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#### Title: Lung cancer risk assessment for workers exposed to polycyclic aromatic 1 hydrocarbons in various industries 2

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#### Pascal Petit<sup>a</sup>, Anne Maître<sup>a,b,\*</sup>, Renaud Persoons<sup>a,b</sup>, Dominique J. Bicout<sup>a,c</sup> 4

- 5 6 7 8 <sup>a</sup> Univ. Grenoble Alpes, CNRS, Grenoble INP, TIMC-IMAG, EPSP team (Environment and Health Prediction of Populations), 38000 Grenoble, France
- <sup>b</sup> Grenoble Alpes teaching Hospital, CHUGA, Occupational and Environmental Toxicology Laboratory, Biochemistry
- Toxicology and Pharmacology Department, Biology and Pathology Institute, F-38000 Grenoble, France
- 9 <sup>c</sup> VetAgro Sup, Biomathematics and Epidemiology Unit, Veterinary Campus of Lyon, F-69280 Marcy l'Etoile, France
- 10
- 11 \* Corresponding authors at: Laboratoire TIMC-IMAG (UMR 5525 CNRS - UGA), Equipe EPSP, Faculté de
- 12 Médecine de Grenoble, Domaine de La Merci, 38706 La Tronche Cedex, France.
- 13 E-mail address: anne.maitre@univ-grenoble-alpes.fr

### 14 ABSTRACT

- 15
- 16 *Background:* Millions of workers are exposed to carcinogenic polycyclic aromatic hydrocarbon (PAH) mixtures.
- 17 The toxicity of PAH mixtures is variable and depends on the composition of the mixture, which is related to the
- emission sources. Although several indicators exist, the cancer risk estimation associated with occupational
   exposure to PAHs is poorly known.
- 20 *Objectives:* To assess the risk of lung cancer associated with PAHs in several industries using the atmospheric 21 concentrations of benzo[a]pyrene (BaP) as a proxy.
- *Methods:* A total of 93 exposure groups belonging to 9 industries were investigated. Eight indicators found in the
   literature were compared to assess risks. A consensual indicator was used to estimate lung cancer risks.
- 24 *Results:* Approximately 30% of the exposure groups were above the maximal risk level of the European Union
- 25 (10<sup>-4</sup>). The risk probabilities were >10<sup>-3</sup> for coke and silicon production; >10<sup>-4</sup> for the manufacturing of carbon
- 26 products and aluminum production;  $>10^{-5}$  for foundries and combustion processes;  $>10^{-6}$  for the use of
- 27 lubricating oils and engine exhaust emissions; and  $>10^{-7}$  for bitumen. The risk probabilities were highly variable
- 28 within industries (from 1 to 1,000 likelihood). A total of 27 (95% CI: 0.1-54) contemporary additional lung
- cancer cases could be expected per year in the French exposed population based on estimations using publisheddata.
- 31 Conclusion: This study provides an overview of cancer risk estimation in many industries. Despite efforts and
- 32 changes that had been made to decrease risks, PAHs remain a sanitary threat for people exposed to these
- 33 pollutants in occupational environments.
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- 35
- 36 Keywords: PAHs, human lung cancer risk assessment, risk probability, inhalation exposure, modeling

#### 37 **1. Introduction**

Lung cancer is among the most encountered cancer in France, with 45,222 new cases (30,401 men and
14,821 women) estimated for the year 2015 (INCa 2017a). Between 5 and 15% of these cases are
believed to solely derive from occupational exposure to chemicals such as asbestos, polycyclic
aromatic hydrocarbons (PAHs), fibers or dust (IARC 2018; INCa 2017b).

PAHs are a group of widespread persistent organic pollutants that are naturally found in the 42 environment. PAHs form a family that includes more than 100 molecules composed of at least two 43 44 fused benzene rings (Achten and Anderssson 2015; Kim et al. 2013; Wickliffe et al. 2014). Although 45 PAHs can be emitted by natural sources (e.g., forest fires, volcanic eruptions), anthropogenic activities 46 contribute most to PAH emissions (Li et al. 2013). PAHs are always emitted in complex mixtures 47 during the combustion process or the distillation of coal and oil (Kim et al. 2013). PAH mixtures are 48 composed of a particulate (heavier compounds, potentially carcinogenic) and gaseous phases (lighter 49 compounds, less toxic) (Park et al. 2002). The general population is mainly exposed to PAHs by 50 inhalation of cigarette fumes for smokers (Ramirez et al. 2011) and ingestion of smoked food for non-51 smokers (Ravindra et al. 2008). Workers are mainly exposed to PAHs via inhalation and, to a less 52 extent, cutaneous absorption (Ravindra et al. 2008).

PAHs are among the most toxic carcinogens currently known. The carcinogenicity of PAHs is mostly 53 54 caused by their ability to attach DNA, thus generating several disorder effects that often lead to tumor 55 initiation (Boström et al. 2002; Misaki et al. 2016; Zaccaria et al. 2013). Several epidemiological 56 studies have incidentally shown an association between exposure to PAHs and an increased risk of 57 developing lung, skin and bladder cancers (Armstrong et al. 2003; Boffetta et al. 1997; Bosetti et al. 58 2007; Böstrom et al. 2002; Ifegwu and Anyakora 2015; Kim et al. 2016, Rota et al. 2014). More recent 59 studies have suggested that PAHs are responsible for an increased risk of developing breast, kidney, 60 prostate, larynx, blood (leukemia), brain and colorectal cancers (Clapp et al. 2008; Hamidi et al. 2016;

61 Korsh et al. 2015; Pan et al. 2005; White et al. 2016).

PAHs are mainly encountered in occupational settings, where exposure can be high. The total airborne concentration levels and relative proportions of concentrations (profiles) of PAH congeners in mixtures are highly variable and depend on emission sources, which differ from industrial to other sectors (Maître et al. 2018, Manoli et al. 2004; Petit et al. 2017a). Occupational exposure varies over several orders of magnitude (Maître et al. 2018; Petit et al. 2017a). Because of the wide range of chemical compositions and concentrations in PAH mixtures, the toxicity of PAH mixtures is variable and depends on the emission sources.

Occupational exposure to PAHs is mainly associated with lung cancer. In the year 2000, it was
estimated that 3% of lung cancer was attributable to occupational exposures in men exposed to PAHs
in France (Boffetta et al. 2010), which is similar to results found in Italy (2.9%, 95% CI: 0.1%-5.9%)
for the period from 2002-2005 (De Matteis et al. 2012). The attributable fraction of lung cancer among

73 this 3% of PAH exposed male workers was estimated to be equal to 27% (Boffetta et al. 2010). Thus, 74 occupational exposure to PAHs was thought to be responsible for 188 lung cancer cases among 75 exposed male workers in France in 2000 (Boffetta et al. 2010) and for 131 (95% CI: 5-266) in Italy in 2005 (De Matteis et al. 2012). In 2015, the International Agency for Research on Cancer (IARC) 76 estimated that occupational exposure to PAHs in France was responsible for 14 new lung cancer cases 77 78 in men (IARC 2018). More accurately, using the previously mentioned attributable fractions and the 79 incidence of the lung cancer, we estimated that between 12 to 37 lung cancer cases would be expected 80 in France in 2015 among male occupationally exposed to PAHs<sup>1</sup>.

Millions of workers are exposed to PAHs in numerous industries, such as aluminum production,
silicon production, electrode production or road paving (Burstyn et al. 2002, Marczynski et al. 2009).
However, there is a lack of knowledge regarding the quantitative assessment of PAH carcinogenic
risks.

85

The aim of this study was to assess the PAH occupational lung cancer risk in various industries and occupations. To achieve this goal, two issues must be considered: how such risk estimation can be performed, and which PAH congener or combination of PAH congeners should be used.

89 Regarding the how, the most commonly encountered approach is to use an indicator that quantitatively 90 estimates exposure risk by calculating a probability corresponding to the chances of an additional 91 human cancer over a certain period of time (usually a lifetime exposure). For example, a probability of  $10^{-6}$  means that there is one chance in a million of observing an additional case of cancer for a lifetime 92 93 exposure. Several indicators exist and are mainly used in environmental studies. The simplest 94 indicator consists of multiplying the exposure concentrations (of a chosen PAH congener or 95 equivalent) by a unit risk, such as the inhalation unit risk (IUR) for inhalation exposure (Callen et al. 96 2014; Hsu et al. 2014; Jia et al. 2011). Other more elaborated indicators take into account different 97 parameters of the exposure conditions and/or human characteristics to minimize the uncertainties of 98 the risk estimation (Petit et al. 2018, in preparation). Probabilistic cancer risk assessments are valuable 99 tools but can be problematic because approaches differ between countries and organizations and 100 because they often result in uncertainty ranges that include the risk considered acceptable (Slob et al. 2014). The provision of a range (e.g., 95% CI), however, is paramount because it demonstrates 101 102 whether knowledge about cancer risk is poor and because it is preferable to single values that can be misleading and might lead to incorrect decisions (Slob et al. 2014; Du et al. 2014). To our knowledge, 103 104 there is no guide, recommendation or gold standard concerning the best choice and condition for using 105 these indicators. In addition, the indicators found in the literature provide risks that vary over several

<sup>&</sup>lt;sup>1</sup>lung cancer incidence for male in France for the year 2015 (30401) × attributable fraction of lung cancer associated to occupational exposure to chemicals (5% to 15%) × attributable fraction of lung cancer associated to occupational exposure in men exposed to PAHs in France (3%) × attributable fraction of lung cancer among the 3% of PAH exposed male workers (27%).

orders of magnitude, which is problematic because, depending on the indicator chosen, decisions will be completely different and could be misleading or incorrect (Petit et al. 2018, in preparation). In addition, it also limits the ability to provide consistency, to assess changes in risk, to compare risks, or to weigh the benefits of risk management options versus costs. Therefore, all indicators found in the literature were compared to confirm this result using our data, and a consensual indicator was used to perform the risk estimation.

Benzo[a]pyrene (BaP), the only PAH classified as a proven human carcinogen (IARC 2017) or in 112 113 most cases, the benzo[a]pyrene toxic equivalent concentration (BaPeq), are used as proxy for the risk 114 estimation (Cincinelli et al. 2007; Liu et al. 2013). The BaPeq approach is believed to take into 115 account the total carcinogenic potency arising from exposures to a mixture of various PAH 116 compounds with different toxicities. In this approach, the concentration of a given carcinogenic 117 congener is expressed as a BaP equivalent concentration using a toxic equivalent factor (TEF) that utilizes BaP as a reference compound to adjust its original concentration depending on toxicity 118 119 differences between both congeners (Boström et al. 2002). Ultimately, BaPeq corresponds to the sum 120 of the BaP concentration and of all congener BaP equivalent concentrations. The TEFs and PAH congeners used for the BaPeq calculation vary between authors. Some, for instance, include all PAHs 121 classified as carcinogens by the IARC while some include all 16 EPA (Environmental Protection 122 123 Agency) PAHs. In addition, the use of TEF is a matter of debate, as their construction is not 124 necessarily based on the inhalation route and as they could misestimate the actual risk when dealing 125 with complex mixtures (Boström et al. 2002; Dreij et al. 2017). Indeed, BaPeq is based on the additive 126 effect of each PAH congener toxicity within mixtures. However, predicting the effects of the whole 127 PAH mixture on risk remains a challenge because both antagonistic and synergic effects/interactions 128 have been observed during in vitro studies, even when dealing with simple binary mixtures (Genies et 129 al. 2016; Jarvis et al. 2014; Tarantini et al. 2011). In addition, when calculating BaPeq concentrations, 130 only a handful of PAH congeners among hundreds are taken into account, which could underrepresent 131 the carcinogenic potency (Samburova et al. 2017). Finally, BaPeq may not be a better index of PAH mixtures than BaP, in particular because the TEFs assigned to each PAH congener are very low 132 (Maître et al. 2018). Consequently, our analysis focused on BaP concentrations to estimate lung cancer 133 134 risk. However, the results of the lung cancer risk estimation using BaPeq are also provided for comparative purposes in the main tables and in more detail in the Supplemental Material. 135

- 136
- 137 **2.** Materials and Methods
- 138

#### 2. Wraterials and Wrethous

### 2.1 Data origin, selection and description

139 The data used in this study were from the Exporisq-HAP database (E-HAP), which includes 140 measurements of atmospheric PAHs consistently performed with the same sampling strategy and 141 analysis. A detailed description of the sampling procedure is presented in the Supplemental Material. 142 The creation and construction of the database is detailed in a previous work (Petit et al. 2017b). The E-143 HAP contained 1729 air samplings (personal and area) comprising the concentrations (in ng/m<sup>3</sup>) of 17 PAHs over short-term sampling ( $\leq 2$  h) and long-term sampling (>2 h) durations. The industrial 144 landscape found in the E-HAP is organized into three imbricated hierarchical levels of increasing 145 description. Each sampling was assigned a level 1 (L1G), level 2 (L2G) and level 3 (L3G) exposure 146 group. L1Gs, which typically refer to product/raw material characteristics, were subdivided into L2Gs 147 corresponding to the exposure source characteristics (locations and/or operations with different 148 149 emission sources). In addition, L2Gs were split into L3Gs that typically referred to a task or a series of 150 tasks that appeared to be the most homogeneous during the work study (Petit et al. 2017b). Levels 1, 2 and 3 were the least, intermediate and most accurate levels, respectively, of the description of the 151 152 occupational context. A detailed description and additional information (e.g., process description) for 153 each exposure group are also available (Petit et al. 2017b).

Samplings were performed in nine L1Gs: aluminum production, silicon production, coke production, manufacturing of carbon products, foundries, combustion processes, use of lubricating oils, engine exhaust emissions, and bitumen (road paving). Each measurement was associated with additional information, such as the sampling time or protective equipment.

158 For the purpose of assessing the lung cancer risk, only personal samplings carried out for long-term 159 durations were included in this study. Samplings with a missing measurement (or concentration) and samplings with no duration were excluded. Data below the limit of quantification (LOQ) were 160 replaced by LOO/2. Exposure groups (L1Gs, L2Gs, L3Gs) gathering at least six samplings were 161 162 included. The exposure used to estimate the risk was representative because only long-term personal sampling were used and because these samplings were not worst-case samplings or regulatory 163 samplings (Petit et al. 2017b). The BaP and BaPeq concentrations were used to assess human lung 164 cancer. A detailed description of the calculation of the BaPeq concentrations are presented in the 165 Supplemental Material. A comparison between risks calculated using the BaP and BaPeq 166 167 concentrations was performed using Fleiss' Kappa (see Supplemental Material).

Although it is possible to estimate the cancer risk of each exposure group, the reliability of the estimation depends on the concentration dispersion (given by the geometric standard deviation for lognormal distributed concentrations), with a higher degree of reliability when the dispersion is low. The BaP concentrations were assumed to be log-normally distributed as exposure concentrations usually follow a lognormal distribution in industrial hygiene (Rappaport 1991). Therefore, the degree of confidence of the concentration can be expressed as a confidence interval (CI), as illustrated in Equation 1 with the 95% CI.

175

176

$$95\% CI (C) = [GM/GSD^2; GM \times GSD^2]$$
<sup>[1]</sup>

where GM is the concentration geometric mean and GSD is the concentration geometric standarddeviation.

179 The 95% CI was always provided to account for uncertainties associated to the exposure variability.

- 180 The exposure groups with the lowest concentration dispersion possible are important for the greatest
- accuracy concerning the components of the worker exposures (Petit et al. 2017b) and thus the best risk
- 182 estimation possible.

#### 183 2.2 Comparison of risks assigned by each indicator found in the literature

- The risk indicators found in the literature for inhalation exposure are listed in Table 1. The formulas shown in Table 1 slightly differ from those found in the mentioned references because they were modified such that each indicator (probability) had to range between 0 and 1 following the transformation:
- 188 *"Modified formula" = 1 exponential (- "formula found in the literature")*

189 The former formulas were recovered in a low concentration limit. All of the risk indicators had a 190 similar functional form (Equation 2) to the exposure concentration and differed in expression of the 191 coefficient ( $\alpha$ ) multiplied by the concentration.

192

$$R = 1 - e^{-\alpha \times C}$$
 [2]

- - -

193 where *R* is a given risk indicator, *C* is the pollutant concentration and  $\alpha$  represents a falloff coefficient 194 used to calculate the given risk indicator (Table 1, Supplemental Material), for example,  $\alpha =$ 195  $\frac{ET \times EF \times ED \times IUR}{4T}$  for the indicator RC and  $\alpha = IUR$  for the indicator LCR.

196 All of the parameters used for the calculations of the risk indicators are shown in Table S1. Following the convention that is typically used in France, we considered that workers weighed, on average, 70 kg 197 198 and were exposed to a constant concentration C of PAHs over 8 hours per day, 5 days a week, 250 days a year for 45 years, corresponding to an exposure duration T = 45 years. For IUR and CSF, the 199 200 values defined by the Office of Environmental Health Hazard Assessment (OEHHA) were used. Both 201 the IUR and CSF values were defined assuming that an individual was continuously exposed on a 202 daily basis with a lifetime inhalation exposure to an agent. Because we were investigating 203 occupational exposures, the IUR and CSF values were rescaled to 45 years of exposure using a cross product, i.e.,  $IUR_{occupation} = IUR_{lifetime} \times 45/70$ . In occupational settings, people are not exposed 204 24h a day and 365 days a year. This discontinuity in the exposure was taken into account in all 205 206 indicators with the exception of LCR (Table 1). Thus, adapting LCR to account for the exposure 207 discontinuity led to LCR = RC, so that only the RC indicator was kept in further analyses.

Indicator	Abbreviation	Expression as $1 - e^{-\alpha \times C}$	Reference
Modified lung cancer risk	LCR	$LCR = 1 - e^{-IUR \times C}$	Callen et al. 2014; Hsu et al. 2014; Jia et al. 2011; Lin et al. 2008; Liu et al. 2010; Ramirez et al. 2011; Wang et al. 2012
Modified cancer risk	RC	$RC = 1 - e^{-\left(\frac{ET \times EF \times ED \times IUR}{AT}\right) \times C}$	Irvine et al. 2014
Modified incremental lifetime cancer risk	ILCR	$\begin{split} ILCR_{1} &= 1 - e^{-\left(\frac{CSF \times \sqrt[3]{BW/70} \times EF \times ED \times IR}{BW \times AT \times PEF}\right) \times C} \\ ILCR_{2} &= 1 - e^{-\left(\frac{CSF \times \sqrt[3]{BW/70} \times EF \times ED \times IR \times cf}{BW \times AT}\right) \times C} \\ ILCR_{3} &= 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times ET}{BW \times AT}\right) \times C} \\ ILCR_{4} &= 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times AT}{BW \times AT}\right) \times C} \\ ILCR_{5} &= 1 - e^{-\left(\frac{CSF \times IR \times EF \times ED \times AT}{BW \times AT}\right) \times C} \end{split}$	Huang et al. 2016; Soltani et al. 2015 Chen and Liao 2006; Hoseini et al. 2016; Singh et al. 2016; Wang et al. 2014 Hu et al. 2007; Li et al. 2013; Qu et al. 2015 Li et al. 2014 Yu et al. 2015
Modified risk	RM	$RM = 1 - e^{-\left(\frac{(IR_a \times EF \times ED \times ET) \times (IUR \times BW \times cf)}{BW \times AT \times IR_b}\right) \times C}$	Amarillo et al. 2014

208 Table 1. Risk indicators found in the literature to estimate lung cancer risk due to PAH exposure

209 Note: A: inhalation absorption factor, AT: averaging time, BW: body weight, C: given PAH

210 concentration, cf: conversion factor, CSF: inhalation cancer slope factor, ED: exposure duration, EF:

211 exposure frequency, IUR: inhalation unit risk, ET: exposure time, PEF: particles emission factor, IR:

inhalation rate, IRa: inhalation rate in  $m^3$ /hour, IRb: inhalation rate in  $m^3$ /day.

213 214

#### 2.3 Risk assessment using a consensual risk indicator

215 As there is no guide or recommendations about the choice and condition for using these indicators, all 216 of them were used in the first instance for all exposure groups constituting at least 6 long-term 217 samplings (Table S2). The reliability of the agreement between all of the indicators was assessed using 218 Fleiss' Kappa. If all of the indicators provided similar results (with at least substantial agreement, 219 corresponding to Fleiss' Kappa > 0.6) for a given concentration, one was kept for further calculations. 220 Otherwise, when the indicators provided dissimilar results, we constructed a consensual risk indicator (CRI) that combined the outputs of all of the indicators to perform the risk estimation. The purpose of 221 222 the consensual risk indicator (CRI) was to aggregate the outputs of all indicators given in Table 1 to produce a single combined probability distribution for the risk estimation (Petit et al. 2018, in 223 preparation). 224

The simplest strategy to construct a consensual indicator is to use a similar relation to Equation 2(Petit et al. 2018, in preparation):

227

228

Consensual risk indicator = 
$$CRI = 1 - e^{-\beta C}$$
 [3]

where *C* is the pollutant concentration and the coefficient  $\beta$ , which can be considered an effective IUR, is obtained from a linear combination of falloff coefficients of all indicators as follows:

231

$$\beta = \sum_{i=1}^{n} \omega_i \alpha_i$$
<sup>[4]</sup>

where *n* is the total number of indicators,  $\omega_i$  ( $0 \le \omega_i \le 1$  and such that all  $\omega_i$  sum to 1) is a weight 233 234 attributed to the indicator  $R_i$  shown in Table 1 and  $\alpha_i$  is the falloff coefficient of  $R_i$  following the 235 parameters shown in Table S1. Equation 3 with Equation 4 was derived from the linear approximation of the linear combination of  $R_i$  with weight  $\omega_i$ . Therefore, such a relationship remained valid for 236 concentrations smaller than  $C_{max} = 2\beta / variance(\beta)$  above which the linear approximation broke 237 238 down. The  $\omega_i$  were obtained using an optimization procedure, which consisted of attributing weights 239 according to the inverse of the square Euclidean distance in the rank between each indicator and their rank barycenter, under the condition that all weights sum to one. As a result of this procedure, 240 241 indicators closest to the barycenter were attributed the highest weights compared with those farthest 242 from the barycenter.



$$\frac{\Delta CRI}{CRI} = \frac{\Delta\beta}{\beta} + \frac{\Delta C}{C}$$
[5]

where  $\Delta\beta$  and  $\Delta C$  are the absolute error of  $\beta$  and C, respectively. In addition, the relative error for  $\beta$  is constant while the relative error of the concentration is variable, depending on the exposure group considered.

Uncertainties on the concentrations are provided in Equation 1. Regarding the uncertainty associated with the falloff factor  $\beta$ , we used the weighed standard deviation of  $\beta$ . However, to generate percentile values of the risk from which the 95% CI of the risks are derived, several simulations of the CRI presented in Equation 3 were run using a lognormal distribution for concentrations (as described in Section 2.1) and assuming for  $\beta$  a normal distribution with mean and standard deviation described above.

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256

### 2.4 Decision rule regarding the risk estimation/ranking

257 There are different thresholds provided by agencies and governments around the world to assign a risk. For instance, a probability >  $10^{-6}$  is considered unacceptable by the US EPA, a probability of  $10^{-4}$ 258 is considered the maximal risk level in the European Union, while a probability >  $10^{-3}$  is considered a 259 high priority by the US EPA and a significant risk level by the US Supreme Court. The threshold 260 considered acceptable for occupational exposure is always greater than the threshold for the general 261 262 population. Based on the different existing thresholds that can be found in the literature, a decision 263 rule was used to rank risks (Table 2). The decision rule was developed in such a way that a factor of 264 10 (one order of magnitude) separated two consecutive classes (very low, low, moderate, high and 265 very high) to allow an easy comparison with the existing risk threshold deemed relevant or applicable 266 to a study/country. As each exposure group consisted of several samplings (at least 6), a distribution of 267 risks/probabilities was subsequently generated. Therefore, the rule consisted of comparing the 90<sup>th</sup> percentile (P<sub>0.90</sub>) of the distribution of risks to different thresholds. In the Results and Discussion 268 sections, the presented risk is always the 90<sup>th</sup> percentile of the distribution of risks. 269

**Table 2.** Decision rule for lung cancer risk estimation

Situation	Risk ranking	Interpretation
$P_{0.90} > 10^{-3}$ $10^{-4} < P_{0.90} \le 10^{-3}$	Very high risk High risk	> 1/1000 chance of observing one additional lung cancer over a period of 45 years of work > 1/10000 chance of observing one additional lung cancer over a period of 45 years of work
$10^{-5} < P_{0.90} \le 10^{-4}$ $10^{-6} < P_{0.90} \le 10^{-5}$	Moderate risk	> 1/100000 chance of observing one additional lung cancer over a period of 45 years of work > 1/1000000 chance of observing one additional lung cancer over a period of 45 years of work
P <sub>0.90</sub> ≤ 10 <sup>-6</sup>	Very low risk	< 1/1000000 chance of observing one additional lung cancer over a period of 45 years of work

271 Note:  $P_{0.90}$ : 90<sup>th</sup> percentile of the risk probability distribution.

272 2.5 Expected number of additional lung cancer cases per year in France

273 Let  $P(\tau)$  denote the probability of the occurrence of lung cancer after an exposure of duration  $\tau$ , and 274  $N(\tau)$  be the number of individuals who were exposed to the pollutant of interest for a time period  $\tau$ , 275 such that the total exposed population is  $N_{exp} = \sum_{\tau=0} N(\tau)$ . It follows that the expected number of 276 additional lung cancers  $E(\tau)$  after an exposure of duration  $\tau$  can be obtained as,

277 
$$E(\tau) = N(\tau) \times P(\tau) = N(\tau) \times [1 - exp\{-\beta C_{\tau}(\tau/T)\}]$$
 [6]

where  $C_{\tau}$  is the (constant) mean concentration of the pollutant that the population has been exposed to over the exposure of duration  $\tau$  and T = 45 years is the maximal occupational exposure duration. For the sake of illustration, we consider three occupational exposure durations, 15 years, 30 years and 45 years, and aggregate the exposed population,  $N_{exp} = N_{\leq 15} + N_{15-30} + N_{>30}$ , into three subpopulations,  $N_{\leq 15}$ ,  $N_{15-30}$  and  $N_{>30}$  corresponding to the population in the exposure time intervals from 0 to 15 years, > 15 to 30 years, and > 30 years, respectively. For an occupational exposure of a given duration, we obtain the expected number of additional lung cancers as

285
$$\begin{cases} E_{15} = N_{\le 15} \times \left[1 - exp\left\{-\frac{\beta C_{15}}{3}\right\}\right] \\ E_{30} = N_{15-30} \times \left[1 - exp\left\{-\frac{2\beta C_{30}}{3}\right\}\right] \\ E_{45} = N_{>30} \times \left[1 - exp\left\{-\beta C_{45}\right\}\right] \\ E_{e} = N_{exp} \times \left[1 - exp\left\{-\beta C_{45}\right\}\right] \end{cases}$$
[7]

where  $E_e$  is the expected number of additional lung cancers among the total exposed population after an exposure of duration 45 years,  $E_{45}$  is the expected number of additional lung cancers among the  $N_{>30}$  subpopulation after an exposure of 45 years,  $E_{30}$  is the expected number of additional lung cancers among the  $N_{15-30}$  subpopulation after an exposure of 30 years and  $E_{15}$  is the expected number of additional lung cancers among the  $N_{\le 15}$  subpopulation after an exposure of 15 years.

291 This approach was used to estimate the expected contemporary number of additional lung cancer cases per year in France in each L1G. We mean that the estimation can be performed either retrospectively 292 293 or prospectively depending on the time origin used for the exposure periods. In the retrospective scheme, the exposure had started 45 years prior, and the estimation then provides the number of 294 295 additional lung cancers that would currently be expected; whereas in the prospective scheme, the first 296 exposure occurred at the time of the measurements (between 2000 and 2014), and then the estimation reflected the number of additional lung cancers that would be expected in the next 30-45 years. If the 297 number of people exposed and condition of exposure did not change over time, then this approach 298 299 would provide the expected number of additional lung cancer cases per year in France in each L1G.

The French population of workers potentially exposed to PAHs was estimated in each L1G. The total

301 L1G workforce was estimated through the national statistics, national studies and grey literature

302 (AFA, 2016; DARES, 2014; FFF, 2014, 2016; FIM, 2016; FNTP, 2017; INSEE, 2017; Ministère du

303 Travail, 2016; Pompiers, 2017; SCF, 2017). The exposed populations,  $N_{\leq 15}$ ,  $N_{15-30}$  and  $N_{>30}$ , were

determined from the E-HAP data, and we assumed that the BaP concentrations were identical for all exposure durations,  $C_{15} = C_{30} = C_{45}$ . The distribution of the BaP and BaPeq concentrations provided the distributions of the expected numbers of lung cancers, from which the summary statistics are reported.

No estimation of the expected number of additional lung cancer was performed for L2Gs and L3Gs because it is currently not possible to estimate the total number of workers for these groups. These groups are too accurate and specific to be found in national statistics, national studies or grey literature. Indeed, the available French national statistics and national studies only provide information regarding industries and sometimes jobs, which are too generic (not sufficiently descriptive) in comparison to L2Gs and L3Gs, which refer to locations/operations and tasks, respectively (Petit et al. 2017b).

- 315
- **316** 2.6 Software

317 Data analyses and all calculations were performed with R software 3.1.0® (R Core Team, Vienna,
318 Austria) for Windows 7©.

319

#### **320 3. Results**

The measurement campaigns were carried out from 2000 to 2014. A total of 93 exposure groups were
studied (Table S2). Among them, 9 were L1Gs, 35 L2Gs and 49 L3Gs.

- 323
- 324 3.1 Risk indicator comparison

325 Regardless of the exposure group considered, ILCR1 always assigned the same risk: very low risk of lung cancer (90<sup>th</sup> percentile of the risk probability distribution  $\leq 10^{-6}$ ) (Table S2). Among all 326 indicators, ILCR4 always assigned the highest risk. This risk was 74.9, 124.7, 126.3, 224.4, 227.3 and 327 4.3x10<sup>11</sup> times higher than the one assigned by ILCR5, ILCR3, ILCR2, RM, RC and ILCR1, 328 respectively. ILCR2 and RC provided almost the same results, with 91 similar risk assignments of 93 329 possible. ILCR3 and RM provided almost the same results, with 92 similar risk assignments of 93 330 possible. Regardless of the L1G considered, Fleiss' Kappa was very low (ranging from -0.01 for 331 bitumen and aluminum production to 0.30 for silicon production). The overall Fleiss' Kappa was low 332 333 (0.29), denoting only a fair agreement between all indicators (Table S2), which confirmed the 334 usefulness of using CRI.

335

#### 3.2 Estimation of lung cancer risk using CRI

336 Using all the indicators shown in Table 1 to construct CRI,  $\beta_{BaP} = 2.93 \times 10^{-4} \text{ m}^3/\mu \text{g} \pm 7.14 \times 10^{-5} \text{ m}^3/\mu \text{g}$ 

- 337 was determined for the  $\beta$  value, which must be compared with IUR =  $7.1 \times 10^{-4} \text{ m}^3/\mu \text{g}$  (see Table S1). 338 We used this  $\beta$  in the CRI to perform the risk estimation as the highest BaP and BaPeq concentrations
  - 13

- in the E-HAP were 65  $\mu$ g/m<sup>3</sup> and 106  $\mu$ g/m<sup>3</sup>, respectively, which were lower than the maximum concentration allowed for using this approach (BaP C<sub>max</sub> = 115 mg/m<sup>3</sup>).
- Among the existing indicators found in the literature, both ILCR3 and RM approaches were closest (factor 1.1) to the conclusions attained with CRI. The obtained results using  $\beta$  were 125 times lower than those that would have been obtained with ILCR4 and 1.1 to 1.7 times lower if ILCR3 or ILCR5 had instead been used. By contrast, the use of this  $\beta$  provided results 1.1 to 1.8 times higher than if
- RM, ILCR2 or RC had been used and  $3.4 \times 10^9$  times higher than if ILCR1 had been chosen.
- The estimated risks where 1.1 to 2.2 times higher (factor, on average, of 1.3) when BaPeq was used instead of BaP (Table S3). BaP and BaPeq provided similar results when assigning risk, with almost perfect agreement between them (Fleiss' Kappa of 0.92). Only 6 groups were assigned with different lung cancer risks when using the BaP and BaPeq concentrations (Tables 3 and S3). In these cases, the risk attributed to the BaPeq concentrations was always greater than the risk attributed with BaP concentrations, which was not surprising because the BaPeq concentrations were always higher than the BaP concentrations.
- 353 Table 3 synthetizes all the lung cancer risks estimated using CRI. The risk reliability of CRI mostly 354 depended on measurement uncertainties and was usually highest for exposure groups with highest description accuracy. The relative error associated with  $\beta$  ( $\sigma/\beta$ ) was equal to 0.24. By contrast, the 355 relative error associated with the concentration ( $\sigma/\mu_c$ , where  $\mu_c$  is the arithmetic mean concentration) 356 357 was, on average, equal to 1.6 (min: 0.5, max: 8.3) for the BaP and 1.5 (min: 0.5, max: 8.2) for the 358 BaPeq. The relative error associated with the concentration was highest for L1Gs: 3.1 on average 359 (min: 1.4, max: 8.3) for the BaP and 3.1 on average (min: 1.4, max: 8.2) for the BaPeq. Regarding 360 L2Gs, this relative error was, on average, equal to 1.6 (min: 0.5, max: 4.9) for both the BaP and BaPeq. The relative error associated with the concentration was lowest for L3Gs: 1.2 on average (min: 361 0.5, max: 3.5) for BaP and 1.2 on average (min: 0.5, max: 3.4) for BaPeq. These observations are not 362 surprising because the more detailed the level of description, the lower the dispersion of the BaP 363
- 364 concentrations.
- Based on the total of 93 exposure groups studied, 16% were estimated to have a very high risk (90<sup>th</sup> percentile > 10<sup>-3</sup>), 15% a high risk (10<sup>-4</sup> < 90<sup>th</sup> percentile  $\le 10^{-3}$ ), 27% a moderate risk (10<sup>-5</sup> <90<sup>th</sup> percentile  $\le 10^{-4}$ ), 25% a low risk (10<sup>-6</sup> < 90<sup>th</sup> percentile  $\le 10^{-5}$ ) and 17% a very low human risk of lung cancer (90<sup>th</sup> percentile  $\le 10^{-6}$ ) (Table 3).
- Regarding L1Gs, French workers exposed to PAHs via products derived from coal (coke, aluminum,silicon production, manufacturing of carbon products and foundry) were the most at risk of developing
- a lung cancer. Coke production had the highest risk of lung cancer, with a chance of three in a
- 372 thousand of an additional human lung cancer over 45 years of work. A very high risk of lung cancer
- 373 was also estimated for silicon production  $(1.1 \times 10^{-3})$ , which was almost four times higher than the risk
- of manufacturing carbon product  $(2.5 \times 10^{-4})$ . There was an estimated risk of  $1.0 \times 10^{-4}$  for aluminum

- production,  $1.8 \times 10^{-5}$  for foundries,  $1.5 \times 10^{-5}$  for combustion processes,  $1.9 \times 10^{-6}$  for engine exhaust emissions,  $1.7 \times 10^{-6}$  for the use of lubricating oils, and  $5.0 \times 10^{-7}$  for bitumen.
- The risks were highly variable within L1Gs (up to 3 orders of magnitude in terms of likelihood). 377 Regarding coke production, all exposure groups had either a very high (between 2.0x10<sup>-3</sup> and 6.7 x10<sup>-</sup> 378 <sup>3</sup>) or a high risk (from  $3.9 \times 10^{-4}$  to  $8.7 \times 10^{-4}$ ). For silicon production, lung cancer risks were most of the 379 time greater (up to 6 likelihood) for tasks near the furnaces (maintenance activities and masonry) than 380 near composite electrodes. The only exceptions were for the fluke damage and resistors dismantling 381 382 activities. A high risk was found for all activities performed near Söderberg electrodes. Manufacture 383 was the L2G with the lowest risk of lung cancer. In aluminum production, the risk of lung cancer was 384 most of the time moderate ( $\leq 10^{-4}$ ), with the exception of the aluminum L1G itself, the maintenance of the paste tower and furnace L2G and its electricians L3G as well as the prebaked anode production – 385 386 paste tower L2G, which demonstrated a high risk of lung cancer. With the exception of the cathode graphitization (moderate risk), all exposure groups in the manufacture of carbon products 387 demonstrated a high risk ( $\leq 10^{-3}$ ) of lung cancer. For foundries, risks in steel foundries (2.4x10<sup>-5</sup>) were 388 24 times higher than in aluminum foundries. In the aluminum foundry, risks of lung cancer were either 389 low ( $\leq 10^{-5}$ ) or very low ( $\leq 10^{-6}$ ). In addition, the driver and smelter had a risk of  $1.4 \times 10^{-6}$ , which was 390 approximately twice as high as the risk of the caster  $(6.6 \times 10^{-7})$ . For the steel foundry, the risk was 391 392 always moderate.
  - 393 With the exception of the firefighters and chimney sweepers from combustion processes, all exposure 394 groups that used products derived from petroleum had either a low or a very low risk of lung cancers. All exposure groups with a low risk of lung cancer used only products derived from petroleum, with 395 396 the exception of the aluminum foundries (Table 3). All exposure groups exposed to engine exhaust emissions had a probability that never exceeded 4.6x10<sup>-6</sup> (for roadwork mechanics). Roadwork 397 398 mechanics had a 2-3 times higher risk than heavy truck and agricultural mechanics. Workers using a 399 hedge trimmer had a 3 times higher risk than workers using a brushwood clearer. Underground drivers 400 had a ten times higher risk than open space drivers. With the exception of discharge mold and 401 vehicles, all exposure groups using lubricating oils had a very low risk of lung cancer. All workers exposed to bitumen (road paving) had a very low risk of lung cancer, with the exception of workers 402 applying hot bitumen in a tunnel using hot bitumen  $(1.2 \times 10^{-6})$ . This activity had a three times higher 403 404 risk when performed with hot bitumen rather than warm bitumen.

#### Table 3. Estimated risk of human lung cancer in nine L1Gs and all their L2Gs and L3Gs using the 405

#### 406 BaP concentrations

	_	BaP level Risk				BaPeq			
Level groups	N	GM (na/m <sup>3</sup> )	5 <sup>th</sup> p. (ng/m <sup>3</sup> )	95 <sup>th</sup> p. (na/m <sup>3</sup> )	90 <sup>th</sup> p.	5 <sup>th</sup> p.	95 <sup>th</sup> p.	Ranking	Ranking (Table S3)
1. Aluminum production	138	55	8.0	464	1.0x10-4	1.5x10-6	1.7x10-4	High	High
1.1 Prebaked anode production – paste tower	30	74	10	1156	2.2x10-4	1.0x10-6	4.1x10-4	High	High
1.1.1 Manufacture operator	7	84	36	285	7.5x10-5	5.4x10-6	1.0x10-4	Moderate	Moderate
1.1.2 Watchperson, heat attendant	18	43	7.7	486	8.7x10-5	9.9x10-7	1.5x10-4	Moderate	High
1.2 Prebaked anode production – furnace	24	24	7.9	67	1.9x10-5	1.8x10-6	2.5x10-5	Moderate	Moderate
1.2.1 Gas attendant, Overhead crane operator	16	24	7.4	73	1.9x10-5	1.8x10-6	2.5x10-5	Moderate	Moderate
1.2.2 Heat attendant mason	8	25	8.9	54	1.9x10-5	1.9x10-6	2.5x10-5	Moderate	Moderate
1.3 Maintenance of the paste tower and furnace	22	94	19	511	1.2x10-4	3.8x10-6	1.9x10-4	High	High
1.3.1 Maintenance operator	6	73	29	345	7.6x10-5	3.8x10-6	1.1x10-4	Moderate	Moderate
1.3.2 Mechanic	9	207	78	696	1.9x10-4	1.2x10-5	2.7x10-4	High	High
1.3.3 Electrician			=	183	5.3x10-5	2.3x10-6	7.8x10-5	Moderate	Moderate
1.4 Ramming: electrolysis construction and furnace restoration	5/	48	/.8	201	6.6x10-5	1.7x10-6	1.0x10-4	Moderate	Moderate
1.4.1 Tank construction: using small seals	14	23	4.0	148	3.8x10-5	6.4x10-7	6.3x10-5	Moderate	Moderate
1.4.2 Tank construction: using large seals	20	33 70	/.0	240	4.4x10-5	1.2x10-6	6.9x10-5	Moderate	Moderate
	204	104	50	243	7.9x10-5	4.3X10-6	1.1x10-4	Moderale	woderale
2. Silicon production	109	704	0.0	/10/	1.1x10-3	9.6x10-7	2.5x10-3	Very high	Very high
2.1 Composite electrodes	108	1200	34 62	11000	1.9x10-3	1.2x10-5	3.7x10-3	Very high	Very high
2.1.1 Paste loading in the electrode	57	01/	02 80	5882	3.9x10-3	2.2X10-5	7.4x10-3	Very nigh	Very high
	12			1007	1.6X10-3	2.4X10-5	2.6X10-3	very nign	very nign
2.2 Soderberg electrodes	13	17/	20	1188	2.3x10-4	3.6X10-6	3.9X10-4	High	High
					2.7X10-4	5.0X10-0	4.2X10-4		High
2.3 Manulacture	112	23	4.Z 5.4	202	3.4x10-5	7.8X10-7	5.6X10-5	Moderate	Moderate
2.3.1 FOSIS CITIET	42	24	5.4	260	4.0X10-5	6.6X10-7	6./XIU-5	Moderate	Moderate
2.3.2 Caster	54	20	3.5	179	3.4x10-5 3.2v10-5	5.7v10-7	5.1X10-5	Moderate	Moderate
2.4 Hoat attendant mason	25		$ \frac{0.0}{4.2}$	23026	0.2×10-3	2.4×10.6	0.5×10.0	Vory high	Vorubiah
2.4 1 Intervention in furnace	19	3448	441	26244	9.3X10-3	2.4X10-0	2.5X10-2 86v10-3	Very high	Very high
2.5 Appual maintonanco	62	497		16219	1 0 1 0 2	5 6v10 6	2 9 10 2	Very high	Very high
2.5 A Plate and/or ring dismantling	27	2480	298	25713	1.9X10-3	5.0X10-0	3.0X10-3	Very high	Very high
2.5.2 Besistors dismantling	7	513	93	3731	4.0x10-3	1 1 1 10-5	1 Qv10-3	Very high	Very high
2.5.3 Fluke damage	22	101	35	449	8.9x10-5	6.9x10-6	1.0x10-0	Moderate	High
3. Manufacturing of carbon products	107	67	1.7	921	2 5x10-4	6 7x10-7	5 5x10-4	High	High
3 1 Cathodes production	107	67	1.7	921	2.5x10-4	6.7x10-7	5.0x10 4	High	High
3.1.1 Baw cathode extruding	.52	161	48	1006	2.0×10-4	6.1v10-6	3 / 10-1	High	High
3.1.2 Cathode baking	18	47	0.77	1130	6 7×10-4	0.1110-0	2 0v10-3	High	Vory high
3.1.2 Cathode graphitization	8	87	25	34	1 1 1 1 0 5	1.0×10.7	1 6 1 0 5	Madarata	Mederate
2.1.4 Laboratory applyzin	7	50	1 9	256	1.1X10-5	4.2810-7	1.0X10-5	Nioderale	Widderate
4 Foundrise	50	1.6	0.42	200	1.2x10-4	9.3×10-7	2.2810-4	Higri Maalawata	Higri Maalawata
4. Foundiles	15	4.0	0.42	12	1.8x10-5	4.6X10-8	3.8X10-5	Moderate	Widderate
4.1 Aluminum	15	0.56	0.03	2.0	9.9X10-7	1./X10-8	1./X10-6	Very low	LOW
4.1.1 Driver, Smeller	7	0.72	0.13	2.3	1.4X10-6	1.6X10-8	2.5X10-6	LOW	LOW
	35			121	0.0X10-7	2.0×10.7	1.1110-0	Mederate	Mederate
4.2 Steel	6	22	5.5	837	2.4X10-5	$2.2 \times 10^{-7}$	4.3X10-3	Moderate	Ligh
4.2.2 Crucible activity	6	19	3.6	61	2.2x10-5	2.4X10-7	1.7x10-4 4 4x10-5	Moderate	Moderate
4 2 3 Heat attendant mason	21	6.7	1.0	43	1.2x10-5	1 7x10-7	2 2x10-5	Moderate	Moderate
5. Use of lubricating oils	89	0.80	0.03	87	1.2×10-5	1.0v10-8	2.2×10-5	Low	Low
5.1 Undercutting	14	0.00	0.00	17	F 0x10 7	E 1v10 0	2.9X10-0	Vorulow	Vondow
5.1.1 Undercutting help-undercutting	7	0.00	0.20	1.7	5.0x10-7	5.1X10-0	0.5X10-7	Very low	Very low
5.2 Turning	43	0.48		32	6.0x10-7	1.0×10.0	0.6×10.7	Verylow	
5.2.1 Mechanic	30	0.27	0.03	0.62	0.3x10-7 2 4x10-7	1.9×10-0	3.0x10-7	Very low	Very low
5.3 Dischargo mold	13			18	4 9 10 6	2.0×10.7	7.0×10.6		
5.4 Vohiolog	13	$\frac{1}{2}$			4.0010-0	1.0×10.7	7.0010-0		
5.4 1 Mechanic driver	9	17	0.66	4.5	2.1X10-0	1.0X10-7	2.9X10-0	Low	LOW
6 Engine exhaust emissions	263	0.70	0.03	8.4	1.4×10-0	1.1.10.0	2.5×10.6		Low
6.1 Highwaye	13	0.70	0.00	0.4	0.1210-7	1.1X10-8	0-01xc.c	Vonulaw	Vonulaw
6.1.1 Administration Toll collector	23	0.09	0.03	0.70	2.1X10-7	3.1X10-9	3.0X1U-7	Very low	Very low
6.1.2 Highway services	15	0.18	0.03	1.2	3.4v10-7	4.5x10-9	5 6x10-7	Very Iow	Very Iow
6 2 Heavy Truck (HT) garage + Roadwork + 2-Stroke opgings	50		0 18	9.8	2 1 1 1 0 6	3 6v10 0	3.5×10.6		
6.2.1 HT mechanic	28	1.3	0.27	8.5	2.1X10-0 1 9x10-6	2.0x10-8	2 9x10-0	Low	
	_0		0.27	0.0	1.0710-0		2.0710-0		
								16	

6.2.2 Roadwork mechanic	9	0.96	0.15	36	4.6x10-6	7.1x10-9	1.0x10-5	Low	Low
6.2.3 Agricultural mechanic	12	1.5	0.50	6.1	1.3x10-6	9.9x10-8	1.8x10-6	Low	Low
6.3 Light Vehicles garage	70	1.0	0.21	6.6	1.2x10-6	4.3x10-8	1.9x10-6	Low	Low
6.3.1 Mechanic (all engines)	56	0.97	0.21	6.8	<u>1.1x10-6</u>	4.6x10-8	1.7x10-6	Low	Low
6.4 Driver: HT, delivery, roadwork, bus	15	0.54	0.21	1.5	3.7x10-7	5.0x10-8	4.8x10-7	Very low	Very low
6.5 Downtown	- 11 -	2.1	0.98	4.0	1.3x10-6	2.1x10-7	1.7x10-6	Low	Low
6.5.1 Sewage worker	6	1.9	0.86	4.0	1.4x10-6	1.7x10-7	1.8x10-6	Low	Low
6.6 Use of 2-Stroke and 4-Stroke engines	30	2.5	0.83	11	2.3x10-6	1.6x10-7	3.2x10-6	Low	Low
6.6.1 Brushwood clearer	7	1.6	0.81	4.4	1.2x10-6	1.4x10-7	1.6x10-6	Low	Low
6.6.2 Hedge trimmer	8	3.1	0.97	15	3.5x10-6	1.5x10-7	5.2x10-6	Low	Low
6.7 Generator	8	0.95	0.17	8.3	2.1x10-6	2.1x10-8	3.7x10-6	Low	Low
6.8 Closed environment	35	0.33	0.03	18	2.7x10-6	1.3x10-9	7.5x10-6	Low	Low
6.8.1 Underground – driver	9	2.4	0.23	8.2	4.3x10-6	6.4x10-8	7.3x10-6	Low	Low
6.8.2 Work in tunnel	21	0.05	0.03	0.68	6.6x10-8	2.3x10-9	1.1x10-7	Very low	Very low
7. Combustion processes	36	4.2	0.25	65	1.5x10-5	5.0x10-8	3.2x10-5	Moderate	Moderate
7.1 Firefighter	7	28	7.3	77	3.0x10-5	1.4x10-6	4.4x10-5	Moderate	Moderate
7.2 Chimney sweeper	10	12	2.8	51	1.3x10-5	6.1x10-7	1.8x10-5	Moderate	Moderate
7.3 Household garbage incinerator	17	1.2	0.20	25	3.5x10-6	1.5x10-8	7.2x10-6	Low	Low
7.3.1 Operating household garbage incinerator	13	1.2	0.19	10	2.8x10-6	2.7x10-8	5.2x10-6	Low	Low
8. Bitumen/road paving	75	0.27	0.03	2.8	5.0x10-7	6.5x10-9	8.7x10-7	Very low	Very low
8.1 Road paving: application of hot bitumen(>150°C)	61	0.28	0.03	3.0	5.4x10-7	6.8x10-9	9.7x10-7	Very low	Very low
8.1.1 Tar application	27	0.18	0.03	2.5	4.5x10-7	3.4x10-9	8.5x10-7	Very low	Very low
8.1.2 Coating application	11	0.14	0.03	0.25	1.1x10-7	9.8x10-9	1.5x10-7	Very low	Very low
8.1.3 Work in tunnel	17	0.80	0.17	3.9	1.2x10-6	2.7x10-8	1.8x10-6	Low	Low
8.2 Application of warm bitumen (≤150°C) in tunnel	8	0.18	0.03	1.8	4.2x10-7	3.6x10-9	7.7x10-7	Very low	Very low
9. Coke production	84	932	90	11310	2.8x10-3	1.3x10-5	5.4x10-3	Very high	Very high
9.1 Coke pusher	14	872	67	5945	6.7x10-3	3.3x10-6	1.8x10-2	Very high	Very high
9.2 Furnace door settings	10	412	107	4184	8.7x10-4	8.6x10-6	1.5x10-3	High	Very high
9.3 Coke withdrawn	8	531	244	1364	3.9x10-4	4.2x10-5	5.1x10-4	High	High
9.4 Furnace battery cleaning-up	16	1035	99	4912	2.0x10-3	2.7x10-5	3.5x10-3	Very high	Very high
9.5 Watchperson	12	499	9.2	16428	3.5x10-3	2.5x10-6	9.0x10-3	Very high	Very high
9.6 Mason	18	1544	371	12317	2.3x10-3	4.9x10-5	3.6x10-3	Very high	Very high
9.6.1 Furnace	12	822	318	2540	6.9x10-4	5.9x10-5	9.5x10-4	High	High
9.6.2 Work in gallery	6	6112	1923	14029	5.7x10-3	4.1x10-4	7.9x10-3	Very high	Very high

Note: 5<sup>th</sup> p.: 5<sup>th</sup> percentile, 90<sup>th</sup> p.: 90<sup>th</sup> percentile, 95<sup>th</sup> p.: 95<sup>th</sup> percentile, GM: geometric mean, N: 407 number of samples. Groups with one number correspond to level 1 exposure groups (L1Gs), while 408 409 L2Gs are preceded by two numbers and L3Gs by three numbers. Level 1 was related to product/raw material characteristics. Level 2 referred to exposure source characteristics (e.g., locations and/or 410 411 operations with different emission sources). Level 3 corresponded to a task or a series of tasks. The sum of L2Gs is not necessarily equal to the total number of their L1G, as L2Gs with less than 6 long-412 term samplings are not shown here. The sum of L3Gs is usually not equal to the total number of their 413 L2G, as L3Gs with less than 6 long-term samplings are not shown here. The 5<sup>th</sup> and 95<sup>th</sup> percentiles 414 correspond to the lower and upper bounds of the 95% confidence interval, respectively. See Table 2 415 for the risk ranking decision rule and interpretation. 416

- 417 3.4 Estimation of exposed workers and number of additional lung cancer cases per year in418 France
- 419 Fig. 1 displays the number of exposed workers  $(N(\tau))$  (on the left) and the expected number of 420 additional lung cancer cases per year in France  $(E(\tau))$  (on the right) for each exposure duration  $\tau$ .
- 421 Table 4 reports  $N(\tau)$  and the associated  $E(\tau)$  calculated for the period from 2000-2014 for each L1G
- 422 and  $\tau$  based on the BaP or BaPeq concentrations.
- 423 In the selected L1Gs, approximately 3.7 million French workers were potentially at risk of PAH
- 424 exposure, most of whom (99%) were employed in L1G using products derived from petroleum (Fig. 1,
- 425 Table 4). Among them, only 11% were exposed at the time of monitoring  $\leq 15$  years, while 41% were
- 426 exposed >15-30 years and 48% > 30 years. More than 60% of the workers were exposed > 30 years in
- 427 aluminum, silicon production and manufacturing of carbon products. Regarding foundries, 74% of the
- 428 workers were exposed >15-30 years. For the remaining L1Gs, at least 40% of the workers were
- 429 exposed >15-30 years and at least 40% > 30 years.
- 430 A total of 27 (95% CI: 0.14-54) cases of additional lung cancer ( $E_e$ ) could potentially be expected per
- 431 year in France if all workers had been exposed for 45 years (Table 4). This estimation was higher
- 432 when using BaPeq (37, 95% CI: 0.57-67), which is not surprising as BaPeq  $\geq$  BaP by definition (Table
- 433 4). Both estimates can be compared to the number of lung cancer cases that would be expected in 2015
- 434 in France among men occupationally exposed to PAHs. Using the incidence of the lung cancer and the
- 435 attributable fractions mentioned in the Introduction section, between 12 and 37 cases would be436 expected.
- 437 The largest number of  $E_e$  was found in coke production and combustion processes, followed by engine 438 exhaust emissions, silicon production, the use of lubricating oils, aluminum production, manufacturing 439 of carbon products, foundries and bitumen. The largest number of expected additional lung cancer 440 cases was not necessarily found for L1Gs that used products derived from coal, where exposure levels 441 are highest. Although lung cancer risks were high or very high for L1Gs that used products derived from coal, the exposed population in these groups was far smaller (1,000 - 40,000 workers) than for 442 L1Gs using products derived from petroleum (100,000 to 2 millions) where lung cancer risks are low 443 444 or very low. Nevertheless, coke production was the L1G with the highest expected additional lung 445 cancer cases despite the small population exposed (4,100 workers).
- 446 Regardless of the L1G, the number of additional lung cancer cases was highest for  $E_e$ , followed by 447  $E_{45}$ ,  $E_{30}$ , and  $E_{15}$ . In addition, the sum of  $E_{45}$ ,  $E_{30}$  and  $E_{15}$  was always inferior to  $E_e$  because of the 448 cumulative effect of the cancer risk.

$\begin{array}{c c c c c c c c c c c c c c c c c c c $	110	~	$N(\tau)$	$E(\tau)_{2000-2014}$	$E( au)_{2000-2014}$		
45 years         4,100         11 (10,05, 22)         16 (0.26, 29)           Coke production         15 - 30 years         1,700         3.1 (0.01, 6.2)         4.5 (0.07, 7.9)           415 years         350         0.32 (0.002, 0.63)         0.46 (0.007, 0.81)         4.5 (0.07, 7.9)           Silicon production         - 30 years         1,500         1.6 (0.001, 3.8)         2.7 (0.01, 5.6)           Silicon production         - 30 years         150         0.05 (2410-5, 0.59)         0.42 (0.001, 0.88)           415 years         150         0.05 (5410-5, 0.13)         0.09 (3410-4, 0.19)         0.42 (0.001, 0.88)           415 years         10,700         1.1 (0.02, 1.8)         1.4 (0.05, 2.2)         1.5 -30 years           Aluminum production         15 - 30 years         2,600         0.18 (0.003, 0.29)         0.23 (0.008, 0.35)           45 years         3.00 years         2,600         0.18 (0.002, 1.8)         1.4 (0.05, 2.2)           Manufacturing of carbon products         45 years         3.00 years         1.000, 1.2)         0.79 (0.008, 1.5)           15 - 30 years         1,200         0.20 (5x10-4, 0.44)         0.30 (0.003, 0.56)         1.5 -30 years         1.200, 1.2)         0.79 (0.008, 1.5)           6.000         0.12 (3110-4, 0.25)         0.18 (0.002, 0.34) </td <td>EIG</td> <td>ι</td> <td>N(l)</td> <td>BaP: P<sub>90</sub> (95% CI)</td> <td colspan="2">BaPeq: P<sub>90</sub> (95% CI)</td>	EIG	ι	N(l)	BaP: P <sub>90</sub> (95% CI)	BaPeq: P <sub>90</sub> (95% CI)		
Coke production         > 30 years         2,000         5.6 (0.03, 11)         8.2 (0.13, 14)           15 - 30 years         1,700         3.1 (0.01, 6.2)         4.5 (0.07, 7.9)           45 years         1,500         1.6 (0.001, 3.8)         2.7 (0.01, 5.6)           Silicon production         15 - 30 years         1500         1.6 (0.001, 3.8)         2.7 (0.01, 5.6)           Silicon production         15 - 30 years         150         0.32 (2.10-4, 0.59)         0.42 (0.001, 0.8)           45 years         150         0.05 (5x10-5, 0.13)         0.09 (3x10-4, 0.19)         1.4 (0.05, 2.2)           Aluminum production         30 years         7,800         0.80 (0.01, 1.3)         1.0 (0.04, 1.6)           45 years         3.00         0.12 (x10-4, 0.02)         0.23 (0.008, 0.35)         1.5 (x10-4, 0.02)           Manufacturing of carbon products         45 years         3.00         0.80 (0.01, 1.2)         0.79 (0.008, 1.5)           5 - 30 years         2.100         0.53 (0.002, 1.8)         1.2 (0.01, 2.3)         1.5 (0.02, 0.3)           Foundries         15 - 30 years         1.200         0.20 (5x10-4, 0.4, 0.25)         0.18 (0.002, 0.3)           6 combustion processes         15 - 30 years         1.500         0.13 (3x10-5, 0.02)         0.02 (2x10-4, 0.03) <tr< td=""><td></td><td>45 years</td><td>4,100</td><td>11 (0.05, 22)</td><td>16 (0.26, 29)</td></tr<>		45 years	4,100	11 (0.05, 22)	16 (0.26, 29)		
Coke production         15 – 30 years         1,700         3.1 (0.01, 6.2)         4.5 (0.07, 7.9)           45 years         350         0.32 (0.002, 0.63)         0.46 (0.007, 0.81)           530         530 years         1,500         1.6 (0.001, 3.8)         2.7 (0.015, 5.6)           Silicon production         15 - 30 years         350         0.25 (2x10-4, 0.59)         0.42 (0.001, 0.8)           45 years         10,700         1.1 (0.02, 1.8)         1.4 (0.05, 2.2)         1.4 (0.05, 2.2)           Aluminum production         530 years         7,800         0.80 (0.01, 1.3)         1.0 (0.04, 1.6)           15 - 30 years         2,600         0.18 (0.003, 0.29)         0.23 (0.002, 1.6)         1.2 (0.01, 2.3)           Aluminum production         15 - 30 years         2,100         0.53 (0.001, 1.2)         0.79 (0.008, 1.5)           45 years         3.00         0.83 (0.002, 1.3)         0.88 (0.008, 1.7)         0.33 (0.003, 0.29)         0.33 (0.003, 0.29)           Manufacturing of carbon products         > 30 years         2,600         0.18 (0.002, 1.3)         0.88 (0.008, 1.7)           50 years         1,200         0.20 (5x10-4, 0.44)         0.30 (0.003, 0.29)         0.23 (0.003, 0.29)           45 years         1,820         0.81 (0.002, 0.34)         0.18 (0.002, 0.34		> 30 years	2,050	5.6 (0.03, 11)	8.2 (0.13, 14)		
≤ 15 years         350         0.32 (0.002, 0.63)         0.46 (0.007, 0.81)           Silicon production         45 years         1,500         1.6 (0.001, 3.8)         2.7 (0.01, 5.6)           Silicon production         15 - 30 years         350         0.25 (2x10-4, 0.59)         0.42 (0.001, 0.88)           ≤ 15 years         150         0.05 (5x10-5, 0.13)         0.09 (3x10-4, 0.19)           Aluminum production         > 30 years         7.800         0.80 (0.01, 1.3)         1.0 (0.04, 1.6)           15 - 30 years         2.600         0.18 (0.003, 0.29)         0.23 (0.008, 0.35)         ≤ 15 years           Manufacturing of carbon products         45 years         3.300         0.83 (0.002, 1.8)         1.2 (0.01, 2.3)           Manufacturing of carbon products         45 years         3.20 years         1.200         0.20 (5x10-4, 0.24)         0.30 (0.003, 0.56)           ≤ 15 years         0         0 (0, 0)         0         0         0         0         0         0         0         0.22 (2x10-4, 0.25)         0.48 (0.002, 0.34)         1.5         30 years         1.500         0.22 (5x10-4, 0.25)         0.48 (0.002, 0.34)         1.5         30 years         1.500         0.25 (0.004, 0.25)         0.44 (0.004, 0.30 (0.004, 0.71)         1.5 -30 years         1.200 0.00         0	Coke production	15 – 30 vears	1,700	3.1 (0.01, 6.2)	4.5 (0.07, 7.9)		
		≤ 15 vears	350	0.32 (0.002, 0.63)	0.46 (0.007, 0.81)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		45 years	1,500	1.6 (0.001, 3.8)	2.7 (0.01, 5.6)		
Silicon production         15 - 30 years         350         0.25 (2x10-4, 0.59)         0.42 (0.001, 0.88)           <15 years		> 30 years	1,000	1.1 (0.001, 2.5)	1.8 (0.006, 3.8)		
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Silicon production	15 – 30 years	350	0.25 (2x10-4, 0.59)	0.42 (0.001, 0.88)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		≤ 15 years	150	0.05 (5x10-5, 0.13)	0.09 (3x10-4, 0.19)		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		45 years	10,700	1.1 (0.02, 1.8)	1.4 (0.05, 2.2)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Aluminum production	> 30 years	7,800	0.80 (0.01, 1.3)	1.0 (0.04, 1.6)		
≤ 15 years         300         0.01 (2x10-4, 0.02)         0.01 (5x10-4, 0.02)           Manufacturing of carbon products         45 years         3,300         0.83 (0.002, 1.8)         1.2 (0.01, 2.3)           > 30 years         2,100         0.53 (0.001, 1.2)         0.79 (0.008, 1.5)           15 - 30 years         2,100         0.20 (5x10-4, 0.44)         0.30 (0.003, 0.56)           ≤ 15 years         0         0 (0, 0)         0 (0, 0)           Foundries         45 years         32,830         0.60 (0.002, 1.3)         0.88 (0.008, 1.7)           > 30 years         6,600         0.12 (3x10-4, 0.25)         0.18 (0.002, 0.34)           15 - 30 years         1,830         0.01 (3x10-5, 0.02)         0.02 (2x10-4, 0.03)           2 (0mbustion processes         > 30 years         165,000         2.5 (0.008, 5.3)         3.4 (0.03, 6.4)           15 - 30 years         165,000         2.5 (0.008, 5.3)         3.4 (0.03, 6.4)           15 - 30 years         150,000         2.8 (9x10-4, 0.59)         0.38 (0.004, 0.71)           Engine exhaust emissions         > 30 years         890,000         1.7 (0.1, 3.1)         2.0 (0.03, 3.4)           15 - 30 years         45 years         2,300,000         3.8 (0.02, 7.0)         4.4 (0.08, 7.6)           Lise of lubricatin	Aluminum production	15 – 30 years	2,600	0.18 (0.003, 0.29)	0.23 (0.008, 0.35)		
$ \begin{array}{l lllllllllllllllllllllllllllllllllll$		≤ 15 years	300	0.01 (2x10-4, 0.02)	0.01 (5x10-4, 0.02)		
$ \begin{array}{l lllllllllllllllllllllllllllllllllll$		45 years	3,300	0.83 (0.002, 1.8)	1.2 (0.01, 2.3)		
	Manufacturing of carbon products	> 30 years	2,100	0.53 (0.001, 1.2)	0.79 (0.008, 1.5)		
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Manufacturing of carbon products	15 – 30 years	1,200	0.20 (5x10-4, 0.44)	0.30 (0.003, 0.56)		
Foundries         45 years         32,830         0.60 (0.002, 1.3)         0.88 (0.008, 1.7)           > 30 years         6,600         0.12 (3x10-4, 0.25)         0.18 (0.002, 0.34)           15 - 30 years         24,400         0.30 (7x10-4, 0.62)         0.44 (0.004, 0.84)           ≤ 15 years         1,830         0.01 (3x10-5, 0.02)         0.02 (2x10-4, 0.03)           Combustion processes         45 years         400,000         6.2 (0.02, 13)         8.2 (0.08, 16)           > 30 years         165,000         2.5 (0.008, 5.3)         3.4 (0.03, 6.4)         15 - 30 years           2 50 years         55,000         0.28 (9x10-4, 0.59)         0.38 (0.004, 0.71)           45 years         2,000,000         3.8 (0.02, 7.0)         4.4 (0.08, 7.6)           > 30 years         890,000         1.7 (0.01, 3.1)         2.0 (0.03, 3.4)           15 - 30 years         253,000         0.16 (9x10-4, 0.30)         0.19 (0.003, 0.32)           Use of lubricating oils         15 years         253,000         1.1 (0.006, 2.0)         1.3 (0.02, 2.2)           < 15 years		≤ 15 years	0	0 (0, 0)	0 (0, 0)		
Foundries> 30 years6,6000.12 (3x10-4, 0.25)0.18 (0.002, 0.34) $15 - 30$ years24,4000.30 (7x10-4, 0.62)0.44 (0.004, 0.84) $\leq 15$ years1,8300.01 (3x10-5, 0.02)0.02 (2x10-4, 0.03) $45$ years400,0006.2 (0.02, 13)8.2 (0.08, 16) $> 30$ years165,0002.5 (0.008, 5.3)3.4 (0.03, 6.4) $15 - 30$ years180,0001.8 (0.006, 3.8)2.5 (0.02, 4.7) $\leq 15$ years55,0000.28 (9x10-4, 0.59)0.38 (0.004, 0.71) $45$ years2,000,0003.8 (0.02, 7.0)4.4 (0.08, 7.6) $= 15$ years2,000,0003.8 (0.02, 7.0)4.4 (0.03, 0.4) $= 15$ years2,000,0001.7 (0.01, 3.1)2.0 (0.03, 3.4) $= 15$ years253,0001.1 (0.006, 2.0)1.3 (0.02, 2.2) $\leq 15$ years1.30 years857,0001.1 (0.01, 4.030)0.19 (0.003, 0.32) $= 15$ years1.30 years632,0001.1 (0.01, 1.8)1.2 (0.04, 1.9)Use of lubricating oils15 - 30 years632,0001.9 (0.02, 3.3)2.1 (0.07, 3.4) $15 - 30$ years430,0000.44 (x10-4, 0.07)0.04 (0.001, 0.07) $\leq 15$ years110,0000.06 (7x10-4, 0.10)0.07 (0.002, 0.12) $> 30$ years60,0000.03 (4x10-4, 0.05)0.04 (0.001, 0.07) $\leq 15$ years12000.002 (3x10-5, 0.003)0.003 (9x10-5, 0.004) $\leq 15$ years12000.002 (3x10-5, 0.003)0.003 (9x10-5, 0.004) $\leq 15$ years3.692,43027 (0.14, 54)37 (0.57, 67)		45 years	32,830	0.60 (0.002, 1.3)	0.88 (0.008, 1.7)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Foundries	> 30 years	6,600	0.12 (3x10-4, 0.25)	0.18 (0.002, 0.34)		
	i oundries	15 – 30 years	24,400	0.30 (7x10-4, 0.62)	0.44 (0.004, 0.84)		
$ \begin{array}{c} \mbox{Combustion processes} & \begin{array}{c} 45 \ years & 30 \ years & 165,000 & 2.5 \ (0.02, 13) & 8.2 \ (0.08, 16) \\ > 30 \ years & 165,000 & 2.5 \ (0.008, 5.3) & 3.4 \ (0.03, 6.4) \\ 15 - 30 \ years & 55,000 & 2.8 \ (9x10-4, 0.59) & 0.38 \ (0.004, 0.71) \\ \leq 15 \ years & 2,000,000 & 3.8 \ (0.02, 7.0) & 4.4 \ (0.08, 7.6) \\ > 30 \ years & 890,000 & 1.7 \ (0.01, 3.1) & 2.0 \ (0.03, 3.4) \\ 15 - 30 \ years & 857,000 & 1.1 \ (0.006, 2.0) & 1.3 \ (0.02, 2.2) \\ \leq 15 \ years & 253,000 & 0.16 \ (9x10-4, 0.30) & 0.19 \ (0.003, 0.32) \\ \end{array} \right. \\ \begin{array}{c} 45 \ years & 1,130,000 & 1.9 \ (0.02, 3.3) & 2.1 \ (0.07, 3.4) \\ 15 - 30 \ years & 632,000 & 1.1 \ (0.01, 1.8) & 1.2 \ (0.04, 1.9) \\ 15 - 30 \ years & 632,000 & 1.1 \ (0.016, 0.83) & 0.53 \ (0.02, 0.87) \\ \leq 15 \ years & 430,000 & 0.48 \ (0.006, 0.83) & 0.53 \ (0.02, 0.87) \\ \leq 15 \ years & 632,000 & 0.04 \ (4x10-4, 0.07) & 0.04 \ (0.001, 0.07) \\ \leq 15 \ years & 68,000 & 0.04 \ (4x10-4, 0.07) & 0.04 \ (0.001, 0.07) \\ \leq 15 \ years & 68,000 & 0.04 \ (4x10-4, 0.05) & 0.04 \ (0.001, 0.07) \\ \leq 30 \ years & 68,000 & 0.03 \ (4x10-4, 0.02) & 0.02 \ (5x10-4, 0.03) \\ \leq 15 \ years & 110,000 & 0.06 \ (7x10-4, 0.02) & 0.02 \ (5x10-4, 0.03) \\ \leq 15 \ years & 38,000 & 0.01 \ (2x10-4, 0.02) & 0.02 \ (5x10-4, 0.03) \\ \leq 15 \ years & 3.692,430 & 27 \ (0.14, 54) & 37 \ (0.57, 67) \\ Total & \begin{array}{c} 45 \ years & 1,766,550 & 13 \ (0.07, 27) & 19 \ (0.29, 33) \\ 15 - 30 \ years & 1,535,250 & 7.5 \ (0.04, 15) & 10 \ (0.15, 18) \end{array} \right. $		≤ 15 years	1,830	0.01 (3x10-5, 0.02)	0.02 (2x10-4, 0.03)		
$\begin{array}{c c} \mbox{Combustion processes} & > 30 \ years & 165,000 & 2.5 \ (0.008, 5.3) & 3.4 \ (0.03, 6.4) \\ 15 - 30 \ years & 180,000 & 1.8 \ (0.006, 3.8) & 2.5 \ (0.02, 4.7) \\ \leq 15 \ years & 55,000 & 0.28 \ (9x10-4, 0.59) & 0.38 \ (0.004, 0.71) \\ 45 \ years & 2,000,000 & 3.8 \ (0.02, 7.0) & 4.4 \ (0.08, 7.6) \\ > 30 \ years & 890,000 & 1.7 \ (0.01, 3.1) & 2.0 \ (0.03, 3.4) \\ 15 - 30 \ years & 857,000 & 1.1 \ (0.006, 2.0) & 1.3 \ (0.02, 2.2) \\ \leq 15 \ years & 253,000 & 0.16 \ (9x10-4, 0.30) & 0.19 \ (0.003, 0.32) \\ \leq 15 \ years & 1,130,000 & 1.9 \ (0.02, 3.3) & 2.1 \ (0.07, 3.4) \\ 15 - 30 \ years & 632,000 & 1.1 \ (0.01, 1.8) & 1.2 \ (0.04, 1.9) \\ 15 - 30 \ years & 632,000 & 1.1 \ (0.01, 1.8) & 1.2 \ (0.04, 1.9) \\ 15 - 30 \ years & 68,000 & 0.04 \ (4x10-4, 0.07) & 0.04 \ (0.001, 0.07) \\ \leq 15 \ years & 110,000 & 0.06 \ (7x10-4, 0.10) & 0.07 \ (0.002, 0.12) \\ > 30 \ years & 60,000 & 0.3 \ (4x10-4, 0.05) & 0.04 \ (0.001, 0.07) \\ \leq 15 \ years & 110,000 & 0.06 \ (7x10-4, 0.02) & 0.02 \ (5x10-4, 0.03) \\ \leq 15 \ years & 12,000 & 0.02 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 12,000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,2000 & 0.002 \ (3x10-5, 0.003) & 0.003 \ (9x10-5, 0.004) \\ \leq 15 \ years & 1,505,250 & 7.5 \ (0.04, 15) & 10 \ (0.15, 18) \\ \end{cases}$		45 years	400,000	6.2 (0.02, 13)	8.2 (0.08, 16)		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Compustion processes	> 30 years	165,000	2.5 (0.008, 5.3)	3.4 (0.03, 6.4)		
	Compassion processes	15 – 30 years	180,000	1.8 (0.006, 3.8)	2.5 (0.02, 4.7)		
		≤ 15 years	55,000	0.28 (9x10-4, 0.59)	0.38 (0.004, 0.71)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		45 years	2,000,000	3.8 (0.02, 7.0)	4.4 (0.08, 7.6)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Engine exhaust emissions	> 30 years	890,000	1.7 (0.01, 3.1)	2.0 (0.03, 3.4)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		15 – 30 years	857,000	1.1 (0.006, 2.0)	1.3 (0.02, 2.2)		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		≤ 15 years	253,000	0.16 (9x10-4, 0.30)	0.19 (0.003, 0.32)		
Use of lubricating oils> 30 years $632,000$ $1.1 (0.01, 1.8)$ $1.2 (0.04, 1.9)$ $15 - 30$ years $430,000$ $0.48 (0.006, 0.83)$ $0.53 (0.02, 0.87)$ $\leq 15$ years $68,000$ $0.04 (4x10-4, 0.07)$ $0.04 (0.001, 0.07)$ Bitumen/road paving $45$ years $110,000$ $0.06 (7x10-4, 0.10)$ $0.07 (0.002, 0.12)$ $> 30$ years $60,000$ $0.03 (4x10-4, 0.05)$ $0.04 (0.001, 0.07)$ $15 - 30$ years $38,000$ $0.01 (2x10-4, 0.02)$ $0.02 (5x10-4, 0.03)$ $\leq 15$ years $12,000$ $0.002 (3x10-5, 0.003)$ $0.003 (9x10-5, 0.004)$ $45$ years $3,692,430$ $27 (0.14, 54)$ $37 (0.57, 67)$ Total $15 - 30$ years $1,535,250$ $7.5 (0.04, 15)$ $10 (0.15, 18)$		45 years	1,130,000	1.9 (0.02, 3.3)	2.1 (0.07, 3.4)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Use of lubricating oils	> 30 years	632,000	1.1 (0.01, 1.8)	1.2 (0.04, 1.9)		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		15 – 30 years	430,000	0.48 (0.006, 0.83)	0.53 (0.02, 0.87)		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		≤ 15 years	68,000	0.04 (4x10-4, 0.07)	0.04 (0.001, 0.07)		
Bitumen/road paving         > 30 years         60,000         0.03 (4x10-4, 0.05)         0.04 (0.001, 0.07)           15 - 30 years         38,000         0.01 (2x10-4, 0.02)         0.02 (5x10-4, 0.03)           ≤ 15 years         12,000         0.002 (3x10-5, 0.003)         0.003 (9x10-5, 0.004)           45 years         3,692,430         27 (0.14, 54)         37 (0.57, 67)           Total         15 - 30 years         1,535,250         7.5 (0.04, 15)         10 (0.15, 18)		45 years	110,000	0.06 (7x10-4, 0.10)	0.07 (0.002, 0.12)		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Bitumen/road paving	> 30 years	60,000	0.03 (4x10-4, 0.05)	0.04 (0.001, 0.07)		
≤ 15 years         12,000         0.002 (3x10-5, 0.003)         0.003 (9x10-5, 0.004)           45 years         3,692,430         27 (0.14, 54)         37 (0.57, 67)           > 30 years         1,766,550         13 (0.07, 27)         19 (0.29, 33)           15 - 30 years         1,535,250         7.5 (0.04, 15)         10 (0.15, 18)	Bitumeninoad paving	15 – 30 years	38,000	0.01 (2x10-4, 0.02)	0.02 (5x10-4, 0.03)		
45 years         3,692,430         27 (0.14, 54)         37 (0.57, 67)           Total         > 30 years         1,766,550         13 (0.07, 27)         19 (0.29, 33)           15 - 30 years         1,535,250         7.5 (0.04, 15)         10 (0.15, 18)		≤ 15 years	12,000	0.002 (3x10-5, 0.003)	0.003 (9x10-5, 0.004)		
> 30 years         1,766,550         13 (0.07, 27)         19 (0.29, 33)           15 - 30 years         1,535,250         7.5 (0.04, 15)         10 (0.15, 18)		45 years	3,692,430	27 (0.14, 54)	37 (0.57, 67)		
15 – 30 years 1,535,250 7.5 (0.04, 15) 10 (0.15, 18)	Tatal	> 30 years	1,766,550	13 (0.07, 27)	19 (0.29, 33)		
	IOTAI	15 – 30 years	1,535,250	7.5 (0.04, 15)	10 (0.15, 18)		
≤ 15 years 390.630 0.88 (0.004, 1.8) 1.2 (0.02, 2.2)		≤ 15 years	390.630	0.88 (0.004, 1.8)	1.2 (0.02, 2.2)		

449 Table 4. Exposed population and number of additional lung cancer cases per year in France

Note: 95% CI: 95% confidence interval,  $\tau$ : exposure duration,  $N(\tau)$ : exposed population.  $N_{exp} =$ 450  $N_{\leq 15} + N_{15-30} + N_{>30}$ .  $N_{exp}$ : total exposed population,  $N_{\leq 15}$ : population exposed  $\leq 15$  years,  $N_{15-30}$ : 451 population exposed 15-30 years,  $N_{>30}$ : population exposed > 30 years.  $E(\tau)$ : expected number of 452 453 additional lung cancers in France after an exposure of duration  $\tau$ ,  $E_e$ : expected number of additional 454 lung cancers among the total French exposed population after an exposure of 45 years,  $E_{45}$ : expected 455 number of additional lung cancers among the  $N_{>30}$  French subpopulation after an exposure of 45 456 years,  $E_{30}$ : expected number of additional lung cancers among the  $N_{15-30}$  French subpopulation after 457 an exposure of 30 years,  $E_{15}$ : expected number of additional lung cancers among the  $N_{\leq 15}$  French 458 subpopulation after an exposure of 15 years. Beware  $E_e \neq E_{15} + E_{30} + E_{45}$  because of the cumulative 459 effect of the cancer risk.

**Expected lung cancer cases** 

Exposed population



**Figure 1.** Rough estimation of the expected number of additional lung cancer cases per year in France in each L1G using BaP concentrations

 $P_{0.05:}$  5<sup>th</sup> percentile,  $P_{0.90:}$  90<sup>th</sup> percentile,  $P_{0.95:}$  95<sup>th</sup> percentile. Where there is only one bar colored in red, it means that  $P_{0.90}=0$ .  $N_{exp} = N_{\le 15} + N_{15-30} + N_{>30}$ .  $N_{exp}$ : total exposed population,  $N_{\le 15}$ : population exposed from 0 to 15 years,  $N_{15-30}$ : population exposed from 15 to 30 years,  $N_{>30}$ : population exposed for more than 30 years.  $E(\tau)$ : expected number of additional lung cancers in France after an exposure of duration  $\tau$ ,  $E_e$ : expected number of additional lung cancers among the total French exposed population after an exposure of 45 years,  $E_{45}$ : expected number of additional lung cancers among the  $N_{>30}$  French subpopulation after an exposure of 45 years,  $E_{45}$ : expected number of 15 years. Beware  $E_e \neq 470$   $E_{15} + E_{30} + E_{45}$  because of the cumulative effect of the cancer risk.

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### 2 4. Discussion

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Risk indicators found in the literature provide extremely different risk probabilities for the same given
concentration (Fleiss' Kappa: 0.29, Table S2). In addition to the fair agreement between existing
indicators, there is, to our best knowledge, no guide, recommendation or gold standard concerning the
best choice and condition for using these indicators. This information confirms the utility of using
CRI.

479 The risk of lung cancer was found to be highly variable between and within exposure groups (up to 480 1,000 likelihood), showing that it was essential to focus on the most detailed level of description 481 available (i.e., the L3G) because these groups had the lowest concentration dispersion and best risk 482 reliability. A strategy to improve the risk reliability would be to lessen measurement uncertainties as 483 they accounted for most of the uncertainties in the risk estimation. One strategy to diminish the 484 concentration dispersion and improve the risk reliability would be to perform other measurements 485 and/or to acquire a more detailed description of exposure groups that cannot currently be considered as 486 having a low concentration dispersion (Petit et al. 2017b). Differences in the risk of lung cancer observed between and within groups may derive from several determinants of exposure, such as 487 ventilation, raw material composition, distance from the emission source or process type and 488 489 temperature, a topic that had been previously addressed (Maître et al. 2018). For instance, lung cancer 490 risk among people working on Söderberg electrodes was 8 times lower than among those working 491 near composite electrodes. This difference can be explained by the pouring of spherical pitch paste 492 into electrodes during composite electrodes loading, which generates an important aerosol, in contrast 493 to Söderberg electrodes, in which large paste cylinders are dropped into the electrode column semi-494 automatically with far less emissions.

495 Workers who were the most at risk of lung cancer were those exposed to PAH mixtures via products 496 derived from coal, while the least at risk were those exposed to PAH mixtures via products derived 497 from petroleum. Workers in coke production, where levels and risks were very high, necessitate a particular focus, regardless of the activity considered. In silicon production, a particular emphasis 498 should be placed on maintenance work in the furnace, annual maintenance activities and paste loading 499 500 of composite electrodes. In aluminum production, efforts should be focused towards maintenance 501 tasks, the paste tower and ramming. In the manufacture of carbon products, raw cathode extrusion is 502 of concern, and steel foundries should focus on the fusion furnace operator. Efforts are still needed to 503 decrease exposures and therefore risks, especially in exposure groups using products derived from coal 504 where the risk can exceed  $10^{-3}$ . A perspective to diminish the risk of human lung cancer would be to 505 set/undertake/implement, when feasible and relevant, product modifications (raw materials, such as ramming paste, containing no PAH or containing less and less PAH, especially BaP), process 506 507 modifications (decrease of the temperatures), collective protective equipment, and, as a last resort, 508 personal protective equipment (PPE).

509 However, these results must be considered carefully because other routes of exposure (skin absorption 510 in particular, which is known to lead to potentially high PAH exposure) were not taken into account. Taking into account several routes of exposure would require the use of additional formulas and/or 511 512 new models (Park 2018). Estimated risks were most certainly overestimated because PPE were not 513 taken into account. Although, on average, 65% of the workers were wearing gloves and 43% were wearing a respiratory mask, there was no information regarding the PPE efficiency. PPE efficiency is 514 highly variable and depends mostly on how they are used, stored and replaced by the workers (Chen et 515 516 al. 2012). Additionally, PPE varies from one company to another, and thus it is impossible to 517 determine whether the worker has worn the PPE during the entire shift. For these reasons, correction for factors that take into account PPE was not used in the risk estimation. Biological monitoring is a 518 519 good complementary approach to airborne monitoring to account for PPE, other routes of exposure 520 and individual factors. As a result, biological monitoring was always performed simultaneously with 521 airborne monitoring among workers included in the E-HAP (Barbeau et al. 2015; Lutier et al. 2016).

522 Estimated risks are only valid for a given moment (when the campaigns of measurement were carried 523 out) and a given exposure duration. Indeed, the exposure duration has a great influence on the 524 estimated risk and number of potential additional lung cancer cases (Table 4, Fig. 1). In addition, exposure conditions do not necessarily remain the same over 45 years because levels can vary 525 526 throughout time, processes can be improved and because the product composition can change (Creely 527 et al. 2007; Peters et al. 2015). Additionally, it is becoming increasingly common that people perform 528 different jobs, activities and tasks during their entire professional career, which must be taken into 529 account when estimating risks (Kienzler et al., 2016). Although knowledge of the cursus laboris of 530 each worker (Marchand 1956; Martin 1990; Martin and Robaux 1989) is paramount for a more 531 accurate risk estimation, it can be rather complex if not impossible to establish (Lentz et al. 2015). In 532 addition, a multitude of individual factors (e.g., genetic susceptibility, preexisting diseases) can have a 533 great influence on the estimated risk and number of potential additional cancer cases; however many 534 uncertainties persist regarding these factors (Abt et al. 2010; Gallagher et al. 2015; Setton et al. 2013; 535 Shen et al. 2014).

536 It was found that additional lung cancer cases in France could be expected in all L1Gs (Fig. 1, Table 537 4), for which epidemiological studies have demonstrated a significant positive association between exposure to PAHs and human lung cancer risk. There are, however, a few exceptions: silicon 538 production, for which there is a paucity of studies, and combustion processes, in particular firefighters 539 540 (approximately 280,000 workers exposed to PAHs (Pompiers, 2017) with a risk of  $3.0 \times 10^{-5}$ ), for 541 which studies are scarce because of the emergency context associated with such jobs. In addition, 542 some epidemiological studies have shown a significant association between exposure to PAHs in public work, road paving and human lung cancer risk (Boffetta et al. 1997; Rota et al. 2014). Here, 543 these occupations demonstrated low risks (from  $5.0 \times 10^{-7}$  for bitumen application to  $4.3 \times 10^{-6}$  for 544 545 underground drivers), and no additional lung cancer cases would be expected in bitumen/road paving,

546 even if 10 times more people were exposed. These differences could be explained by the finding that 547 epidemiological studies investigate retrospective exposures (tumorigenesis may span more than 20 to 40 years) and that changes in the exposure conditions occurred and lowered exposure levels over these 548 past decades. Indeed, for road paving, the product composition (use of products derived from 549 petroleum instead of from coal) and the decrease in application temperature significantly lowered 550 exposure levels (Burstyn et al. 2002; Spickenheuer et al. 2011) and therefore risks. These variations 551 may derive from several determinants of exposure, such as ventilation, raw material composition or 552 553 process temperature. These features most certainly explained the smaller number of additional lung 554 cancer cases for exposures that occurred between 2000 and 2014 than prior to 2000 (Boffetta et al. 555 2010; De Matteis et al. 2012).

556 Based on the lung cancer risks calculated in this study and on the estimated number of exposed 557 workers in each L1G, a rough estimation of the expected contemporary number of additional lung 558 cancer cases in each L1G was performed (Fig. 1). This value is a rough estimation because of all the 559 mentioned uncertainties and because the precise number of exposed workers was not accurately 560 known. For example, the number of people who used lubricating oils was overestimated because many 561 workers who answered that they were using mineral oils were in fact using synthetic oils (Ministère du 562 Travail, 2016). The incidence of lung cancer may be underestimated because the smoking prevalence 563 was not taken into account (50% of workers in the E-HAP were smokers, with even a greater % before 564 2000) (Shen et al. 2014).

The largest number of expected additional lung cancer cases was not necessarily found for L1Gs that 565 566 used products derived from coal because the number of exposed workers was far smaller (1,000 -567 40,000) than in L1Gs using products derived from petroleum (100,000 to 2 millions). Overall, a total 568 of 27 (95% CI: 0.14-54) additional lung cancer could be expected per year in France among the 3.7 569 million workers estimated to be exposed to PAHs (37, 95% CI: 0.57-67) if the BaPeq was used instead 570 of the BaP). These values only indicate the likelihood of lung cancer and not whether they will or will 571 not occur. This number might be underestimated because workers exposed to PAHs from other 572 industries (e.g., aerospace, use of creosote, recycling, tire production, naval industries) are not currently in the E-HAP. The contemporary number of additional lung cancer cases in France was 573 574 found to be 7 and 5 times lower than the number of lung cancer cases estimated for the year 2000 in 575 France (Boffetta et al. 2010) and 2005 in Italy (De Matteis et al. 2012), but it was within the range of 12-37 cases that would be expected in 2015 using the attributable fractions and the incidence of the 576 577 lung cancer mentioned in the Introduction section. In contrast, our estimation was 2 times higher than the estimation of the IARC (2018) for 2015. The estimation proposed by the IARC (2018) could, 578 579 however, be an underestimation because the study (SUMER study) they used to estimate the number of exposed workers (approximately 1.5 million) to PAHs was incomplete. For example, workers 580 581 exposed to combustion processes, such as firefighters, were not taken into account, and for engine

exhaust emissions, only people exposed to diesel exhaust were taken into account; other exhaustemissions were not considered to be exposed to PAHs in the SUMER study.

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The risk estimation was not performed for all individual PAHs other than BaP because the BaP is the 585 only PAH with an inhalation unit risk (IUR) for lung cancer. Other available IURs were either 586 established for another toxic effect (e.g., nasal respiratory epithelial adenoma and nasal olfactory 587 588 epithelial neuroblastoma for naphthalene) or derived using a potency equivalency factor (TEF) 589 procedure, for which TEFs were not necessarily based on the inhalation route nor on the same animal 590 models (OEHHA 2017). Assessment of the mixture toxicity is, however, paramount but very 591 challenging because it requires the identification of a suitable/genuine proxy that is representative of 592 the whole mixture toxicity. BaP might not be sufficient to fully estimate the cancer risk of the whole PAH mixture. BaPeq is often used as a proxy in this regard, but its use is highly discussed, as 593 594 explained in the Introduction section. Currently, there is no clear agreement concerning which PAH 595 congeners should be reported (Boström et al. 2002). The highest burden of hazardous effects of PAH 596 mixtures is commonly represented by heavier PAHs (composed of at least 4 benzene rings, such as 597 BaP) that can be absorbed onto particles (in contrast to the lighter PAHs that are predominantly in the 598 gas phase). In addition, the absorption of some PAHs onto particles could also have an impact on the 599 cancer potency of PAH mixtures. In fact, particles carry many other compounds (not just PAHs) with 600 carcinogenic properties (Boström et al. 2002; Buonanno et al. 2015), and the effects of PAH exposure 601 alone cannot be easily separated from those of particles (Guerreiro et al. 2016). The study of exposure 602 functions (Petit et al. 2017a) is thus important to determine "typical source mixtures" (signature) 603 because the PAH mixture composition and toxicity vary substantially due to the multitude of emission 604 sources. The identification of suitable markers for assessing the mixture toxicity is needed but very 605 challenging due to the interactions among the components of a mixture (cocktail effects) (Boström et al. 2002). Tools (e.g., exposure functions, correlation network analysis) and models (e.g., 606 607 physiologically-based pharmacokinetic) considering these interactions are needed and are being 608 developed (Lentz et al. 2015; Petit et al. 2017a).

Despite efforts and changes that had been made in the past to decrease exposure levels and risks,
PAHs remain a sanitary threat for people who are exposed to these pollutants in occupational
environments. Further efforts, changes and appropriate safe PAH guidelines are still needed to better

612 protect the populations exposed to PAHs and thus reduce the number of lung cancer cases.

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### Exposed population



### Expected lung cancer cases

## Coke production

Overall

## Combustion processes

## Engine exhaust emissions

## Silicon production

## Use of lubricating oils

## Aluminum production

# Manufacturing of carbon products

### Foundries

### Bitumen / road paving 45 55 50

