

Radionuclides Biokinetics Database (EULEP)

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ABSTRACT

The overall aim of the EU Fifth Framework Programme Concerted Action RBDATA-EULEP was to provide information to improve the assessments of intakes of radionuclides and of the resulting doses. This involved a review of the behaviour of radionuclides following intake, and the transfer of expertise on methodology by organising small training workshops. The main activity was the development of an electronic database, effectively an annotated bibliography, with the electronic format facilitating extension, updating, and information retrieval. It consists of linked tables of references and experiments, with details and comments on the materials, procedures and results. By the end of the project in December 2004 it contained information on over 900 inhalation, 500 ingestion and 400 injection experiments from nearly 700 references. To meet the further aim of providing easy access to the database over the Internet, a web site was developed on which the database can be searched and information retrieved. Prospective users include: groups developing standards for internal dosimetry, scientists conducting research on radionuclide biokinetics, and health physicists assessing the consequences of accidental intakes.

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EXECUTIVE SUMMARY

The overall aim of this Concerted Action was to provide information to improve the reliability of assessments of intakes of radionuclides and of the resulting doses delivered either to workers or, in the case of releases to the environment, to the general public. This was achieved by (i) carrying out a review of the biokinetic behaviour of radionuclides, following their entry into the human body by any route, and (ii) transferring expertise on methodology by organising small workshops and training courses. The project consisted of two Work-packages:

Work-package 1: Review of radionuclide biokinetics

The consortium collated and analysed information from the literature on experimental studies relating to the biokinetics of radioactive compounds. A wide range of radionuclides was covered, with emphasis on the actinides (e.g. uranium, plutonium), fission products (e.g. caesium, strontium) and activation products (e.g. cobalt). The review of inhaled materials included derivation from the data of values of parameters describing absorption from the lungs to the blood, for use with the Human Respiratory Tract Model (HRTM) described in Publication 66 of the International Commission on Radiological Protection (ICRP). Other reviews dealt with ingested materials, and the systemic behaviour (including excretion) of radionuclides after entry into the blood by injection or after wound contamination. Ingestion and injection studies are often essential to interpreting data from inhalation experiments.

An existing electronic database (developed by members of the consortium during the Fourth Framework Programme) was enhanced and extended for use in this project. From reviews of the literature, further data were entered, extending the content from 103 references with information on 288 experiments, to 698 references, with information on 1888 experiments (936 inhalation, 514 ingestion and 438 injection), greatly exceeding the original target of at least 300 references with information on 900 experiments. To derive HRTM parameter values from experimental data requires a parameter-fitting computer program. A suitable program previously developed by one of the partners was distributed to the others, and training in its use was provided. To meet the further aim of providing easy access to the database over the Internet, a web site was developed on which the database can be searched and information retrieved.

It is considered that there are three groups of potential users of the database:

Groups of experts involved in developing guidance or standards relating to exposure to radioactive materials, in particular members of the ICRP Task Group on Internal Dosimetry, who are developing revisions of ICRP Publications 30/68 and 54/78.

Scientists involved in research on radionuclide biokinetics.

Health physicists who need to assess the consequences of accidental intakes of radioactive materials.

Work-package 2: Guidance on methodology to determine biokinetics

The second activity concerned the transfer of expertise on methodology on (i) experimental methods related to biokinetics such as inhalation facilities, *in vitro* dissolution techniques, and analytical methods, and (ii) computer modelling to derive absorption parameter values from experimental data. As a contribution to the education of young scientists in the general area of radiation protection dosimetry, short workshops were organised in France (June 2002, January 2003) and Germany (October 2003).

CONTENTS

1	Introduction	1
1.1	Work-package 1: Review of radionuclide biokinetics	1
1.2	Work-package 2: Guidance on methodology to determine biokinetics	1
2	Scientific and technical description of the results	2
2.1	Work-package 1: Review of radionuclide biokinetics	2
2.1.1	Adaptation of an existing electronic database	2
2.1.2	Data entry	9
2.1.3	Derivation of HRTM absorption parameter values from experimental data	14
2.1.4	Provision of access to the database through the Internet	14
2.2	Work-package 2: Guidance on methodology to determine biokinetics	16
2.2.1	Course 1 Experimental techniques	16
2.2.2	Course 2 Interpretation of experimental data	17
3	Acknowledgements	17
4	References	18
APPENDIX A	Glossary	20

1 INTRODUCTION

The overall aim of this Concerted Action was to improve the reliability of assessments of intakes of radionuclides and of the resulting doses delivered either to workers or, in the case of releases to the environment, to the general public. The objectives, as described in the agreed Technical Annex to the contract, were as follows. They remained essentially unchanged throughout the course of the project.

The project consists of two Work-packages:

1.1 Work-package 1: Review of radionuclide biokinetics

The consortium will collate and analyse information from the literature on experimental studies on the biokinetics of compounds of radionuclides of relevance to occupational and public exposure. Part of the work will focus on a review of *in vitro* and *in vivo* experiments with materials likely to be inhaled. Where appropriate, data will be expressed in terms of absorption parameter values which can be used with the ICRP (International Commission on Radiological Protection) Publication 66 Human Respiratory Tract Model (HRTM) to calculate dose coefficients and interpret whole body monitoring or bioassay data (ICRP 1994a, 2002).

Other reviews will provide biokinetic parameter values for ingested materials, and for the systemic behaviour of radionuclides after entry into the blood either by injection or after wound contamination. A wide range of radionuclides will be covered with emphasis on actinides and fission products that are currently encountered in facilities within the EU. Easy access to the database, which will also give information on the quality of the data and on their interpretation, will be provided via the Internet through a web site.

1.2 Work-package 2: Guidance on methodology to determine biokinetics

The second activity concerns the transfer of expertise on methodology to determine radionuclide biokinetics and the development of common approaches to dose assessment. This will include experimental methods related to biokinetics such as inhalation facilities and instillation methods, *in vitro* dissolution techniques, analytical methods, and also computer modelling to derive absorption parameter values from experimental data. Short workshops on some of these topics will be organised as a contribution to the education of young scientists in the general area of radiation protection dosimetry.

This project aims to build a comprehensive database in the field of radiation protection which is expected to be of immediate value, and will also provide input into any future Euratom directive. It will give strong support to the ICRP by analysing and collating the literature reviews which are essential for the development of the new biokinetic models

that are required for the forthcoming revision of Publications 30, 54, 68 and 78 on radiation doses to workers.

The publication of the HRTM, the forthcoming new human alimentary tract (HAT) model, and the development of new systemic models necessitate a re-interpretation of existing data.

This proposal is intended to provide a comprehensive and up-to-date database of high scientific quality and easy accessibility via the Internet. In addition, through a common approach developed by the participants, it will give guidance on the interpretation of experimental data and the derivation of absorption parameter values.

2 SCIENTIFIC AND TECHNICAL DESCRIPTION OF THE RESULTS

2.1 Work-package 1: Review of radionuclide biokinetics

2.1.1 Adaptation of an existing electronic database

An existing electronic database, developed by some members of the consortium during the Fourth Framework Programme, as a task of a EULEP-EURADOS Action Group (Bailey et al, 2000a; 2000b), was enhanced and extended for use in this project. Experience in the Fourth Framework Programme had shown its potential in the collation of data from experimental studies. Essentially, it provides an annotated bibliography: a listing of papers relating to a topic, with a summary of the relevant information, and, importantly, comments on each major aspect of the paper and the experiments described in it. Moreover, the electronic format provides some distinct advantages over a traditional hard copy, in particular:

- Development. The database can continually be extended and updated to provide more complete coverage of the topic and to widen its scope. Revisions can be distributed at negligible cost, e.g., by electronic mail.
- Retrieval of information. Information relevant to a particular issue can be found either by means of a "Query", which selects records according to chosen criteria, e.g. all experiments involving a selected element and chemical form, or simply by searching a table for selected text, using the "Edit/Find" feature.

A description follows below at a similar level of detail to that given in publications based on conference presentations (Bailey et al., 2000b; 2003, 2004). Full details are given in the User Guide (Bailey, 2005).

Records are stored in four main tables: one for *References* and three for *Experiments: Inhalation, Ingestion and Injection*.

The screenshot shows the Microsoft Access interface for the 'References' table. The window title is 'Microsoft Access - [References]'. The menu bar includes File, Edit, View, Insert, Format, Records, Tools, Window, and Help. The toolbar contains various icons for file operations and data manipulation. The main form area is titled 'References' and features a 'Find Experiments' button. The form fields are as follows:

- Ref No:
- Authors:
- Title:
- Publication:
- Volume: Pages: Date:
- Comment:
- Abstract:
- Entered by:
- Paper:
- Spreadsheet:

The status bar at the bottom indicates 'Record: 699 of 699' and provides a note: 'Self-explanatory. Up to 255 characters. Use format as in existing records'.

Figure 1 Data entry and viewing screen for references

The *References* table contains information about each publication (Reference) reporting relevant experiments. Figure 1 shows the data entry screen (“Form”) for References, from the current version:

- Citation details: authors; title; publication; volume; pages; date.
- Comment: *e.g.*, whether it contains the original data, an analysis of HRTM parameter values or a review giving only a summary; cross-references to other related references.
- Abstract, taken from the Reference if it has one; if not, written by the person entering the record.
- Record of data entry and of any updating.
- The “Paper” field gives a link to a separate document file (if available, Table 1), containing the text of the reference: typically used for documents which are unpublished, or where copyright is owned by a partner in the consortium.
- The “Spreadsheet” field gives a link to a separate spreadsheet, (if available, Table 1), which might contain tabulated data and/or calculations based on results in the reference. A spreadsheet might well contain such information relating to more than one experiment, and is therefore identified by the number of the principal Reference to which it relates.

The *Experiments* tables summarise information on each experiment, in three sections, which give information about the material studied, experimental methods and results.

Table 1 Spreadsheets and documents linked to the database (December 2004)

Spreadsheets (*.xls)			Documents (*.doc or *.pdf)
Ref 1 Stather 1975	Ref 342 Boback 1975 G	Ref 597 Snipes 1983	R159 Bailey 1998.pdf
Ref 34 Stradling 1996	Ref 344 Morrow 1964	Ref 601 Zhou 2004	R297 Newton 2000.doc
Ref 42 Ramounet 1998	Ref 359 Patrick 1977	Ref 602 Cheng 2002	R342 Boback 1975 G IDEAS 84.doc
Ref 157 Ham 2000	Ref 372 Cheng 1999	Ref 607 Felicetti 1974	R343 Marsh 1996.doc
Ref 163 Mishima 1985	Ref 392 Schiessle 1964	Ref 608 Thomas 1973	R346 Bailey 2002.pdf
Ref 198 Sullivan 1985	Ref 406 Spencer 1960	Ref 613 Djuric 1962	R428 Fractional dissolution rates.doc
Ref 199 Harrison 1979	Ref 428 Cuddihy 1978	Ref 614 Newton 1994	R653 Newton 2004.doc
Ref 203 Harrison 1986	Ref 572 Zhou 2003	Ref 625 Dobryakova 1970	
Ref 204 Harrison 1987	Ref 590 Thind 1995	Ref 696 Slouka 1970a	
Ref 205 Stather 1980	Ref 592 Lang 1995	Ref 697 Slouka 1970b	
Ref 206 Sullivan 1979			

Thus the *Inhalation Experiments* table summarises information on each experiment giving information about dissolution in the respiratory tract and absorption to blood. Although called *Inhalation*, it includes experiments in which the material was instilled (injected) into the lungs, and *in vitro* experiments designed to assess dissolution in the lungs, including cell studies. Figure 2 shows the data entry screen for Inhalation Experiments.

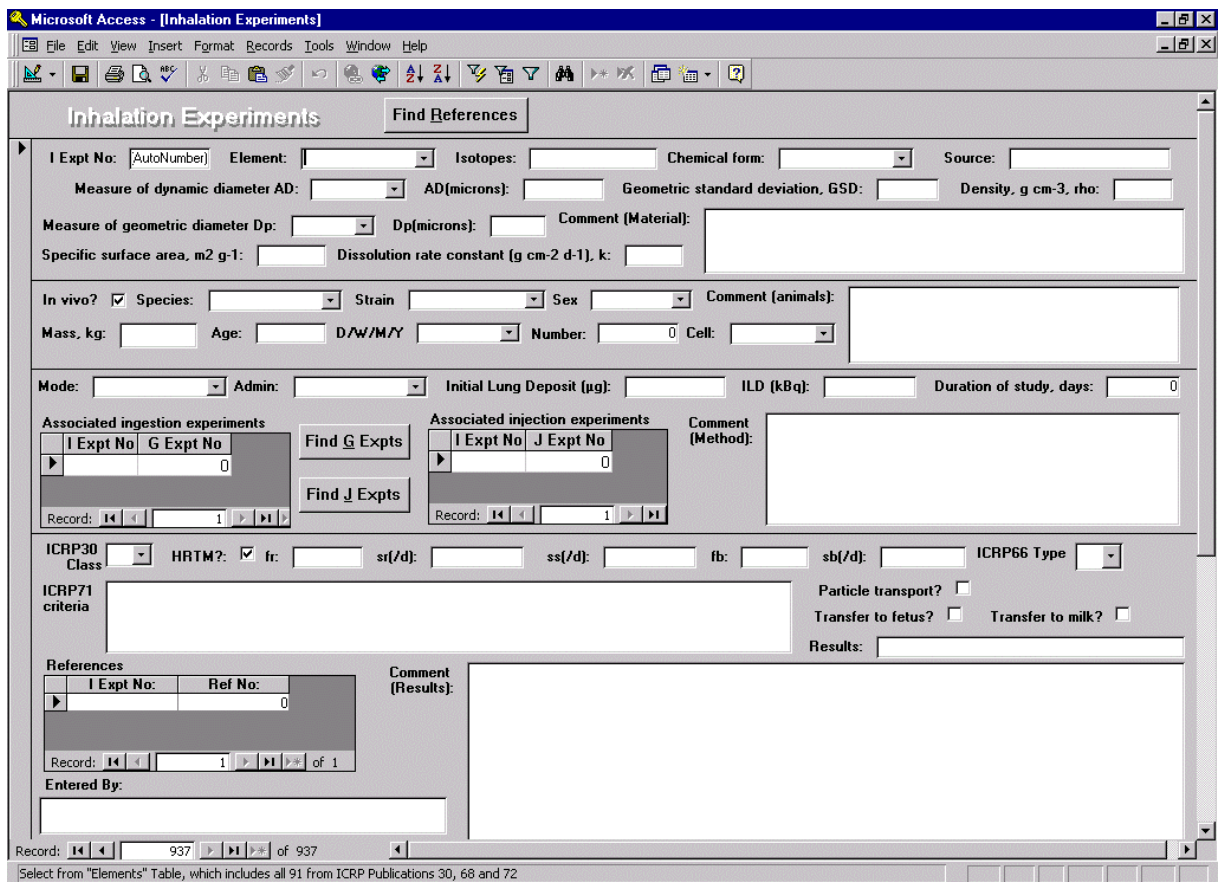


Figure 2 Data entry and viewing screen for Inhalation Experiments

The first section contains information about the material:

- Element; isotopes; chemical form; source (e.g., name of facility or laboratory where the material was prepared).
- Characteristics of the size distribution: median; geometric standard deviation.
- Density; specific surface area.
- Comment on the material (e.g., method of preparation).

The second section contains information about the experimental method:

- Species; strain; age; mass; sex; and number.
- Mode of administration: route, e.g., inhalation; single, multiple or chronic.
- Initial lung deposit (μg , Bq).
- Duration of experiment (study) in days.
- Links to any associated ingestion and injection experiments.

Comments on the method (e.g., duration of administration, anaesthetics used).

The third section contains information about the results:

- Assessment of whether derivation of HRTM parameter values is feasible from the results.
- HRTM parameter values if derived: f_r (fraction dissolved rapidly), s_s (slow dissolution rate) etc.
- The “Results” field gives a link to a separate spreadsheet, (if available, Table 1), which might for example contain a table giving organ distribution at a series of times after administration, taken from a graph in the original paper, or calculations to derive parameter values.
- Comments on the results, in particular how the HRTM parameter values were derived, and cross-references to results of closely related experiments.
- Record of data entry and of any updating.

The corresponding *Ingestion* and *Injection Experiments* tables are similar, but generally simpler than the *Inhalation Experiments* tables, requiring less information about the material. The *Ingestion Experiments* table has specific fields to give: status (fed or ‘fasted’, i.e. before breakfast); factor investigated in the study (e.g., mass, chemical form); links to any associated injection experiments. Figure 3 shows the data entry screen for Ingestion Experiments.

The *Injection Experiments* table has a specific field to give the route of administration (e.g., intravenous, intramuscular). Figure 4 shows the data entry screen for Injection Experiments.

Microsoft Access - [Ingestion]

File Edit View Insert Format Records Tools Window Help

Ingestion Find References

G Expt No: [AutoNumber] Element: [] Isotopes: [] Chemical form: []

Source: [] Comment (Material): []

Species: [] Strain: [] Sex: [] Mass, kg: []

Age: [] D/W/M/Y [] Number: [0] Comment (animals): []

Admin: [] Status: [] Factor studied: [] Duration of study, days: []

Amount (µg): [] Comment (Method): []

Amount (µg/kg): []

Amount (kBq): []

Amount (kBq/kg): []

Transfer to fetus? Comment (Results): []

Transfer to milk?

F1: []

Results: []

References

G Expt No:	Ref No:
[]	[0]

Record: [1] of 1

Associated injection experiments

G Expt No	J Expt No
[]	[0]

Record: [1] of 1

Entered by: []

Record: [515] of 515

Select from "Elements" Table, which includes all 91 from ICRP Publications 30, 68 and 72

Figure 3 Data entry and viewing screen for Ingestion Experiments

Microsoft Access - [Injection]

File Edit View Insert Format Records Tools Window Help

Injection Find References

J Expt No: [AutoNumber] Element: [] Isotopes: [] Chemical form: []

Source: [] Comment (Material): []

Species: [] Strain: [] Sex: [] Mass, kg: []

Age: [] D/W/M/Y [] Comment (animals): []

Number: [0]

Admin: [] Route: [] Duration of study, days: []

Amount (µg): [] Comment (Method): []

Amount (µg/kg): []

Amount (kBq): []

Amount (kBq/kg): []

Transfer to fetus? Transfer to milk?

Results: []

References:

J Expt No:	Ref No:
[]	[0]

Record: [1] of 1

Entered by: []

Record: [439] of 439

Select from "Elements" Table, which includes all 91 from ICRP Publications 30, 68 and 72

Figure 4 Data entry and viewing screen for Injection Experiments

The *References* table is linked to each table of *Experiments* through a “junction table”, which enables each reference to be linked to any number of experiments (and *vice-versa*). Many experiments are reported in several publications, each of which could refer to several experiments. While it is clearly preferable to refer to publications in peer-reviewed journals, often the results first appear in a laboratory report, and sometimes, presumably for reasons of space or style, the external publication only includes some of them, or only a graphical summary. The database structure is shown in Figure 5.

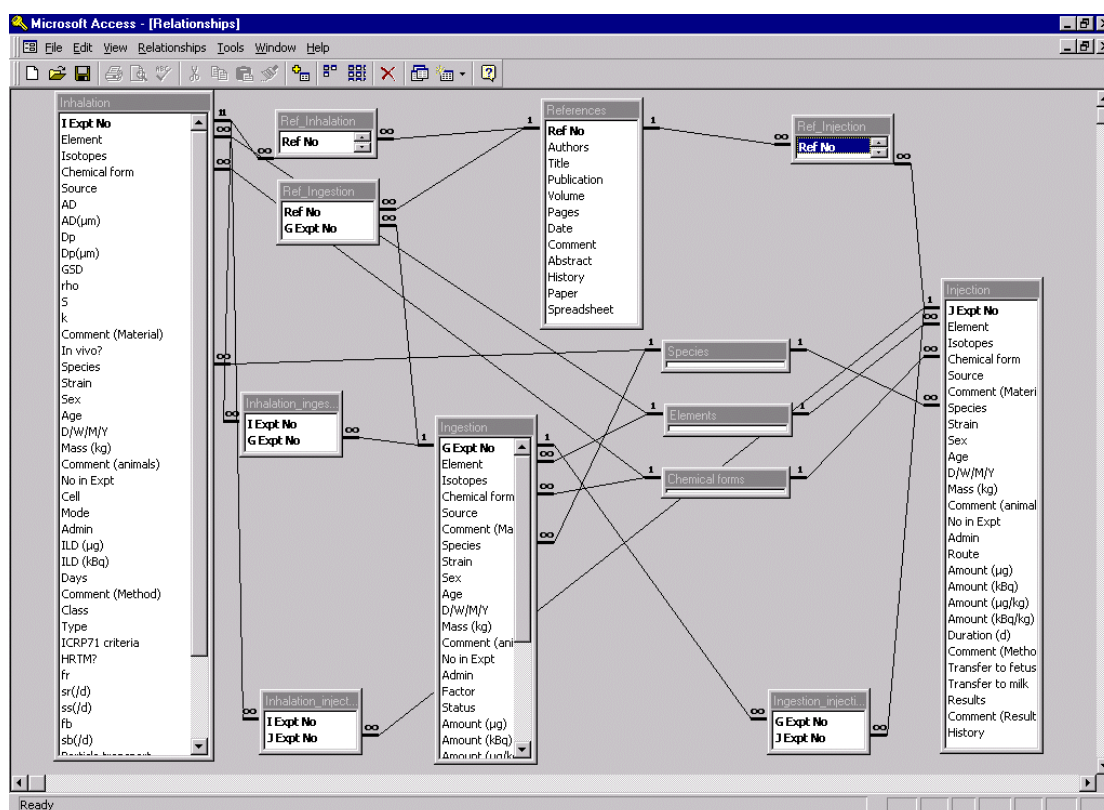


Figure 5. Structure of the database showing the relationships between the tables of data. “Junction” tables allow each record in the References Table to be linked to more than one record in each of the Inhalation, Ingestion and Injection Experiments Tables. Similarly a record in the Inhalation Experiments Table can be linked to more than one record in the References Table and to more than one record in each of the Ingestion and Injection Experiment Tables.

Wherever possible, data are entered by selecting text from drop-down lists. This makes entry easier, and also facilitates retrieval of information, by avoiding the use of a variety of terms for the same concept.

The Main Menu screen (Figure 6) provides the central point of reference for navigating the database. Buttons on it activate queries to provide listings of the experiments relating to a route of intake, for a selected element and chemical form, or for references by a chosen author. Other buttons open the References and Experiment Forms, and other functions as mentioned below.

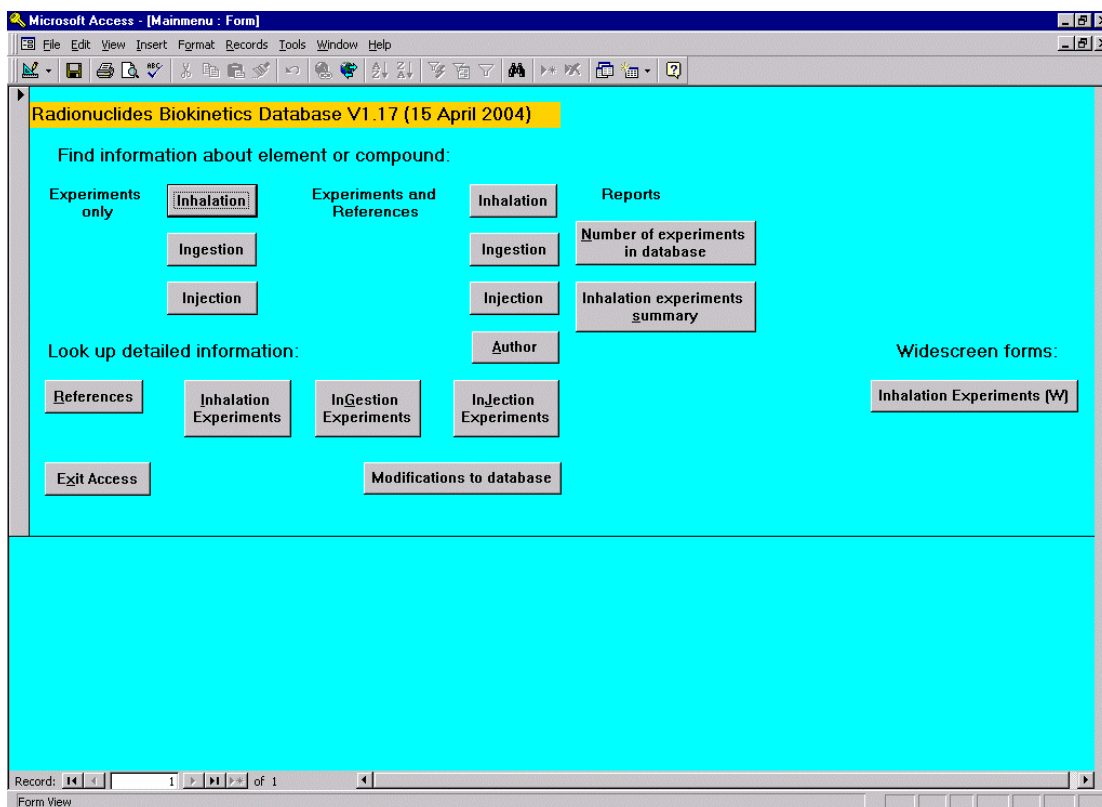


Figure 6. Main Menu screen: buttons on the upper part activate queries to find the experiments and publications (references) relating to a route of intake, for a selected element and chemical form. Searches can also be made for all publications by a chosen author. Buttons on the lower part open forms displaying summaries of information about each reference and experiment (Figures 1–4).

During the course of the project, several improved versions were produced, as described in the following paragraphs. There were also additions to the data entry tables (chemical forms, species, etc) and drop-down lists. A number of changes to the existing database (V1.01) had been agreed before the formal start of the project. They were implemented and the revision, designated V1.12, was distributed in February 2001. Further revisions (but with fewer changes in total) were distributed in June 2001 (V1.13), February 2002 (V1.14), March 2002 (V1.15 and an updated User Guide), December 2002 (V1.16) and April 2004 (V1.17 and an updated User Guide).

The main changes were as follows:

- *General:* The database was transferred from MS ACCESS V2 to ACCESS97. The data entry and review Forms for the main records (References and the three types of Experiments) were redesigned on the basis of a larger screen size (800x600 pixels). For Inhalation Experiments, which has the largest number of fields, a “Large” or “Widescreen” version was added (at 1024x768 pixels) “Inhalation Experiments (Large)”. This enabled the complete form to be on screen at once, without the need for scrolling.
- *Main menu:* New buttons were added: “Author” which runs a new Query to find all references by a specified author (first author or co-author); “Number of

experiments in database” which activates a new Report tabulating the number of experiments in the database of each type, and for each element (Table 2, Section 2.2.1.2); *Inhalation experiments summary*” which activates a new Report tabulating a summary of the inhalation experiments for a specified element. A button was also added to open the new “Modifications to database” Form (see below).

- *“References” Table and Form:* New Fields “Paper” added [originally OLE Object, but subsequently changed to hyperlink] and “Spreadsheet” [hyperlink]. These are used to link to a document (eg WORD or pdf file) or spreadsheet, respectively, related to that Reference (Table 1).
- *References, all Experiment Tables, and associated Forms:* Field “History” [memo] added and corresponding field “Entered by”. This is used to document the name of the person entering the record (and the date), and subsequent modifications. The method of linking to related documents and spreadsheets was changed from OLE (object linking and embedding) to hyperlinks. This had several advantages, including easier linking to new files, faster scrolling through records, and reduced file size.
- *All Experiment Tables and associated Forms:* New fields were added for: Strain; Sex; Mass; Age (D/W/M/Y); Transfer to fetus; Transfer to milk.
- *Inhalation Experiments Table:* Sub-forms were added to allow an experiment to be linked to more than one ingestion experiment and more than one injection experiment. A new field: “ICRP 30/68 class” (D/W/Y), and a check-box to identify experiments that gave useful information on particle transport rates, were added.
- *Ingestion Experiments Table:* A sub-form was added to allow an experiment to be linked to more than one injection experiment. New fields were added relating to the amount administered: “ $\mu\text{g}/\text{kg}$ ” and “ kBq/kg ”.
- *Injection Experiments Table:* “admin” field was added for consistency with the inhalation and ingestion experiments tables. New fields were added relating to the amount administered: “ $\mu\text{g}/\text{kg}$ ” and “ kBq/kg ”.
- *Elements Table:* Extended to include all 91 elements covered in ICRP Publications 30 and 68 (ICRP 1979, 1994b).
- *Modifications to database:* A new Table, with associated Form, was added. It is used (mainly by the database manager) to document changes to the Master database: both changes to its structure and to the data, e.g. entry of blocks of data.

Disclaimer Form: extended with: “It should be noted that comments and inferences made reflect the judgements of those who entered the information, and may be subjective in nature. Users should consult the original publications for full details and to draw their own conclusions.” Macros were changed, so that the database opens with the disclaimer, and the user has to click “OK” (signifying acceptance) to reach the Main menu.

2.1.2 Data entry

At the end of the Fourth Framework Programme in June 1999, the database contained 103 References, with information on 288 experiments (Table 2). (This had been increased to 376 experiments by the start of this project in January 2001). The stated aim of the project was to increase this to about 900 experiments by the original end date

of the contract (December 2003), i.e., to add about 200 experiments per year. As shown in Figure 7, a much higher rate of record entry was achieved throughout. At the end of December 2004 the database contained 698 references, with information on 1888 experiments (936 inhalation, 514 ingestion and 438 injection), greatly exceeding the original target. **This is the main achievement of the project.** There is sufficient content that it has now become useful to search for information. The usefulness has increased with increasing number of records, and as its coverage of each element became more comprehensive.

During the Fourth Framework Programme, the emphasis was placed on inhalation as the route of entry, and this is reflected in the initial distribution of records between the three routes of entry (1999, Figure 8). During this project, all three routes were considered explicitly, and the proportion of ingestion and injection experiments initially rose quickly, and then remained stable.

Table 2. Progress in entering information into RBDATA.

	References	Experiments			Total
		Inhalation	Ingestion	Injection	
June 1999	103	218	35	35	288
January 2001	163	257	68	51	376
December 2001	275	343	211	128	682
December 2002	469	595	333	241	1170
December 2003	584	800	450	364	1614
December 2004	698	936	514	438	1888

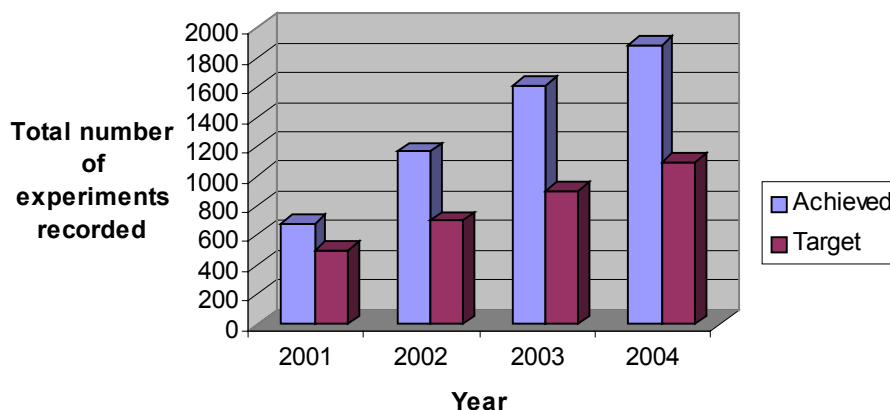


Figure 7. Progress in data entry: total number of experiments recorded by the end of each year of the project, compared to target.

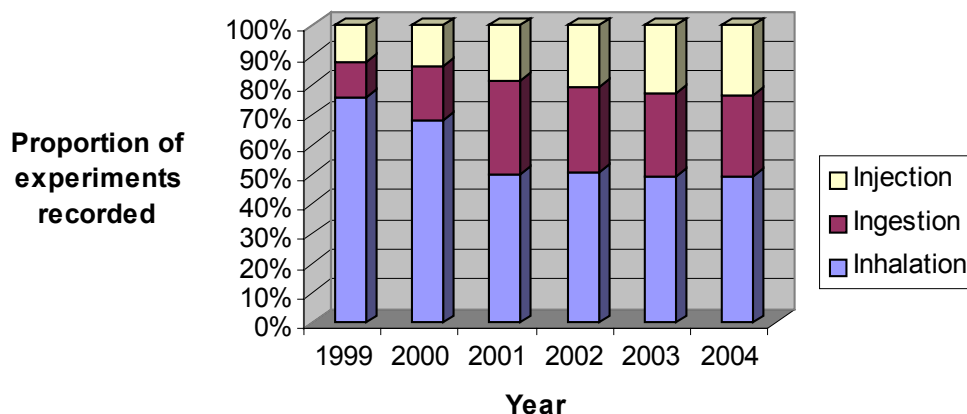


Figure 8. Progress in data entry: number of experiments of each type recorded by the end of each year.

As shown in Table 3, there is some information relating to 62 out of the 91 elements covered in ICRP Publications 30, 68 and 72. However, as shown in Figure 9, there are no entries yet for 29 elements, and less than four entries each for 14 other elements. As might be expected most entries relate to important actinides, fission and activation products. More than 50% of the records relate to six elements: plutonium (19%), uranium (11%), cobalt (8.3%), americium (5.0%), strontium (4.2%), and neptunium (3.7%). Figure 10 shows the distribution of records between elements, with the twelve elements having most entries identified.

By the end of the project there were also more than 30 spreadsheets and 7 documents (Section 2.2.1.1) linked to the database (Table 1).

As noted above, some additional fields were included during the programme, after some records had been entered. It was therefore necessary to review and update many records, especially those entered before January 2001.

Table 3 Numbers of each type of experiment in the database (December 2004)

Element	January 2001				December 2004				Additions			
	Inhalation	Ingestion	Injection	Total	Inhalation	Ingestion	Injection	Total	Inhalation	Ingestion	Injection	Total
Actinium	2			2	2		1	3			1	1
Aluminium		1	2	3		1	2	3				
Americium	23			23	67	11	16	94	44	11	16	71
Antimony					17	4	1	22	17	4	1	22
Arsenic		1		1	2	1		3	2			2
Barium			1	1	26	10	10	46	26	10	9	45
Berkelium							1	1			1	1
Beryllium						6	26	32		6	26	32
Bismuth					9	1	7	17	9	1	7	17
Cadmium		1		1		2		2		1		1
Caesium	8	3	2	13	25	11	5	41	17	8	3	28
Calcium			1	1	4	15	8	27	4	15	7	26
Californium					3		4	7	3		4	7
Carbon					10			10	10			10
Cerium	4			4	16	9	14	39	12	9	14	35

RADIONUCLIDES BIOKINETICS DATABASE (EULEP)

Element	January 2001				December 2004				Additions			
	Inhalation	Ingestion	Injection	Total	Inhalation	Ingestion	Injection	Total	Inhalation	Ingestion	Injection	Total
Chromium					7	1	1	9	7	1	1	9
Cobalt	69	20	19	108	80	41	35	156	11	21	16	48
Curium	3				28	6	4	38	25	6	4	35
Einsteinium					3	1	6	10	3	1	6	10
Europium					1	4	2	7	1	4	2	7
Gadolinium					7	3	6	16	7	3	6	16
Gold					2			2	2			2
Hafnium					3			3	3			3
Hydrogen					3			3	3			3
Indium					16	1	2	19	16	1	2	19
Iodine					5	1		6	5	1		6
Iridium					1	4	6	11	1	4	6	11
Iron	1			1	10	4	3	17	9	4	3	16
Lanthanum	1	1	2	4	2	1	2	5	1			1
Lead		1		1	27	12	9	48	27	11	9	47
Manganese	1			1	6	10	12	28	5	10	12	27
Mercury	1			1	8	5	5	18	7	5	5	17
Neptunium	1	29	7	37	9	48	13	70	8	19	6	33
Niobium					9	7	17	33	9	7	17	33
Phosphorus						1	2	3	0	1	2	3
Plutonium	66	10	9	85	187	111	66	364	121	101	57	279
Polonium					2	2	1	5	2	2	1	5
Promethium						1	1	2		1	1	2
Protactinium	1			1	1			1				
Radium					9		2	11	9		2	11
Ruthenium	2			2	9	28	10	47	7	28	10	45
Scandium							1	1			1	1
Selenium						16	20	36		16	20	36
Silicon					7			7	7			7
Silver	1			1	3	8	10	21	2	8	10	20
Sodium					2	2	2	6	2	2	2	6
Strontium			1	1	17	46	17	80	17	46	16	79
Sulphur					2			2	2			2
Tantalum	1				2	1		3	1	1		2
Technetium						9	5	14	0	9	5	14
Tellurium					9	20	15	44	9	20	15	44
Terbium	6			6	6			6				
Thallium					9	1	4	14	9	1	4	14
Thorium	5		6	11	31		9	40	26	0	3	29
Tin					1	6	9	16	1	6	9	16
Titanium					4			4	4			4
Tungsten					1	2	1	4	1	2	1	4
Uranium	57	1	1	59	186	8	16	210	129	7	15	151
Vanadium							3	3			3	
Yttrium					4	3	3	10	4	3	3	10
Zinc	2			2	13	22	14	49	11	22	14	47
Zirconium	2			2	23	7	9	39	21	7	9	37
Total	257	68	51	376	936	514	438	1888	679	446	387	1512

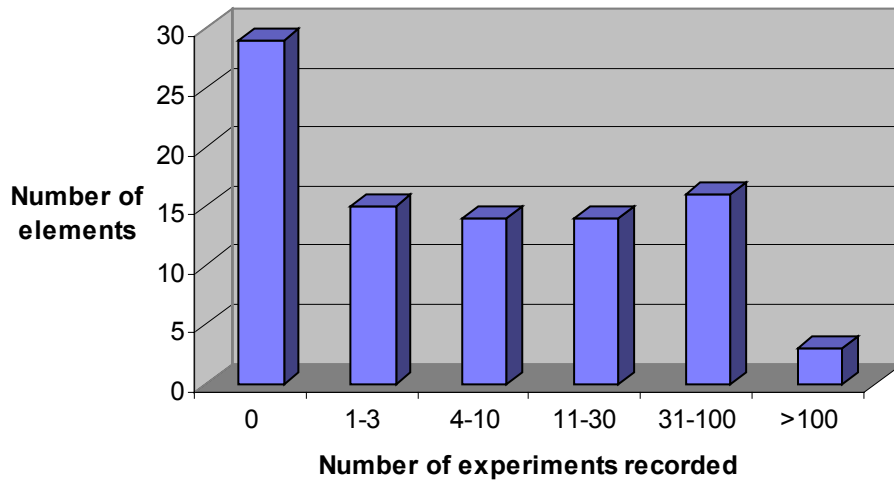


Figure 9 Number of elements (from the 91 considered in ICRP Publications 30, 68 and 72) with a given range of number of entries. Thus, for 16 elements there are between 31 and 100 experiments recorded

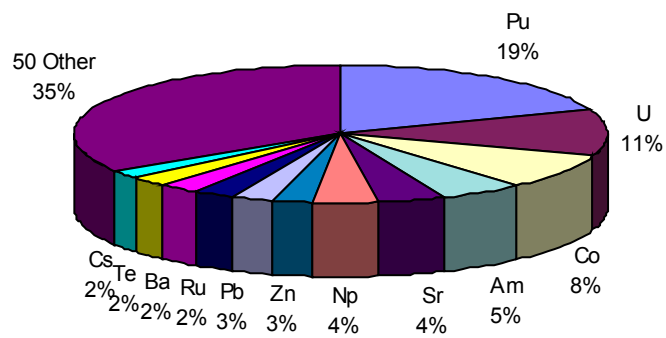


Figure 10 Distribution of records among the 62 elements: the 12 with most entries are identified. A figure of 2% represents 40–50 entries.

2.1.3 Derivation of HRTM absorption parameter values from experimental data

It is not a simple task to derive values of the parameters that define absorption to blood for use in the HRTM from *in vivo* experimental data. A suitable parameter-fitting program (GIGAFIT, Graphically Interactive General Algorithm for FITting, Birchall et al., 1995) has been developed at NRPB and was already used by a few of the members. A workshop to train other members in the use of this software was held at NRPB in June 2001. The workshop involved the participants working through a series of examples of increasing complexity, using GIGAFIT.

A method that had been developed at CEA (Ramounet et al., 2000) to obtain estimates of the rapid fraction (f_r) and the slow dissolution rate (s_s) for relatively insoluble (Type S) materials was also described at the workshop. The amount absorbed into blood, $B(\tau)$ at time τ after intake was obtained by multiplying the amount in skeleton by a factor of approximately two for plutonium and three for americium. This was related to f_r and s_s using the cumulative lung activity as follows:

$$B(\tau) = f_r \text{ IDLD} + s_s \sum_0^{\tau} \text{ DLD}$$

where $\sum \text{ DLD}$ is the cumulative deep lung deposit from time 0 to time τ , expressed in terms of IDLD, the initial deep lung deposit. A plot of $B(\tau)/\sum \text{ IDLD}$ versus time gives f_r as the intercept and s_s as the gradient. An advantage was that it gave estimates of errors on the values of the parameters.

2.1.4 Provision of access to the database through the Internet

A web site was developed by NRPB IT (Information Technology) Systems Group using Macromedia Dreamweaver UltraDev 4. This enables it to be run on a Windows server, with a user's own web browser. A web site was set up on an NRPB server with the domain name www.rbdata.org. Access to it is restricted by means of required username and password, which are provided by the database manager to appropriate users.

Figure 11 shows the "Welcome" page of the web site. It displays a logo, brief description, and acknowledgement to the EC Contract support.

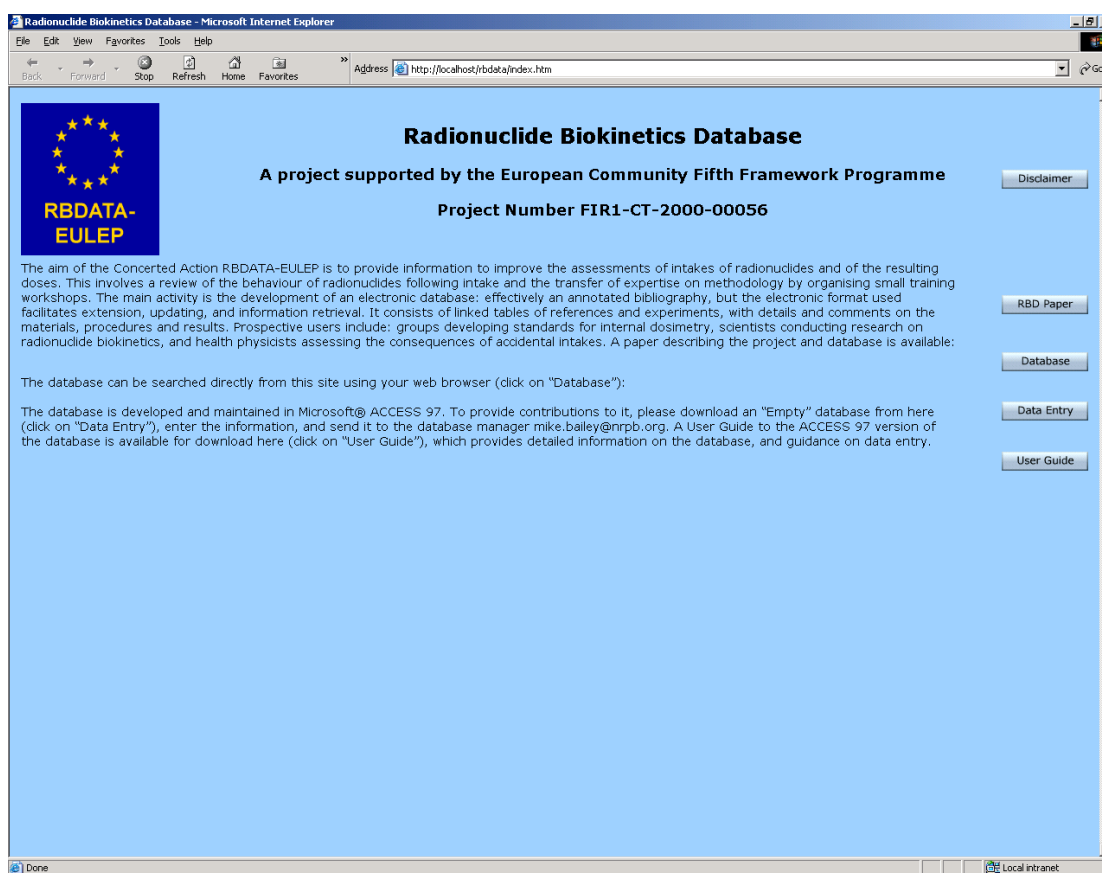


Figure 11. Welcome page of the web site www.rbdata.org

Buttons provide the following functions:

Disclaimer

Information similar to the “about” screen of the database.

RBD paper

Further information: the text of the paper by Bailey et al (2003) as a pdf.

Data Entry

This downloads a blank copy of the ACCESS database. A user can contribute to the database by entering information, and returning it to the database manager (mike.bailey@hpa-rp.org.uk)

User Guide

This downloads a copy of the User Guide to the ACCESS 97 version of the database (Bailey, 2005, as a pdf), which provides detailed information on the database, and guidance on data entry.

Database

This opens the “Home” page of the web site, giving direct access to the database contents, using a web browser (Figure 12). This provides most of the search and display functions available from the “Main screen” of the ACCESS database (Figure 6):

- Find information on each type of experiment (inhalation, ingestion or injection) according to element and chemical form, giving the Experiment (record) numbers, summary information, and (optionally) the numbers and summary information about the References linked to the experiments found.
- Find all References by a specified author.
- View the detailed information in each record: i.e. each Reference or Experiment.
- View the table giving the number of Experiments in the database for each element and type of Experiment (inhalation, ingestion or injection).

It also enables identification of all the references linked to a selected experiment (Inhalation, Ingestion or Injection).

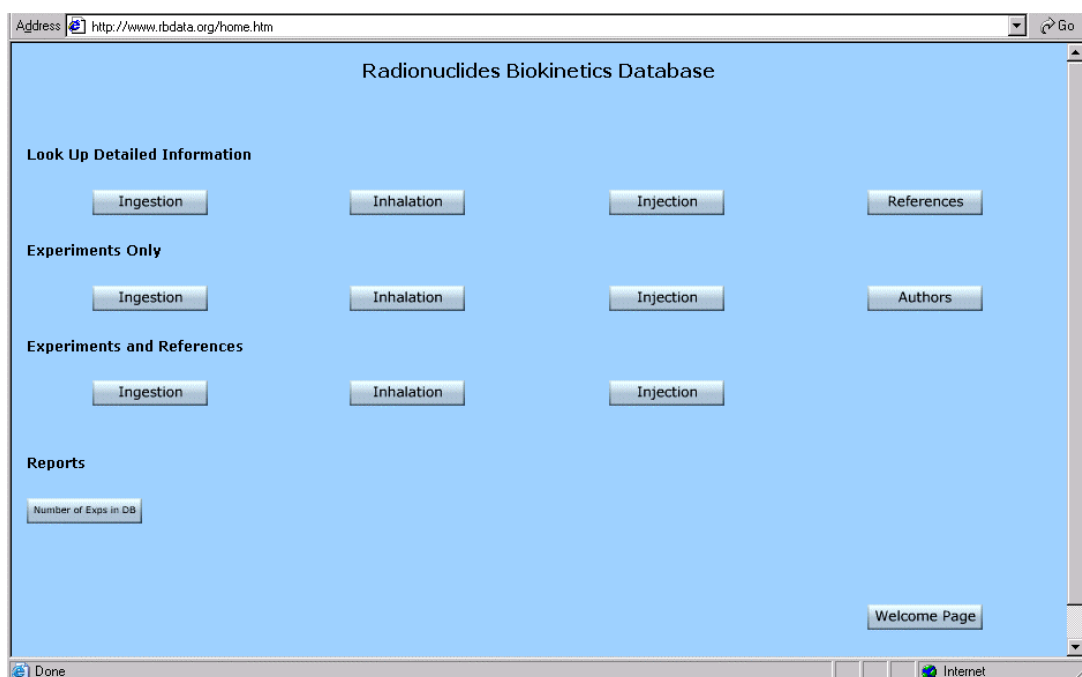


Figure 12. RBDATA web site home page

2.2 Work-package 2: Guidance on methodology to determine biokinetics

The second activity concerned the transfer to young scientists of expertise on (i) experimental methods related to biokinetics such as inhalation facilities, *in vitro* dissolution techniques, and analytical methods, and (ii) computer modelling to derive absorption parameter values from experimental data. Short workshops were organised for this purpose.

2.2.1 Course 1 Experimental techniques

A general course on experimental techniques was held on 13/14 October 2003 at GSF Munich. It consisted of three presentations, including a talk on human biokinetic studies, and a visit to the experimental facilities at GSF. It was attended by young scientists from

GSF, IRSN, NRPB and CIEMAT (Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas, Spain).

Short courses (1–2 days) on specific topics were also arranged for young scientists from the members' institutes. Courses took place on inhalation of radioactive materials at CEA, Bruyères-le-Châtel (June, 2002) and on *in vitro* dissolution techniques and aerosol characterisation at IRSN, Pierrelatte (October, 2002). The course at CEA involved practical demonstrations on exposure by inhalation and a tour of the CEA facilities. The course at IRSN included formal lectures and practical experience on *in vitro* techniques and aerosol characterisation and also involved a visit to the IRSN laboratories.

2.2.2 Course 2 Interpretation of experimental data

This course was held at GSF Munich on 14/15 October 2003, following Course 1, to minimise costs for those students from IRSN, CIEMAT, GSF and NRPB who attended both. It included training in the use of the parameter-fitting program (GIGAFIT) that was developed at HPA-RPD (formerly NRPB) (Section 2.1.3).

An additional short course for CEA staff was held in January 2003. This involved a member of staff from NRPB visiting CEA to discuss and give guidance on analysis of plutonium lung clearance experiments. The advice was promulgated in a collaborative paper (Rateau-Matton et al., 2005).

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The partner institutes (EULEP members as identified on the title page) therefore provided staff time and other resources.

The identified lead scientist from each member institute was as follows:

HPA-RPD	M R Bailey (Co-ordinator)
IRSN	V Chazel
CEA	P Fritsch
GSF	W G Kreyling
AEAT	D Newton
UWC	D M Taylor
KI	M Svartengren (following the death of P Camner)

Contributions from other staff at these institutes are gratefully acknowledged, including:

- HPA-RPD N Stradling (Leader of Work Package 2).
 A Hodgson (Course trainer; participant at meetings; contributor to database records)
 S Wenman-Bateson and P Lomas (web site development).
 F Smith (database development)
- IRSN F Pacquet, M Donnadiou-Claraz, F Petitot (participants at meetings)
- CEA E Ansoborlo (original co-ordinator of proposal, participant at meetings; contributor to database records)
 B Ramounet-Le Gall, J Delforge (participants at meetings)

In addition, M Á Morcillo Alonso of CIEMAT contributed database records.

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On 1 April 2005 NRPB became the Radiation Protection Division (RPD) of the Health Protection Agency (HPA).

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APPENDIX A Glossary

AEAT	AEA Technology
Bq	Becquerel (one nuclear transformation per second)
CEA	Commissariat à l'Energie Atomique
CIEMAT	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas
D	Germany
Σ DLD	cumulative deep lung deposit
EC	European Commission
EU	European Union
EULEP	European Late Effects Project Group
EURADOS	European Radiation Dosimetry Group
F	France
f_r	Fraction of particulate matter in the respiratory tract that dissolves rapidly
GIGAFIT	Graphically Interactive General Algorithm for FITting
GSF	Forschungszentrum für Umwelt and Gesundheit, GmbH
HAT	Human Alimentary Tract
HRTM	Human Respiratory Tract Model
ICRP	International Commission on Radiological Protection
IDEAS	General guidelines for the estimation of committed dose from incorporation monitoring data (EC 5 th Framework Project)
IDLD	initial deep lung deposit
INDOS	ICRP Task Group on Internal Dosimetry
IPSN	Institut de Protection et de Sûreté Nucléaire
IRSN	Institut de Radioprotection et de Sûreté Nucléaire
IT	Information technology
KI	Karolinska Institute
MS	Microsoft®
NRPB	National Radiological Protection Board
RBDATA	Radionuclides Biokinetics Database
SCK•CEN	Belgian Nuclear Research Centre
SE	Sweden
s_r	Rapid dissolution rate (of particles in the respiratory tract)
s_s	Slow dissolution rate (of particles in the respiratory tract)
UK	United Kingdom
UWC	University of Wales, Cardiff