

CEA-EXPO: A facility exposure matrix to assess passed exposure to chemical carcinogens and radionuclides of nuclear workers

M. TELLE-LAMBERTON^{1,2}, P. BOUVILLE¹, D. BERGOT¹, M. GAGNEAU¹,
S. MAROT¹, J.M. GIRAUD³, J.M. GELAS⁴

(Manuscript received 29 September 2004, accepted 24 January 2005)

ABSTRACT A “Facility-Exposure Matrix” (FEM) is proposed to assess exposure to chemical carcinogens and radionuclides in a cohort of nuclear workers. Exposures are to be attributed in the following way: a worker reports to an administrative unit and/or is monitored for exposure to ionising radiation in a specific workplace. These units are connected with a list of facilities for which exposure is assessed through a group of experts. The entire process of the FEM applied in one of the nuclear centres included in the study shows that the FEM is feasible: exposure durations as well as groups of correlated exposures are presented but have to be considered as *possible* rather than *positive* exposures. Considering the number of facilities to assess (330), ways to simplify the method are proposed: (i) the list of exposures will be restricted to 18 chemical products retained from an extensive bibliography study; (ii) for each of the following classes of facilities: nuclear reactors, fuel fabrication, high-activity laboratories and radiation chemistry, accelerators and irradiators, waste treatment, biology, reprocessing, fusion, occupational exposure will be deduced from the information already gathered by the initial method. Besides taking into account confusion factors in the low doses epidemiological study of nuclear workers, the matrix should help in the assessment of internal contamination and chemical exposures in the nuclear industry.

Key-words: job exposure matrix / chemical exposure / nuclear workers / epidemiology

RÉSUMÉ CEA-EXPO : Une matrice installations-expositions pour évaluer les expositions internes aux radionucléides et les expositions chimiques des travailleurs du nucléaire.

Une matrice emplois-expositions (MEX) est proposée pour évaluer l'exposition aux cancérigènes chimiques et aux radionucléides d'une cohorte de travailleurs du nucléaire. Les expositions sont attribuées de la façon suivante : un travailleur est rattaché à une unité administrative et/ou surveillé pour les rayonnements ionisants à un lieu de travail déterminé. Ces unités sont reliées à une liste d'installations pour lesquelles un groupe d'experts évalue les expositions. La réalisation complète de la

¹ IRSN/DRPH/SRBE/LEPID, B.P. 17, 92262 Fontenay-aux-Roses Cedex, France.

² Present address: Institut de Veille Sanitaire, Département Santé Travail, 12 rue du Val d'Osne, 94415 St Maurice Cedex, France.

³ CEA, 31-33 rue de la Fédération, 75752 Paris Cedex 15, France.

⁴ COGEMA, 2 rue Paul Dautier, B.P. 4, 78141 Vélizy-Villacoublay Cedex, France.

matrice emplois-expositions pour l'un des centres nucléaires inclus dans l'étude montre que celle-ci est réalisable. Les durées d'exposition ainsi que les groupes d'expositions corrélées sont présentées mais doivent être considérés comme des expositions *potentielles* plus que *réelles*. Étant donné le nombre d'installations à expertiser (330), une méthode simplifiée est proposée : (i) la liste d'expositions sera restreinte aux 18 produits chimiques retenus après une étude bibliographique détaillée ; (ii) pour chaque classe d'installations : réacteurs, fabrication de combustible, laboratoires haute-activité et radiochimie, accélérateurs et irradiateurs, traitement de déchets, biologie, retraitement, fusion, les expositions seront déduites de l'information recueillie par la méthode initiale. En plus de la prise en compte des facteurs de confusion dans l'étude épidémiologique sur les faibles doses chez les travailleurs du nucléaire, la matrice aidera à l'évaluation historique de la contamination interne et des expositions chimiques dans l'industrie nucléaire.

1. Background

As part of the cohort study on the effects of ionizing radiation among the 50,000 nuclear workers employed by the CEA-COGEMA group, it was decided to assess their exposure to the carcinogenic substances used in the work-place. In the nuclear industry, workers are predominantly exposed to X and gamma rays and exposure to these radiation types is relatively well measured by ongoing monitoring (use of personal dosimeters), as required by government regulations. Up to now, the literature reports a link between X and gamma radiation in nuclear industry work, and the following disorders: leukaemia (Wiggs *et al.*, 1991; Gribbin *et al.*, 1993; Omar *et al.*, 1999; Ritz *et al.*, 1999; Telle-Lamberton *et al.*, 2004; Zablotska *et al.*, 2004; Carpenter *et al.*, 1994; Cardis *et al.*, 1995; Muirhead *et al.*, 1999), multiple myeloma (Omar *et al.*, 1999; Cardis *et al.*, 1995; Muirhead *et al.*, 1999; Iwasaki *et al.*, 2003) and lung cancer (Wiggs *et al.*, 1991; Ritz *et al.*, 1999; Beral *et al.*, 1988; Ritz, 1999). However, workers involved in nuclear fuel fabrication and reprocessing as well as research, use many carcinogenic substances. Results from the literature suggest that the detrimental effects of radiation are not specific and that cofactors, such as internal contamination or chemical products, may be involved. Unfortunately, those exposures are more difficult to measure.

In this context, it appeared useful to determine the carcinogens – in addition to X- and γ -rays – to which the 50,000 radiation workers of the CEA-COGEMA group included in the cohort study had been exposed. Our objective was two-fold: to develop a tool for assessing the occupational exposure to carcinogens of the CEA-COGEMA workers, and to eliminate the possible role of these exposures as confounding factors in the analysis of the relation between ionising radiation and cancer (stratified sub-group analysis). To carry out this goal, a working group was brought together, made up of the medical co-ordinators of CEA and of COGEMA, together with specialists in occupational medicine, radiation protection, toxicology, history of science and techniques, and epidemiology.

The group faced the following choice: occupational exposures could be studied either individual by individual, using “hazard forms” completed by the occupational medicine department, or through an assessment of the exposures in the different facilities where the workers were employed.

The hazard forms list the exposures associated with the job description of the worker concerned. Hazard forms have existed since the end of the 1950s, albeit inconsistently, depending on the specific workplace. Their usefulness has been demonstrated for a cohort composed of 400 workers (Baysson *et al.*, 2000). Nonetheless, generalizing this method to 50,000 workers presents the following problems: (i) the data from the hazard forms alone are sometimes quite fragmentary; recourse to workers’ memories can be required on a case-by-case basis (Jéjati *et al.*, 1998); (ii) these forms were shaped into a systematic structure only recently, which means that mass data entry would be inordinately difficult; (iii) the hazards mentioned are those assessed by an occupational physician and can vary from one physician to another, as well as from one period to another; they can also be influenced by the existence of money compensation for work with some hazards.

In this context, we decided to proceed through an assessment of exposures in the facilities and develop a “facility-exposure” matrix (FEM), by analogy with the job-exposure matrices commonly used in occupational epidemiology and developed substantially during the 1980s (Goldberg *et al.*, 1993; Bouyer and Hemon, 1994). They have been particularly useful for retrospective exposure assessment in large-scale studies for which individual exposure assessments by a direct method were impossible (Guenel *et al.*, 1993; Moulin *et al.*, 1997). Their performances have been assessed in smaller case-control studies, by comparison with individual exposure methods such as subject self-assessment, questionnaires about work, and expert assessment by industrial hygienists (Ahrens *et al.*, 1993; Orłowski *et al.*, 1993; Stengel *et al.*, 1993). To validate them, it is also possible to consider already-known associations between exposures and diseases, as was done for the MATEX matrix for EDF-GDF workers (Imbernon *et al.*, 1995). The conclusions of these validation studies encourage the further development of job-exposure matrices in occupational epidemiology.

Performances of Job-Exposure Matrices can be improved by including the following two elements: the probability of exposure in a given job, rather than a binary “yes/no” exposure variable and the definition of matrices specific for given plants or industrial sectors. The probability of exposure estimated by the proportion of workers exposed in a given job improves estimation of the odds-ratio and avoids the loss of statistical power associated with a dichotomous assessment (Bouyer and Hemon, 1993). Another means of improving the performance of

a matrix is to introduce not only the occupation but also the industrial sector or the facility or the work environment. Accuracy improves, with a reduction in the classification errors and a consequent improvement in statistical power (Bouyer and Hemon, 1994), as mentioned by several studies (Kauppinen and Partanen, 1988; Heineman *et al.*, 1994; Kelsh *et al.*, 2000). Considering the difficulties of using jobs, as defined in the personnel files, which are not precise enough to be associated with occupational risks, we decided to develop a Facility-Exposure Matrix, “CEA-EXPO”, rather than, a Job-Exposure Matrix. In our context, facilities carry out specific industrial activities, from which possible exposures can be deduced as will be seen in the results section.

2. Method

2.1. The original facility-exposure matrix method

Exposures were to be attributed the following way:

worker → facility → exposure.

Into this path two intermediate variables had to be introduced: the administrative department to which the worker reported and the different workplaces where he was monitored for exposure to ionising radiation, the only usable information available in the workers' files.

We thus had to follow this path:

worker → administrative department or workplace → facility → exposure.

Before establishing this correspondence, it was necessary to define and delimitate facilities in a relevant way and to choose the exposures to assess. Then, exposures had to be collected facility by facility and, finally, the connection between workers and facilities had to be made.

Two lists of facilities were available to define our own classification: the nomenclature of “basic nuclear facilities” (installations nucléaires de base: INB) and this of “facilities requiring classification for environmental protection” (installations classées pour l'environnement: ICPE). The first defines industrial units to be considered when safety requirements have to be satisfied. It may be for instance a nuclear reactor or a radiological laboratory. The second is used for non radiological environmental regulations; it may be for instance a decommissioned nuclear facility. We used these two lists and added some facilities not fitting within these nomenclatures for historical reasons, either because they were closed before

the nomenclatures existed or for practical necessity such as defining a group for the radiation protection department, whose personnel are by definition mobile and not assigned to a particular facility. The following elements had to be collected to describe each facility: (i) key-dates (including construction, activation and, when relevant, closing, and decommissioning); (ii) administrative units that owned the facility. The latter information was essential because it was required to link workers and facilities. The first priority was to gather these data for the basic nuclear facilities as it concerned the large majority of workers. ICPE would be treated at a second stage.

The definition of exposures was based upon the list of products classified 1, 2A and 2B by IARC (IARC, 1998). The working group determined what products among this list were used at CEA and COGEMA over time. Other exposures were added to the list: toxic products which carcinogenicity has not been proven but widely used in the company and radiological exposures inaccurately measured by individual dosimeters.

The expert assessments necessary to associate the facilities with carcinogen exposures required a close collaboration between researchers and those working in the facilities. First, in order to obtain information on the exposures, meetings were held with personnel who had worked in the facility for a long period and who knew its industrial risks. They were chosen by the working group which included members who knew the personnel for long. Most of them were former health physicists or safety engineers. The meetings were moderated by an epidemiologist, a chemist, and a historian. The following information was collected for each substance retained in the matrix and for the entire lifetime of the facility: (i) approximate number of workers at the facility; (ii) percentage of workers concerned by exposure (*probability* of exposure); (iii) *frequency* of exposure (daily, frequent, occasional); (iv) *intensity* of exposure (possible, low, medium, high); (v) product handling; (vi) physico-chemical form of radionuclides. Second, the information collected during the meeting was synthesised in a table. Finally, this table was validated by subsequent feedback from participants at the meeting.

The association between workers and facilities through administrative units or workplaces necessitated a substantial task to be done through archives and interviews with employed or retired experts. The task consisted in decoding administrative unit codes and monitoring work site codes, *i.e.* finding their exact meaning, and associating them to facilities.

When the whole process described above was carried out, descriptive analyses of exposures were performed: percentage of workers exposed, and duration of exposures. Correlation analyses were also carried out in order to synthesize the

information gathered on the facilities and to define groups of correlated exposures to be considered as one confusion factor in the epidemiological analysis. These correlation analyses were made using the principal component analysis (PCA) method (Saporta, 1990). PCA allows the identification of groups of variables that are interrelated *via* phenomena that cannot be observed (Burstyn, 2004). It consists in systematically examining correlations between variables considered in the analysis. It identifies independent factors that explain the maximum amount of mutual correlation. These factors can be used further in the epidemiological analysis to make adequate adjustments. Included in this PCA were the exposure durations to products in the matrix as well as the cumulative radiation doses measured for workers from 1967 through 1994 (doses of beta, X + gamma and neutrons).

The entire original approach was applied to the Grenoble nuclear site.

2.2. Method of validation of the FEM

A validation of the exposure assessment method was carried out in Fontenay-aux-Roses site, the oldest nuclear research centre in France. The facility retained was a priori the most complicated place to assess. It is a very old facility which has had very heterogeneous activities using a lot of chemical or radiological substances. The validation consisted in comparing the assessment, through the method described above, with an assessment through an examination of archives concerning the facility. This assessment was undertaken by a specialist in the history of science and techniques. The method is extensively described in (Straus, 1996). It consisted in a systematic examination of archives of the facility for the period 1961–1980. Without knowing the results of the experts assessment, the historian reported in the same grid the dates for which a document existed proving the presence of the product in the facility. On purpose, no extrapolation was made between two dates if the product was to be found in archives dating from two different dates. The two grids were then superposed to examine the coherence.

2.3. Method of simplification of the FEM

Considering the huge task ahead, the working group looked for ways to simplify the original method. In order to reduce the number of exposures to assess, it was decided to conduct an extensive bibliographic study on the carcinogenic effects of the products retained in the initial list, and to retain only products whose carcinogenicity was similar to that of ionising radiation. In order to carry out extrapolation from information already gathered, categories of facilities with similar industrial activities were defined by the working group.

3. Results

3.1. Definition of the exposures

Products were defined by the working group on the basis of IARC classification (products in classes 1, 2A and 2B (IARC, 1998)) and as mentioned above, some products were added because of their toxicity and their widespread use in the company, despite the fact that their carcinogenicity has not been proven (for example, strong acids and dodecane). External exposures to neutrons and to low-energy X-rays were added to the initial list, as were the radionuclides that can lead to internal contamination. This decision was made after a reconstruction of dosimetric practices. This reconstruction, carried out with the aid of another working group, made up of occupational physicians, radiation protection engineers, and epidemiologists, determined that neutron dosimetry had been inadequately documented, that exposure to low-energy X-rays could lead to an overestimation of doses and that individual reconstruction of internal exposure to radionuclides was impossible on the scale of such a cohort study (Telle *et al.*, 1996). This led to the list included in Table I.

3.2. Validation of the exposure assessment method

The exposures assessed in Fontenay-aux-Roses nuclear research by examination of archives and by experts were compared. The archives did not allow us to identify exposures exhaustively. The work involved in finding and sorting through documents was enormous. Only a few discordances were observed: it appears that there was a risk of exposure to aromatic amines and PCB that was never mentioned at the meetings and there were slight discordances about dates of exposure. Among the 24 chemical products detected by the historian, 22 were cited by the experts. All radionuclides detected by the historian were cited by the expert. Experts cited 25 chemical substances and 3 radionuclides not mentioned by the historian.

3.3. Results of the feasibility study

Grenoble CEA nuclear centre contains three experimental reactors, including one training reactor; it also has two analytic laboratories and a waste treatment plant.

The worker files gave the workplace, coded by UDT (dosimetric monitoring unit). We were able to cross-check these UDTs with the corresponding facilities and thus trace workers through these facilities. Between 1967 and 1994, 1 949 agents passed through these six Grenoble facilities. The exposure at facilities being identified by year, it was possible to calculate the exposure durations. It must be borne in mind, however, that these are *possible* and not *positive* exposures.

TABLE I
Products included in the original matrix.
Produits inclus dans la matrice d'origine.

exposure	IARC classification*	EEC classification**
<i>chemical exposures</i>		
strong acids		
hydrochloric	n.c.	n.c.
nitric	n.c.	n.c.
sulfuric	1	n.c.
perchloric	n.c.	n.c.
sulfochromic	n.c.	n.c.
sulfamic	n.c.	n.c.
hydrofluoric acids and fluorides	n.c.	n.c.
asbestos	1	1
aromatic amines	1	n.c.
aniline	2B	n.c.
antimony and compounds	2B	n.c.
arsenic	1	1
solvents		
benzene	1	1
toluene	2B	2
xylene	3	n.c.
chloroform	2B	3
carbon tetrachloride	2B	3
trichloroethylene	2A	3
perchloroethylene	2A	n.c.
carbon sulfide	n.c.	n.c.
dodecane	n.c.	n.c.
aromatic and paraffinic diluents	n.c.	n.c.
tert-butyl-benzene	n.c.	n.c.
beryllium	1	2
cadmium and compounds	1	2
chrome and compounds	1	1
cobalt and compounds	2B	n.c.
gasoline	2B	2
tar and derivatives	1	2
cutting oils or lubricants	1	1
mineral oils	1	1

TABLE I (Continued).

Exposure	IARC classification*	EEC classification**
insecticides	2A	3
carpentry and joinery	1	n.c.
heavy metals		
lead	2B	1
mercury	3	n.c.
nickel and compounds	1	1
pcb	2A	n.c.
silica sio2	1	n.c.
bases	2B	n.c.
sodium hydroxide	n.c.	n.c.
potash	n.c.	n.c.
ammonia	n.c.	n.c.
hydrazine	2B	2
organophosphorous compounds	2A	n.c.
tri-butyl-phosphate	n.c.	n.c.
thenoyltrifluoroacetone	n.c.	n.c.
<i>other chemical exposure</i>	n.c.	n.c.
tri-lauryl-amine	n.c.	n.c.
alcohols	n.c.	n.c.
acetone	n.c.	n.c.
nitrogen oxide	n.c.	n.c.
talc	n.c.	n.c.
silver salts	n.c.	n.c.
hydrogen peroxide	n.c.	n.c.
DTPA	n.c.	n.c.
oxalic oxide	n.c.	n.c.
amides	n.c.	n.c.
di-amides	n.c.	n.c.
pyridinic compounds	n.c.	n.c.
sulfured or nitrogenated compounds	n.c.	n.c.
<i>lab animal care</i>	n.c.	n.c.
<i>ultra-violet rays</i>	2A	n.c.
<i>internal radiological exposures</i>	n.c.	n.c.
plutonium and transplutoniums		
plutonium	1	n.c.
americium	n.c.	n.c.

TABLE I (Continued).

Exposure	IARC classification*	EEC classification**
curium	n.c.	n.c.
californium	n.c.	n.c.
uranium		
natural	n.c.	n.c.
less than 3% enrichment	n.c.	n.c.
3 to 30% enrichment	n.c.	n.c.
30 to 90% enrichment	n.c.	n.c.
more than 90% enrichment	n.c.	n.c.
thorium	1	n.c.
neptunium	n.c.	n.c.
radon	1	n.c.
radium	1	n.c.
fission products		
cesium	n.c.	n.c.
iodin	1	n.c.
others	n.c.	n.c.
activation products		
cobalt	n.c.	n.c.
others	n.c.	n.c.
other radionuclides,		
tritium	n.c.	n.c.
phosphore 32	1	n.c.
carbon 14	n.c.	n.c.
sulfur 35	n.c.	n.c.
<i>other radiological exposures</i>		
low energy X rays	n.c.	n.c.
neutrons	n.c.	n.c.

* (1) "Sufficient evidence" of carcinogenicity in humans, (2) "Limited evidence" of carcinogenicity; (2A) probable carcinogenicity; (2B) possible carcinogenicity, (3) "Inadequate evidence" of carcinogenicity. (n.c.) not classified.

** (1) "proven carcinogen", (2) "must be treated as a carcinogen", (3) "possible carcinogen", (n.c.) not classified.

Possible exposures with the highest frequency and the highest duration of exposures were: cutting oil, uranium and neutrons (Tab. II). Behind these come benzene, toluene, xylene, and sodium hydroxide. Among the occasional exposures over a long period of time, we note: cobalt, tritium, plutonium, mineral oils, carbon, mercury, cadmium, and neptunium. On the other hand, there was almost no exposure to acids. Among the products for which the frequency of use or

TABLE II
Mean durations of possible exposures for workers of the Grenoble basic nuclear facilities.
Durées moyennes des expositions potentielles pour les travailleurs des installations nucléaires de base de Grenoble.

daily or frequent exposure		occasional exposure		other exposures (frequency not specified)	
exposure	mean (yrs)	exposure	mean (yrs)	exposure	mean (yrs)
cutting oils	4.9	cobalt, tritium	5.3	asbestos	4.6
slightly enriched uranium	4.7	plutonium	4.7	cesium, iodines	3.6
neutrons	4.1	mineral oil	4.4	tetrachloroethylene	3.2
uranium enriched more than 30%	4.1	carbon 14, carbon tetrachloride	4.4	silica	2.5
benzene, toluene, xylene	2.9	mercury	4.2	americium	1.2
sodium hydroxide	2.3	cadmium	3.7	radon	1.1
thorium	1.4	neptunium	3.3	sulphuric acid	0.2
hydrochloric acid	1.4	oxalic acid	2.7	chrome and compounds	0.1
TTA	1.1	lead	2.5	gasoline	0.1
		trichloroethylene	1.9	aromatic amines	0.04
		perchloroethylene	1.8	tributylphosphate (TBA)	0.04
		low-energy X-rays	1.8		
		potash, ammonia, phosphorus, sulphur	1.2		
		chloroform	1.1		
		nitric acid	0.8		
		perchloric acid	0.2		
		carbon sulphide	0.2		

exposure could not be determined, some were present over a significant period of time: asbestos, cesium, iodine, and tetrachlorethylene.

A principal component analysis (PCA) (Saporta, 1990) was then carried out. Four groups of closely inter-correlated exposures were deduced from this analysis, shown in Table III, in decreasing order of exposure.

3.4. Progress of the assessment through the original FEM method

Progress on the matrix has varied between centres. A list of 330 facilities at 14 nuclear centres has been established and indicates the extent of the work ahead. For more than 300 facilities, complete expert appraisals for tritium and neutrons

TABLE III

Exposures, grouped according to the principal component analysis (classed within each group in decreasing order of exposure duration).

Expositions regroupées par analyse en composantes principales (classées au sein de chaque groupe par ordre décroissant de durée d'exposition).

group 1	group 2	group 3	group 4
cobalt	silica SiO ₂	nitric acid	sodium hydroxide
tritium	oxalic acid	benzene	trichloroethylene
cutting oils	tetrachloroethylene	toluene	tars and derivatives
asbestos	cesium	xylene	low-energy x-rays
uranium	iodines		perchloroethylene
plutonium	other solvents		gasoline
carbon tetrachloride	neutrons		sulfuric acid
mineral oils	cadmium and compounds		carbon sulphide
carbon 14	other heavy metals		perchloric acid
mercury	neptunium		thorium
	other fission products		radon
	lead		americium
			chloroform
			ultraviolets
			TTA
			other radionuclides
			potash
			ammonia
			sulphur 35
			phosphorus 32

have been completed. Detailed characteristics cited above concerning facilities were collected for more than half of them. For 51 facilities, local expert meetings have taken place to assess all the exposures (chemicals and radionuclides). Validation of the original method was very encouraging: the analysis of the results obtained at Fontenay-aux-Roses and our comparison of them with the data from the archives showed a high consistency. The analysis of exposures at Grenoble showed that development of the matrix was possible on condition that (i) the codes for workplace or administrative department included in the worker files could be associated with facilities (ii) we accept a possible rather than real exposure estimate. The whole process, however, was considered to be much too time consuming. The group thus decided to define a simplified matrix, with a simpler method of assessing exposure.

3.5. Proposed simplified method

3.5.1. New list of exposures

Chemical carcinogens to retain were those which could provoke ionizing radiation related cancers (confusion factors). The extensive bibliographical study led us to consider the following list: hydrofluoric acid and its fluorinated derivatives (involved in haematopoietic, broncho-pulmonary, prostate, and bladder cancers); asbestos (broncho-pulmonary, pleural, peritoneal, ovarian, and digestive cancers); aromatic amines (bladder and skin cancers); antimony (broncho-pulmonary cancers); arsenic (broncho-pulmonary, skin, liver, and larynx cancers); benzene (leukemia); beryllium (broncho-pulmonary cancers); cadmium (broncho-pulmonary and prostate cancers); chrome (broncho-pulmonary, liver, and nasal and sinus cancers); tar and its polycyclic aromatic hydrocarbon derivative (skin, broncho-pulmonary, prostate, and bladder cancers); aliphatic hydrocarbons (haematopoietic cancers); cutting oils (skin, digestive and nasal and sinus cancers); hydrazine (broncho-pulmonary, liver, blood, and nasal and sinus cancers); UV (skin cancers); nickel (broncho-pulmonary, nasal and sinus, and digestive cancers); PCB (polychlorinated biphenyls: haematopoietic cancers); silica (broncho-pulmonary cancers). Electromagnetic fields were added to the list due to the use of particle accelerators in nuclear research centres.

3.5.2. Extrapolation of detailed exposures

The following classes of facilities were judged by the working group as being fairly homogeneous due to their occupational exposures patterns: (i) nuclear reactors or piles (light-water, heavy-water, graphite gas); (ii) fuel fabrication; (iii) high-activity laboratories, and radiation chemistry; (iv) accelerators and irradiators; (v) waste treatment; (vi) biology; (vii) reprocessing; (viii) fusion; (ix) others.

On the basis of this classification, we shall synthesise the information gathered for each type of facility and extrapolate this synthesis to facilities which could not be assessed in detail. Two preliminary stages will be necessary: (i) classify each of the 51 facilities in the above mentioned list, (ii) check if for each class of facility, enough information is available, (iii) check if the information gathered for each class is enough homogeneous to extrapolate. In case of too much lack of information, detailed assessments will continue on adequate facilities. In case of too heterogeneous exposure for one class of facilities, this one will be redefined.

3.5.3. Detailed assessment for tritium, neutrons and low energy X-rays

Considering the importance of exposure to tritium, neutrons and low energy X-rays exposures in the calculation of external dose of radiation, it was decided that we shall carry out an expert assessment for each facility for tritium, neutrons, and low-energy X-rays.

4. Conclusion

In order to assess retrospective carcinogenic exposures (other than ionising X- and gamma- radiation) among workers at CEA and COGEMA (roughly 50,000 workers), we developed a Facility-exposure matrix (FEM), CEA-EXPO, derived from the job-exposure matrix method. 330 facilities were listed and exposures assessed in detail for 51 of them by experts.

The validation study made for one of Fontenay-aux-Roses' historical facilities with both expert assessment and examination of archives showed that the former is preferable.

The feasibility of merging the worker files with the files containing facility exposure information was tested at six basic facilities at the Grenoble centre. We ascertained that this linkage is possible, on condition that efforts focus on reconstructing the various acronyms included in these files for the administrative departments and work places. In addition, we have calculated the exposure durations. These results provide a map of the exposures at the facilities concerned. They must, however, be interpreted cautiously, as the presence of a substance does not necessarily engender a toxic risk for the worker (concept of possible exposures).

We also examined the correlations between the various exposures. They indicate exposure groups that ought to be considered together for the facilities concerned, to avoid spreading ourselves too thin over factors that cannot be differentiated in the further epidemiological analysis.

At that stage, a simplified method was envisaged. A bibliographic report about the toxicity of the carcinogenic products used at CEA and COGEMA helped us identify the substances mostly likely to be cofactors for radio-induced diseases. It led to a simplified list of 18 exposures.

A second simplification of the method consisted in classifying the different facilities into 8 relatively homogenous groups (plus one "others"). The information collected for the first 51 facilities, together with the assessment of the working group, will enable adequate attribution of occupational exposures to each

group. Specific expert assessments are underway for neutrons and tritium (as a whole-body dose) as well as for low-energy X-rays (which could cause bias in the measurement of the whole-body dose).

The following priorities have been defined for the next phase of the project, in agreement with the working group: (i) identify from the worker, administrative and dosimetric files the facilities where each worker worked (this involves translating the codes of administrative departments and work places into facilities); (ii) conduct a specific expert assessment for neutrons, tritium and low-energy X-rays; (iii) construct a simplified matrix in attributing occupational exposures to each large category of facilities (iv) validate the final method. Individual hazard forms could be used to make this validation on a sample of workers representative of all the activities of CEA-COGEMA group. It will then be possible, when studying the association between external ionising radiation and cancers, to take other exposures into account by performing stratified Poisson regression. The matrix will allow a stratification distinguishing workers not exposed to chemical carcinogens from possibly exposed workers.

Other uses of the matrix can be described: it can help in assessing exposures for special case-control studies within the cohort, together with other traditional methods such as self-reported evaluation, or data from occupational medicine departments. It can also be a tool for occupational physicians in the assessment of past exposures of their patients. Thus, it should go beyond clarifying the effect of low doses of ionising radiation, and should help in the study of other occupational hazards in the nuclear industry as are internal contamination and chemical exposures. When validated, the simplified matrix could be used in other similar nuclear facilities since to our knowledge only one matrix of this type exists in these industries (Ruttenber *et al.*, 2001).

***Acknowledgments.** We would like to thank the members of the working group constituted to develop this matrix: Bernard Auriol, Denis Bard, Georges Bataller, Paul Beau, Francis Bermann, Françoise Couleru, Daniel Delacroix, Thierry Desse, Monique Duchaud, Annie Eskenazy, Marianne Estrabaud, Odile Frossard, Jean-Marie Gelas, Jean-Michel Giraud, Michel Girod, Philippe Hubert, Pierre Joudrier, Jean-Pierre Le Goff, René Le Tule, Marie-Pascale Lizée, François Pic, Jean-Philippe Planchet, Christine Riasse, Philippe Royer, André Straus, Jean Tourte. We also thank very much former workers who helped us in assessing facilities' exposures, whose names cannot be mentioned exhaustively here. We thank Joelle Févotte for her fruitful reading of the manuscript and Jo Ann Cahn for her help in the English translation. This project received funding from the Ligue nationale contre le cancer in its program of aid towards research in cancer epidemiology.*

REFERENCES

- Ahrens W., Jockel K.H., Brochard P., Bolm-Audorff U., Grossgarten K., Iwatsubo Y., Orłowski E., Pohlabein H., Berrino F. (1993) Retrospective assessment of asbestos exposure – I. Case-control analysis in a study of lung cancer: efficiency of job-specific questionnaires and job exposure matrices, *Int. J. Epidemiol.* **22**, S83–S95.
- Baysson H., Laurier D., Tirmarche M., Valenty M., Giraud J.M. (2000) Epidemiological response to a suspected excess of cancer among a group of workers exposed to multiple radiological and chemical hazards, *Occup. Environ. Med.* **57**, 188-194.
- Beral V., Fraser P., Carpenter L., Booth M., Brown A., Rose G. (1988) Mortality of employees of the Atomic Weapons Establishment, 1951-82, *Br. Med. J.* **297**, 757-770.
- Bouyer J., Hemon D. (1993) Comparison of three methods of estimating odds ratios from a job exposure matrix in occupational case-control studies, *Am. J. Epidemiol.* **137**, 472-481.
- Bouyer J., Hemon D. (1994) Job exposure matrices, *Rev. Epidemiol. Sant. Publ.* **42**, 235-245.
- Burstyn I. (2004) Principal Component Analysis is a powerful instrument in occupational hygiene inquiries, *Ann. Occup. Hyg.* **48**, 655-661.
- Cardis E., Gilbert E.S., Carpenter L., Howe G., Kato I., Armstrong B.K., Beral V., Cowper G., Douglas A., Fix J., *et al.* (1995) Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries, *Radiat. Res.* **142**, 117-132.
- Carpenter L., Higgins C., Douglas A., Fraser P., Beral V., Smith P. (1994) Combined analysis of mortality in three United Kingdom nuclear industry workforces, 1946-1988, *Radiat. Res.* **138**, 224-238.
- Goldberg M., Kromhout H., Guenel P., Fletcher A.C., Gerin M., Glass D.C., Heederik D., Kauppinen T., Ponti A. (1993) Job exposure matrices in industry, *Int. J. Epidemiol.* **22**, S10-S15.
- Gribbin M.A., Weeks J.L., Howe G.R. (1993) Cancer mortality (1956-1985) among male employees of Atomic Energy of Canada Limited with respect to occupational exposure to external low-linear-energy-transfer ionizing radiation, *Radiat. Res.* **133**, 375-380.
- Guenel P., Nicolau J., Imbernon E., Warret G., Goldberg M. (1993) Design of a job exposure matrix on electric and magnetic fields: selection of an efficient job classification for workers in thermoelectric power production plants, *Int. J. Epidemiol.* **22**, S16-S21.
- Heineman E.F., Cocco P., Gomez M.R., Dosemeci M., Stewart P.A., Hayes R.B., Zahm S.H., Thomas T.L., Blair A. (1994) Occupational exposure to chlorinated aliphatic hydrocarbons and risk of astrocytic brain cancer, *Am. J. Ind. Med.* **26**, 155-169.
- IARC (1998) IARC monographs on the evaluation of carcinogenic risks to humans, List of IARC evaluations.
- Imbernon E., Goldberg M., Bonenfant S., Chevalier A., Guenel P., Vatre R., Dehay J. (1995) Occupational respiratory cancer and exposure to asbestos: a case-control study in a cohort of workers in the electricity and gas industry, *Am. J. Ind. Med.* **28**, 339-352.
- Iwasaki T., Murata M., Ohshima S. (2003) Second analysis of mortality of nuclear industry workers in Japan, 1986-1997, *Radiat. Res.* **159**, 228-38.
- Jéjati H., Laurier D., Tirmarche M., Valenty M., Giraud J. (1998) Étude de cohorte en milieu professionnel: utilisation des fiches de nuisances et de la mémoire collective afin de reconstituer des expositions multiples., *Rev. Méd. Trav.* **25**, 51.
- Kauppinen T., Partanen T. (1988) Use of plant- and period-specific job-exposure matrices in studies on occupational cancer, *Scand. J. Work. Environ. Health* **14**, 161-167.
- Kelsh M.A., Kheifets L., Smith R. (2000) The impact of work environment, utility, and sampling design on occupational magnetic field exposure summaries, *Am. Industr. Hyg. Ass. J.* **61**, 174-182.

- Moulin J.J., Romazini S., Lasfargues G., Peltier A., Bozec C., Deguerry P., Pellet F., Wild P., Perdrix A. (1997) Development of a job-exposure matrix in the heavy-metal industry in France, *Rev. Epidemiol. Sant. Publ.* **45**, 41-51.
- Muirhead C.R., Goodill A.A., Haylock R.G., Vokes J., Little M.P., Jackson D.A., O'Hagan J.A., Thomas J.M., Kendall G.M., Silk T.J., Bingham D., Berridge G.L. (1999) Occupational radiation exposure and mortality: second analysis of the National Registry for Radiation Workers, *J. Radiol. Prot.* **19**, 3-26.
- Omar R.Z., Barber J.A., Smith P.G. (1999) Cancer mortality and morbidity among plutonium workers at the Sellafield plant of British Nuclear Fuels, *Br. J. Cancer.* **79**, 1288-1301.
- Orlowski E., Pohlabein H., Berrino F., Ahrens W., Bolm-Audorff U., Grossgarten K., Iwatsubo Y., Jockel K.H., Brochard P. (1993) Retrospective assessment of asbestos exposure – II. At the job level: complementarity of job-specific questionnaire and job exposure matrices, *Int. J. Epidemiol.* **22**, S96-S105.
- Ritz B. (1999) Radiation exposure and cancer mortality in uranium processing workers, *Epidemiology* **10**, 531-538.
- Ritz B., Morgenstern H., Froines J., Young B.B. (1999) Effects of exposure to external ionizing radiation on cancer mortality in nuclear workers monitored for radiation at Rocketdyne/Atomics International, *Am. J. Ind. Med.* **35**, 21-31.
- Ruttenber A.J., McCrea J.S., Wade T.D., Schonbeck M.F., LaMontagne A.D., Van Dyke M.V., Martyny J.W. (2001) Integrating workplace exposure databases for occupational medicine services and epidemiologic studies at a former nuclear weapons facility, *Appl. Occup. Environ. Hyg.* **16**, 192-200.
- Saporta G. (1990) *Probabilités, analyse des données et statistique*. Paris, Éditions Technip.
- Stengel B., Pisani P., Limasset J.C., Bouyer J., Berrino F., Hemon D. (1993) Retrospective evaluation of occupational exposure to organic solvents: questionnaire and job exposure matrix, *Int. J. Epidemiol.* **22**, S72-S82.
- Straus A. (1996) Pré-étude concernant l'INB 57 (communication personnelle).
- Telle M.A., Bergot D., Bard D. (1996) Effects of protracted exposures to low doses of ionising radiations: reconstructing exposures of the French Atomic Energy Commission (CEA) workforce, *9th International Congress on Radiation Protection*, 14-16 May 1996, Vienne.
- Telle-Lamberton M., Samson E., Caër S., Bergot D., Bard D., Bermann F., Gélas J.M., Giraud J.M., Hill C., Hubert P., Néron M.O., Quesne B., Tirmarche M. (2004) External radiation exposure and cancer mortality among French CEA and COGEMA workers. EPICOH – Seventeenth Symposium on Epidemiology in Occupational Health. Melbourne, Australia, October, *Occup. Environ. Med.* **61**, e18.
- Wiggs L.D., Cox-DeVore C.A., Wilkinson G.S., Reyes M. (1991) Mortality among workers exposed to external ionizing radiation at a nuclear facility in Ohio, *J. Occup. Med.* **33**, 632-637.
- Zablotska L.B., Ashmore J.P., Howe G.R. (2004) Analysis of mortality among Canadian nuclear power industry workers after chronic low-dose exposure to ionizing radiation, *Radiat. Res.* **161**, 633-641.