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1 **Methods for the assessment of health risk induced by contaminants in** 2 **atmospheric particulate matter: a review**

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12
13 **Keywords:** cancer risk, exposure pathways, non-cancer risk, particulate matter.

14 15 **Abstract:**

16 Air pollution is a major issue for human health with more than 7 million premature deaths per
17 year due to indoor and outdoor air pollution. Exposure to particulate matter is correlated with
18 adverse health effects in the short and long run. Evaluating the health risk from exposure to
19 particulate matter is challenging because particulate matter contains many contaminants and
20 observed diseases result from multiple causes. Here we review advanced methods for the
21 evaluation of cancer and non-cancer risks induced by exposure to contaminants in particulate
22 matter. Contaminants include polycyclic aromatic hydrocarbons, phthalates, dioxins, furans,
23 dioxin-like polychlorobiphenyls, and major and trace elements. We discuss risk assessment by
24 ingestion, inhalation, and dermal contact, and for population age categories. We observe that
25 the highest contributions to cancer risk come from benzo[a]pyrene, indeno[1,2,3-c,d]pyrene,
26 benzo[k]fluoranthene, dibenz[a,h]anthracene, chromium, arsenic, cadmium, and cobalt.

27 28 **Contents:**

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37

38 Abbreviation list:

ABS	Dermal adsorption factor
ADD	Average daily dose
ADI	Acceptable daily intake
AF	Dermal adherence factor
AT	Average timing
BW	Body weight
C_i	Concentration of species i in air
CR	Cancer risk
CSF	Cancer slope factor
DL-PCBs	Dioxin-like polychlorobiphenyls
EC	Exposure concentration in air
ED	Exposure duration
EF	Exposure frequency
ET	Exposure time
GIABS	Gastrointestinal absorption factor
HI	Hazard index
HQ	Hazard quotient
ILCR	Incremental lifetime cancer risk
IR_{ing}	Soil intake rate
IR_{inh}	Inhalation intake rate
IUR	Inhalation unit risk
LADD	Lifetime average daily dose
LCR	Lifetime cancer risk
MRL	Minimal risk level
PAHs	Polycyclic aromatic hydrocarbons
PCDD	Dioxins
PCDF	Furans
RBA	Relative bioaccessibility
RfC	Reference concentration
RfD	Reference dose
SA	Exposed skin surface area
SBET	Simple bioavailability extraction test
TEF	Toxic equivalent factor
TEQ	Toxic equivalent concentration
USEPA	United States environmental protection agency
WHO	World health organization

39

40 **1 Introduction**

41 Rapid industrialization around the world has led to an important economic prosperity and an
42 increase in the living standards. This evolution was also accompanied by the deterioration of
43 the environmental balance and a drastic decrease in air quality (Fowler *et al.* 2020). The effects
44 of air pollution on human health have returned as a top priority at the end of the XXth and at the
45 beginning of the XXIst century as new epidemiological evidence emerged (Fowler *et al.* 2020).
46 According to the world health organization, air pollution was responsible for about 7 million
47 premature deaths worldwide in 2016 (WHO 2016). In 2013, the international agency for
48 research on cancer (IARC) has classified outdoor air pollution and particularly particulate
49 matter as Group 1 “carcinogenic to humans” (Loomis *et al.* 2013). Particulate matter is
50 nowadays considered as one of the most challenging issues in the environmental field because
51 of its effect on human health (Mark Goldberg 2008, Anderson *et al.* 2012, Thurston *et al.* 2017,
52 Cochard *et al.* 2020). Epidemiological, biomedical, and clinical studies indicate that long-term
53 exposure to particulate matter will increase the probability of having strokes, myocardial
54 infarcts, vascular dysfunction, hypertension, heart insufficiency and heart failure (Du *et al.*
55 2016, Lelieveld and Münzel 2020, Manisalidis *et al.* 2020, Manojkumar and Srimuruganandam
56 2021). Long-term exposure to air pollution can be also related to chronic asthma, pulmonary
57 insufficiency, and might even promote lung cancer (Xing *et al.* 2016, Manisalidis *et al.* 2020).
58 As for the respiratory system, short-term exposure to particulate matter is closely correlated to
59 cough, shortness of breath, asthma, and chronic obstructive pulmonary disease (Manisalidis *et*
60 *al.* 2020).

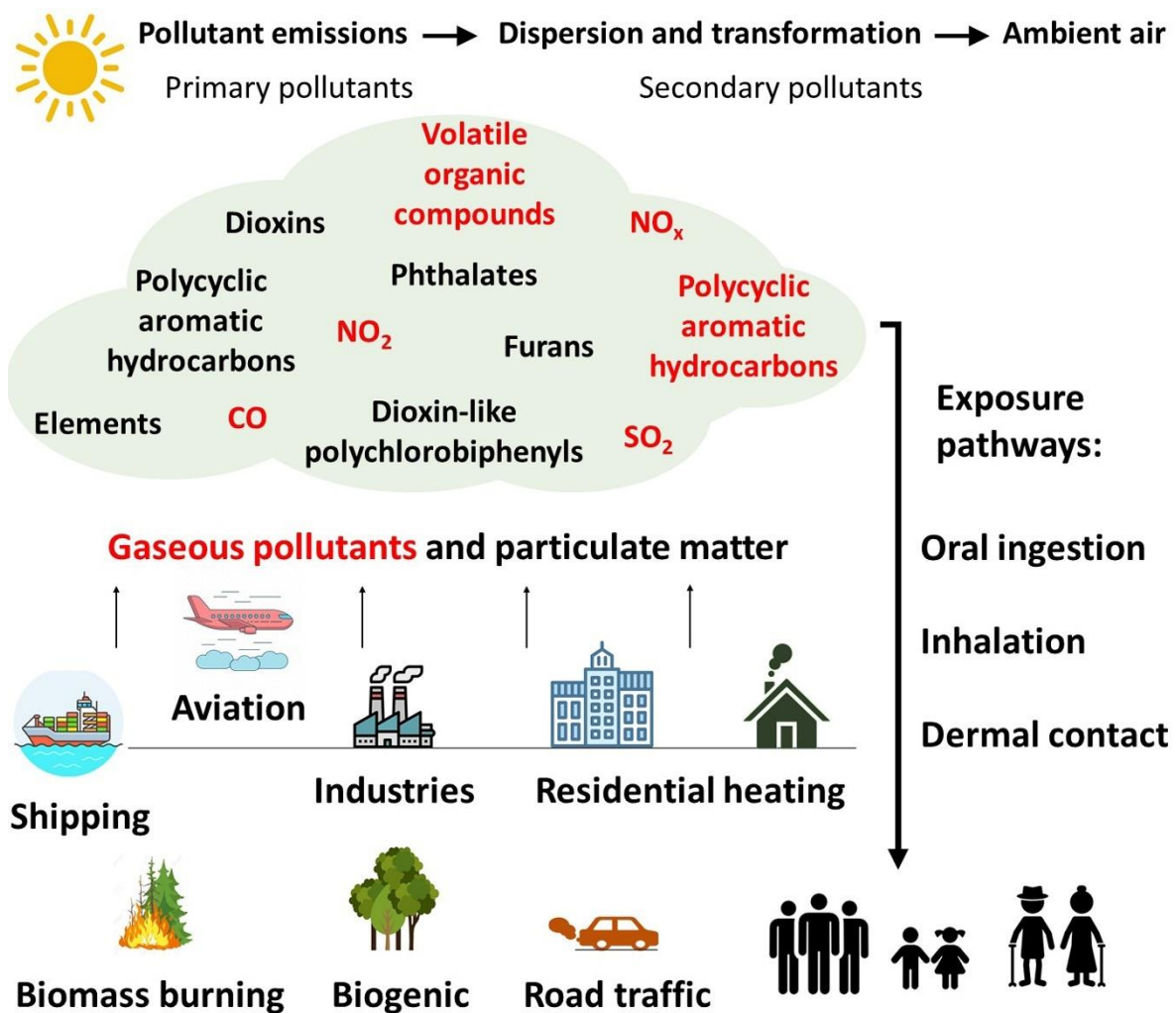
61 Atmospheric particles represent a complex mixture of inorganic species such as elements,
62 water-soluble ions, etc., organic species such as polycyclic aromatic hydrocarbons (PAHs),
63 alkanes, hopanes, etc., and a biological fraction including pollen, spores, etc. The composition
64 of these particles varies strongly and depends on the source of emissions (Sitaras and Siskos
65 2008, Mukherjee and Agrawal 2017, Yu and Park 2021), the reactivity of the atmosphere and
66 the atmospheric lifetime (**Fig. 1**). The exposure to the different atmospheric contaminants can
67 happen via three major routes: inhalation, ingestion and dermal absorption (**Fig. 1**). However,
68 the physical and chemical properties of the substance will dictate the manner in which the
69 substance enters the human body. Airborne particles might enter the human body via the
70 respiratory system. The penetration and the interaction of these particles with the human
71 respiratory tract are controlled by the size, the shape and the composition of the particles as
72 well as the geometry of the airways (Schwartz and Neas 2000, Bell *et al.* 2009, Cochard *et al.*

73 2020). Once inhaled, particulate matter and associated chemicals are either exhaled or deposited
74 in the respiratory tract. Large particles, that have a diameter higher than 10 μm , can be retained
75 in the oro-pharyngeal region due to impaction. Coarse particles, having a diameter between 2.5
76 and 10 μm can be deposited in the tracheobronchial region. Fine and ultrafine particles, having
77 a diameter below 2.5 μm and 0.1 μm respectively, can reach the alveoli and small conducting
78 airways due to gravitational sedimentation (Thakur *et al.* 2020). Additionally, particulate matter
79 deposition and accumulation might also occur at carinal ridges due to inertial impact and lower
80 clearance efficiency (Martonen *et al.* 1994). On the other hand, the non-respirable particulate
81 matter can enter the human body via the oral route. The absorption of the particulate matter
82 chemical components, leading to the introduction into the vascular system is the most important
83 in the small intestine compared to other organs in the gastrointestinal tract (Asante-Duah 2019).
84 As for the dermal route, the skin provides a major interface between the body and the
85 environment. However, the most common route of a toxicant via the skin is a passive diffusion
86 through the epidermis into the dermis where the toxicant might enter a blood vessel (Asante-
87 Duah 2019). Upon contact with skin or organs in the human body, chemicals may cause
88 different health effects from a simple irritation to a severe tissue destruction (Anderson and
89 Meade 2014).

90 Health risk assessment studies aim at estimating the nature and the probability of adverse health
91 effects in humans who may be exposed to chemicals in contaminated media (USEPA 2022a).
92 These studies differ from epidemiological by their objectives. Epidemiological studies evaluate
93 if past chemical exposures may be responsible for documented health problems in a specific
94 group of the population. On the other hand, health risk assessment studies estimate whether
95 current or future exposures will pose risks to a broad population (OEHHA 2001). The latter
96 studies are based on the evaluation of the cancer and the non-cancer health risks. According to
97 the national air toxics assessment glossary, the cancer risk represents the incremental
98 probability that an individual might develop cancer over a lifetime as a result of a specific
99 exposure to a carcinogenic chemical (USEPA 2022b). On the other hand, the non-cancer risk
100 represents the probability to develop health complications other than cancer such as
101 cardiovascular and respiratory diseases as a result of exposure to chemical pollutants. The
102 evaluation of the health risks associated with the exposure to pollutants is an important step
103 leading to the development of effective risk management policies in a population.

104 Health risk assessment tools such as the environmental benefits mapping and analysis program-
105 community edition (BenMap-CE), the CO-benefits risk assessment (COBRA), the air quality+

106 (Air Q+), the household air pollution intervention tool (HAPIT), and others are widely used
 107 (Glorennec and Monroux 2007, Gao *et al.* 2015, Farzaneh 2017, 2019). However, these tools
 108 only assess the health risks of major pollutants such as sulfur oxides, nitrogen oxides, ozone
 109 and particulate matter (Hassan Bhat *et al.* 2021). The present paper is a comprehensive review
 110 of the published methods for the assessment of the health risks due to the exposure to different
 111 classes of compounds in particulate matter. This paper also develops the methodology for the
 112 evaluation of the cancer and the non-cancer risks for the different exposure pathways and for
 113 different age categories. The review also aims to further understand which species and/or
 114 classes of compounds appears as the most problematic to human health, and to understand the
 115 limitations of health risk evaluation methods.



116
 117 **Fig. 1:** Exposure cycle to air pollutants emitted by different natural and anthropogenic sources,
 118 dispersed in ambient air while undergoing transformations before reaching humans and
 119 impacting their health.

120 **2 Health risk assessment and epidemiological studies**

121 Health risk assessment and epidemiological studies are both important but have different aims.
122 The scientists that are searching for relationships between the exposure to chemicals and
123 observed health problems in a population usually conduct an epidemiology study (OEHHA
124 2001). On the other hand, health risk assessment methodologies are used to estimate if a current
125 or a future exposure to chemicals might pose a health risk to a population. The epidemiological
126 study has the advantage to be based on a known illness while the health risk assessment is a
127 probabilistic method for occurrence of pathologies and is used as a preventive tool. The
128 methods used in the health risk evaluation cannot be used to link health problems to past
129 chemical exposures. As well, both epidemiological or health risk assessment studies cannot
130 prove that a specific chemical caused an individual's illness (OEHHA 2001).

131 Since the early 1980s, health risk assessment methods began to develop and is increasingly
132 being used to inform major policy decisions (McClellan 1999). In the same period,
133 toxicological data have formed the foundation for many hazard and dose-response assessments
134 (Krewski *et al.* 1990, Déglin *et al.* 2021). In parallel, health risks in human population were
135 increasingly being assessed by the use of empirical data for epidemiological studies (Nurminen
136 *et al.* 1999). The latter studies are considered important for the interpretation of relationships
137 between putative causal agents and health outcomes in human populations (Déglin *et al.* 2021).
138 These studies can yield more defensible estimates of likely human health risk than those
139 obtained from biologic models based on animal studies (Nurminen *et al.* 1999). That is why
140 risk assessors rely on both toxicological and epidemiological studies when investigating the
141 association between the chemical exposure and the adverse health effects. Epidemiological
142 studies can also contribute to update and modify exposure data due to continuous surveillance
143 of animal and human data, both in terms of exposure and associated health outcomes (Maffini
144 *et al.* 2021). Conversely, epidemiological and risk assessment studies operate in parallel lines
145 due to the inherent limitations and challenges of observational epidemiological studies (Déglin
146 *et al.* 2021).

147

148 **3 Steps for risk assessment evaluation**

149 The risk assessment process is described by four steps: hazard identification, exposure
150 assessment, dose-response assessment, and risk characterization (USEPA 1991c, OEHHA
151 2001, WHO 2021). In the first step of the risk assessment process, scientists determine the types

152 of health problems caused by the exposure to a specific chemical. This step can be accomplished
153 by reviewing studies investigating the effects of the considered species on humans and
154 laboratory animals (OEHHA 2001). "Hazard identification" also includes the determination of
155 hazardousness of a species by international organizations and to which extent (WHO 2021).
156 Then, "exposure assessment" is considered as the process of estimating the magnitude, the
157 frequency, and the duration of the exposure as well as the exposure pathway of a chemical
158 present in the atmosphere (USEPA 1991c). All of this information is combined with factors
159 related to individuals such as body weight, breathing rates or daily activity patterns in order to
160 estimate the quantity of the chemical that is entered into the body. Some of these parameters
161 also differ by age and sex. Hence, the relationship between the likelihood and the severity of
162 adverse health effects, and the amount of the exposure to the chemical is described by the "dose-
163 response assessment". The dose-response relationship often differs between chemicals in
164 general and between the ones that can cause cancer compared to those that can cause other
165 kinds of health problems (OEHHA 2001). Finally, the risk characterization step combines the
166 information developed in the previous steps in order to estimate the risk in an exposed
167 population.

168

169 **4 Cancer and non-cancer risk assessment**

170 4.1 Cancer risk assessment

171 According to the United States environmental protection agency, there is no exposure that have
172 "zero risk" while evaluating cancer risk unless there is a clear evidence otherwise (USEPA
173 1991a). Even an exposure to a very low concentration of cancer-causing pollutant can increase
174 the risk of cancer assuming a linear correlation between dose and response.

175 The cancer risk evaluation is based on carcinogenic chemicals where risk estimates are assigned
176 to a probability that an individual might develop a cancer over a lifetime as a result of an
177 exposure to a carcinogenic chemical. By that, the cancer risk is usually expressed as the
178 maximum number of cases of cancer projected to occur in a population of 1 million due to the
179 exposure to the cancer-causing substances over a 70-years lifetime (OEHHA 2001). The cancer
180 risk associated with a chemical in a specific exposure pathway will be the product of a lifetime
181 average daily dose by a carcinogenic slope factor (USEPA 1989a).

182

183 4.2 Non-cancer risk assessment

184 Historically, scientists have assumed that some molecular events can evoke mutagenic changes
185 in a cell that leads to damage multiplication and carcinogenicity (Haber *et al.* 2012). This
186 phenomenon is considered as a non-threshold effect because response generation is probable at
187 all exposure levels. The non-cancer risk represents the risk of developing health problems other
188 than cancer. The non-cancer effect is assumed to have a certain threshold or a certain value
189 below which no response is generated. This is mainly due to adaptive protective mechanisms
190 in the cells against toxic effects (Haber *et al.* 2012). Non cancer health effects, such as asthma,
191 nervous system disorders, birth defects, cardiovascular diseases and problems in the
192 development of children, become more severe as the exposure to chemical increases (OEHHA
193 2001).

194 The safe threshold doses, which are used for the non-cancer risk evaluation, are designated
195 differently by a number of health agencies worldwide. This threshold dose is reported as a
196 reference dose (RfD) or reference concentration (RfC) by the United States environmental
197 protection agency (USEPA 1994), or an acceptable daily intake (ADI) by the world health
198 organization (Lu 1988). Other agencies reported this threshold dose as a tolerable intake (TI)
199 such as the international program on chemical safety (IPCS 1994), or a minimal risk level
200 (MRL) such as the United States agency for toxic substances and disease registry (ATSDR)
201 (Pohl and Abadin 1995).

202 According to the United States environmental protection agency, the calculated hazard for a
203 non-cancer health effect is not a probability but a measured ratio of the magnitude of a
204 receptor's potential exposure usually called the average daily dose (ADD) to a standard
205 exposure level such as the reference concentration (RfC) or the reference dose (RfD) (USEPA
206 1989b). This ratio is also called "Hazard quotient" (HQ) and is calculated for a specific species
207 in a specified exposure pathway. Additionally, the hazard index (HI) is defined as the sum of
208 more than one hazard quotient for multiple substances considering one pathway or multiple
209 exposure pathways considering one substance (USEPA 1991c).

210

211 **5 Risk assessment methodology**

212 Health risk assessment methods consider several parameters in order to evaluate the severity of
213 the exposure. These factors include the dose or the intake rate, the characteristics of the exposed
214 individuals the concentrations of the pollutant and other parameters related to the harmfulness

215 of the compounds on human health. The characteristics of the exposed individuals are mainly
 216 the body weight, the duration and the frequency of the exposure. In this section, the
 217 methodology for the evaluation of the risk related to the exposure to different classes of
 218 compounds will be presented, also taking into consideration the three major exposure pathways:
 219 inhalation, ingestion, and dermal contact.

220 5.1 Method developed by the United States environmental protection agency

221 The health risk assessment presented by the United States environmental protection agency was
 222 first developed and published in 1989 and 1991 (USEPA 1989c, 1991c). This method was
 223 applied since then to different classes of compounds in particulate matter depending on the
 224 availability of reference values for the different species and the different exposure pathways.
 225 Both non-cancer and cancer risk evaluation need to consider a daily exposure dose, expressed
 226 in mg/kg/day, or a daily exposure concentration, expressed in mg/m³. For the non-cancer risk,
 227 the daily exposure dose is referred to as an average daily dose (ADD_i) and the daily exposure
 228 concentration is referred to as an exposure concentration in air (EC_i).

229 The average daily dose (ADD_i) for the different exposure pathways, and the exposure
 230 concentration (EC_i) for inhalation are estimated as follows (Eq. 1 to Eq. 4):

$$231 \quad ADD_{i-inhalation} = \frac{C_i \times IR_{inh} \times ED \times EF \times 10^{-6}}{BW \times AT} \quad (Eq. 1)$$

$$232 \quad ADD_{i-ingestion} = \frac{C_i \times IR_{ing} \times ED \times EF \times 10^{-6}}{BW \times AT} \quad (Eq. 2)$$

$$233 \quad ADD_{i-dermal} = \frac{C_i \times SA \times AF \times ABS \times ED \times EF \times 10^{-6}}{BW \times AT} \quad (Eq. 3)$$

$$234 \quad EC_i = \frac{C_i \times ET \times ED \times EF \times 10^{-6}}{AT} \quad (Eq. 4)$$

235
 236 Detailed information of each parameter used in the different formulas is given in **Table 1**. The
 237 concentration of the species (C_i) is usually considered as the average concentration during the
 238 sampling or exposure period. Some of the parameters presented in the formulas are related to
 239 the exposed individual such as the inhalation (IR_{inh}) and ingestion (IR_{ing}) rates and the body
 240 weight (BW) while other parameters are more related to the frequency (EF) and the duration of
 241 the exposure (ED) to an agent (**Table 1**). However, for the evaluation of the cancer risk, the
 242 exposure period during which the dose is averaged is usually lifetime or 70 years (USEPA

243 2011). Accordingly, the lifetime average daily dose (LADD_i) for the different exposure
244 pathways can be calculated using Eq. 1 to 4 with lifetime that corresponds to 25500 days
245 replacing the average timing calculated as $AT = ED \times 365$ days (USEPA 1989c, 2011) (**Table**
246 **1**).

247 Additionally, exposure parameters also vary depending on the exposure pathway, the age group
248 chosen such as newborns, children, adolescents, or adults, the sex, and the exposed population,
249 e.g. residents, indoor workers, outdoor workers, etc.. These parameters should be site-specific
250 and should be chosen based on demographic data and exposure factors related to the country or
251 the region. If no data available, default values can be used. For instance, the default body weight
252 (BW) for a newborn between 0 and 1 year is 7.8 kg, while for a child between 1 and 11 years,
253 the body weight is 25 kg, for an adolescent between 12 and 18 years, the body weight is 61 kg,
254 and for an adult, the body weight is 70 kg (**Table 1**). The United States environmental protection
255 agency has published an exposure factor handbook that was updated in 2011 in order to provide
256 statistical data on the various factors used in the assessment of the exposure to air contaminants
257 for assessors inside the agency as well as outside (USEPA 1997a, 2011). The handbook also
258 contain data for the assessment of the exposure to soil and water contaminants.

259 Furthermore, the Chinese research academy of environmental sciences (CRAES) has also
260 published a Chinese exposure factors handbook for children and adults for the Chinese
261 population (Duan *et al.* 2015, Duan 2016). This data is mainly used by assessors in China since
262 the exposure parameters highly reflects the Chinese population.

263

264 5.1.1 Non-cancer risk assessment

265 The non-cancer risk assessment is based on the comparison between the average daily dose
266 (ADD_i) representing the exposure estimate and the reference dose (RfD_i) or the comparison
267 between the exposure concentration in air (EC_i) to the reference concentration for inhalation
268 (RfC_i). The reference dose (RfD_i), expressed in mg/kg/day, is defined as an estimate of a daily
269 exposure of the human population including sensitive groups that is likely to be without an
270 appreciable risk of deleterious effects during a lifetime (USEPA 2022a). Additionally, the
271 reference concentration (RfC_i) is a similar term that is used to assess inhalation risks and is
272 expressed in mg/m³. The ratios between ADD_i and RfD_i or RfC_i are called hazard quotients
273 (HQ_i) and are calculated following either Eq. 5a or Eq. 5b (USEPA 1989c, 1991c, 2011):

274
$$HQ_i = \frac{ADD_i}{RfD_i} \text{ (Eq. 5a)}$$

275
$$\text{or } HQ_i = \frac{EC_i}{RfC_i} \text{ (Eq. 5b)}$$

276 The reference dose (RfD_i) and the reference concentration (RfC_i) values found in the literature
 277 for different species in various classes such as PAHs, elements, phthalates, dioxins, furans and
 278 dioxin-like polychlorobiphenyls and different exposure pathways are presented in **Table 2**. For
 279 non-standard populations, no correction is needed for the reference dose and the reference
 280 concentration values (USEPA 2011). This is due to the idea that the integrated risk information
 281 system (IRIS) does not consider a 70 kg body weight assumption in the determination of RfD_i
 282 and RfC_i. Additionally, the dermal reference dose (RfD_{dermal}) can be determined from oral
 283 reference dose (RfD_{oral}) values if a gastrointestinal absorption factor (GIABS) is available as
 284 follows:

285
$$RfD_{dermal} = RfD_{oral} \times GIABS \text{ (Eq. 6)}$$

286 A default value for gastrointestinal absorption factor of 1 is used except for inorganic
 287 compounds such as Sb, Ba, Be, Cd, Cr(VI), Mn, Ni, Ag and V that were assigned values of
 288 0.15, 0.07, 0.007, 0.025, 0.025, 0.04, 0.04, 0.04 and 0.026, respectively (USEPA 2004b).

289 A receptor might also be exposed to different chemicals associated with non-cancer effects. By
 290 that, the non-cancer risk values can be presented either by species for the different exposure
 291 pathways, or by the sum of species for a specific exposure pathway, or by the sum of species
 292 for all exposure pathways (USEPA 1989c, 1991c, 2011). In order to distinguish between the
 293 different definitions, we will describe each one separately.

294 The total hazard quotient (total HQ_i) is defined as the non-cancer risk for a species in the
 295 different exposure pathways assuming additive effects and is calculated as follows (Eq.7):

296
$$\text{Total } HQ_i = HQ_{i-inhalation} + HQ_{i-ingestion} + HQ_{i-dermal} \text{ (Eq. 7)}$$

297 In order to calculate the non-cancer risk for a family of chemicals in a specific exposure
 298 pathway, the hazard index (HI) is used and will be calculated as follows (Eq.8):

299
$$HI_{inhalation/ingestion/dermal} = \sum_i HQ_{i-inhalation/ingestion/dermal} \text{ (Eq. 8)}$$

300 Finally, in order to evaluate the total non-cancer risk for a specific family for the combined
301 exposure pathways, the total hazard index (THI) is calculated as follows (Eq. 9):

302
$$Total\ HI = THI = HI_{inhalation} + HI_{ingestion} + HI_{dermal} \quad (Eq. 9)$$

303 Generally, the higher hazard quotient, total hazard quotient, hazard index and total hazard index
304 values above 1, the greater is the level of concern and the higher the probability of occurrence
305 for hazardous non-cancer effects (USEPA 2011).

306

307 5.1.2 Cancer risk assessment

308 The cancer risk (CR_i) for a specific chemical in one exposure pathway is calculated as follows
309 (Eq.10a and Eq.10b), considering the exposure concentration (EC_i) or the lifetime average daily
310 dose ($LADD_i$):

311
$$CR_{i-inhalation} = EC_i \times IUR_i \quad (Eq. 10a)$$

312
$$or \quad CR_{i-inhalation/ingestion/dermal} = LADD_i \times CSF_i \quad (Eq. 10b)$$

313 IUR_i is the inhalation unit risk for a chemical expressed in m^3/mg used to calculate the cancer
314 risk associated with the inhalation pathway (USEPA 1997a). CSF_i is the cancer slope factor for
315 a chemical in a specific exposure pathway expressed in $kg \cdot day/mg$. Cancer slope factors (CSF)
316 and inhalation unit risk (IUR) values found in the literature for different species and classes of
317 compounds in particulate matter are presented in Table 2. According to USEPA (1997a), cancer
318 slope factors and inhalation unit risk values are corrected for non-standard populations, i.e.
319 body weight (BW) different than 70 kg, by multiplying the values by $\sqrt[3]{\frac{BW}{70}}$.

320

321

322

323 Table 1: Exposure parameters through inhalation, ingestion, and dermal contact (*USEPA: United States environmental protection agency)

Exposure parameters	Unit	Availability of data	Reference
Concentration in air	C_i	ng/m ³	
Inhalation intake rate	IR_{inh}	m ³ /day	Short-term and long-term exposure values for inhalation are available for different age groups in the USEPA* exposure handbook 20 m ³ /day for an adult and 10 m ³ /day for a child (USEPA 2011)
Soil intake rate	IR_{ing}	mg/day	Data is available for different age groups in the USEPA* exposure handbook 100 mg/day for a child and 50 mg/day for and adult (USEPA 2011)
Body weight	BW	kg	Body weight is considered a demographic parameter. The use of specific data for the country or the region is recommended. If no data available, default body weight values for different age groups and sex found in the USEPA* exposure handbooks: 7.8 kg for newborns (0 to <1 year), 25 kg for children (1 to <12 years), 61 kg for adolescents (12 to <18 years) and 70 for adults (18 to 70 years) (USEPA 1991c, 1997a, 2011)
Exposure frequency	EF	days/year	225 days for outdoor workers, 250 days for indoor workers and 350 days for residents (USEPA 2002, 2004b)
Exposure time	ET	h/day	6 hours for a child, and 8 hours for an adult (Liu <i>et al.</i> 2018, Dahmardeh Behrooz <i>et al.</i> 2021)
Exposure duration	ED	years	Exposure durations can be found in the USEPA* exposure handbook for different age groups: 1 for newborns (0 to <1 year), 11 for children (1 to <12 years), 6 for adolescents (12 to <18 years) and 52 for adults (18 to 70 years) (USEPA 2011)
Average timing	AT	days	AT = ED x 365(days) for non-carcinogens AT = 70 years x 365 for carcinogens (USEPA 1989c)
Exposed skin surface area	SA	cm ²	Exposed skin surface area can be found in the exposure handbook. The default exposed surface area is 2800 cm ² for a child, 5700 cm ² for an adult, 3300 cm ² for an outdoor worker and 3300 cm ² for a construction worker (USEPA 2002, 2011)
Dermal adherence factor	AF	mg/cm ²	0.2 mg/cm ² for a child, 0.07 mg/cm ² for an adult resident, and 0.2 mg/cm ² for an adult worker (USEPA 2002)
Dermal adsorption factor	ABS	-	0.13 for polycyclic aromatic hydrocarbons 0.03 for As 0.001 for Cd 0.01 for other elements (USEPA 2002, 2011)

325 Table 2: Values of the reference dose (RfD), reference concentration (RfC), cancer slope factor (CSF), and inhalation unit risk (IUR) reported in
 326 the literature for the different species

Compound	Reference dose (RfD) (mg/kg/day)			Reference concentration (RfC) (mg/m ³)	Cancer slope factor (CSF) (kg·day/mg)			Inhalation unit risk (IUR) (m ³ /mg)
	Dermal	Ingestion	Inhalation		Dermal	Ingestion	Inhalation	
Polycyclic aromatic hydrocarbons								
benzo[a]pyrene	-	3 x 10 ^{-4 c}	-	2 x 10 ^{-6 c}	25 ^a	7.3 ^a	3.85 ^a	6 x 10 ^{-1 c}
Dioxins, furans, dioxin-like polychlorobiphenyls								
2,3,7,8-tetrachlorinated dibenzo-p-dioxin	-	7 x 10 ^{-10 c}	-	4 x 10 ^{-8 c}	-	1.3 x 10 ^{5 c}	-	3.8 x 10 ^{4 c}
Phthalates								
bis(2-ethylhexyl)phthalate	-	2 x 10 ^{-2 c}	-	-	-	1.4 x 10 ^{-2 c}	8.4 x 10 ^{-3 b}	2.4 x 10 ^{-3 c}
butyl benzyl phthalate	-	2 x 10 ^{-1 c}	-	-	-	1.9 x 10 ^{-2 c}	-	-
diethylphthalate	-	8 x 10 ^{-1 c}	-	-	-	-	-	-
dibutylphthalate	-	1 x 10 ^{-1 c}	-	-	-	-	-	-
Elements								
aluminum	-	1 ^c	-	5 x 10 ^{-3 c}	-	-	-	-
antimony metallic	-	4 x 10 ^{-4 c}	-	3 x 10 ^{-4 c}	-	-	-	-
arsenic, inorganic	1.23 x 10 ^{-4 d}	3 x 10 ^{-4 c,d}	3.01 x 10 ^{-4 d}	1.5 x 10 ^{-5 c}	1.5 ^{e,g}	1.5 ^c	15.1 ^{e,d}	4.3 ^c
barium	-	2 x 10 ^{-1 c}	-	5 x 10 ^{-4 c}	-	-	-	-
cadmium	1 x 10 ^{-5 d}	1 x 10 ^{-3 c}	1 x 10 ^{-5 d}	1 x 10 ^{-5 c}	-	-	6.3 ^e	1.8 ^c
chromium (VI)	6 x 10 ^{-5 d}	3 x 10 ^{-3 c,d}	2.86 x 10 ^{-5 d}	1 x 10 ^{-4 c}	20 ^g	5 x 10 ^{-1 c}	41 ^c	84 ^c
cobalt	1.6 x 10 ^{-2 d}	3 x 10 ^{-3 c}	5.71 x 10 ^{-6 d}	6 x 10 ^{-6 c}	-	-	9.8 ^e	9 ^c
copper	1.2 x 10 ^{-2 d}	4 x 10 ^{-2 c,d}	6.9 x 10 ^{-4 d}	-	-	-	-	-
iron	-	7 x 10 ^{-1 c}	-	-	-	-	-	-
lanthanum	-	5 x 10 ^{-5 c}	-	-	-	-	-	-
lead	5.2 x 10 ^{-4 d}	3.52 x 10 ^{-3 d}	3.5 x 10 ^{-5 d}	-	8.5 x 10 ^{-3 g}	8.5 x 10 ^{-3 c}	4.2 x 10 ^{-2 e}	1.2 x 10 ^{-5 h}
manganese	1.84 x 10 ^{-3 d}	1.4 x 10 ^{-1 c}	1.43 x 10 ^{-5 d}	5 x 10 ^{-5 c}	-	-	-	-
mercury	3 x 10 ^{-4 c}	3 x 10 ^{-4 c}	3 x 10 ^{-4 c}	3 x 10 ^{-4 c}	-	-	-	-
nickel	9 x 10 ^{-5 d}	2 x 10 ^{-2 c,d}	9 x 10 ^{-5 d}	9 x 10 ^{-5 c}	-	-	0.84 ^d	0.26 ^c
strontium	-	6 x 10 ^{-1 c}	-	-	-	-	-	-
thallium (soluble salts)	-	1 x 10 ^{-5 c}	-	-	-	-	-	-
tin	-	6 x 10 ^{-1 c}	-	-	-	-	-	-
vanadium	-	5 x 10 ^{-3 c}	-	1 x 10 ^{-4 c}	-	-	-	8.3 ⁱ
zinc	6 x 10 ^{-2 d}	3 x 10 ^{-1 c,d}	3 x 10 ^{-1 d}	-	-	-	-	-

327 ^a(Peng *et al.* 2011); ^b(OEHHA 2011); ^c(USEPA-IRIS 2022) ;^d(Hao *et al.* 2020); ^e(Bello *et al.* 2017); ^f(USEPA 2009);
 328 ^g(USEPA 2004b); ^h(CalEPA 2022); ⁱ(PPRTV 2022); ^j(USEPA 1997b); ^k(RAIS 2022).

329 Additionally, dermal cancer slope factor can be determined from oral cancer slope factor values
330 if a gastrointestinal absorption factor (GIABS) is available (Eq.11):

$$331 \quad CSF_{dermal} = \frac{CSF_{oral}}{GIABS} \quad (Eq. 11)$$

332 The total cancer risk for a species is calculated as the sum of the different risks associated with
333 the different exposure pathways and is presented as follows (Eq.12):

$$334 \quad Total \ CR_i = CR_{i-inhalation} + CR_{i-ingestion} + CR_{i-dermal} \quad (Eq. 12)$$

335 The cancer risk for a family of chemicals associated with a specific exposure pathway is
336 estimated as follows (Eq.13):

$$337 \quad CR_{inhalation/ingestion/dermal} = \sum_i CR_{i \ inhalation/ingestion/dermal} \quad (Eq. 13)$$

338 The cumulative cancer risk (CCR) as the risk attributed to a family of compounds in the
339 combined three exposure pathways is calculated as follows (Eq.14):

$$340 \quad Cumulative \ CR = CCR = CR_{inhalation} + CR_{ingestion} + CR_{dermal} \quad (Eq. 14)$$

341 The United States environmental protection agency considers a risk level of 10^{-6} (one additional
342 case per one million people) as the threshold limit (USEPA 1991b). More concern should be
343 given regarding these chemicals when the risk level exceeds the threshold. Additionally, values
344 between 10^{-6} and 10^{-4} denote a potential risk and values higher than 10^{-4} indicate a high potential
345 cancer risk (Chiang *et al.* 2009).

346 Furthermore, the cancer risk can be calculated for different age categories and summed together
347 in order to obtain an average lifetime cancer risk (LCR) or an incremental lifetime cancer risk
348 (ILCR) (OEHHA 2012):

$$349 \quad LCR = Cumulative \ CR_{Newborn} \times \frac{ED_{newborn}}{70} + Cumulative \ CR_{child} \times \frac{ED_{child}}{70} \\ 350 \quad + Cumulative \ CR_{adolescent} \times \frac{ED_{adolescent}}{70} \\ 351 \quad + Cumulative \ CR_{adult} \times \frac{ED_{adult}}{70} \quad (Eq. 15)$$

352
353

354 5.1.3 Concentration of the species in the risk assessment evaluation

355 The risk assessment in air samples can be evaluated for the exposure to the gas-phase
356 compounds as well as the particulate phase. Therefore, several classes of compounds are usually
357 used for the assessment of the cancer and the non-cancer risk such as elements, PAHs,
358 phthalates, dioxins, furans, and dioxin-like polychlorobiphenyls.

359 PAHs refer to lipophilic chemical compounds that are formed by two or more aromatic rings
360 that are environmentally persistent with various structures and toxicity (Halek *et al.* 2010,
361 Abdel-Shafy and Mansour 2016). Phthalates are a class of human-made chemicals that are
362 commonly used to increase the flexibility of plastic products, especially in poly(chloride)vinyl
363 (PVC) products (USEPA 2012). Dioxins, furans, and dioxin-like polychlorobiphenyls are semi-
364 volatile persistent organic pollutants that can be transported far from their emission sources
365 (Srogi 2008, Koukoulakis *et al.* 2020). Even if these organic and inorganic species are found in
366 low amounts in particulate matter, it has been shown that they largely contribute to the
367 particulate matter toxicity (Akhtar *et al.* 2010, Fortoul *et al.* 2015, Bandowe and Meusel 2017).
368 On the other hand, ammonium, sulfate, sea salts, and crustal elements that contribute largely to
369 particulate matter mass contribute the least to the toxicity (Borm *et al.* 2007). The assessment
370 for elements and phthalates is usually done by evaluating the risk of each species. The reason
371 is that some of them are considered carcinogenic while others can only be evaluated for their
372 non-cancer risks. For example, diethylphthalate and dibutylphthalate are only evaluated for
373 their non-cancer risks due the fact that no cancer slope factor or inhalation unit risk values were
374 found for these species in order to assess their cancer risk. On the other hand, bis(2-
375 ethylhexyl)phthalate and butyl benzyl phthalate are evaluated for both cancer and non-cancer
376 risks due to the availability of reference coefficients in the literature (**Table 2**).

377 Among PAHs, dioxins, and furans, benzo[a]pyrene (B[a]P) and 2,3,7,8-tetrachlorodibenzo-p-
378 dioxin (2,3,7,8-TCDD) are known to be carcinogenic to humans (IARC 2021). A toxic
379 equivalent factor (TEF) was introduced to assign toxicity values for the different congeners
380 based on the toxicity of either B[a]P or 2,3,7,8-TCDD reported as 1 (Nisbet and LaGoy 1992,
381 Van den Berg *et al.* 2006).

382

383

384

385 Table 3: Toxic equivalent factor (TEF) values for the different polycyclic aromatic
 386 hydrocarbons (PAHs) and their derivatives

Compound name	Toxic equivalent factor (TEF) value
acenaphthylene	0.001 ^a
1-methylnaphthalene	0.0025 ^b
2-methylnaphthalene	0.001 ^a
acenaphthene	0.001 ^a
fluorene	0.001 ^a
7H-benzo[c]fluorene	20 ^e
anthracene	0.01 ^a
phenanthrene	0.001 ^a
1-methylphenanthrene	0.001 ^e
fluoranthene	0.001 ^a
pyrene	0.001 ^a
cyclopenta[c,d]pyrene	0.01 ^e
1-methylpyrene	0.001 ^e
benz[a]anthracene	0.1 ^a
chrysene/triphenylene	0.01 ^a
5-methylchrysene	1 ^e
benzo[b]fluoranthene	0.1 ^a
benzo[k]fluoranthene	0.1 ^a
benzo[a]pyrene	1 ^a
benzo[e]pyrene	0.002 ^d
dibenz[a,h]anthracene	5 ^a
benzo[g,h,i]perylene	0.01 ^a
indeno(1,2,3-C,D)pyrene	0.1 ^a
dibenzo[a,l]pyrene	0.001 ^e
dibenzo[a,e]pyrene	10 ^e
dibenzo[e,l]pyrene	1 ^e
dibenzo[a,i]pyrene	10 ^e
dibenzo[a,h]pyrene	10 ^e
5-nitroacenaphthene	0.01 ^d
2-nitrofluorene	0.01 ^b
9-nitroanthracene	0.0032 ^c
3-nitrofluoranthene	0.0026 ^c
1-nitropyrene	0.1 ^b
6-nitrochrysene	10 ^b

387 ^a(Nisbet and LaGoy 1992), ^b(Collins *et al.* 1998), ^c(Durant *et al.* 1996), ^d(Hester and Harrison
 388 1998), ^e(Iakovides *et al.* 2021)

389
 390 The health risk evaluation for the PAHs and dioxins/furans classes of compounds is conducted
 391 using the benz[a]pyrene equivalent concentration (B[a]P_{eq}) and the toxic equivalent
 392 concentration of 2,3,7,8-tetrachlorinated dibenzo-p-dioxin (WHO-TEQ) using the following
 393 formulas (Eq.16a and Eq.16b):

394
$$\text{WHO - TEQ} = \sum_{i=1}^n C_i \times \text{TEF}_i \quad (\text{Eq. 16a})$$

395
$$\text{B[a]P}_{\text{eq}} = \sum_{j=1}^n C_j \times \text{TEF}_j \quad (\text{Eq. 16b})$$

396 C_i and C_j , expressed in ng/m^3 , are the concentrations of the dioxins, furans and dioxin-like
397 polychlorobiphenyls congeners, and PAHs and their derivatives, respectively. TEF_i and TEF_j
398 correspond to the toxic equivalent factor compared to 2,3,7,8-TCDD and B[a]P, respectively
399 (Nisbet and LaGoy 1992, Collins *et al.* 1998, Van den Berg *et al.* 2006). The values of toxic
400 equivalent factors, TEF_i and TEF_j are found in **Table 3** and **Table 4**. The calculated B[a]P_{eq} or
401 WHO-TEQ are added in Equations 1 to 4 to calculate the daily dose or exposure concentration
402 and then the non-cancer or cancer risks.

403

404 5.2 Other parameters and formulas included in the assessment of the health risk

405 5.2.1 Cancer risk for phthalates

406 In the evaluation of the cancer risks for phthalates, Zhang *et al.* (2019b) applied the same
407 formulas presented in section 3.1.2 to calculate the lifetime average daily dose for inhalation.
408 However, an additional factor related to the age sensitivity factor was added to the calculations
409 of the 70-years lifetime cancer risk when considering different age categories in the
410 calculations. The authors have added an age sensitivity factor (ASF) of 10 for infants between
411 the age of 0 and 2, 3 for toddlers between the age of 3 and 6, 3 for adolescents between the age
412 of 7 and 16, and 1 for adults between the age of 17 and 70 based on the reported of the office
413 of environmental health hazard assessment (OEHHA). OEHHA developed these ASF to take
414 into account the higher sensitivity to carcinogens during early-life exposure (OEHHA 2015)
415 but are not highly used in the literature to calculate the health risk for the different age
416 categories.

417

418 5.2.2 Cancer risk for polycyclic aromatic hydrocarbons

419 Several papers estimating the health risk due to the exposure to PAHs only consider the
420 inhalation pathway and calculate a lifetime excess cancer risk (ECR). The formula used for the
421 calculation of excess cancer risk related to PAHs exposure is the same as Eq.10a but instead of

422 multiplying an exposure concentration by the inhalation unit risk, the assessors directly use the
 423 B[a]P_{eq} (Yang *et al.* 2017, Song *et al.* 2019, Pateraki *et al.* 2020, Tsai *et al.* 2020).

424

425 Table 4: Available toxic equivalent factor (TEF) values presented by the world health
 426 organization (WHO) in 1998 and re-evaluated in 2005 for dioxins, furans and dioxin-like
 427 polychlorobiphenyls (Van den Berg *et al.* (2006)

	WHO 1998	WHO 2005
Dioxins (PCDDs)		
2,3,7,8-tetrachlorinated dibenzo-p-dioxin	1	1
1,2,3,7,8-pentachlorinated dibenzo-p-dioxin	1	1
1,2,3,4,7,8-hexachlorinated dibenzo-p-dioxin	0.1	0.1
1,2,3,6,7,8-hexachlorinated dibenzo-p-dioxin	0.1	0.1
1,2,3,7,8,9-hexachlorinated dibenzo-p-dioxin	0.1	0.1
1,2,3,4,6,7,8-heptachlorinated dibenzo-p-dioxin	0.01	0.01
octachlorinated dibenzo-p-dioxin	0.0001	0.0003
Furans (PCDFs)		
2,3,7,8 tetrachlorinated dibenzofuran	0.1	0.1
1,2,3,7,8 pentachlorinated dibenzofuran	0.05	0.03
2,3,4,7,8 pentachlorinated dibenzofuran	0.5	0.3
1,2,3,4,7,8 hexachlorinated dibenzofuran	0.1	0.1
1,2,3,6,7,8 hexachlorinated dibenzofuran	0.1	0.1
2,3,4,6,7,8 hexachlorinated dibenzofuran	0.1	0.1
1,2,3,7,8,9 hexachlorinated dibenzofuran	0.1	0.1
1,2,3,4,6,7,8-heptachlorinated dibenzofuran	0.01	0.01
1,2,3,4,7,8,9-heptachlorinated dibenzofuran	0.01	0.01
octachlorinated dibenzofuran	0.0001	0.0003
Dioxin-like polychlorobiphenyls (DL-PCBs)		
3,4,4',5-tetrachlorobiphenyl	0.0001	0.0003
3,3',4,4'-tetrachlorobiphenyl	0.0001	0.0001
2,3',4,4',5'-pentachlorobiphenyl	0.0001	0.00003
2,3',4,4',5-pentachlorobiphenyl	0.0001	0.00003
2,3,4,4',5-pentachlorobiphenyl	0.0005	0.00003
2,3,3',4,4'-pentachlorobiphenyl	0.0001	0.00003
3,3',4,4',5-pentachlorobiphenyl	0.1	0.1
2,3',4,4',5,5'-hexachlorobiphenyl	0.00001	0.00003
2,3,3',4,4',5-hexachlorobiphenyl	0.0005	0.00003
2,3,3',4,4',5'-hexachlorobiphenyl	0.0005	0.00003
3,3',4,4',5,5'-hexachlorobiphenyl	0.01	0.03
2,3,3',4,4',5,5'-heptachlorobiphenyl	0.0001	0.00003

428

429 The United States environmental protection agency proposed $6 \times 10^{-7} (\text{ng}/\text{m}^3)^{-1}$ as the inhalation
 430 unit risk value for B[a]P_{eq}. However, inhalation unit risk value was reported as 8.7×10^{-5}

431 $(\text{ng}/\text{m}^3)^{-1}$ by the world health organization (WHO 2000), and $1.1 \times 10^{-6} (\text{ng}/\text{m}^3)^{-1}$ by the office
432 of environmental health hazard assessment (OEHHA 2009).The two latter agency used a
433 method that does not take into consideration the different exposure parameters but only
434 considers the pollutant concentration and a fixed unit risk leading to an overestimation or an
435 underestimation of the real risk. Consequently, the United States environmental protection
436 agency method can contribute to more accurate results based on the different exposure pathways
437 and the age categories.

438

439 5.2.3 Non-cancer and cancer risks for elements

440 For the elements, a dimensionless average annual excess risk for an individual (R) can be used
441 to calculate the cancer and the non-cancer risks using the average daily dose (ADD_i) and the
442 lifetime daily dose ($70 \times \text{RfD}_i$), respectively, as follows (Eq. 17-18) (Chen *et al.* 2015, Wang *et*
443 *al.* 2018):

$$444 \quad R(\text{non} - \text{carcinogenic}) = \frac{10^{-6} \times \text{ADD}_i}{70 \times \text{RfD}_i} \quad (\text{Eq. 17})$$

$$445 \quad R(\text{carcinogenic}) = \frac{1 - e^{-\frac{\text{LADD}}{\text{CSF}}}}{70} \quad (\text{Eq. 18})$$

446 In this calculation, the threshold value above which the risk is unacceptable for cancer risk is
447 also 10^{-6} , whereas the risk level of 10^{-3} per year or higher is considered serious and a high
448 priority for attention (Wang *et al.* 2018). The acceptable value for the non-cancer risk is lower
449 than one.

450 Other papers integrated the bioaccessibility of the elements in the health risk evaluation. The
451 bioaccessibility represents the fraction of the species concentration that is released from the
452 environmental matrix into a synthetic biological fluid and becomes available for absorption
453 (Expósito *et al.* 2021). Therefore, the bioavailability, considered as the fraction of the species
454 in the exposure media absorbed by the organism, is influenced by the bioaccessibility since
455 solubilization is required for crossing membranes in the body (USEPA 2007). By that, the
456 bioaccessible fraction represents the maximum amount of the species that can be absorbed
457 (Manjón *et al.* 2020). Hu *et al.* (2011) estimated the relative bioaccessibility (RBA) of the
458 elements using a simple bioavailability extraction test (SBET) and integrated them to the

459 estimation of the cancer risk and the hazard quotient through ingestion pathway as follows
460 (Eq.19a and Eq.19b):

$$461 \quad HQ_{ingestion} = \frac{ADD_i \times RBA}{RfD_i} \quad (Eq. 19a)$$

$$462 \quad CR_{i-ingestion} = LADD_i \times RBA \times CSF_i \quad (Eq. 19b)$$

463 Where RBA is the relative bioaccessibility corresponding to the ratio of the elements' contents
464 extracted using the simple bioavailability extraction test method to their total contents in the
465 study. According to the study, the highest bioaccessibility rates were observed for Cd, Zn and
466 Pb with values exceeding 60%. On the other hand, the lowest values were attributed for Cr, Co,
467 and Ni with mean values of bioaccessibility ranging between 12 and 19%. These values were
468 also applied by Iakovides *et al.* (2021) that added the relative bioaccessibility parameter to the
469 different formulas used for the calculations of the cancer risk in the three exposure pathways.

470 Furthermore, Nie *et al.* (2018) evaluated the bioaccessibility of the elements through different
471 simulated body fluids in order to have different contact interfaces between human body and
472 particulate elements. Nie *et al.* (2018) used artificial lung fluid, artificial sweat, and artificial
473 gastric juice, and phosphate buffered saline solution. The trace elements that have the highest
474 bioaccessibility in artificial lung fluid and in artificial sweat were As, Cu, Pb and V (60-80%).
475 V, Cu, As, and Mn had the highest values in phosphate buffered saline solution (62-82%), and
476 V, Pb, Cu, and Mn in artificial gastric juice (67-84%). According to Mishra *et al.* (2021), the
477 concentration of the bioaccessible fraction is more relevant than the total concentration of the
478 element for a better and more accurate risk assessment of the element toxicity. Up to our
479 knowledge, there were no other study using the bioaccessible fraction of other species in the
480 risk assessment evaluation.

481

482 **6 Risk assessment studies**

483 The health risk related to particulate matter exposure is generally evaluated by studying the
484 cancer and non-cancer risks of one or several classes of compounds such as PAHs, phthalates,
485 dioxins, furans, dioxin-like polychlorobiphenyls, and elements as mentioned earlier.

486 Table 5: Selection of health risk assessment studies reported in the literature for polycyclic aromatic hydrocarbons (PAHs), elements, phthalates,
 487 dioxins and furans (PCDD/Fs), and dioxin-like polychlorobiphenyls (DL-PCBs)

Site (Country)	Risk evaluation	Class of compounds	Total cancer risk values	Total non-cancer risk values	Exposure pathways	Age categories	Problematic species	Reference
Zouk Mikael and Fiaa (Lebanon)	Cancer and non-cancer risk	PAHs Elements Phthalates PCDD/Fs and DL-PCBs	$0.4 - 1.4 \times 10^{-5}$ $2.5 - 4.4 \times 10^{-5}$ $3.8 - 5.1 \times 10^{-7}$ 4×10^{-7}	$0.1 - 0.4$ $0.3 - 1.2$ $0.001 - 0.1$ $0.01 - 0.06$	Inhalation, ingestion, and dermal contact	Newborns, children, adolescents, and adults	Sum of PAHs reported to benzo[a]pyrene, As, Co, Cr(VI), Ni and V	Fadel <i>et al.</i> (2022)
Thohoyandou (South Africa)	Cancer and non-cancer risk	Elements	3.4×10^{-6}	$0.54 - 1.18$	Inhalation	Lifetime	Ni	Edlund <i>et al.</i> (2021)
Tangshan (China)	Cancer and non-cancer risk	Elements	$0.4 - 1.5 \times 10^{-4}$	$2.8 - 2.81$	Inhalation	Children and adults	Mn, As, Cd, and Cr(VI)	Fang <i>et al.</i> (2021)
Abuja (Nigeria)	Cancer and non-cancer risk	Elements	$1.4 - 4.0 \times 10^{-10}$	$10^{-5} - 10^{-4}$	Inhalation, ingestion, and dermal contact	Children and adults	-	Sulaymon <i>et al.</i> (2020)
Sha-Lu area (Taiwan)	Cancer risk using a unit risk for inhalation	Elements	8.2×10^{-5}	-	Inhalation	Lifetime	As and Cr(VI)	Tsai <i>et al.</i> (2020)
Iasi (Romania)	Cancer and non-cancer risk	Elements	$6.3 - 8.0 \times 10^{-6}$	$0.2 - 0.3$	Inhalation	Lifetime	As and Cr(VI)	Galon-Negru <i>et al.</i> (2019)
Barcelona (Spain)	Cancer and non-cancer risk	Elements	$2.3 - 3.1 \times 10^{-5}$	below 1	Inhalation	Lifetime	Cr(VI)	Sánchez-Soberón <i>et al.</i> (2015)
Nicosia (Cyprus)	Cancer risk	PAHs Elements	7.1×10^{-4} 7.7×10^{-4}	-	Inhalation, ingestion, and	Lifetime	Sum of PAHs As, Ni, and Pb	Iakovides <i>et al.</i> (2021)

					dermal contact			
Penteli, Votanikos, and Tourlos (Greece)	Cancer risk using a unit risk for inhalation	PAHs	$0.3 - 2.6 \times 10^{-7}$	-	Inhalation	Lifetime	benzo[a]pyrene	Pateraki <i>et al.</i> (2020)
Harbin (China)	Cancer and non-cancer risk	PAHs	4.1×10^{-4}	-	Inhalation, ingestion, and dermal contact	Children, adolescents, and adults	Benzo[a]pyrene, indeno(1,2,3-c,d)pyrene, and benzo(k)fluoranthene	Ma <i>et al.</i> (2020b)
Beijing (China)	Cancer risk	PAHs	8.7×10^{-6}	-	Inhalation	Lifetime	Benzo[a]pyrene	Chang <i>et al.</i> (2019)
Jamshedpur (India)	Cancer risk	PAHs	$1.0 - 2.3 \times 10^{-5}$	-	Inhalation	Lifetime	Benzo[a]pyrene, dibenz[a,h]anthracene	Kumar <i>et al.</i> (2019)
Beijing (China)	Cancer risk using a unit risk for inhalation	PAHs	3.0×10^{-4}	-	Inhalation	Lifetime	Sum of PAHs reported to benzo[a]pyrene	Song <i>et al.</i> (2019)
Northern Thailand	Cancer risk	PAHs	$0.8 - 2.6 \times 10^{-3}$	-	Inhalation, ingestion, and dermal contact	Lifetime	Sum of PAHs reported to benzo[a]pyrene	Pongpiachan (2015)
Eleusis (Greece)	Cancer risk	PAHs PCDD/Fs and DL-PCBs	2.4×10^{-5} 1.2×10^{-5}	-	Inhalation	Lifetime	Sum of PAHs reported to benzo[a]pyrene and the sum of PCDD/Fs	Koukoulakis <i>et al.</i> (2020)
Suzhou of Jiangsu province (China)	Cancer risk	PCDD/Fs	$0.2 - 2.7 \times 10^{-5}$	-	Inhalation	Lifetime	Sum of PCDD/Fs reported to 2,3,7,8-TCDD	Sun <i>et al.</i> (2017)
Around metallurgical plants in China	Cancer risk using a unit risk for inhalation	PCDD/Fs, DL-PCBs	Sintering plants: $0.1 - 4 \times 10^{-5}$ Copper plants: $0.05 - 1.1 \times 10^{-4}$	-	Inhalation	Lifetime	Sum of PCDD/Fs reported to 2,3,7,8-TCDD	Yang <i>et al.</i> (2017)

			Aluminum plants: $0.04 - 7.1 \times 10^{-4}$ Lead plant: 2.1×10^{-6}					
Beirut (Lebanon)	Cancer risk	PCDD/Fs	6.5×10^{-5}	-	Inhalation	Different age categories	Sum of PCDD/Fs reported to 2,3,7,8- TCDD	Baalbaki <i>et al.</i> (2016)
Xi'an (China)	Cancer and non-cancer risk	Phthalates	$10^{-12} - 10^{-10}$	$10^{-7} - 10^{-3}$	Inhalation	Lifetime	bis-2- ethylhexylphthalate, and butyl benzyl phthalate	Ma <i>et al.</i> (2020a)
Guangzhou, Shanghai, Beijing, and Harbin (China)	Cancer and non-cancer risk	Phthalates	$10^{-10} - 10^{-7}$	0.01 – 0.02	Inhalation	Infants (0-2 years), toddlers (3-6 years), adolescents (7- 17 years), and adults (17- 0 years)	bis-2- ethylhexylphthalate	Zhang <i>et al.</i> (2019b)

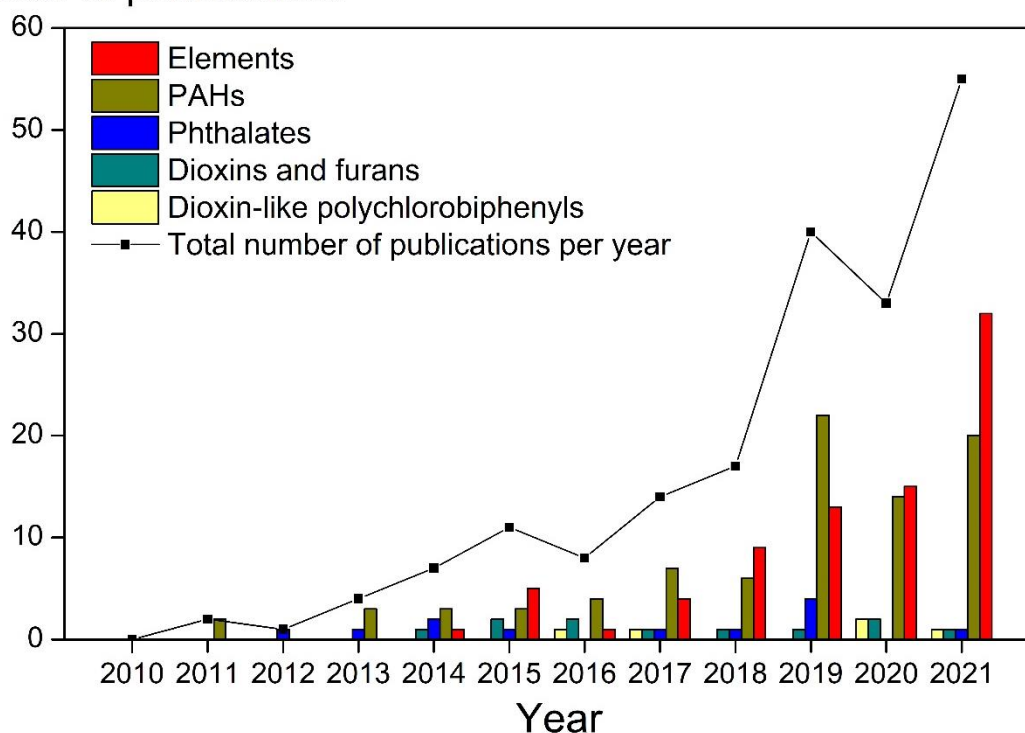
489

490 6.1 Search methodology for risk assessment publications

491 For this review, the authors conducted a literature search using several online literature
492 databases such as Google scholar, Web of Science; ScienceDirect, PubMed, etc.). The keywords
493 searched for were “health risk assessment in particulate matter”, “risk evaluation in particulate
494 matter” as well as the “health risk assessment” for the different classes of compounds in
495 particulate matter such as elements, PAHs, phthalates, dioxins and furans, and dioxin-like
496 polychlorobiphenyls. After obtaining articles using the aforementioned keywords, the articles
497 were then filtered based on the title and the abstract of the research. The authors did not take
498 into consideration publications related to the health risk assessment of PAHs, phthalates,
499 dioxins and furans, and dioxin-like polychlorobiphenyls in the gaseous phase as well as the
500 evaluation of the risk due to the exposure to volatile organic compounds.

501

Number of publications



502

503 **Fig. 2:** Number of articles published related to the health risk evaluation for different classes of
504 compounds in particulate matter (elements, polycyclic aromatic hydrocarbons (PAHs),
505 phthalates, dioxins and furans, and dioxin-like polychlorobiphenyls).

506

507 The evolution of the number of publications between 2010 and 2021 dealing with health risk
508 assessment for the different classes of compounds in particulate matter is presented in **Fig. 2**.
509 Additionally, more details can be found regarding these publications in the supplementary
510 information. The figure shows that the number of publications including the health risk
511 evaluation is highly increasing especially for elements and PAHs in particulate matter.
512 However, few studies were found for phthalates, dioxins, furans, and dioxin-like
513 polychlorobiphenyls.

514

515 6.2 Risk assessment studies per class of compounds

516 **Table 5** presents a selection of papers dealing with the evaluation of the health risk for
517 particulate matter components. In general, most of the studies found in the literature include
518 both the chemical characterization of particulate matter as well as source apportionment and
519 health risk evaluation. Furthermore, most of the studies focus on the exposure through one
520 pathway that is inhalation and one class of compounds as shown in **Table 5**. Literature regarding
521 the comparison of the health risks between different classes of compounds in particulate matter
522 is scarce and more effort should be done in order to further understand the mechanism of
523 interactions between species. Therefore, the presentation and the analysis of the different studies
524 found in the literature will be discussed by class of species.

525 6.2.1 Polycyclic aromatic hydrocarbons

526 PAHs, oxygenated-PAHs, and nitrated-PAHs are mainly emitted from petrogenic, pyrogenic,
527 and biogenic sources and are formed during the incomplete combustion of fossil fuels, natural
528 gas, wood, coke, and organic waste (Abbas *et al.* 2018). PAHs can enter the human body
529 through ingestion, inhalation, and dermal contact. The general population is usually exposed to
530 a mixture of PAHs. The latter are present in the indoor or outdoor air as well as associated to
531 cigarette and wood smokes, biomass and fossil fuels burning. The short-term exposure to PAHs
532 might cause impaired lung function in asthmatics and thrombotic effects for people with
533 coronary heart disease (Kim *et al.* 2013). Additionally, the exposure to high concentrations of
534 pollutant mixtures containing PAHs might result in eye irritation, nausea, vomiting, etc. (Abdel-
535 Shafy and Mansour 2016). On the other hand, some studies have shown that the long-term
536 exposure to PAHs is linked to several health problems such as skin, lung bladder, and
537 gastrointestinal cancers in workers (Abbas *et al.* 2018). Like many carcinogens, PAHs are
538 metabolized enzymatically to various metabolites, of which some are reactive (Rengarajan *et*

539 *al.* 2015). The toxicity, mutagenicity and/or carcinogenic properties of the PAHs have made 16
540 of them listed as priority pollutants (Srogi 2007, Hussar *et al.* 2012): naphthalene,
541 acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene,
542 chrysene, benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene,
543 indeno[1,2,3-c,d]pyrene, dibenz[a,h]anthracene and benzo[g,h,i]perylene.

544 Most of the studies in the literature reported the concentrations of the 16 PAHs to an equivalent
545 concentration of B[a]P considered as a key carcinogenic marker belonging to PAH species. Few
546 studies in the literature added the oxygenated and nitrated derivatives of PAHs in the B[a]P_{eq}
547 calculations (Bandowe *et al.* 2014, de Oliveira Galvão *et al.* 2018, Gao *et al.* 2018, Wei *et al.*
548 2021).

549 As observed in **Table 5**, benzo[a]pyrene, indeno(1,2,3-c,d)pyrene, benzo(k)fluoranthene, and
550 dibenz[a,h]anthracene generally contribute the most to the calculated cancer risk. This is mainly
551 due to their high toxic equivalent factor corresponding values compared to other PAHs (**Table**
552 **3**). These species along with benz[a]anthracene, chrysene, and benzo(b)fluoranthene are
553 classified by the international agency for research on cancer as group 1, 2A, or 2B (IARC 2021).
554 Several studies have reported that adults exhibited a greater cancer risk than children (Gong *et al.*
555 *al.* 2019, Sulong *et al.* 2019, Wang *et al.* 2019, Bai *et al.* 2020). According to Chang *et al.*
556 (2019), Bai *et al.* (2020), a greater cancer risk was observed for male adults due to inhalation
557 exposure while female adults were at higher risk due to ingestion and dermal contact compared
558 to inhalation. Furthermore, several studies have reported that when comparing exposure
559 pathways, higher risk values were observed for dermal contact, then ingestion, and finally
560 inhalation (Tarafdar and Sinha 2019, Iakovides *et al.* 2021, Fadel *et al.* 2022). This observation
561 shows the importance of the evaluation of the three exposure pathways rather than only working
562 on the inhalation pathway. According to Tarafdar and Sinha (2019), the most influential
563 parameter found by sensitivity analysis in the assessment of health risk is the relative skin
564 adherence factor followed by the exposure duration.

565 Anthropogenic activities in urban and industrial areas play an important role in governing
566 cancer risk of human exposure to particulate matter (Pongpiachan 2015). Several studies tried
567 to link the cancer risk values to PAHs emission sources. Chao *et al.* (2019) conducted a source
568 apportionment exercise with only PAHs and concluded that vehicular emissions produce a high
569 cancer risk contribution due to the high proportion of toxic PAHs such as benzo[a]pyrene,
570 indeno(1,2,3-c,d)pyrene, benzo(k)fluoranthene, and dibenz[a,h]anthracene. The same
571 conclusion was also presented by Chen *et al.* (2016), Song *et al.* (2019), Zhang *et al.* (2019c),

572 Mehmood *et al.* (2020), Iakovides *et al.* (2021), Fadel *et al.* (2022). Most of the latter studies
573 also underlined the additional contribution of other sources such as coal combustion from
574 industrial activities, biomass burning, and power plants. According to Ma *et al.* (2020b), the
575 incremental lifetime cancer risk was at least 4 times higher in the heating period using coal as
576 a source of heating compared to the non-heating period.

577

578 6.2.2 Phthalates

579 Phthalates are physically bound to the materials, hence and they can migrate from the matrix
580 into the environment (Xie *et al.* 2005). These compounds are generally emitted into the
581 atmosphere during plastic burning (Simoneit *et al.* 2005, Fadel *et al.* 2021). The major route of
582 exposure for most phthalates is ingestion while inhalation and dermal absorption are considered
583 minor routes (NRC 2008, Boberg *et al.* 2018, Chen *et al.* 2019). The critical age group for this
584 class of chemicals is mainly small children and infants from the mouthing of toys, and other
585 children's products manufactured from polyvinyl chloride (Babich *et al.* 2004). The United
586 States environmental protection agency and several agencies in other countries have classified
587 some of the phthalates as priority pollutants and endocrine disruptors compounds (Xie *et al.*
588 2005). They might interfere with the biosynthesis, secretion, action, or metabolism of naturally
589 occurring hormones (Kavlock *et al.* 1996, Diamanti-Kandarakis *et al.* 2009). The exposure to
590 phthalates might also affect the reproductive systems and children's intelligence (Lu *et al.*
591 2018). Additionally, Hauser *et al.* (2006) found that the DNA damage in human sperm might
592 be related to urinary levels of some phthalates. On an environmental level, dibutylphthalate,
593 bis(2-ethylhexyl)phthalate, and butyl benzyl phthalate have higher toxicity compared to other
594 phthalates to terrestrial organisms, fish, and aquatic invertebrates (USEPA 2012).

595 Other than the reference dose values (RfD) presented by the United States environmental
596 protection agency and presented in **Table 2**, the European food safety authority (EFSA) defined
597 values for tolerable daily intake of phthalates as 0.01 mg/kg for dibutylphthalate and 0.05 mg/kg
598 for bis(2-ethylhexyl)phthalate. On the other hand, the scientific committee on toxicity, eco-
599 toxicity, and the environment (CSTEE) specified that the tolerable daily intake values for the
600 exposure of infants and young children to some phthalates from toys are 37 µg/kg/day for bis(2-
601 ethylhexyl)phthalate, 200 µg/kg/day for butyl benzyl phthalate, and 100 for dibutylphthalate (Ji
602 *et al.* 2014). The daily intake, or the average daily dose, of phthalates to the reference dose
603 showed negligible non-cancer risks since the hazard index values were below the threshold limit

604 of 1 (Sampath *et al.* 2017, Zhang *et al.* 2019b, Ma *et al.* 2020a, Fadel *et al.* 2022). However, it
605 is worth noting that even at doses lower than the reference dose, phthalate exposure might be
606 linked to interrupted semen quality and reproductive hormones in the human population.
607 According to Chen *et al.* (2017) and Maffini *et al.* (2021), the values of reference doses (RfD)
608 for phthalates proposed by the United States environmental protection agency were based on
609 inadequate studies and did not take into consideration the male reproductive toxicity. However,
610 these effects might decrease when the exposure decreases. The latter idea emphasizes on the
611 importance of setting more stringent regulations on phthalates.

612 As for the cancer risk, most of the studies focused on the inhalation pathway (**Table 5**) and
613 found no significant human health risk from particulate matter-bounded phthalates exposure
614 specifically from the exposure to bis(2-ethylhexyl)phthalate (Lu *et al.* 2018, Gadi *et al.* 2019,
615 Li *et al.* 2019, Ma *et al.* 2020a). However, the assessment of the health risk from the inhalation
616 pathway only leads to an underestimation of the risk. Fadel *et al.* (2022) found that cancer risk
617 values for ingestion due to the exposure to bis(2-ethylhexyl)phthalate is at least 6 times higher
618 compared to inhalation, emphasizing on the importance of considering the different exposure
619 pathways. Additionally, several studies have reported that children were subjected to greater
620 phthalates exposure than adults (Zhang *et al.* 2014, Sampath *et al.* 2017), while no significant
621 differences were observed between adult males and females (Lu *et al.* 2018). Monte Carlo
622 simulation was applied by Li *et al.* (2019) in order to estimate the incremental lifetime cancer
623 risk from inhalation on the basis of bis(2-ethylhexyl)phthalate concentrations. They found by
624 sensitivity analysis that the phthalate concentration, the exposure frequency, and the inhalation
625 rate have great contribution on the estimation of the risk while body weight is a less significant
626 parameter. All of these findings were based on the few health risk assessment studies
627 implicating phthalates (**Fig. 2**). That is why it is important to increase phthalate studies in
628 particulate matter as well as the health risk evaluation.

629

630 6.2.3 Dioxins, furans and dioxin-like polychlorobiphenyls

631 Dioxins and furans are generally emitted by vehicular emissions and industrial processes
632 especially industries producing compounds such as chlorophenols and phenoxy herbicides,
633 chlorine bleaching of paper pulp and smelting (Cortés *et al.* 2014). Additionally, these
634 compounds are emitted from high temperature processes such as waste incineration and
635 sintering in iron and steel industries (Anderson and Fisher 2002). Dioxin-like

636 polychlorobiphenyls are not natural substances but were manufactured for use as dielectric
637 fluids, in larger-scale electrical products such as transformers and capacitors, in heat transfer
638 and hydraulic systems and in industrial oils and lubricants (WHO 2010). Several compounds
639 have toxicological effects and can have a significant dioxin-like-toxicity. These agents have the
640 ability to bind to the aryl hydrocarbon receptor or known as AhR. This protein is well known
641 for its role in mediating toxicity and regulating enzymes and other proteins. The aryl
642 hydrocarbon receptor was originally characterized as a regulator of xenobiotic metabolism. In
643 the presence of dioxin-like compounds, this protein also mediates a variety of biological
644 responses leading to hepatocellular damage, thymic involution, immune suppression, and/or
645 tumor promotion (Stevens *et al.* 2009). Other than the reference dose values proposed by the
646 United States environmental protection agency, the world health organization European centre
647 of environment and health formulated tolerable daily intake value between 1 and 4 pg WHO-
648 TEQ/kg/day. On the other hand, the United Kingdom committee on the toxicity of chemicals
649 in food, consumer products and the environment recommended the value of 2 pg WHO-
650 TEQ/kg/day (López *et al.* 2021). While the ingestion is the main pathway for the exposure to
651 dioxins and furans and dioxin-like polychlorobiphenyls, studies in the literature mainly focused
652 on the exposure by inhalation (**Table 5**). Fadel *et al.* (2022) showed that the cancer risk by
653 ingestion is 7-fold higher for adults and 100-fold higher for newborns compared to inhalation
654 and dermal contact. Considering the inhalation pathway, Barbas *et al.* (2018) and López *et al.*
655 (2021) found that the risk assessment due to the exposure of dioxins, furans and dioxin-like
656 polychlorobiphenyls pose a low cancer risk in Madrid and Valencia, two regions in Spain. On
657 the other hand, several other studies found a considerable cancer risk due to the exposure to
658 these pollutants especially in industrial areas and near waste burning activities. The health risk
659 induced by dioxins and furans was worthy of attention as their values exceed the United States
660 environmental protection agency limit in a Chinese and a Greek industrialized sites (Bi *et al.*
661 2020, Koukoulakis *et al.* 2020). Sun *et al.* (2017) evaluated the health risk near different types
662 of factories and found that cancer risk values were the highest near municipal waste incinerators
663 and the lowest near inorganic chemical factories. Yang *et al.* (2017) found that high cancer risk
664 values were observed in sites near secondary aluminum and copper smelters.

665

666

667

668 6.2.4 Major and trace elements

669 Major and trace elements constitute a major concern due to the adverse effects associated with
670 ambient exposure and their deposition (Dahmardeh Behrooz *et al.* 2021). They enter the human
671 body through inhalation, ingestion and dermal contact with potentially damaging and altering
672 the functioning of organs such as the brain, kidney, lungs and also blood (Godwill Azeh Engwa
673 2019). For instance, the exposure to high levels of arsenic might lead to the destruction of
674 vessels, gastrointestinal tissues and can affect the heart and the brain (Martin and Griswold
675 2009). Additionally, the exposure to manganese might lead to neurological disorders (O'Neal
676 and Zheng 2015). The exposure to lead is mainly related to the gastrointestinal tract and central
677 nervous system in adults and children (Martin and Griswold 2009). Also according to
678 Jaishankar *et al.* (2014), the exposure to elevated levels of mercury can damage the kidney, the
679 brain, and developing fetus. The health effects due to the exposure to cadmium are mainly
680 related to the fact that the human body cannot excrete cadmium because cadmium is re-absorbed
681 by the kidney (Godwill Azeh Engwa 2019). Chromium (VI) can cause lung and upper
682 respiratory cancers (Balali-Mood *et al.* 2021). The IARC has classified chromium (VI)
683 compounds, arsenic, cadmium, and nickel as group I carcinogenic to humans (IARC 2021).

684 It has been also reported that children are more susceptible to hazardous metal substances
685 compared to adults (Zhang *et al.* 2019a). The evaluation of the risk due to the exposure to major
686 and trace elements is generally done for the three exposure pathways. The reference dose (RfD),
687 reference concentration (RfC), inhalation unit risk (IUR), and cancer slope factors (CSF) values
688 are available for a large number of elements (Jiang *et al.* 2018, Nirmalkar *et al.* 2021, Fadel *et al.*
689 2022, Priyan R *et al.* 2022). It is worth noting that the toxicity of chromium is reported to its
690 hexavalent state. Therefore, the chromium concentration is generally divided by 7 to estimate
691 Cr(VI) concentration, given the assumed Cr(VI)/Cr(III) concentration ratio of 1 to 6 (USEPA
692 2004a, Farahmandkia *et al.* 2017, Kermani *et al.* 2018, Dahmardeh Behrooz *et al.* 2021).
693 Additionally, it is also assumed that the measured arsenic is totally inorganic (Huang *et al.*
694 2014).

695 For the non-cancer risk, several elements can be included in the evaluation such as Al, As, Ba,
696 Cd, Co, Cr, Cu, Fe, Hg, La, Mn, Ni, Pb, Sb, Sn, Sr, Tl, V and Zn due to the availability of
697 reference concentrations and reference doses values in the literature (**Table 2**). Several studies
698 have reported that Mn, As and Ni contribute the most to the non-cancer values (Zhang *et al.*
699 2019a, Hao *et al.* 2020, Sulaymon *et al.* 2020, Dahmardeh Behrooz *et al.* 2021, Duan *et al.*
700 2021, Fang *et al.* 2021). This might be mainly due to the low values of the reference doses

701 leading to high values of hazard quotient and hazard index. Studies show that the non-cancer
702 value of an element in one or/and several exposure pathways is usually below the threshold
703 limit of 1. However, when considering the total risk for all the elements, it has been shown that
704 the population near the sampling sites were at high risk of having non-cancer health effects
705 (Díaz and Rosa Dominguez 2009, Zhang *et al.* 2018, Fadel *et al.* 2022). The non-cancer risk
706 has been found higher for children compared to adults in some studies (Dahmardeh Behrooz *et*
707 *al.* 2021, Fadel *et al.* 2022).

708 As for the cancer risk, Cr (VI) and As generally show the highest proportion of the total cancer
709 risk value followed by Cd and Co (Wang *et al.* 2018, Galon-Negru *et al.* 2019, Liu *et al.* 2019,
710 Hao *et al.* 2020, Duan *et al.* 2021, Fang *et al.* 2021). These elements show high values of the
711 cancer slope factors especially for the inhalation pathway leading to high values of cancer risk
712 (**Table 2**). Consequently, when trying to attribute cancer risk values for the different emission
713 sources, the sources that emit Cr, As, Cd and Co are the ones that show the highest contributions.
714 Major sources related to significant cancer risk values obtained are mainly road traffic and
715 industrial sources, and more specifically coal combustion plants (Duan *et al.* (2021), Fang *et al.*
716 (2021), Liu *et al.* (2018), Galon-Negru *et al.* (2019), Tsai *et al.* (2020), (Chen *et al.* 2021)).
717 Sensitivity analysis using tornado plots were examined by Roy *et al.* (2019) for the ingestion
718 and the inhalation pathways. The results of this analysis showed that the dermal adherence factor
719 and the exposure duration were recognized as the predominant factors for cancer risk values.
720 Additionally, a negative correlation was found with body weight for cancer risk calculations
721 via inhalation pathway.

722

723 **7 Strengths and limitations of the health risk evaluation**

724 The main goal of a health risk assessment is to apply a transparent procedure to analyze the
725 consequences of exposures to potentially harmful agents (Glorennec *et al.* 2012). Health risk
726 assessment might aid policy makers in implementing new strategies to prevent from adverse
727 health effects related to particulate matter exposure. The method is cost-efficient, standardized,
728 and requires no health data (Edlund *et al.* 2021). Health risk assessment allows to easily assess
729 the potential consequences of a given exposure situation (Glorennec *et al.* 2012) and to point
730 out the most problematic species for risk management.

731 However, this assessment presents limitations and uncertainties. Health risk assessment
732 methods assume independence between toxic actions within and across compounds. Actually,

733 the interactions between the different contaminants on health, defined as cocktail effect
734 reflecting synergism or antagonism action is not well defined (Edlund *et al.* 2021, Fadel *et al.*
735 2022). Then, there is no available method for the calculation of health risk hazards due to
736 exposure to a combination of several air contaminants. Consequently, the total cancer and non-
737 cancer risks cannot be calculated when considering exposure to several classes of compounds
738 since.. . Additionally, these studies do not account for the variability in the toxicity of a certain
739 exposure depending on particle composition or differences in population sensitivity (Edlund *et*
740 *al.* 2021). Furthermore, uncertainties accompany risk assessment studies especially in the
741 choice of exposure parameters and reference values (Hao *et al.* 2020). Due to the lack of local
742 data for exposure parameters in a considerable number of countries, the evaluation is based on
743 the standard parameters proposed by different agencies and that might not be suitable to the
744 studied population. That is why, exposure parameters should be carefully chosen in order to
745 reflect the characterization of the population.

746

747 **8 Conclusion and future directions**

748 Health risk assessment studies estimate the health impact from exposure to pollutants and
749 chemicals that affect air quality. This review presents the published methods used for the
750 evaluation of the cancer and non-cancer risks due to the exposure to different classes of
751 compounds in atmospheric particles. The most employed method is the one developed by the
752 United States environmental protection agency (USEPA). Furthermore, several parameters can
753 be added to this method such as the bioaccessibility of the species, age sensitivity factor, etc.

754 Most of the published papers in the literature regarding the human health risk evaluation in
755 particulate matter focused on the following classes of compounds: PAHs, phthalates, dioxins,
756 furans, dioxin-like polychlorobiphenyls, and major and trace elements. For some of these
757 classes, the assessment was only based on the inhalation pathway while it is important to note
758 that ingestion and dermal pathway might highly contribute to the risk values. Among PAHs,
759 benzo[a]pyrene, indeno(1,2,3-c,d)pyrene, benzo(k)fluoranthene, and dibenz[a,h]anthracene
760 contribute the most to the cancer risk calculated. On the other hand, the evaluation of the cancer
761 risk is based on the bis(2-ethylhexyl)phthalate for phthalates, on the equivalent concentration
762 of 2,3,7,8-tetrachlorinated dibenzo-p-dioxin for dioxins, furans, and dioxin-like
763 polychlorobiphenyls, and the equivalent concentration of benzo[a]pyrene for PAHs. As for

764 elements, the most problematic species are Cr, As, Cd, and Co that show a high contribution to
765 the cancer risk in different studies.

766 Despite the limitations, the results of health risk assessment studies are of utmost importance
767 and might facilitate policy-decision making by focusing on the most problematic species. Since
768 chromium (VI) is considered as one of the species leading to high cancer risk values, efforts
769 should be made in order to analyze chromium (VI) rather than estimating the concentration of
770 chromium (VI) from the total chromium concentration. On the other hand, several attempts
771 were made in a qualitative way in order to link health risk values and the emission sources.
772 Endeavors were also done in a quantitative way to link source apportionment results applied to
773 one class of compounds, such as PAHs or elements, to the cancer and non-cancer risks.
774 However, additional efforts should be made regarding this matter by including much more
775 problematic species and emission source markers in order to better relate the health impact to
776 the different sources. Additionally, more work should be done to determine local exposure
777 parameters and local demographic data in order to reduce the uncertainty of the evaluation.
778 Efforts should be also made to have a better knowledge on the toxicity of several species in the
779 above-mentioned classes of compounds in order to add them to the global assessment.
780 Reference doses or concentrations for the different exposure pathways are still missing
781 especially for phthalates. Furthermore, since studies started adding the bioaccessibility values
782 to the calculations of the health risk, future studies should be focalized on the determination of
783 bioaccessibility values for different classes of compounds in particulate matter. Finally, future
784 toxicological studies should be focused on the evaluation of the cocktail effect between the
785 different classes of compounds. Such researches could contribute to the improvement of the
786 health risk assessment model for a better estimation of the cumulative cancer and non-cancer
787 risks, especially in population exposed to a mixture of contaminants.

788

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804

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