

$$k_{\text{tb}_B, \text{tb}_B} := -(k_{\text{tb}_B, \text{bladder}})$$

$$k_{\text{other}, \text{other}} := 0$$

$$q0_{\text{other}} := 0$$

Note that the initial contents are expressed in terms of atoms, which have no dimensions or units.

$$q0_{\text{xfer}} := 1.0$$

Calculate the eigensystem.

$$\gamma := \text{eigenvals}(k^T)$$

$$V := \text{eigenvecs}(k^T)$$

$$c := V^{-1} \cdot q0$$

$$j := \text{xfer}.. \text{other}$$

$$C_j := c_j \cdot V_{\text{urine}, j}$$

Define the cumulative (q_u) and 24-hour incremental (Δe_u) urinary excretion functions...

$$q_u(t) := \sum_{j = \text{xfer}}^{\text{other}} C_j \cdot \exp(\gamma_j \cdot t)$$

$$\Delta e_u(t) := (q_u(t) - q_u(t - 1 \cdot \text{day}))$$

... and the instantaneous urinary excretion function (Q_u).

$$Q_u(t) := \sum_{j = \text{xfer}}^{\text{other}} \gamma_j \cdot C_j \cdot \exp(\gamma_j \cdot t)$$

Here are some examples of the functions in use.

$$t := 10 \text{ day}$$

$$q_u(t) = 2.238 \times 10^{-1}$$

$$\Delta e_u(t) = 1.720 \times 10^{-2}$$

The coefficients and rate constants for IMBA bioassay model.

$$i := 1..6$$

$$\gamma_i C_i =$$

0.0000000000	day ⁻¹
0.0000000000	
0.0096389857	
0.0323679517	
0.0005238865	
-0.0425308239	

$$\gamma_i =$$

0.0000000000	day ⁻¹
0.0000000000	
-12.0000000000	
-0.0693147181	
-0.0173286795	
-2.7725887222	

Compare the Mathcad calculations with IMBA.

$$\lambda := \frac{\ln(2)}{4485 \text{ day}}$$

$$t := 1..100$$

Incremental 24-hour urinary excretion, which is the IMBA "Urine" bioassay type.

$$\Delta e_u(t \cdot \text{day}) \cdot \exp(-\lambda \cdot t \cdot \text{day}) =$$

	1
1	1.8210 · 10 ⁻²
2	2.8780 · 10 ⁻²
3	2.7656 · 10 ⁻²
4	2.5874 · 10 ⁻²
5	2.4165 · 10 ⁻²
6	2.2568 · 10 ⁻²
7	2.1077 · 10 ⁻²
8	1.9686 · 10 ⁻²
9	1.8387 · 10 ⁻²
10	1.7176 · 10 ⁻²

Instantaneous urinary excretion, which is IMBA "User Defined" bioassay type.

$$Q_u(t \cdot \text{day}) \cdot \exp(-\lambda \cdot t \cdot \text{day}) =$$

	1
1	2.8053 · 10 ⁻²
2	2.8509 · 10 ⁻²
3	2.6765 · 10 ⁻²
4	2.5003 · 10 ⁻²
5	2.3350 · 10 ⁻²
6	2.1807 · 10 ⁻²
7	2.0367 · 10 ⁻²
8	1.9023 · 10 ⁻²
9	1.7769 · 10 ⁻²
10	1.6599 · 10 ⁻²

$$\text{day}^{-1}$$

Output from IMBA using coefficients and rate constants calculated here.

Specified Time (d)	Collection period (d)	Calculated Rate(pCi/d)	Measurement Time (d)
1.000E+00	1.000E+00	1.821E-02	9.000E+01
2.000E+00	1.000E+00	2.878E-02	
3.000E+00	1.000E+00	2.7656E-02	
4.000E+00	1.000E+00	2.5874E-02	
5.000E+00	1.000E+00	2.4165E-02	
6.000E+00	1.000E+00	2.2568E-02	
7.000E+00	1.000E+00	2.1077E-02	
8.000E+00	1.000E+00	1.9696E-02	

Specified Time (d)	N/A	Calculated Value(pCi)	Measurement Time (d)
1.000E+00		2.8053E-02	
2.000E+00		2.8509E-02	
3.000E+00		2.6766E-02	
4.000E+00		2.5003E-02	
5.000E+00		2.335E-02	
6.000E+00		2.1807E-02	
7.000E+00		2.0367E-02	
8.000E+00		1.9023E-02	

For more information on the methods used here consult the following references:

Jacquez, J. A. Compartmental Analysis in Biology and Medicine (Ann Arbor: University of Michigan Press) 1985.

Killough, G. G., Eckerman, K. F. *A Conversational Eigenanalysis Program for Solving Differential Equations*, in Computer Applications in Health Physics, Proceedings of the Seventeenth Midyear Topical Symposium of the Health Physics Society, 1984.

E. Polig *Modeling the Distribution and Dosimetry of Internal Emitters: A Review of Mathematical Procedures Using matrix Methods* Health Physics (81)5:492-501; 2001.

Potter, C. A. "Application of the ICRP Clarification of the Tritium Metabolic Model" Health Physics (87), pp 375-381, 2004.