Estimate of the number of cases of certain types of cancer that are attributable to occupational factors in France

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FOREWORD

This work was carried out as part of an expert report for the commission set up by article L.176-2 of the Social Security Code. This commission, whose role is to carry out a regular assessment of the proportion of ailments covered by the Occupational Accidents and Occupational Diseases Scheme (AT-MP), in order to regulate the financial balances between different branches of the Sickness Insurance Scheme, meets every three years. In 2002, the presidency of this commission was held by Madame Lévy-Rosenwald, a Senior Councillor in the Cour des Comptes (Government Accounting Office) and the commission made its report in September 2002.

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CONTENTS

1 THE CONTEXT

Diseases of occupational origin are numerous and diverse (cancers, hearing disorders, respiratory diseases, musculo-skeletal disorders, psychological and depressive disorders, dermatological and allergic disorders, occupational asthma, reproductive disorders, cardio-vascular diseases etc.). Besides the physico-chemical and biological agents, nowadays we are aware of the considerable effect of the psychosocial factors associated with the way the work is organised, the consequences of which for people's health affect both the somatic and mental spheres (1-3). Diseases of an occupational origin weigh heavily on the population's health and are one of the major sources of social inequalities with regard to people's health [4]. Thus the role of exposure to physico-chemical agents in the working environment is such that it is estimated that about half the social differences with regard to mortality due to lung cancer recorded in industrialised countries can be explained by workplace exposure; these social differences are very marked, with three times as many manual workers dying from lung cancer as managerial staff [5]. The place of cases of occupational exposure is of the same order of magnitude for bladder cancers, for which occupational factors account for half the social differences observed for this disease [6].

Despite the considerable importance of occupational diseases, there is only a limited amount of information available in the international literature aimed at making a quantitative assessment of the proportion and number of cases of illnesses attributable to occupational factors, and there is even less information available in France. This is all the more harmful as this type of data can be of considerable help in drawing up priorities in terms of prevention, by indicating the origin of the main risk factors associated with many public health problems as well as the contribution they make. Moreover, the cost of shouldering the burden of occupational diseases in medical and economic terms is a considerable one for the community, and our system of social security lays down specific procedures for financing these costs which need to be based on reliable data. This, moreover, is the role of the Commission, set up by article L.176-2 of the Social Security Code, for which this work was originally accomplished.

However, assessing the number of diseases attributable to occupational factors poses certain methodological problems and involves the availability of reliable epidemiological data. In fact, among the diseases liable to be caused by occupational factors, with very few exceptions, nothing distinguishes them in medical terms from those which might be due to other known or unknown factors: so it is not enough simply to list the cases of a particular disease to be informed about their origin. Moreover, the majority of diseases for which there are occupational risk factors are of multifactorial origin and the part played by occupational factors in their appearance on the scale of the population as a whole may be of greater or lesser significance. Only epidemiological data make it possible to estimate, within the population as a whole, the "fraction attributable to occupational factors", by correlating the risk of disease with the proportion of the population exposed to the factors which are a cause thereof.

The work reported here is restricted to estimating the proportion, within the male French population, of certain types of cancer for which there is a recognised occupational origin. In fact, despite the large number of diseases that have their origin partly in the occupational environment, it is almost only for cancers that we have epidemiological data based on the international literature and on French data, that make it possible, despite various limits which will be mentioned further on in the text, to estimate with sufficient reliability the fraction attributable to factors of an occupational origin in the French population. Particular attention will be devoted to lung cancer (the second cause of incident cancers and the first cause of death due to cancer among men in France) for which certain occupational risk factors are well established, and to cancers for which victims are compensated on the grounds of occupational diseases within the French system.

2 METHODS OF CALCULATING THE FRACTIONS ATTRIBUTABLE TO OCCUPATIONAL EXPOSURE

The proportion (or fraction) of cases attributable to a factor measures the impact of a risk factor within the population. As the majority of diseases are multifactorial, this fraction assesses the proportion of the number of cases of a disease explained by exposure to this factor within a population.

From a methodological point of view, the principle of calculating the number of cases of a disease attributable to a risk factor within a population assumes that it has been established (by epidemiological and other studies) that the factor is a cause of the disease (relationship of a causal nature). Knowledge of the *"relative risk"* [1] which associates the factor and the disease, and the proportion of people exposed to the factor within the population enables to estimate the attributable risk fraction (ARF) to this factor in the following way [7]:

$$ARF = P_E (RR-1) / [P_E (RR-1) + 1]$$

where P_E is the proportion of subjects exposed to the risk factor within the population, and RR the relative risk

This simple formula can be adapted to more complex situations, in particular when there are more detailed data on the relative risks associated with different levels of exposure, or on the relative risks associated with exposure to several risk factors [7]. Other methods of calculation exist in particular for calculating attributable fractions in case-control studies carried out among the general population on the basis of the data from the sample studied [8-9]. When the attributable risk fraction is established, knowledge of the total number of cases of the disease in the population as a whole makes it possible to calculate the number of cases attributable to the factor, simply by multiplying the attributable fraction of the risk by the total number of cases of the disease.

The fraction of risk attributable to a factor, which assesses the proportion of cases of a disease explained by exposure to this factor within a population, is not a universal item of data: it depends not only, as we have seen, on the relative risk of the disease associated with a factor, but also on the proportion of subjects exposed within the population. So, the fraction of risk of lung cancers attributable to asbestos in a country is determined by the proportion of people exposed to this agent. The attributable risk fraction therefore is specific to a given population, and may vary considerably from one population to another. Consequently it is not possible to simply use the data published in the international scientific literature and automatically apply them to the French population in order to find out the numbers of cases attributable to various occupational factors. However, data from countries with a comparable level of industrialisation enable to estimate the order of magnitude of the proportion of these cancers that are attributable to occupational factors.

There are only rare studies that make it possible to assess the prevalence of lifelong exposure to carcinogenic agents within the French population as a whole. The SUMER survey which was carried out in 1994 gives a cross-sectional picture of cases of exposure during that particular year, but the validity of the estimates of prevalence is uncertain [10]; moreover, the period concerned is recent and does not make it possible to take into account the largely deferred nature of the carcinogenic effects of exposure. For two agents, asbestos and wood dust, specific studies of lifelong occupational exposure in France were available, making it possible to estimate the number of men exposed at least once in their lives [11-13]. For these two factors, the attributable risk fractions were therefore calculated on the basis of different hypotheses of relative risk, with the latter coming either from the international literature (lung cancer and asbestos) [15-19,

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[1] *That is to say the measurement of the strength of the association between exposure to the factor and the risk of disease: a relative risk of 2 signifies that a person exposed to the factor has twice as much risk of being affected by the disease as a person who is not.*

22-23], or from a large French case-control study [27-28]. As regards the fraction of mesotheliomas attributable to asbestos, the estimate was calculated directly from a recent case-control study (National Mesothelioma Surveillance Programme; personal communication).

In the absence of sufficiently reliable French exposure data, we relied on the international literature, which puts forward estimates of the attributable risk fraction for various occupational carcinogens. We selected studies carried out in various countries which seemed the most sound in terms of exposure assessment and protocol quality, and validated our choices using literature reviews. These data concern countries of a comparable level of industrialisation to that of France, and the attributable risk fractions are likely to be of a similar order of magnitude. However, there are undoubtedly differences as regards specific cancers or agents, because of the epidemiological profile that is appreciably different for certain cancers, and various industrial characteristics that are peculiar to France. Calculating the number of cases in France using attributable risk fractions from the literature was done taking the extreme values of the latter, in order to offer low and high estimates; in the majority of cases, we favoured the conservative (that is to say the lowest) hypothesis.

Depending on the types of cancer and agents, the data used are therefore of different origin and nature: (*I*) estimates of attributable risk fractions drawn from the international literature concerning countries of a comparable level of industrialisation to that of France: (*ii*) French data allowing, either the direct calculation of an attributable risk fraction or the application of relative risks to data regarding the prevalence of lifelong exposure (asbestos and wood dust).

According to the availability of data, we restricted the estimation of the attributable fractions to certain cancers which are the subject of a Table of Compensation of Occupational Disease [14] in France, for which there is a recognised causal relationship with an occupational agent classified in group 1 (recognised carcinogens) of the International Agency for Cancer Research - IARC). Only cancers for which we had at our disposal, either French data on exposure to occupational carcinogens at population level that were regarded as sufficient, or when credible attributable fractions have been published in the international literature have been included. Squamous cell skin cancers for which compensation is paid have been excluded, because there are no data on their incidence within the French population. The selected cancers were lung cancer, pleural mesothelioma, bladder cancer, nasal cancers, and leukaemia. The calculations were confined to men.

3 CANCERS OF OCCUPATIONAL ORIGIN

Many factors in the occupational environment constitute human carcinogens [15], and these factors form by far the most numerous group among those which have currently been identified: they represent about half the physical and chemical agents, compounds and industrial processes which appear among the factors currently classified in group 1 (recognised carcinogens), and more than two thirds of those classified in group 2A (probable carcinogens) by the IARC.

3.1 Tables of occupational diseases

The Social Security Code (art. L 461-1 Title V) specifies "Any disease designated in a table of occupational diseases and contracted in the conditions mentioned in this table shall be presumed to be of occupational origin". The conditions laid down in the tables of occupational diseases are concerned with a description of the disease for which victims are paid compensation and the circumstances of exposure to an occupational factor (list of types of work that may be restrictive or indicative, claim period[2], exposure periods). A

[2] *The claim period is the time that has elapsed between the cessation of exposure and the occurrence of the disease.*

presumption of occupational origin applies to the occupational diseases listed in the tables once all the conditions laid down therein are fulfilled. There are two official lists of tables of occupational diseases, one for the General Social Security Scheme and one for the Agricultural Scheme [14].

A number of recognised carcinogens, classified in group 1 by the IARC are not covered in France by a table of occupational diseases. Amongst these are: crystalline silica, cadmium, beryllium, unrefined mineral oils, coal gasification, the rubber and leather industries, for which the occupational disease tables do not mention cancer.

Tables compensating for occupational cancers under the General Social Security Scheme

- T 4 (leukaemia and exposure to benzene)
- T 6 (leukaemia, lung cancer, osseous sarcoma and exposure to ionising radiation
- T 10 b (lung cancer and exposure to chromic acid)
- T 15 b (bladder cancer and exposure to aromatic amines)
- T 16 a (lung cancer, bladder cancer, epithelioma of the skin and exposure to coal tar, coal oil, pitches and soots from burning coal)
- T 20 D (epithelioma of the skin, angiosarcoma of the liver and exposure to arsenical fumes or dust)
- T 20 a (lung cancer and exposure to arsenical fumes or dust)
- T 30 C, D, E and 30 a (pleural mesothelioma, primitive pleural tumours, lung cancer and inhalation of asbestos dust)
- T 36 a (epithelioma of the skin and exposure to oil derivatives)
- T 37 b (lung cancer, nasal cancer and exposure to nickel matte grilling)
- T 44 a (lung cancer associated with siderosis and exposure to the inhalation of iron oxide fumes or dust)
- T 45 (cancer of the liver secondary to occupational hepatitis C or D)
- T 47 (cancers of the ethmoid and facial sinuses and exposure to wood dust)
- T 52 (cancer of the liver and exposure to vinyl chloride)
- T 70 b (lung cancer and joint exposure to cobalt and tungsten carbide before sintering)
- T 81 (lung cancer and exposure to bis(chloromethyl)ether)

The majority of the tables of occupational diseases mention restrictive claim periods and limitative lists of types of work giving entitlement to compensation.

Compensation of cancers on the grounds of occupational diseases is considered as particularly worrying in France, since only a small fraction of cancers of occupational origin are in fact compensated on these grounds [15]. One of the aims of this work is to try to assess the extent of this phenomenon for cancers compensated on the grounds of occupational diseases and for which we have sufficient epidemiological data.

3.2 Results

3.2.1 Lung cancer

3.2.1.1 *Lung cancer and all exposures*

Lung cancer is particularly frequent in the world and many etiological factors of occupational origin have been identified [16]. It is also the cancer site for which the number of cases induced by occupational factors is the greatest in industrialised countries. Doll & Peto has estimated that in the United States, 10 to 15% of lung cancers among men and about 5% among women show a considerable occupational etiological element [17]. More recently, other authors [16] have estimated in the same country that these proportions were 9% among men and 3% among women. The proportion of the risk of lung cancer attributable to occupational factors has been estimated at 18% of lung cancers among men in the Nordic countries [18]. A recent Swedish study estimates the fraction of lung cancers attributable to certain occupational exposure factors (diesel fumes, asbestos, and various combustion products) at 9.5% among men in the Swedish population [19], and in Finland 29% of all deaths due to lung cancer are estimated to be of an occupational origin [20] (14% of which are due to exposure to asbestos, 2.7% to exposure to crystalline silica, 0.2% to cadmium, 1.6% to hexavalent chromium, 1.5% to nickel, 4.5% to radon and 3% to occupational passive smoking). Finally, according to Kogevinas et al. [21] this fraction is estimated at 13% among men for Europe as a whole.

Applying these fractions to the annual number of incident cases and deaths due to lung cancer observed in the French population makes it possible to give an order of magnitude to the annual number of cases that one would expect among men due to occupational exposure to a carcinogenic factor (Table 1). According to the hypotheses adopted, this number works out at between 2,713 and 6,051 for new cases occurring annually and between 2,433 and 5,427 for annual deaths due to lung cancer, out of all cases and deaths occurring within the population.

Table 1. Estimate of the fraction of lung cancers attributable to occupational exposure among men in France

		Estimate of the fraction attributable to occupational exposure *AF*			
		International Literature		Number of cancers attributable to occupational exposure *N2 = N1 X AF*	
	Number of cases in France *N1*	Lower hypothesis (a)	Upper hypothesis (b)	Lower hypothesis (a)	Upper hypothesis (b)
Mortality due to lung cancer for 1999 (CépiDC INSERM) Men	20,867	13%	29%	2,713	6,051
Lung cancer Incidence 1995 (Francim network, Ministry of Health) Men	18,713	13%	29%	2,433	5,427

(a) attributable fractions estimated by Kogévinas et al. for Europe
(b) attributable fractions estimated by the Finnish Institute of Occupational Health, Finland

Please note: the data on incidence and mortality do not refer to the same year, which explains the difference between mortality and incidence.

3.2.1.2 *Lung cancer and exposure to asbestos*

Asbestos is the occupational lung cancer risk factor for which we have the best-established data. An estimate of the proportion of retired people in France who have been exposed to asbestos in the course of their working lives has been carried out using two different methods [11-12]. These estimates show that about 25% of men aged 55 and over had been exposed to asbestos during their working lives; taking into account current data, it is reasonable to estimate that this proportion is lower among younger ones. In the work presented here, the proportion of men between 35 and 54 years of age exposed to asbestos during their working lives has been estimated at 10% and we have gone on the assumption that none of the men below 35 years of age had been exposed.

Based on this information, we calculated the proportion of cases of lung cancer attributable to asbestos exposure, assuming that exposure to asbestos increases the risk of lung cancer by 50%. This relative risk of 1.5 is reasonable considering the levels of exposure encountered; it is a lower estimate from the international epidemiological literature, the relative risks associated with higher levels of exposure to asbestos being appreciably higher.[22].

This estimate shows (Table 2) that 12% of lung cancers in men of over 55 and about 7% of those in men of between 35 and 55 can be attributed to exposure to asbestos in the course of their working lives. Applying these estimated proportions to the number of deaths due to cancer in the same age brackets, yields a figure of 2,087 deaths due to lung cancer among men of 55 and over that are attributable to exposure to asbestos and 173 among men between 35 and 54 years of age (Table 2). The same fractions applied to the data on incidence yields a figure of 1,849 incident cases of cancer among men of 55 and over and 160 among those between 35 and 54 years of age attributable to

exposure to asbestos. So both in terms of mortality and incidence, over 2,000 cases of lung cancer are attributable annually to occupational exposure to asbestos among men in France.

The fractions for lung cancer attributable to exposure to asbestos in the data from recent international literature vary for men between 10-20% [23-24, 26] and 14% [20]. When applying these fractions from the international literature to the French data on incidence and mortality, the number of annual deaths attributable to occupational exposure to asbestos is between 2,086 and 4,172 among men, and the number of incident cancers between 1,871 and 3,742 (Table 2).

Table 2. Estimate of the fraction and number of lung cancers attributable to exposure to asbestos among men in France

		Estimate of the fraction attributable to exposure to asbestos (a) *AF*					
	Number of cases France *N1*	French data	International literature	Finnish data	Number of cancers attributable to exposure to asbestos *N2 = N1 X FA*		
		(1)	(2)	(3)	(1)	(2)	(3)
Mortality 1999 (b)							
Men ≥ 55 yrs	17,397	12%			2,087		
Men 35-54 yrs	3,465	7%			242		
Men total	20,867		10-20%	14%	2,329	2,086-4,172	2,921
Incidence 1995 (c)							
Men ≥ 55 yrs	15,406	12%			1,849		
Men 35-54 yrs	3,212	7%			225		
Men total	18,713		10-20%	14%	2,074	1,871-3,742	2,620

a: attributable fractions estimated in France (1) and in the international literature (2) (3)
b: source : CepiDC INSERM
c: source : Cancer in France, Ministry of Health, Francim network

3.2.2 Pleural mesothelioma and exposure to asbestos

Asbestos is the only recognized risk factor for pleural mesothelioma[3]. The data used are taken from the *Programme National de Surveillance du Mésothéliome (PNSM)/National Mesothelioma Surveillance Programme,* which was set up in 1998. This programme brings together several teams and gathers information on all cases of pleural mesothelioma from 21 French departments. From these observed cases, an estimate of the incidence of pleural mesotheliomas is made for the country as a whole. This estimate shows that for the year 1998 the incidence of mesothelioma was about 650 cases among men and 150 among women [25]. By comparing the exposure to asbestos of the cases with that of randomly selected controls, the PNSM was able to estimate the fraction attributable to exposure to asbestos at 85% of mesotheliomas in men. This proportion is comparable with the estimates from the international literature on the subject which range from 80 to 90% [23, 26, 30-31].

When applying this proportion to the numbers of incident cases of mesothelioma for the year 1998, it was estimated that between 537 and 578 new cases occurring during 1998 were attributable to occupational exposure to asbestos in men in France (Table 3).

Table 3: Estimate of the number of incident cases of mesothelioma attributable to exposure to asbestos among men in France in 1998

		Estimate of the fraction attributable to exposure to asbestos (a) *AF*					
Number of incident cases in France (1998, PNSM) *N1*		French data (PNSM)	International literature	Finnish data	Number of mesotheliomas attributable to asbestos exposure *N2 = N1 X AF*		
		(1)	(2)	(3)	(1)	(2)	(3)
Total	770-844						
Men	632–681	85%	88%	85%	537-578	556-599	537-578
Women	138-163	-	-	-	-	-	-

a: attributable fractions estimated in France on the basis of the data provided by the PNSM (1) and that found in the international literature (2) (3)

[3] *Except erionite, which is only found in certain regions of Turkey.*

3.2.3 Bladder cancer

Mortality due to bladder cancer is almost twice as low as the incidence of this type of cancer. The number of deaths due to malign tumours of the bladder in France was 3,470 in 1999 among men [32]. The estimate for the number of new cases of bladder cancers was 7,815 cases among men in 1995 [33]. Mortality from bladder cancers has been increasing regularly since 1975, as has the incidence of such cancers [33].

According to most authors the proportion of bladder cancers attributable to occupational causes varies from about 5 to 25%. It is the second most frequent site for the incidence of occupational cancers in the United States and in the United Kingdom, after cancers of the respiratory system [24, 34-35].

The only occupational risk factors for bladder cancer that are recognised for compensation in France are certain aromatic amines (Table of Occupational Diseases 15 b) and work involving the use of tars, oils and pitches in the manufacture of aluminium by electrolysis using the continuous anode process (Table of Occupational Diseases 16 a).

As no lifelong exposure data for men are available in France for these two agents, the only estimates of the fraction of bladder cancers attributable to occupational factors which could be made were based on data from the international literature (Table 4). The latter estimates the proportion of bladder cancers attributable to exposure to occupational agents at about 10% (USA) [35] and 8% (Europe) [21]. Finnish data from Nurminen & Karjalainen [20] estimate the fraction of bladder cancers in men that are attributable to exposure to aromatic amines at 5.4% and the fraction attributable to exposure to aromatic polycyclic hydrocarbons at 1.9%, with the total proportion of occupational bladder cancer among men in Finland being estimated at 14.2%.

According to the hypotheses applied the numbers of cases of bladder cancer attributable to occupational exposure which would be likely to occur each year in men in France would be between 625 and 1,110 and these factors would give rise to between 347 and 492 deaths due to bladder cancer. Relying on the Finnish data, the estimated number of bladder cancers attributable to aromatic amines and aromatic polycyclic hydrocarbons in France at 570 (422 + 148) – and these would be likely to give rise to 253 deaths (187 + 66) (Table 4).

Although these numbers are based on proportions of bladder cancers attributable to occupational exposure gleaned from the international literature, the data from American, European and Finnish studies suggest estimates of several hundreds of annual incident cancers in France.

Table 4. Estimate of the fraction of bladder cancers (ICD-9 188) attributable to occupational exposure among men in France

Number of cases in France *N1*		Occupational agent	Estimate of the fraction attributable to occupational exposure (a) *AF* International literature	Finnish data	Number of cases attributable to occupational exposure *N2 = N1 X FRA*	
			(1)	(2)	(1)	(2)
Mortality 1999 (b) Men	3,470	All	10%	14.2%	347	492
		Aromatic amines	-	5.4%		187
		PAH	-	1.9%		66
Incidence 1995 (c) Men	7,815	All	8–10%	14.2%	625-781	1,115
		Aromatic amines	-	5.4%		422
		PAH	-	1.9%		148

a: attributable fractions estimated in the international literature (1) and in Finland (2)
b: source : CepiDC Inserm
c: source : Cancer in France, Ministry of Health, Francim network

3.2.4 Sinonasal cancers and exposure to wood dust

The carcinogenic effects of wood dust have been known for many years. wood dust induces rare cancers (nose, nasal cavities and facial sinuses) for which the main known risk factors are occupational: wood dust, nickel and chromium, the leather industry and formaldehyde. In France, Table of Occupational Diseases No. 47 only compensates for cancers of the ethmoid and facial sinuses: this table does not include cancers of the nasal cavities (ICD-9 160.0) although these are strongly associated with exposure to wood dust [13, 27-29]. It should also be pointed out that Table of Occupational Diseases 37a for its part compensates for primitive cancers of the ethmoid and facial sinuses, in relation to work involving operations on nickel matte grilling.

Several studies have estimated the fraction of these cancers that are attributable to occupational factors. This fraction has been estimated at 25% of this type of cancers in the USA [17]; more recently, a study by Kogevinas [29] suggested a figure of 39% for the proportion of occupational factors as a whole for cancers of the nose and sinuses. A recent work by M. Carton and M. Goldberg (Inserm, Unité 88) in collaboration with the Occupational Health Department of the Health Surveillance Institute, as a supplement to the recently published data [13], yields an estimate of the proportion of men who had been exposed to wood in the course of their working lives at 9% (personal communication). The relative risks of the appearance of cancer of the sinuses and nasal cavities associated with occupational exposure to wood dust vary considerably depending on the histological type of cancer: very high relative risks (relative risks of 12 to 41, according to the studies, for occupations exposing people to wood dust such as joiners, cabinet makers) are reported for adenocarcinomas which are particularly frequent forms in France [27, 36].

We calculated the fraction of cancers of the nose and facial sinuses attributable to exposure to wood in France on the basis of a RR = 10 (a low hypothesis in view of the proportion of adenocarcinomas in France which is about 50%) and a prevalence of lifelong exposure of 9% among men. On these bases, 45% of these cancers are related to exposure to wood dust in France, that is to say 113 incident cases of cancer for the year 1997. Using international data the number of incident sinonasal cancers attributable to occupational exposure in France can be estimated at between 60 and 102 annually (Table 5). In 1999, 67 cancers of the ethmoid and facial sinuses were recognized under the terms of Table 47 of the General Social Security Scheme (60 in 2000).

A comparison of the fractions of cancers attributable to exposure to wood dust estimated in Finland and in France shows that this fraction seems greater in France. This could be explained by the difference in woodworking methods between the two countries and the type of wood used: France uses much more hard wood in the wood processing industry (especially in the manufacture of furniture).

Table 5. Estimate of the fraction of cancers of the nasal cavities, ethmoid and facial sinuses attributable to occupational exposure among men in France (ICD-9 160.0 – 160.2-160.8)

Number of cases in France (Men) *N1*	Occupational agent	Estimate of the fraction attributable to wood dust exposure (a) *AF* French data (1)	International literature (2)	Finnish data (3)	Number of cases attributable to wood dust exposure *N2 = N1 X AF* (1)	(2)	(3)
Incidence (ethmoid, nasal cavities, facial sinuses) 1997 (b) 250	All	-	25 – 41 %	24,0 %	-		250
	Wood dust	45,0 %	-	15,7 %	113		
	Nickel-Chromium	-	-	7,3 %	-		

a: Attributable fractions estimated in France (1), in the international literature (2) and in Finland (3)
b: Source: Cancer Incidence in Five Continents – IARC, WHO 1997: incidence rate between 0.9 and 1.5/100,000 men according to French cancer registers (250 cases corresponds to the lower rate, that is to say 0.9/100.000)

3.2.5 Leukaemia and occupational exposure

The role of exposure to benzene in the appearance of leukaemia has been established for a long time. This disease is the subject of Table 4 of Occupational Diseases in the General Social Security Scheme. The occupational risk factors associated with the appearance of leukaemia are essentially benzene and ionizing radiation. There are no published French data currently available for estimating the fraction of leukaemias that are related to occupational exposure. The frequency of lifelong exposure to benzene in the French population has not been documented so far, so the estimates proposed in Table 5 come solely from the international literature. In the USA the proportion of leukaemias that are of occupational origin among men is estimated at 10% [17]; in Europe, it is estimated at 5% [21]. In the Finnish study, this fraction is estimated at 18.5% [20].

According to these different hypotheses, between 112 and 413 new cases of leukaemia among men in France would therefore have been attributable in 1995 to occupational exposure (Table 6).

Table 6. Estimate of the fraction of leukaemias attributable to occupational exposure among men in France (ICD-9 204-208)

	Number of cases in France (Men) *N1*	Occupational agent	Estimate of the fraction attributable to occupational exposure (a) *AF* French data (1)	International literature (2)	Finnish data (3)	Number of cases attributable to occupational exposure *N2 = N1 X AF* (1)	(2)	(3)
Leukaemia incidence (1995) (b)	2,233	All	-	5–10%	18.5	-	112-224	413

(a) : attributable fractions estimated on the basis of data from the international literature (2) and Finnish data (3)
(b) Source: Cancer in France, Ministry of Health, Francim network.

3.3 Summary: comparison of the estimates with the number of cancers for which compensation was paid on the grounds of an occupational disease

As we have already mentioned in the Foreword, it is rare to come across available data that would enable one to estimate directly the number of cases of cancer that are attributable to occupational exposure in France. However, there is a certain amount of information available at international level that makes it possible to make reasonably close estimates for a certain number of them. They are summarized in Table 7 which also shows the number of cancers that were compensated on the grounds of an occupational disease in the course of the year 1999 [37].

Table 7. Number of cases of occupational cancer recognised by the General Social Security Scheme in 1999 and estimates of the overall number of attributable cases inclusive of all schemes (men, all France)

		Cases compensated under General SS Scheme (a)		Number of cases attributable among men in France		
				Application of attributable AF		
				International		French
Cancer	Occupational agent	Table of occupational diseases	1999 (a)	Lower hypothesis	Upper hypothesis	
Leukaemia	Benzene	4	16	-	-	-
Leukaemia	Ionizing radiations	6	11	-	-	-
Total leukaem	**-**	**-**	**27**	**112 (b)**	**413 (b)**	**-**
Lung	Ionizing radiations	6	7			
Lung	Chromic acid	10ter	6			
Lung	Coal tar	16bis	5			
Lung	Arsenic	20bis	1			
Lung	Asbestos	30 C & 30bis	438	1 871 (b)	3 742 (b)	2074 (b)
Lung	Nickel	37ter	1			
Lung	Cobalt, tungsten	70ter	0			
Lung	Bischloromethylether	81 A	0			
Total Lung	**-**	**-**	**458**	**2 433 (b)**	**5 427 (b)**	
Pleural meso	Asbestos	30 D	267	537 (c)	599 (c)	537–578(c)
Other pleur tum	Asbestos	30 E	20			
Peritoneal meso	Asbestos	30 D	11			
Pericardial meso	Asbestos	30 D	2			
Total meso	**Asbestos**		**310**			
Bladder	Aromatic amines	15ter	4	-	422	-
Bladder	Coal tar	16bis	3	-	148	-
Total Bladder		**-**	**7**	**625 (b)**	**1115 (b)**	**-**
Sino nasal	Nickel	37ter	0	18 (d)		-
Sino nasal	Wood dust	47	67	40 (d)	-	113 (d)
Total Sinonasal	**All agents**	**-**	**67**	**60 (d)**	**102 (d)**	**-**
Hepatocell carc	Hepatitis B/C	45	0			
Oss sarcoma	Ionizing radiations	6	0			
Angiosarcoma	Vinyl chloride	52	0			
Total			**869**			

a: Quarterly industrial accident statistics – CNAMTS – Paris, March 2002 – definitive data drawn up on, pages 39-56.

b: Estimates of the number of cases attributable to occupational factors out of the 1995 incident cases. Source: Cancer in France, Incidence and Mortality, situation in 1995, trends between 1975 and 1995. Francim, Ministry of Health, Paris.

c: Estimate of the number of attributable cases out of the incident cases estimated by the National Mesothelioma Monitoring Programme, year 1998, BEH no. 03/2002, 2002 : 11-13

d: Estimate of the number of attributable cases out of the incident rates estimated by the IARC, for the year 1997: Cancer incidence in five continents, vol. VII, Edit DM Parkin, SL Whelan, J. Ferlay, L. Raymond and J. Young. IARC Scientific Publications, no. 143, Lyon 1997, p. 989.

On the basis of the attributable risk fractions reported in the international literature, the annual numbers of cases of lung cancer due to exposure to an established carcinogen would be between 2,713 and 6,051 for incident cases, and between 2,433 and 5,427 for deaths, according to different hypotheses. In 1999, compensation was paid for 458 lung cancers on the grounds of occupational diseases in France by the General Social Security Scheme.

There are available French data for estimating the number of pleural mesotheliomas and lung cancers attributable to exposure to asbestos among men in the French population, which can be regarded as realistic when compared with the estimates made in countries with a comparable level of industrialization. The data from the *National Mesothelioma Surveillance Programme (PNSM)* allowed for a reliable estimate of the number of mesotheliomas which occurred in France in 1998 and the fraction that may be attributed to occupational exposure to asbestos among men. This fraction works out at over 550

cases of mesothelioma among the male population that may be attributed to occupational exposure to asbestos. Despite the efforts devoted over the last few years in France to compensating mesotheliomas, the number of mesotheliomas compensated in the Tables of Occupational Diseases is still well below the actual number that are occurring, since in 1999 only 297 cancers of the pleura were compensated under the General Social Security Scheme (which covers about 80% of the population).

Taking into account the data available on the prevalence of exposure to asbestos in France, the estimated fraction of lung cancers attributable to this agent is 12% among men of 55 years and over, and 5% among 35-54 year olds, and the estimated number of incident cases in the year 1995 is over 2,000; estimates of the number of cases of lung cancers among French men range between 1,871 and 3,742 when applying the data from the international literature. In 1999 compensation payments for lung cancer under Tables 30 and 30*a* of the General Social Security Scheme accounted for 438, out of a total of 458 lung cancer cases compensated under the terms of the Tables of Occupational Diseases as a whole.

With regard to bladder cancer**,** the attributable risk fractions used are those from the international literature, in the absence of information on the proportion of men exposed to the established occupational risk factors for bladder cancer in France. According to the references used, the number of new cases of bladder cancer attributable to occupational exposure would have been between 625 and 1,110 for men in 1995 in France. However, the number of bladder cancers for which compensation was paid under the General Social Security Scheme in France was a mere seven in 1999.

French data on the prevalence of exposure to wood dust in France made it possible to estimate the number of cancers of the nose and facial sinuses that could have been attributed to exposure to wood dust in men in 1997 at a figure of 113. As with mesothelioma, despite the very strong association between occupational exposure and the disease, we found that this cancer was undercompensated, with the number of cases recognised in 1999 by the General Social Security Scheme being 67. It should be noted that this figure of 113 expected cases is probably an underestimate itself, as the calculation of this number of expected cases was made by applying the attributable fraction to the lowest observed rate of incidence in the eight French cancer registers published by the IARC in 1997. There is a large discrepancy between the data on mortality and the data on incidence, which poses a problem of reliability; no other data was available.

According to different hypotheses, between 112 and 413 incident leukaemias among men in France would have been attributable in 1995 to occupational factors, whilst in 1999, 27 cases were compensated as occupational diseases by the General Social Security Scheme (15 on the grounds of exposure to benzene, and 11 on the grounds of exposure to ionising radiation).

4 DISCUSSION

This work is concerned with estimating the number of deaths and/or incident cases that could be attributed annually to established occupational risk factors in France for certain types of cancer. These estimates have been based on data on the exposure of the male French population, when such data were available, and on estimates of attributable risk fractions taken from the international literature.

Estimating risk fractions attributable to a particular factor is an exercise whose results depend on the quality of the data available for making the calculations. Uncertainties which may arise are concerned with whether there is a causal relationship between exposure to the factor and the disease, the value of the relative risks, and the prevalence of exposure. The relative risks must be adjusted to take into account known confounding factors [38]; they may be estimated directly from the population to which the estimates of attributable fractions apply [8 – 9], or come from summaries of the literature, but at all events, the value used for the calculation must take into account the different levels of exposure that are encountered in the general population [39]. Ideally the prevalence of exposure should reflect the lifelong frequency of exposure among those subjects among the population to which the results apply [40].

In this work, only agents for which a causal relationship with the cancer studied was established by IARC have been taken into account.

When we have directly calculated an attributable risk factor (mesothelioma and asbestos), the value of the relative risk came from data from a case–control study on pleural mesothelioma in the general population produced by the PNSM that can reasonably be considered as representative of the French situation [25]. For the fraction of sinonasal cancers attributable to wood dust, the value of the relative risk came from a substantial multicentric French study, in which relative risks adjusted for various confounding factors have been established on a population base that may also be regarded as representative of France [27]. When we have used French exposure data to which relative risks established elsewhere have been applied (lung cancer and asbestos, cancer of the nose and wood dust), the data concerned the lifelong frequency of exposure of men in the French population [11 – 13]. When we have used estimates of attributable fractions taken from the international literature, only studies regarded as of a sufficient quality by various authors have been included [7-9, 38-40]. These data came from countries with a level of industrialization comparable to that of France; there are undoubtedly differences with regard to specific cancers or agents, because of various industrial characteristics peculiar to France and the epidemiological profile of certain cancers, which varies from one country to another, but it may be considered that on the whole such differences do not introduce major distortions, as can be seen from the results when it has been possible to estimate French attributable fractions directly, which are of an order of magnitude generally close to what was found in the international literature.

The estimates of the number of cases which could be attributed to occupational risk factors use the latest cancer incidence data published for France: those for the year 1995 (bladder cancers, lung cancers, leukaemia), those for the year 1997 for sinonasal cancers, and those for the year 1998 for pleural mesotheliomas. The consolidated data on compensation for occupational cancers for their part are more recent (1999). The incidence of the majority of the cancers studied in this work is tending to increase regularly [33], which would tend to minimize the estimates presented here. Moreover, the hypothesis that the proportion of cancers giving rise to compensation is still lower than the figure that can be deduced from the reported estimates is very probable, as a number of occupational factors acknowledged as known carcinogens classified in the IARC's Group 1 are still not the subject of Occupational Disease Tables in France.

The study has focused exclusively on men. Indeed, although the part played by occupational factors in cancer among women is probably underestimated [39], current data on the occupational exposure of women to occupational cancer-causing agents are still very inadequate. It should be pointed out that the statistics supplied by the Caisse nationale d'assurance maladie des travailleurs salariés (CNAMTS)/Employees' Sickness Insurance Fund of the General Social Security Scheme [37] do not currently make it possible to differentiate between recognized occupational diseases on the basis of gender, and that the proportion of cancers among women that may be attributed to occupational factors should not be disregarded, although it is probably less than among men.

Our estimates have enabled us to put forward upper and lower limits for the numbers of cancers expected annually and to stress the extent of the discrepancy between these numbers and those for compensation payments on the grounds of occupational diseases under the General Social Security Scheme. Indeed, if we apply a reduction of 20% to take into account workers affiliated to other Social Security Schemes, more than 1,600 cases of lung cancer related to occupational exposure to asbestos ought to have been able to be compensated under the General Scheme in 1999, and between 430 and 460 cases of pleural mesothelioma among men in 1998.

It appears that whilst the role of occupational factors in the occurrence of cancers is on the whole largely unrecognised, there exists – depending on the type of cancer – a large disparity in the probability of a cancer being compensated on the grounds of an Occupational Disease. Pleural mesothelioma and cancers of the nose are the least badly recognised, since more than half of those that may be attributed to an occupational origin benefit from compensation under the General Social Security System. This percentage is close to 20% for lung cancers, but this result is explained almost exclusively by exposure to a single causal agent, namely: asbestos. On the other hand, leukaemia (about 10%) and especially bladder tumours (about 1%), are virtually always unrecognised as cancers of an occupational nature. Finally, it seems that when it is a question of a rare cancer that is very strongly associated with a specific agent that is well known to specialised physicians (asbestos, wood dust, in particular), under-recognition is less marked; on the other hand, the more a cancer is frequent and of multifactorial aetiology, the less the occupational origin is taken into account. The example of lung cancer illustrates this situation. In a study by Bergeret *et al.* on lung cancer in the Lyon region [42], an assessment of occupational exposure carried out by industrial hygiene experts showed that 115 of the 516 patients (22.2%) included in their study fulfilled the administrative conditions for compensation as an occupational disease. Not one of them had been issued with an occupational disease certificate. In another set of 327 lung cancers in the Ile-de-France and Basse-Normandie regions between 1994 and 1997, an expert report on their work records concluded that 24.8% of the subjects had definitely been exposed to asbestos during at least one job and that 12.2% had probably been exposed in this way [43]. A study carried out in 1996 into incident cases of lung cancer admitted to a hospital pneumology department in the Ile-de-France region estimated that 24% of the 123 patients who had been questioned about their working lives could be compensated, which represented 15% of the incident cases [44]. These studies, although they throw an interesting light on the subject, cannot be directly extrapolated to the French population as a whole, as they were carried out in particular regions and may reflect specific regional factors with regard to the occupational exposure of the subjects.

Despite the imperfections and methodological limitations of the reported estimates, it is likely that they are realistic and make it possible to assess the extent of the under-compensation of these diseases, even though we systematically chose the most conservative hypotheses. The reasons for such a phenomenon remain to be explained. There are very few works in France – either epidemiological or sociological – which would help to better identify "log jams" in the system of compensating occupational diseases: ignorance or refusal on the part of the patient (or his or her family, especially in the case of sudden death), a lack of knowledge of the occupational origin and application

procedures on the part of the attending physicians, Occupational Disease Tables that are too restrictive (claim periods, restrictive lists of work giving rise to exposure) or too strict an application of the rules by the Social Security bodies.

There are a few indications however showing that at least in the case of some cancers, the bottleneck is to be found mainly upstream of the Social Security bodies, at patient and attending physician level. Several case-control studies carried out by Bergeret *et al*., in the Rhône department between 1983 and 1990 provided a formal assessment on a case by case basis of the criteria for recognising certain cancers as occupational diseases. This analysis showed that ignorance of the potential occupational origin of these cancers among attending physicians and patients constitutes an important obstacle to their recognition as occupational diseases; thus, among the cases of cancer included in these investigations that corresponded to the criteria in the relevant Occupational Disease Tables, only four cases of leukaemia out of 25 that were eligible had given rise to an application (all of which were compensated), and none of the six bladder cancers, or 115 lung cancers corresponding to the criteria for recognition as Occupational Diseases had given rise to a certificate from the attending physician. A study carried out in the Ile-de-France region shows that in 1996, out of 215 declarations of diseases connected with asbestos exposure (53 of which were mesotheliomas), 154 were compensated on the grounds of occupational diseases, that is to say 72% of the declarations and 93% of the cases regarded as characterised diseases. So these studies would tend to suggest that the main problem with the phenomenon of under-compensation of mesotheliomas occurs at patient and attending physician level, before the application [45]. This hypothesis seems to be confirmed by a study included in the *National Mesothelioma Surveillance Programme (*PNSM), aimed at assessing acceptance on the grounds of an Occupational Disease among patients for whom prior occupational exposure to asbestos has been identified. Out of 213 pleural mesothelioma cases covered by the General Scheme diagnosed in 1999 or 2000 in 18 departments, an Occupational Disease Declaration was made for 126 subjects (59%); 121 of these were recognised (96%), and 5 cases (4%) were rejected. Among the 87 patients who did not apply for recognition as cases of occupational diseases, 30 (34.5%) were identified as having had occupational exposure to asbestos in the course of the expert report on their working career. So there is a high frequency of subjects who do not make an application for recognition as cases of Occupational Diseases, even though exposure to asbestos is identified among more than a third of these patients (Pairon JC *et al.* Medico-Social Section of the National Mesothelioma Surveillance Programme: preliminary results. Personal communication). There seems to be a need therefore to continue with the efforts made over the last few years to inform workers, retired people and doctors about the compensation of diseases of an occupational origin.

5 CONCLUSION

This work is the very first approach at quantifying cancers of an occupational origin in France. A number of works that are in progress or in preparation will make it possible to document the matter more satisfactorily in years to come.

Thus, an important study into the occupational risk factors for lung cancer and cancers of the upper airways tract in the French population has just begun (ICARE study, D Luce Inserm Unité 88 and I. Stucker Inserm Unité 170). It will make it possible to verify a number of estimates and to calculate the fractions attributable to a large number of occupational risk factors for these cancers which are particularly frequent in France.

Moreover, the Occupational Health Department of the Health Surveillance Institute (InVS), has launched the MATGENE program, aimed at producing a whole set of job-exposure matrices which will make it possible to assess the exposure of the French population to chemical agents throughout their working careers.

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