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Comparative assessing for radiological, chemical, and physical exposures at the French uranium conversion plant: Is uranium the only stressor?☆

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Abstract

This study presents the pattern of exposure to uranium and other occupational pollutants known to be potentially carcinogenic, mutagenic or toxic and used at the main uranium conversion plant in France. For different uranium compounds specified according to their solubility and purity, and 16 other categories of pollutants: chemicals, fibres, vapours, dust, and heat a time- and plant-specific job exposure matrix (JEM) was created covering the period 1960–2006. For 73 jobs and for each pollutant the amount and frequency of exposure were assessed on a four-level scale by different time periods. The JEM shows 73% sensitivity and 83% specificity. Although exposure assessment was semi-quantitative, the JEM allows computing of individual cumulative exposure score for each pollutant across time. Despite the predominant natural uranium compounds exposure, the amount of exposure to other pollutants such as TCE and other chlorinated products, asbestos, and fibres, is important at the plant. Numerous correlations detected between uranium compounds exposure and exposure to chemicals warrants improving biological monitoring of exposed workers and accounting for associated exposures in epidemiological studies. Results of this study will be used for further investigation of association between exposure and mortality among uranium conversion workers cohort.
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Introduction

Uranium is known for its chemical and radiological toxicity after acute exposure. But there is little evidence on the adverse health effects and particularly on the

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carcinogenic potential of protracted uranium exposure. Cohort studies of workers in the nuclear industry stand out from all other epidemiological studies carried out at the workplace owing to the accuracy of the available exposure data. However, these data are often restricted to external radiation exposure (X- and gamma rays, beta particles or neutrons) for which external dosimetry became systematic for potentially exposed workers as of the early 1950s. Through this monitoring, epidemiologists can use personal irradiation data to determine the risks of occurrence of cancer or non-tumorous pathologies as a function of total received dose during professional life (Cardis et al., 2005, 2007; Guseva Canu et al., 2008c; Rogel et al., 2005; Telle-Lamberton et al., 2004; Telle-Lamberton et al., 2007; Vrijheid et al., 2007). Workers are, however, exposed not only to radiation, but also to other types of pollutant such as chemicals, particle pollutants or asbestos, most of which are carcinogenic. This simultaneous presence of several types of exposure has been described in uranium workers (Guseva Canu et al., 2008a) and is probably significant in many fuel cycle facilities.

With the exception of radiation, direct monitoring of such exposure began relatively recently, as it responds to fresh knowledge in toxicology and to new regulations that also came into effect only very recently (EC, 1998, 2004). It can therefore be assumed that exposure to these factors was greater in the past than now and that new tools, encompassing all types of exposure, whether nuclear, physical or chemical, are required to estimate the risk of cancer and non-tumorous pathologies in workers in the nuclear industry.

Medical records are the main instrument used for monitoring nuclear workers. They include a job description giving details of all types of exposure concerned. Usually, however, different types of exposure are only monitored and documented in medical records in strict accordance with regulatory requirements, while radiotoxicological and whole-body monitoring data on workers only concern exposure to ionising radiation. Furthermore, it is difficult to use these data in epidemiological studies because the medical records of workers in the nuclear industry in France are not computerised and access to them is restricted. Lastly, it is not always feasible to consult medical records for cohort studies as some cohorts may be made up of several thousands of individuals.

Some tools have been developed to overcome these difficulties and some of them take into account some forms of radiation exposure (Boice et al., 2006; Carpenter et al., 1987, 1988; Eheman and Tolbert, 1999; Krishnadasan et al., 2007, 2008; Ritz, 1999; Ritz et al., 1999, 2000, 2006; Rooney et al., 1993; Ruttenber et al., 2001a, b; Wing et al., 1993). One such tool is the job exposure matrix (JEM), which is based on a definition of jobs and the related forms of exposure and includes an assessment of exposure levels (Goldberg et al., 1993; Hoar, 1983). The JEM has sometimes been used in the nuclear field and has provided initial data on some groups of workers (Boice et al., 2006; Carpenter et al., 1988; Eheman and Tolbert, 1999; Henn et al., 2007; Krishnadasan et al., 2007, 2008; Ritz, 1999; Ritz et al., 1999, 2000; Rooney et al., 1993; Ruttenber et al., 2001a, b; Wing et al., 1993). Publications, however, rarely develop information on how these matrices are built or on exposure results, even though such information is crucial for a clear understanding of the environment under study or for a correct interpretation of analysis results. Analysis of the literature (Boice et al., 2006; Carpenter et al., 1988; Eheman and Tolbert, 1999; Henn et al., 2007; Krishnadasan et al., 2007, 2008; Ritz, 1999; Ritz et al., 1999, 2000; Rooney et al., 1993; Ruttenber et al., 2001a, b; Wing et al., 1993) (see summary in Table 1) shows that there are only a few matrices – limited to the description of two or three types of exposure – that are relatively well described and that provide more precise exposure indicators based on measurement data or allow an estimation of cumulated exposure. These are not exhaustive, however, and exclude other types of exposure also found in the workers' occupational environment.

The objective of this study is to investigate exhaustively the exposure to different occupational pollutants at the main uranium conversion plant in France.

Material and methods

The AREVA NC uranium conversion plant in Pierrelatte

The AREVA NC plant in Pierrelatte is located in the south-east of France. It occupies a nuclear production site originally created by the CEA (the French atomic energy commission) in 1960, with a view to building a uranium isotope separation facility for making weapons-grade uranium. The *Compagnie Générale des Matières Atomiques* (COGEMA, which became AREVA NC in May 2006) has been enriching and converting uranium for industrial use since 1976. It is made up of several production facilities, support and maintenance facilities and storage areas. Each facility consists of one or more units and carries out an independent and specific uranium processing activity. Fig. 1 shows how various successive activities have been carried out on the site over the years.

Specific job exposure matrix (JEM) elaboration

The overall procedure is described in Fig. 2. Exposure to uranium-bearing and other chemical compounds used

Table 1. Short review of studies assessing occupational exposure among nuclear workers by using job-exposure matrix approach

Reference, country	Industry, period	Exposure	Exposure estimator	Exposure assessment method	Purpose, study design and main results	Reviewer's comments
Eheman and Tolbert (1999), Germany	All involving radiation exposure, 1960–1980	External radiation dose	Discrete annual dose distribution with 6 dose categories. Distribution of cumulative dose, geometric mean and standard deviation	Published dosimetry data for different occupational groups. Interview for job history Monte Carlo method	To estimate radiation doses and uncertainty for individuals reported occupational radiation exposure in Population-based Case-Control study of non-Hodgkin's lymphoma	Use of radioprotection dosimetry data. No assessment of internal radiation exposure
Krishnadasan et al. (2007), USA	Rocket engine and nuclear power testing facility, 1950–1990	TCE, benzene, hydrazine, PHA, mineral oils	Exposure score for each chemical = intensity of exposure (4-level scale) by 3 time periods × duration of employment	Coding of likelihood and intensity of exposure by job title by hygienist based on knowledge from facility records and workers survey and interviews	To assess a relationship between occupational exposure to chemicals in the Nested Case-Control study of prostate cancer incidence. Dose–response relationship with TCE exposure	Available data on life style habits and familial history of prostate cancer, occupational physical activity intensity. Study with etiological issue
Krishnadasan et al. (2008), USA	Rocket engine and nuclear power testing facility, 1950–1990	Occupational physical activity	Score of occupational physical activity based on intensity (3-level scale) of occupational physical activity for a job held longest × duration of employment	Coding of intensity of physical activity by job title by hygienist based on knowledge from facility records and workers survey and interviews	To assess a relationship between occupational physical activity in the Nested Case-Control study of prostate cancer incidence. No dose–response relationship. Inverse association among aerospace workers but not among radiation workers	Data on life style habits and familial history of prostate cancer, available for a limited number of subjects. Job titles used as an entry to JEM despite discrepancies in physical activity level results among radiation and aerospace workers

Boice et al. (2006), USA	Rocket engine testing facility SSFL, 1948–1999	TCE and hydrazine. Other chemicals as surrogate for exposure to all other chemicals	Potential of exposure (no, possible and likely exposure) and cumulative potential exposure for hydrazine and TCE. Duration of employment as a test stand mechanic for other chemicals	Review of worker's exposure history, year, place, and type of work. Validation based on walkthrough visits, interviews with workers, review of workers' medical records	To assess mortality among rocket engines testing workers. Non-significant relationship between TCE and kidney cancer. No relationship between test stand mechanic job and mortality	Only potential of exposure assessed by crude JEM. Comprehensive review of TCE and hydrazine use at the facility
Ritz et al. (1999), USA	Rocket engine testing facility SSFL, 1950–1990	Hydrazine and other chemicals 1950–1990	Relative intensity of presumptive exposure (4-level scale) by 3 time periods. Time-dependent cumulative exposure score	3 experts consensus based on walkthrough visits, interviews with workers, review of historical facility reports	Retrospective cohort study of cancer incidence and mortality. Dose–response relationship for lung, colorectal, and pancreatic	Workers with low exposure used as reference instead of unexposed workers
Rooney et al. (1993), UK	UK Atomic Energy Authority	13 specific radionuclides; 6 metals: Be, Br, Cd, Pb, Hg, Zn; 3 types of chemicals: aromatic, halogenated, other organic compounds; asbestos, metal dusts, metal fumes	For each radionuclides-level of exposure (none, possible, probable but relatively low, probable but relatively high). For other agents, level of exposure on 3-level scale (none, low, high). Duration of work	Review of worker's exposure history, year, place, and type of work. 125 work areas classified by health physicists or experienced staff in 7 work environments: reactor, reactor maintenance, fuel examination after irradiation, fuel fabrication, decontamination and was disposal and laundry, fuel reprocessing. Records of internal contamination	Case-Control study of prostate cancer among UKAEA workers. Dose–response relationship with radionuclides exposure. No significant findings according to other kinds of exposure	No details on JEM. No reporting of exposure results
Carpenter et al. (1988), USA	Y-12 and ORNL, 1943–1979	26 chemicals or chemical groups including Be, U, Th, carbon dusts, welding fumes,	Rank of potential exposure to each chemical (0 – no, 1 – low, 2 – moderate, 3 – high potential for exposure). Exposure	Subjective evaluation by industrial hygienist of job title/ department combination with accounting for time	Nested case-control of primary CNS cancer. Analyses according exposure status, exposure duration,	No cumulative exposure assessment. No results according to exposure levels. No reference on

Table 1. (*continued*)

Reference, country	Industry, period	Exposure	Exposure estimator	Exposure assessment method	Purpose, study design and main results	Reviewer's comments
		cutting oils, hydrazine	duration = duration of employment in job titles with rank 2 or 3	period, review of industrial processes, on-site visits, interview with people, urinalysis and air monitoring data	employment duration. No significant findings	exposure evaluation report
Wing et al. (1993), USA	ORNL, 1943–1984	Be, Hg, Pb	15 job categories based on potential for similar occupational environment and activities. Time spent in job category	Employment records: job title, department, payment status and monitoring status for Be, Hg, Pb exposure	To consider the role of possible selection and confounding factors on dose-risk estimators in previous cohort study of solid cancer and leukaemia. No significant changes on dose-risk estimates except Hg	
Ritz (1999), USA	Fernald FFMPC, 1951–1990	TCE, kerosene, and cutting oils	Exposure level (0–3) and duration of exposure (with 15 year lag). Internal and external radiation dose	Plant experts: a plant foreman, hygienists, an engineer determined likelihood of chemical exposure for each job title and plant area for 1952–1977 period	Cohort study of chemical exposure effects on cancer mortality with accounting for radiation exposure for specific cancer sites	Good description of highly exposed jobs, jobs with concomitant exposure, cutting oils composition and definition discussed
Ritz et al. (2000), USA	Rocketdyne, 1950–1994	Internal lung dose, asbestos, hydrazine	Exposure level (0–3) defined on job titles. Internal and external radiation dose	? Job titles, employment periods, and job locations used as proxy measures for chemical exposures	Cohort study of internal radiation exposure effect on mortality from specific cancer sites. Dose–response relationship with internal radiation exposure	Results adjusted for chemical exposure are not shown
Ruttenber et al. (2001a), USA		Be, CCl_4, Cr, Pb, Ni, TCE, PCE,		Published estimates. For Be, data from a	Improving estimates of exposure for	Validation of Be exposure estimators.

	Rocky Flats Nuclear weapon facility, 1951–1989	formaldehyde, methylene chloride, asbestos	Time-weighted average (max/min) annual air exposure	100 s personnel air samplers. Estimates for concentration in breathing zone of workers, adjusted for respirator use	epidemiological studies of plutonium workers	Results in % and nb of workers exposed to each agent.
Ruttenber et al. (2001b), USA	Rocky Flats Nuclear weapon facility, 1951–1989	Be, CCl_4, Cr, Pb, Ni, TCE, PCE, formaldehyde, methylene chloride, asbestos	Time-weighted average (max/min) daily air concentration. Cumulative exposure for period of interest = Av. concentration × nb hours worked	Published estimates for similar production process. Hours worked paid/ year from employer's roster	To develop a JEM for epidemiological studies and for determination of eligibility for a medical screening program for highly exposed former workers	No reference of published estimates of exposure levels. No detail on final nb of job groups, on mostly exposed jobs, on 10/20 selected chemicals. Solid estimators allowing accounting for uncertainties. Reporting of exposures according to LOEL
Henn et al. (2007), USA	Chemical laboratories at Y-12, X-10, K-25 and SRS plants, 1943–1998	Organic and inorganic chemicals including radioisotopes	Individual cumulative potential exposure indices (PEIs) = nb of days with task- and time-dependent combination × task- and time-dependent weighting factors	Task-dependent weighting factors determined by industrial hygienists (IH) through jobs review and interviews with workers. Time-dependent weighting factors determined through IH monitoring results	To assess chemical exposure for a mortality study of 6157 chemical laboratory workers	PEIs are not specific of any chemical. Waiting factor for time were established on the basis of exposure trends data available for only 4 chemicals from 54 considered

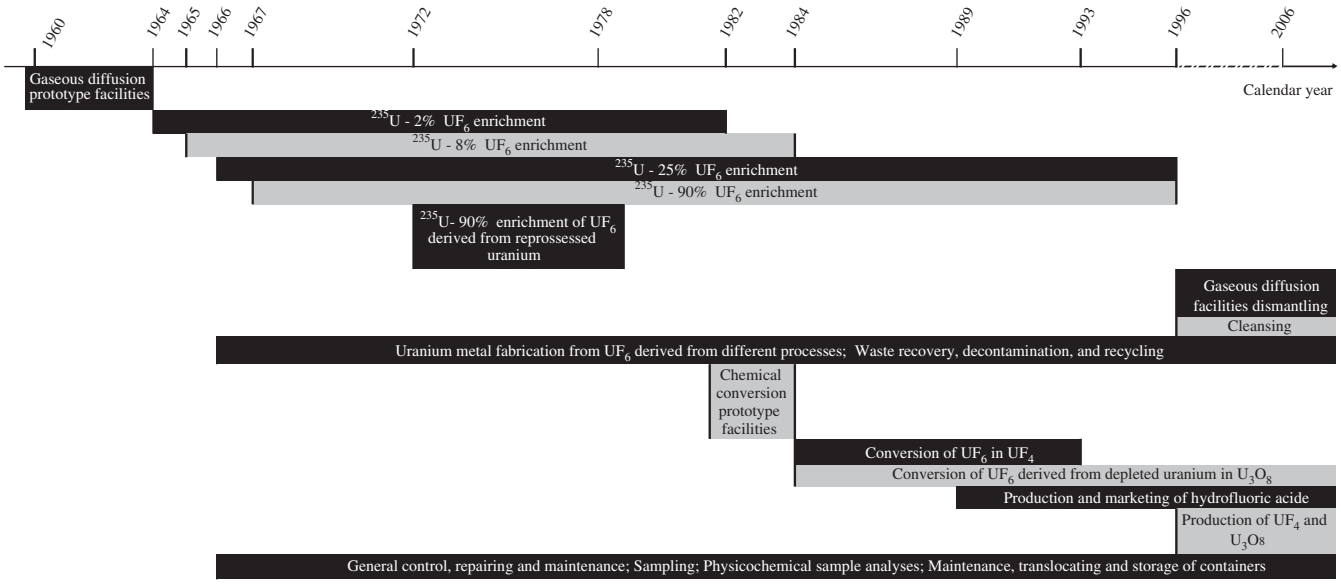

Fig. 1. Development of main industrial activities at the AREVA NC Pierrelatte plant from 1960 to 2006.

on the site was assessed retrospectively, applying a special JEM methodology recently developed for the French nuclear industry (Guseva Canu et al., 2008b). As part of this method, experts in the site's past and present activities define jobs and types of exposure, while certain workers who have performed the different jobs assess exposure levels.

For elaborating the AREVA NC Pierrelatte JEM we invited 13 experts coming from different scientific areas. This variety of specialists ensured that all the jobs at the facility and the related exposure factors were covered, while taking into consideration changes affecting the company, technological processes used, past and present working conditions and the work organisation for each of the plant's facilities.

Definition of types of exposure

Three types of exposure were considered: exposure to uranium-bearing compounds that emit alpha particles and are responsible for internal irradiation, exposure to chemicals classified as carcinogenic, mutagenic and toxic to reproduction (EC, 2004) used on the site (regardless of period) and exposure to physical factors considered relevant for the study of cancers of organs that are particularly sensitive to uranium.

Definition of jobs

Jobs that are characterised by an equivalent exposure level over a period were subdivided into "job-period" pairs. Jobs were identified using a company list of job titles. Each job title groups together employees performing the same activities on identical position in the department or facility. This list was completed with the job titles of shut-down facilities, then simplified by grouping together certain job titles with the same exposure characteristics (e.g. the "Administrative employee with no dosimetric film"). For each job, the calendar periods where exposure was stable were determined. The purpose here was to incorporate a time dimension into the matrix by taking into account changes in strategy, processes, techniques, raw materials and/or products used, as well as the administrative or ergonomic reorganisation of jobs.

Assessment of exposure

Exposure was assessed with the help of active and retired employees of the uranium conversion plant. Hygienists designated active employees to ensure that the various facilities and activities were each represented by at least three workers. Retired employees were selected from the company retiree records. Respondents' answers were voluntary and anonymous. Information was gathered from respondents using a standardised questionnaire. Each respondent was asked to assess only job-period pairs with which he was personally familiar. Exposure was assessed on the basis of a semi-quantitative estimation of two exposure indicators for each job-period pair: frequency of exposure to a product and the quantity of product that the worker handled. A four-level scale was used to estimate exposure frequency (0 = never, 1 = rarely, 2 = occasionally and 3 = frequently) and the quantity of product that the worker was handling at the time of exposure (0 = none, 1 = negligible, 2 = moderate and 3 = significant). The final "frequency and quantity" scores were determined according to statistical criteria (Guseva Canu et al., 2008b). The purpose of the first statistical examination of the scores was to identify any "divergent" respondents

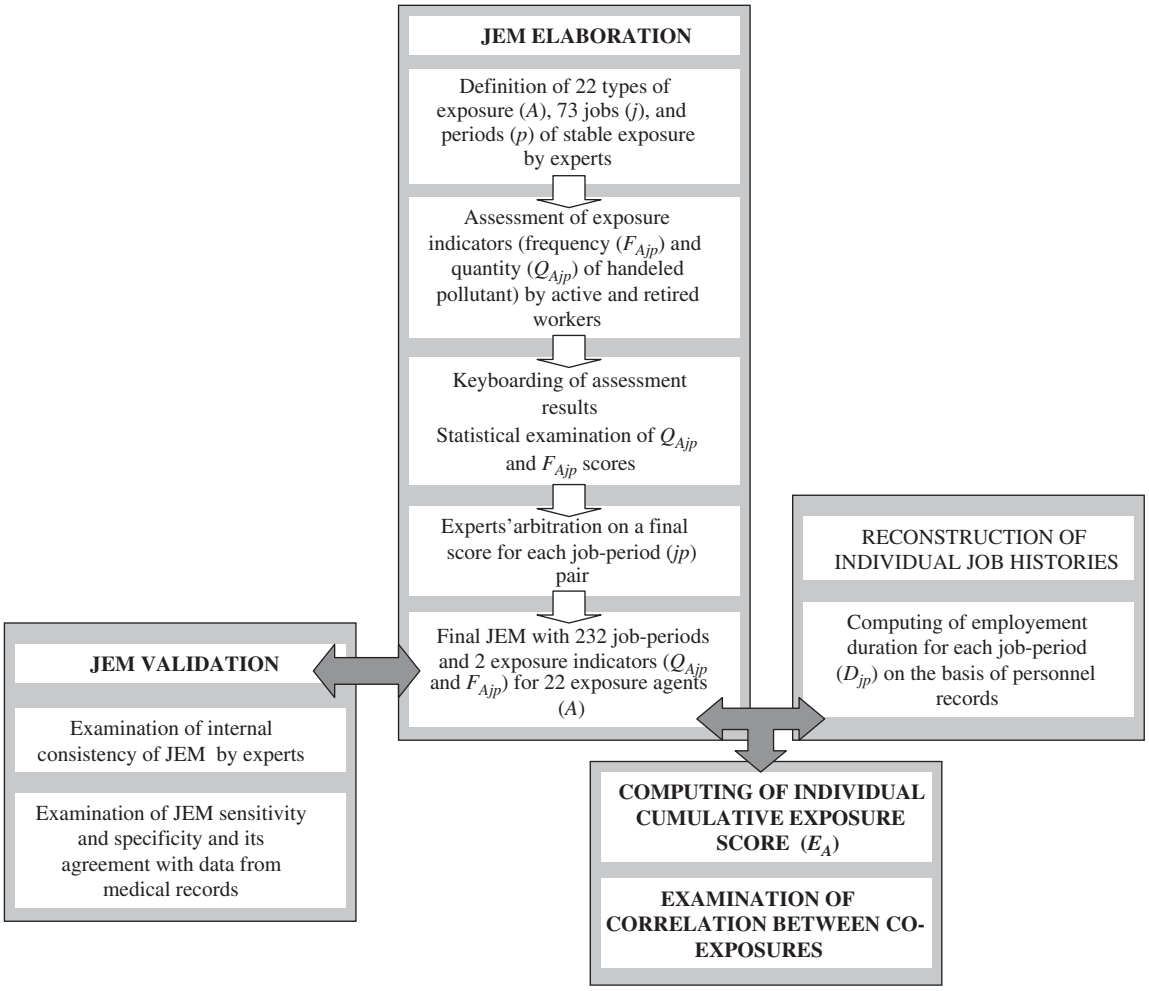

Fig. 2. Flow diagram of the retrospective individual exposure assessment process at the AREVA NC Pierrelatte plant (1960–2006).

whose opinion differed from that of the majority of the group concerning a position occupied for a certain period of time and who gave "extreme" scores for a whole series of exposure agents. The scores given by such respondents were eliminated. The second statistical examination was aimed at eliminating distributions that did not lead to an acceptable final score. These included distributions with a standard deviation of at least 1.5, reflecting too wide a range of opinions, and bi- or multimodal distributions, pointing to the existence of two or more groups of diverging opinion. All the other distributions were accepted and the final scores selected were the arithmetical means rounded up or down to the nearest whole number. The experts examined the distributions of rejected scores during the arbitration session and reached a consensus on a final pass score for each job-period pair.

Validation

In order to validate the JEM, the experts within the facility examined all the results in light of the changes in each job over time and in relation to all the different jobs. An expert from outside AREVA NC compared the results with exposure data in other comparable nuclear facilities. In addition, exposure results from the matrix were compared for validation purposes with results found in the medical records of a random representative sample of workers (1% of the worker population). These records contain job/exposure agent sheets that describe exposure factors known for their toxic effects that are subject to monitoring regulations. They do not, however, include quantitative data on forms of exposure other than irradiation and validation only focuses on a qualitative aspect, identifying exposure factors common to the JEM and job/exposure agent descriptions. A dichotomous variable (exposed/unexposed) was used for all periods and all exposure factors studied to guarantee a uniform comparison of JEM exposure results with medical file results. The kappa (κ) coefficient of agreement was calculated using Fleiss' formula (Fleiss, 1981). Kappa values were interpreted according to the criteria defined by Landis and Koch (1977). Values greater than 0.80 represent very good agreement beyond chance, values between 0.60 and 0.80 represent good agreement, values between 0.40 and 0.60 represent

moderate agreement, values between 0.20 and 0.40 represent fair agreement, and values below 0.20 represent poor agreement. Furthermore, conventional indicators such as sensitivity and specificity were calculated (Last, 1995) to allow overall appraisal of JEM validity.

Estimation of cumulated exposure and co-exposure

The following equation was used to calculate the individual cumulated exposure score for each type of exposure across all jobs of worker's career at the AREVA NC Pierrelatte plant:

$$E_A = \sum_{j=1}^{73} \sum_{p_j} F_{Ajp} \times Q_{Ajp} \times D_{jp}$$

where E_A represents the individual cumulated exposure to an exposure agent A.

For the job j ($j = 1$–73) during the period of stable exposure p_j, F_{Ajp} represents the frequency of exposure to the agent A, Q_{jp} is the quantity of product that the worker handled during exposure to the agent A, and D_{jp} the duration (in years) of the employment in the job-period jp.

The existence of co-exposures and possible correlations between exposure to uranium-bearing compounds and other types of exposure was examined using Spearman's correlation coefficient ρ (Spearman, 1904), using Bonferroni adjustment for multiple comparisons. Cohen's (1988) criteria were used for interpreting correlation results.

Results

JEM structure

All the exposure agents are shown in Table 2. Radiological exposure through internal contamination has been broken down into several factors based on two criteria: (1) the purity of uranium, to make a distinction between compounds derived from natural uranium (NU) and those derived from reprocessed uranium (RPU), which contain traces of fission products and (2) transferability of uranium particles to biological tissue (fast (f), moderate (m), and slow (s)) (ICRP, 1994) after intake. The last characteristic depends on the physical–chemical form of the uranium-bearing compounds (Ansoborlo et al., 2002; Chazel et al., 2001). Heat was considered among associated forms of exposure, even though it is not classified as carcinogenic, mutagenic or toxic to reproduction. It can have a synergistic effect on internal contamination by uranium, for it increases respiratory ventilation and the permeability of the body's biological tissue and alters the deposition of uranium particles taken in via the respiratory tract (ICRP, 1994).

Job-period pairs correspond to job exposure matrix rows.

For each facility, jobs were distinguished for workers and operators in manufacturing and operating jobs, uranium handlers, mechanical maintenance technicians, electrical maintenance technicians, electronic maintenance technicians, supervisors, physical–chemical analysts and so on. Additional distinction of jobs according to working hours was performed to discriminate jobs with fixed working hours and jobs with work in shift (i.e. 8-h shift). In total, 73 jobs were distinguished. These jobs were then divided into 232 job-period pairs where exposure was assumed as stable. This distinction was performed on the basis of knowledge of technical and strategic changes in the activity of each facility (see Fig. 1). Most jobs (59%, i.e. 43 jobs from 73) were divided into four operational periods of 11.5 years in average and median duration of 10 years. Between 1960 and 2006, 22 jobs (30%) – concerned with uranium industrial chemistry for the most part – were operational for two periods after they were started in 1982 or 1984. Four jobs, i.e. 5.5%, went through three operational periods until the gaseous diffusion plant was decommissioned in 1996, while four more recently created jobs were not divided into any particular operational period.

Assessment results

In all, 353 workers took part in the assessment of job-period pairs: 182 active workers out of the 182 contacted and 171 retired workers out of the 550 contacted. This distribution matches the distribution of the plant's pay roll and accounts for more than 10% of the AREVA NC Pierrelatte cohort. The 232 job-period pairs were analysed in terms of exposure to the products defined above. A frequency and quantity of exposure scores were obtained from each analysis. A summary of the scores given by the respondents and a description of the respondents' characteristics can be found elsewhere (Guseva Canu et al., 2008b). The scores underwent statistical processing, following which 96% were accepted. Following the experts' score arbitration session, 230 frequency and 229 quantity scores that had been rejected following statistical processing were accepted.

The JEM consists of a total of 10,296 cells showing final scores in terms of quantity and frequency of exposure to the 22 exposure agents for each of the 232 job-period pairs occupied between 1960 and 2006. The experts reached a consensus for all scores.

Validation results

Expert examination of assessment results showed the JEM to be satisfactory in terms of internal and external consistency. It was found to be a true reflection of actual

Table 2. Summary of exposure agents evaluated in the job exposure matrix and exposure characteristics of the AREVA NC Pierrelatte plant workers ($N = 2709$)

Exposure agents	Detail	Exposed workers *n* (%)	Individual cumulative exposure score in exposed workers Mean ± SD (median)
1. Natural U compounds f[a]	UF_6, UF_4, $UO_2(NO_3)_2$, (UO_4, nH_2O)	2253 (83.23)	67.49 ± 65.32 (44.50)
2. Natural U compounds m[a]	$(U_2O_7)(NH_4)_2$, U_3O_8, UO_2F_2, UO_3	1815 (67.05)	42.93 ± 51.01 (23.21)
3. Natural U compounds s[a]	UO_2	992 (36.65)	42.22 ± 40.52 (16.40)
4. Reprocessed U compounds f[a]	UF_6, UF_4, $UO_2(NO_3)_2$, (UO_4, nH_2O)	851 (31.44)	31.89 ± 40.52 (16.27)
5. Reprocessed U compounds m[a]	$(U_2O_7)(NH_4)_2$, U_3O_8, UO_2F_2, UO_3	656 (24.23)	36.62 ± 43.32 (20.53)
6. Reprocessed U compounds s[a]	UO_2	475 (17.55)	35.40 ± 43.76 (17.95)
7. Chlorinated agents	Perchloroethylene, tetrachloroethene, trichloroethene, dichloromethane, polychlorinated biphenyls (PCBs), carbon tetrachloride	1784 (65.90)	18.49 ± 21.72 (13.37)
8. Fluoride agents	Fluorhydric acid, tungsten hexafluoride, fluorine, potassium fluoride	1652 (61.03)	28.47 ± 42.39 (13.37)
9. Nitrogenous agents	Ammonia, ammonia anhydride, nitrogen acid, nitrous vapours	1415 (47.80)	31.55 ± 45.60 (12.04)
10. Solvents containing aromatic hydrocarbons	Benzene, toluene, xylene, styrene	1255 (46.36)	30.41 ± 39.90 (15.26)
11. Welding fumes	Fumes and metal dusts	425 (15.70)	12.07 ± 14.57 (7.78)
12. Vitreous fibres and rock wool	Rock, slag, and glass wools	1280 (47.28)	21.05 ± 26.05 (10.21)
13. Asbestos	Asbestos fireproofing, insulation, and braids	1894 (69.97)	19.28 ± 18.73 (15.94)
14. Refractive ceramic fibres		555 (20.50)	9.98 ± 7.93 (8.56)
15. Chromate	Potassium dichromate and chromium trioxide	102 (3.77)	7.56 ± 6.18 (6.42)
16. Chlorine trifluoride		1341 (49.54)	14.94 ± 15.35 (10.04)
17. Trichloroethylene (TCE)		1685 (62.25)	27.27 ± 33.57 (15.25)
18. Lead	Paints, plates, and dust	331 (12.23)	8.49 ± 8.32 (6.46)
19. Mercury	Vapours	827 (30.55)	16.46 ± 23.19 (8.96)
20. Silica	Silica gel, silica grains	695 (25.67)	8.71 ± 8.06 (6.73)
21. Hydrazine and other fuels	Hydrazine, domestic fuel, gas-oils, four-star fuel, petroleum	1164 (42.99)	16.18 ± 19.89 (10.29)
22. Heat	Temperature at the workstation $> 30\,^{\circ}C$	2361 (87.22)	54.63 ± 53.71 (34.47)

[a]Uranium compounds were classified in terms of absorption types (f – fast, m – moderate or s – slow) according to the Human Respiratory Tract Model described in ICRP Publication 66 (1994).

Table 3. AREVA NC Pierrelatte job exposure matrix validity characteristics compared to AREVA NC Pierrelatte workers' medical records used as reference

Exposure category	Observed agreement	Kappa coefficient	Sensitivity	Specificity
Uranium compounds derived from NU[a]	0.85	0.66	0.81	0.96
Uranium compounds derived from RPU[b]	0.92	0.83	0.82	0.98
Asbestos	0.61	0.09	1.00	0.60
Vitreous fibres and wools	0.74	0.27	0.50	0.80
Chlorinated agents	0.71	0.42	0.77	0.67
Fluoride agents	0.58	0.15	0.57	0.60
Nitrogenous agents	0.68	0.36	0.59	0.79
Total	0.78	0.56	0.72	0.83

[a]Natural uranium.
[b]Reprocessed uranium.

known exposure levels at different periods of the plant's history and, more generally, throughout the uranium industry. For instance, the JEM shows that since 1982 mechanic maintenance, container maintenance, and dismantling-decontamination technicians at the industrial chemistry division was potentially exposed to slowly soluble reprocessed uranium (RPUs) compounds such as uranium oxide. During the period 1982–1992 this exposure occurred occasionally (frequency = 2) when moderate quantity (quantity = 2) of uranium dioxide were handled. In 1990's the frequency of exposure remained stable when the quantity of handled RPUs compounds increased (frequency = 3) reflecting an increase in division's activity. Similarly, no exposure to RPUs was observed before 1980 among chemical laboratory workers. For the period 1986–1996 we observed higher RPUs exposure level among physical–chemical analysts involved in R&D activities (frequency = 3, quantity = 1) then exposure level observed among physical–chemical analysts involved in routine lab analyses (frequency = 1, quantity = 1).

The comparison of matrix exposure data with data from the workers' medical files used as a reference provided further validation, the results of which are shown in Table 3. For the purposes of comparison, agreement between the two data sources was estimated by actual observation and the κ coefficient. The κ values were interpreted according to Landis and Koch (1977). As far as exposure to uranium-bearing products is concerned, matrix data show very good agreement ($\kappa = 0.83$) with medical file data. There is less agreement for exposure to chemicals. Agreement is poor ($\kappa = 0.09$) in the case of exposure to asbestos. Sensitivity and specificity values observed are close to 1, indicating good matrix performance.

Exposure results

The descriptive statistics of individual cumulative exposure for each category of exposure agent are summarised in Table 2 and Fig. 3. Many jobs concentrate several exposure factors at the same time. Table 4 shows the jobs with the greatest exposure, showing only those jobs that have accumulated the highest exposure levels to more than three categories of exposure agent. The study of these cases of co-exposure reveals many correlations between exposure to uranium-bearing compounds and other types of exposure. Table 5 reveals a highly significant ($p < 0.0001$) positive correlation between exposure to NUf compounds and exposure to heat. This reflects industrial reality and confirms the hypothesis that the two types of exposure behave synergistically. Other strong correlations can be seen for exposure to NUf and NUm compounds, in particular with the exposure to trichloroethylene, fluorinated, and nitrated products and solvents. Correlations between exposure to uranium-bearing compounds derived from reprocessing uranium (RPU) and NUm compounds and exposure to refractory ceramic fibres are also significant. Chlorinated and fluorinated products are high on the list of chemicals. There is a strong mutual correlation between both these types of exposure. Exposure to chromates is the least common among exposure agents as a whole as well as among fibres, particles, vapours and fumes. Exposure to chromates concerns three jobs, all at the physical–chemical analysis laboratory. Asbestos, glass wool, and rock wool are characteristically found in around 50% of jobs. Asbestos exposure correlates with exposure to TCE and other chlorinated products, whereas exposure to glass wool and rock wool correlates with exposure to solvents and welding fumes (data not shown).

Discussion

Validity of study

In order to estimate exposure to uranium-bearing products and other types of product used at the AREVA

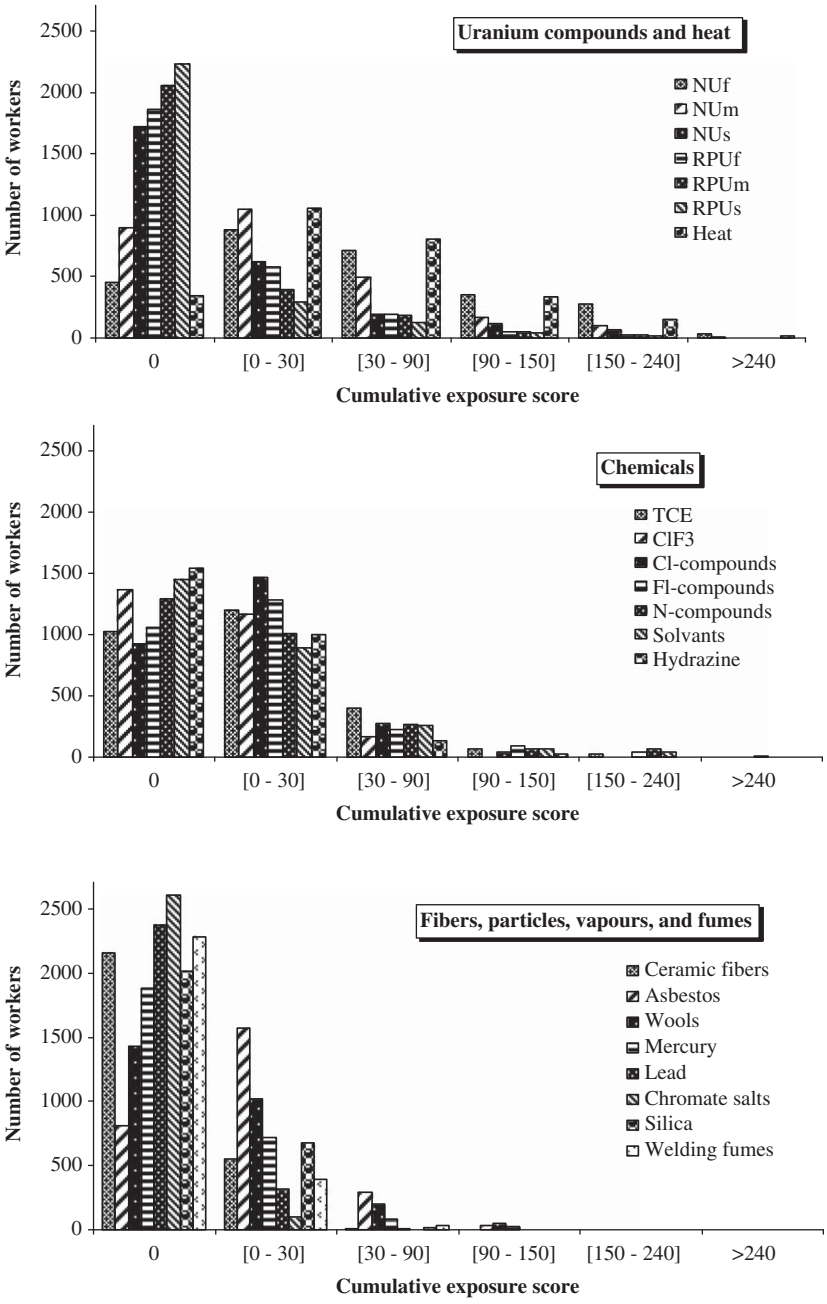

Fig. 3. Cumulative exposure to radiological, chemical and physical stressors of the AREVA NC Pierrelatte workers ($N = 2709$).

NC Pierrelatte plant between 1960 and 2006, a period- and site-specific JEM was created. In this matrix, exposure to chemical products or particles, such as metal dust or fibres, was estimated with the same degree of accuracy as exposure to uranium, the chief exposure agent. The JEM method has been widely discussed already (Goldberg et al., 1993; Guseva Canu et al., 2008b; Hoar, 1983; Kauppinen et al., 1998; Kauppinen, 1994). Compared with other studies that have developed JEMs for nuclear workers (Boice et al., 2006; Carpenter et al., 1987, 1988; Eheman and Tolbert, 1999; Henn et al., 2007; Krishnadasan et al., 2007, 2008; Ritz, 1999; Ritz et al., 1999, 2000; Rooney et al., 1993; Ruttenber et al., 2001a, b; Wing et al., 1993) (Table 1), this study drew largely on the opinions of a multidisciplinary expert committee and an exposure assessment based on workers' knowledge. Any bias related to self-declaration was controlled through the participation of 353 respondents and expert validation of final scores. The use of a standardised questionnaire for data collection limited any respondent-related bias. Lastly, information was statistically processed to reduce the subjectivity of the respondents' answers and obtain a group statistical response. A large number of jobs was discriminated

Table 4. Jobs with the highest cumulated exposure levels for more than 3 categories of exposure agent

Jobs	Exposure agents with the highest scores
Dismantling-decontaminating technician	Compounds derived from RPUf[a] Compounds derived from RPUm[a] Compounds derived from RPUs[a] TCE Fluorinated compounds Mercury Lead Refractive ceramic fibres
Driver at enriched materials chemistry unit	Compounds derived from NUf[a] Compounds derived from NUm[a] TCE Fluorinated compounds Heat
Mechanic at enriched materials chemistry unit	Compounds derived from NUf[a] Hydrazine and other fuels Welding fumes Wools Heat
Technician and operator at container maintenance shop	Compounds derived from RPUf[a] Compounds derived from RPUm[a] Compounds derived from RPUs[a] Fluorinated compounds
Physical-chemistry analysis technician at the plants' main laboratory	Potassium dichromate Mercury Nitrogenous compounds Silica gel, silica grains

[a]Uranium compounds derived from natural (NU) and reprocessed uranium (RPU) were classified in terms of absorption types (f, m or s) according to ICRP (1994).

(73 jobs + "Administrative employee with no dosimetric film" job, considered as not exposed). These jobs were defined on the basis of functions or tasks carried out by the employees as part of their work and at each facility. This discrimination improves the accuracy of the JEM and increases its specificity (Benke et al., 2000; Kauppinen et al., 1998) to take into account all the exposure characteristics specific to the various jobs.

Exhaustive nature of the JEM

In addition to uranium-bearing compounds, the exposure agents studied include all chemicals classified as carcinogenic, mutagenic or toxic to reproduction (EC, 2004), as well as physical factors considered relevant to the study. Our list contains 22 different categories of exposure agents, most of which are commonly used at other nuclear facilities (Table 1). A number of other products, such as cadmium (Rooney et al., 1993), beryllium (Boice et al., 2006; Carpenter et al., 1987, 1988; Rooney et al., 1993; Ruttenber et al., 2001a, b; Wing et al., 1993), nickel (Carpenter et al., 1987, 1988; Ruttenber et al., 2001a, b), zinc (Rooney et al., 1993), cutting oils (Carpenter et al., 1988; Krishnadasan et al., 2007; Ritz, 1999), and formaldehyde (Ruttenber et al., 2001a, b), which have been described as exposure agents in workers in the nuclear sector, were excluded from our JEM, either because they were never used at the plant or because their use entailed no risk of exposure. Cadmium, for example, which is classified as a category 2 carcinogen in its powder form (EC, 2004), is found on the Pierrelatte site as stainless-steel covered plates in annular tanks used as a neutron moderator for uranium waste. In its bulk form, cadmium presents no risk of exposure through inhalation of fumes or dust. It is never in contact with acids and therefore never gives off any toxic gases.

Exposure results at the Pierrelatte plant: strong points and limits

Despite its semi-quantitative basis the JEM allows computing of individual cumulative exposure score for each pollutant across time. It is suitable for chronic exposure to low doses of products but does not take into account cases of accidental exposure. These are listed in the archives for direct consultation and analysis.

Validation results showed that the exposure coding by the JEM seems to be a good reflection of known types of exposure over the plant's various periods of activity. That is especially true for exposure to uranium-bearing compounds, as confirmed by the results of a comparison to check agreement between JEM data and medical record data. Medical surveillance is strictly regulated for the chemo- and/or radiotoxic effects of these known products. The toxic effects of asbestos, rock and glass wools and certain chemicals, however, have long been overlooked and exposure to these products was not subject to regular surveillance by occupational medicine specialists. The first inventory of asbestos in the plant, for example, only dates back to 1997. These products are scored less systematically in job and exposure agent sheets, which probably explains the agreement between results. For this reason, medical files do not represent a

Table 5. Correlation between exposure to uranium compounds and other exposure agents

Exposure agents	Asbestos	Ceramic fibres	Chromate	Trichloro-ethylene	Chlorine trifluoride	Mercury	Lead	Silica	Hydrazine	Chlorinated agents	Fluoride agents	Nitrogenous agents	Solvents	Welding fumes	Wools	Heat
NUf[a]	**0.61***	0.29*	0.10*	**0.72***	0.40*	0.31*	0.25*	0.33*	0.24*	**0.56***	**0.65***	**0.52***	0.43*	0.25*	0.26*	**0.66***
NUm	0.38*	**0.52***	0.20*	0.38*	0.26*	**0.53***	0.16*	0.40*	0.19*	0.42*	**0.55***	**0.59***	0.48*	0.36*	0.47*	0.35*
NUs	0.21*	0.45*	0.31*	0.27*	0.10*	0.40*	0.23*	0.32*	0.17*	0.30*	**0.57***	**0.65***	**0.51***	0.12*	0.24*	0.08*
RPUf	0.03*	0.37*	0.34*	0.10*	−0.01	0.35*	0.16*	**0.57***	0.16*	0.26*	0.37*	0.40*	0.27*	0.28*	0.19*	0.03*
RPUm	−0.08*	0.44*	0.36*	−0.05	−0.04	0.08*	0.23*	0.35*	0.14*	0.15*	0.40*	0.46*	0.23*	0.12*	0.17*	0.01*
RPUs	0.10*	0.37*	0.35*	0.16*	0.11*	0.26*	0.27*	0.31*	0.32*	0.22*	0.40*	0.47*	0.34*	0.03*	0.20*	0.07*

Values of Spearman's correlation coefficient ($N = 2709$).

[a]Uranium compounds derived from natural (NU) and reprocessed uranium (RPU) were classified in terms of absorption types (f, m or s) Values of rho > 0.50 corresponding to a large correlation according to Cohen's criteria are bolded.

*Two-tailed significance test p-value < 0.01.

sufficient source of data for estimating low-level protracted exposure to chemicals and to physical exposure agents in worker cohorts with multiple exposures. The JEM provides more accurate and comprehensive information than the plant's personnel medical records.

The exhaustive nature of the JEM highlights the relative significance of exposure to various agents (Fig. 3). It was thus confirmed that the main type of exposure at the plant is to uranium-bearing compounds, derived mostly from soluble natural uranium. The subdivision of uranium-bearing compounds according to their solubility is an important factor, for it governs the distribution of uranium in the body and its toxic effects. It is through this degree of precision that the JEM reveals that workers involved in processing soluble compounds are co-exposed to heat. This shows that heat must be considered as a synergistic factor in contamination by soluble uranium and should be included as such in analyses. To the best of our knowledge, no previous study has ever taken this factor into account in estimating the risk of exposure to uranium and its effects. The same is true for exposure to mercury vapours, ceramic fibres, and fluorinated products, which are the chemicals with the strongest correlation with exposure to medium-soluble uranium-bearing compounds.

It is difficult to compare these results with those of other, similar studies because few studies give any exposure results. The rare studies that have developed their exposure results in the nuclear sector are those using measurement data (Eheman and Tolbert, 1999; Krishnadasan et al., 2007; Ruttenber et al., 2001b). In addition, exposure results can only be compared if the industrial processes used are comparable. The Pierrelatte plant is the only plant that produces and markets recycled chemicals. Some of its processes, however, may be common to other plants in France and abroad and could be compared with them. For example, in order to describe exposure to the ten chemicals associated with exposure to ionising radiation, Ruttenber et al. (2001b) used the average annual exposure values available for similar processes to those used at the Rocky Flats plant. It is nonetheless regrettable that the authors neither quote these processes nor specify the source of instrument measurement data they use.

The lack of usable instrument measurement data was a major obstacle of this study. Routine job monitoring carried out at the plant does not provide reliable quantitative information, as its purpose is to ensure that workers remain within radiation protection limits and trigger an alarm if the limits are overrun. The values of uranium concentration measurements obtained from air samplers alone are not sufficient to quantify the intake of particles and their use is not recommended (Britcher and Strong, 1994). The results of filter analyses

carried out when the maximum permissible concentration was exceeded and in response to alarms are not available for the period in question. Studies of certain workstations carried out between 1995 and 1997 (Ansoborlo et al., 2002) present concentration results according to the different uranium compounds found at the place of work, together with particle grain size, elemental composition, specific activity and solubility, which are crucial parameters for the estimation of the dose delivered to the body in the event of intake (Ansoborlo et al., 1998, 2002; Chazel et al., 2001). The results of workstations studies, however, cannot be used to quantify exposure in the matrix. Firstly, these studies are very irregular and only target a particular facility at a given time. Secondly, they provide no indication as to exposure prior to 1995 or since 1997. The new regulatory framework of the registration, evaluation, authorisation, and restriction of chemicals (REACH) directive (EC, 2006) provides for generalised use of quantitative measurements of exposure to chemicals, particularly in industry. It promotes the sharing of information among industrial firms with common worker exposure scenarios (Marquart et al., 2007). This would eventually make it possible to enrich the JEM with quantitative exposure estimators obtained from measurement data comparable to other plants in the nuclear sector.

Conclusion and perspectives

Despite the predominant natural uranium compounds exposure, the amount of exposure to other pollutants, such as TCE and asbestos, known as carcinogenic, mutagenic or toxic is important at the plant. Numerous correlations detected between uranium compounds exposure and exposure to chemicals warrants improving workstation monitoring at the plant and biological monitoring of exposed workers. Moreover, these results demonstrate the need to take into account associated exposures in epidemiological studies, especially where carcinogenic effects of protracted uranium exposure are addressed. Results of this study will be applied to further investigation of association between exposure and mortality among uranium conversion workers in France.

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