

This document is the Submitted Manuscript version of a Published Work that appeared in final form in Environmental Research, February 2016.

Online version:

<https://www.sciencedirect.com/science/article/abs/pii/S0013935115301596>

DOI: <https://doi.org/10.1016/j.envres.2015.11.031>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

Carcinogenicity of consumption of red and processed meat:
What about environmental contaminants?

José L. Domingo*, Martí Nadal

*Laboratory of Toxicology and Environmental Health, School of Medicine, IISPV,
Universitat Rovira i Virgili, Sant Llorenç 21, 43201 Reus, Catalonia, Spain*

*Corresponding author.

E-mail address: joseluis.domingo@urv.cat (J.L. Domingo)

29 ABSTRACT

30

31 In October 26, 2015, the International Agency for Research on Cancer (IARC)
32 issued a press release informing of the recent evaluation of the carcinogenicity of red and
33 processed meat consumption. The consumption of red meat and processed meat was
34 classified as “probably carcinogenic to humans”, and as “carcinogenic to humans”,
35 respectively. The substances responsible of this potential carcinogenicity would be
36 generated during meat processing, such as curing and smoking, or when meat is heated at
37 high temperatures (N-nitroso-compounds, polycyclic aromatic hydrocarbons and
38 heterocyclic aromatic amines). However, in its assessments, the IARC did not made any
39 reference to the role that may pose some carcinogenic environmental pollutants, which
40 are already present in raw or unprocessed meat. The potential role of a number of
41 environmental chemical contaminants (toxic trace elements, polycyclic aromatic
42 hydrocarbons, polychlorinated dibenzo-*p*-dioxins and dibenzofurans, polychlorinated
43 biphenyls, polybrominated diphenyl ethers, polychlorinated diphenyl ethers,
44 polychlorinated naphthalenes and perfluoroalkyl substances) on the carcinogenicity of
45 consumption of meat and meat products is discussed in this paper. A case-study, Catalonia
46 (Spain), is specifically analyzed, while the influence of cooking on the concentrations of
47 environmental pollutants is also reviewed. It is concluded that although certain cooking
48 processes could modify the levels of chemical contaminants in food, the influence of
49 cooking on the pollutant concentrations depends not only on the particular cooking
50 process, but even more on their original contents in each specific food item. As most of
51 these environmental pollutants are organic, cooking procedures that release or remove fat
52 from the meat should tend to reduce the total concentrations of these contaminants in the
53 cooked meat.

54

55 *Keywords:* Meat and meat products; environmental contaminants; dietary exposure;
56 cooking; carcinogenicity

57

58

59 **1. Introduction**

60

61 In October 26, 2015, the International Agency for Research on Cancer (IARC)
62 issued a press release (No. 240) on the results of the recent evaluation by this agency,
63 which is the specialized cancer agency of the World Health Organization (WHO), of the
64 carcinogenicity of red and processed meat consumption (IARC, 2015). Based on data of
65 the scientific literature, 22 experts from 10 countries classified the consumption of red
66 meat as “probably carcinogenic to humans” (Group 2A), whereas processed meat was
67 classified as “carcinogenic to humans” (Group 1). Additional information on these
68 assessments has been published in the Lancet Oncology (Bouvard et al., 2015), as an
69 advance of a monograph of the IARC on this subject, whose publication has been already
70 announced (volume 114). Bouvard et al. (2015) reported that the largest body of
71 epidemiological data concerned colorectal cancer. Although the mechanisms responsible
72 of the carcinogenicity of red and processed meat are not clearly established yet, Bouvard
73 et al. (2015) highlighted the presence of N-nitroso-compounds (NOCs), polycyclic
74 aromatic hydrocarbons (PAHs) and heterocyclic aromatic amines (HAAs), well known
75 (or suspected) carcinogenic chemicals, in meat processing such as curing and smoking
76 (NOCs, PAHs), or when meat is heated at high temperatures (HAAs). It is certainly well
77 established that processing and cooking of meats may produce these known or suspected
78 carcinogens (Alaejos et al., 2008; De Mey et al., 2015; Herrmann et al., 2015; Kim et al.,
79 2013; Larsson, 1986; Trafialek and Kolanowski, 2014). However, due to the practically
80 unavoidable presence of other carcinogenic compounds, which are already present in raw
81 or unprocessed meats, we believe that these chemicals are not the only potentially
82 carcinogenic substances in meat and meat products. These other substances are well
83 known environmental pollutants such as some heavy metals, polychlorinated dibenzo-*p*-
84 dioxins and dibenzofurans (PCDD/Fs), dioxin-like polychlorinated biphenyls (PCBs),
85 etc. We feel this is an issue clearly worthy of being taken into account in order to establish
86 the global causes of the carcinogenicity of consumption of red and processed meat.
87 Therefore, the role of a number of environmental pollutants on the potential
88 carcinogenicity of consumption of meat and meat products is discussed in this paper.

89

90 **2. Environmental pollutants in meat and meat products**

91 Meat and meat products have an important nutritional value. There is wide scientific
92 evidence that demonstrates the benefits of meat consumption in a healthy diet. Meat and
93 meat products are a major source of nutrients, being a great source of protein of high
94 biological value, as well as a great source of essential amino acids, B vitamins such as
95 vitamin B12, as well as a number of essential trace elements, with particular relevance
96 for iron (Klurfeld, 2015; McAfee et al., 2010; Murphy et al., 2011; Pereira and Vicente,
97 2013; Zanovec et al., 2010; Zhang et al., 2010). However, it is also known that certain
98 dietary habits can contribute to compromised health by being a source of exposure to
99 toxic contaminants. Specifically, for meat and meat products the health risks for the
100 consumers are mainly related to micropollutants and/or process-induced toxicants.
101 Micropollutants are generated by human activity, or may come from veterinary or plant
102 treatments, being eventually transferred to foodstuffs, including meats. In turn, process-
103 induced toxicants are formed during food processing such as heating or smoking (Engel
104 et al., 2015).

105 Many of these potential toxicants are fat soluble, and therefore, any fatty food
106 often contains higher levels of micropollutants than does vegetable matter. Consequently,
107 an issue of concern related with a frequent consumption of certain foodstuffs (including
108 of course meat and meat products) is the health risks potentially derived from exposure
109 to chemical pollutants contained in those food items. A number of recent studies have
110 shown that highly consumed foods, and with a considerable nutritional value, can be also
111 a potential source of human exposure to various environmental contaminants, whose
112 potential toxicity is well known. These pollutants include inorganic toxic elements such
113 as arsenic (As), cadmium (Cd), mercury (Hg) and lead (Pb), PAHs, pesticides,
114 polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), polychlorinated
115 biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), polychlorinated diphenyl
116 ethers (PCDEs), polychlorinated naphthalenes (PCNs), and perfluoroalkyl substances
117 (PFASs). Information on the human exposure to these inorganic and organic
118 environmental pollutants, many of them persistent organic pollutants (POPs), can be
119 found in a recent review on the presence of nutrients and chemical pollutants in fish and
120 shellfish (Domingo, 2015).

121

122 **3. Balancing health benefits and chemical risks of regular consumption of meat and** 123 **meat products. A case-study: Catalonia, Spain**

124

125 To the best of our knowledge, the most wide and complete surveillance program on
126 the trends in the concentrations of a number of environmental pollutants in food and the
127 human dietary intake of those pollutants, has been performed in our laboratory (Reus,
128 Catalonia, Spain). The surveillance program started in 2000. The first survey (BF1) was
129 performed between 2000 and 2002, when the concentrations of the following
130 contaminants were analyzed in a number of foodstuffs, belonging to various food groups:
131 As, Cd, Hg and Pb (Llobet et al., 2003a), PCDD/Fs (Llobet et al., 2003b), PCBs (Llobet
132 et al., 2003c), PBDEs (Bocio et al., 2003), PCNs (Domingo et al., 2003),
133 hexachlorobenzene (Falcó et al., 2004), PCDEs (Bocio et al., 2004) and 16 PAHs (Falcó
134 et al., 2003). In 2006-2008, we carried out a second survey, and in 2008 we initiated the
135 third and last survey of the program. The results of that case-study (Catalonia)
136 corresponding to meat and meat products are next summarized.

137

138 *3.1. Experimental design*

139

140 The food items analyzed in our first survey (BF1) were the following: fish and
141 shellfish (hake, sardine, mussel) and tinned fish (tuna, sardine); vegetables (lettuce,
142 tomato, potato, green beans, cauliflower); fresh fruits (apple, orange, pear); pulses
143 (lentils, beans); cow milk (whole, semi-skimmed) and dairy products (yogurt, cheese);
144 cereals (bread, pasta, rice); fats (margarine) and oils (olive, sunflower), and hen eggs. The
145 group of meats was made on beef (steak, hamburger), pork (loin, sausage) and lamb
146 (steak) as red meats, and chicken (breast) as white meat, while ham, hot dogs and salami
147 were selected as meat products. All the foodstuffs were randomly obtained in local
148 markets, large supermarkets and grocery stores from seven cities of Catalonia, with a
149 number of inhabitants between 150,000 and 1,800,000. To establish the daily dietary
150 intake of the analyzed pollutants by the population of Catalonia, we multiplied the
151 concentration of the specific contaminant found in each specific food item by the
152 estimated daily consumption of the respective food group. The total dietary intake of each
153 pollutant was then calculated by summing each product over all the food groups. During
154 2006–2008, the second survey (BF2) of the surveillance program was performed. The
155 experimental design of that survey was basically the same than the previous one (BF1),
156 but the number of cities in which food samples were purchased was increased to 12, and
157 a new food group, bakery products, was also included. Finally, the number of fish and
158 shellfish species analyzed was increased from 3 to 14. The last survey (BF3) of the

159 surveillance program started in 2008, being the food items acquired in the same 12 cities
160 of the previous survey (BF2), and divided into the same 12 food groups. In the three
161 surveys of the program, the concentrations of the pollutants in all foodstuffs were
162 analyzed in *composite* samples, which were made up by a minimum of 8 and a maximum
163 of 24 individual samples of each food item. Only edible parts of the foodstuffs were
164 included in the composites. Usually, 2-3 composite samples were prepared for the
165 analysis of each environmental contaminant. For calculations, when the concentration of
166 one of the pollutants was under the limit of detection (LOD), we generally assumed that
167 the value was equal to one-half of the LOD (ND = 1/2 LOD). We next summarize the
168 concentrations of the various environmental pollutants in meat and meat products. Data
169 are grouped according to the chemical characteristics of the environmental contaminants.

170

171 3.2. *Trace elements*

172

173 In the BF1, BF2 and BF3 surveys, among the food groups (11 or 12) in which the
174 foodstuffs were respectively classified, all meat and meat products were taken together
175 as belonging to an only group. For BF1, the concentrations of As, Cd, Hg and Pb were:
176 0.020, 0.005, 0.0015 and 0.0025 $\mu\text{g/g}$ of fresh weight, respectively, while in the BF2 the
177 average concentrations were <0.100 , 0.006, <0.100 and 0.043 $\mu\text{g/g}$ for these same
178 elements. The highest levels of Cd and Pb (the only detected elements) were found in the
179 samples of pork sausage (0.044 and 0.090 $\mu\text{g/g}$, respectively). Finally, in the BF3 the
180 mean concentrations of As, Cd, Hg and Pb in the composite samples of meat and meat
181 products were respectively: 0.013, 0.007, 0.0011 and 0.0072 $\mu\text{g/g}$, with the highest level
182 corresponding to Pb in cured ham (0.172 $\mu\text{g/g}$ of wet weight). For a standard male adult
183 (70-kg, body weight), the exposure to these elements through the diet, with estimated
184 consumptions of meat and meat products of 185 g/day (BF1), 172 g/day (BF2) and 172
185 g/day (BF3), was 4.44, 0.00 and 0.00 $\mu\text{g/day}$ for As; 1.11, 0.00 and 0.80 $\mu\text{g/day}$ for Cd;
186 2.22, 0.00 and 1.76 $\mu\text{g/day}$ for Hg; and 4.44, 7.16 and 10.21 $\mu\text{g/day}$ for Pb (Llobet et al.,
187 2003a; Marti-Cid et al., 2008a; Martorell et al., 2011). The calculations of the dietary
188 exposure to these trace elements in the BF2 and BF3 surveys were carried out assuming
189 ND = 0.

190

191 3.3. *Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs)*

192 In the BF1 survey, the concentrations of PCDD/Fs ranged between 49.82 pg WHO-
193 TEQ/kg of fresh weight for lamb, and 71.20 pg WHO-TEQ/kg of fresh weight for pork
194 and pork products, with an estimated daily intake of 12.09 pg WHO-TEQ from all meat
195 and meat products. This means a percentage of 13% of the total daily dietary intake of
196 PCDD/Fs by a male adult living in Catalonia (Llobet et al., 2003b). In the BF2, the mean
197 concentration of PCDD/Fs in the composite samples of meat and meat products was 17.0
198 pg WHO-TEQ/kg fresh weight, with the lowest and highest values found in veal steak
199 (0.008) and hamburger (0.037), respectively (Llobet et al., 2008). The estimated dietary
200 intake of meat and meats products for an adult male was 2.62 pg WHO-TEQ/day,
201 meaning 10.2% of the total daily dietary intake of PCDD/Fs. In the BF3, the levels of
202 PCDD/Fs in meat and meat products ranged between 5 and 24 ng WHO-TEQ/kg of fresh
203 weight, for the samples of loin of pork and those of hot dogs, with 6 ng WHO-TEQ/kg
204 for veal steak and chicken breast, and 22 ng WHO-TEQ/kg for salami. The mean
205 concentrations of PCDD/Fs in meat and meat products was 11 ng WHO-TEQ/kg, which
206 means an estimated dietary intake of 1.27 pg WHO-TEQ/day (Perelló et al., 2012), with
207 a 10.0% of the total daily dietary intake of PCDD/Fs.

208

209 3.4. Polychlorinated biphenyls (PCBs)

210

211 The concentrations of 11 PCB congeners (IUPAC No. 28, 52, 77, 101, 105, 118,
212 126, 138, 153, 169 and 180) were determined in our BF1 survey. The level of all PCBs
213 in the group of meat and meat products was 373.55 ng/kg of fresh weight, which was
214 equivalent to 47.85 pg WHO-TEQ/kg, when calculated on the basis of the five congeners
215 (IUPAC No. 77, 105, 118, 126 and 169) for which, at that time, values of WHO-TEFs
216 were established (Llobet et al., 2003c). The highest concentration of the sum of all PCBs
217 (pg WHO-TEQ/kg) was detected in the composite samples of pork and pork products
218 (68.17), while the lowest level of that sum was found in the chicken samples (17.65). The
219 estimated intake of PCBs for an adult (20-65 years old) male was 8.85 pg WHO-TEQ/day
220 (5.9% of the total daily dietary intake of PCBs). In the BF2 survey, the concentrations of
221 18 PCB congeners were analyzed. They included the previous 11 congeners, together
222 with PCBs 81, 114, 123, 156, 157, 167 and 189, being the congeners No. 77, 81, 105,
223 114, 118, 123, 126, 156, 157, 167, 169 and 189 classified as dioxin-like PCBs (DL-
224 PCBs). The concentration of all PCBs in the group of meat and meat products was 127.3
225 ng/kg of fresh weight, which was equivalent to 19.0 pg WHO-TEQ/kg (Llobet et al.,

226 2008). The highest concentration of the sum of the 18 PCBs (pg WHO-TEQ/kg) was
227 detected in beef hamburger (67 pg WHO-TEQ/kg), while the lowest levels were found in
228 the veal steak samples (6 pg WHO-TEQ/kg) and those of lamb (7 pg WHO-TEQ/kg) and
229 chicken (7 pg WHO-TEQ/kg). The estimated intake of PCBs for an adult male was 2.24
230 pg WHO-TEQ/day (4.3% of the total daily dietary intake of DL-PCBs).

231 The levels of the same 18 PCB congeners were again determined in the BF3
232 survey. The concentration of all PCBs in the group of meat and meat products was 109.5
233 ng/kg of fresh weight, which was equivalent to 6.0 pg WHO-TEQ/kg (Perelló et al.,
234 2012). The highest concentration of the sum of the 18 PCBs (pg WHO-TEQ/kg)
235 corresponded to the samples of hot dog and salami (both with 11 pg WHO-TEQ/kg),
236 being the lowest levels found in the samples of veal steak samples, loin of pork, chicken
237 breast, and cured and boiled ham (all with 4 pg WHO-TEQ/kg). The estimated intake of
238 DL-PCBs for an adult male living in Catalonia was 0.84 pg WHO-TEQ/day (3.2% of the
239 total daily dietary intake of DL-PCBs).

240

241 3.5. Polybrominated diphenyl ethers (PBDEs)

242

243 In our initial survey (BF1), the mean concentrations of PBDEs (sum tetra- to
244 octaBDEs) were determined (Bocio et al., 2003). In the 15 composite samples of meat
245 and meat products that were analyzed, the PBDE concentrations (ng/kg fresh weight)
246 ranged between 13.5 and 24.9 for hexaBDEs and pentaBDEs, respectively, being the sum
247 of all 5 groups of homologues of PBDEs, 109.2 ng/kg fresh weight. The lowest and
248 highest PBDE levels corresponded to chicken (10 ng/kg fresh weight) and pork and pork
249 products (172 ng/kg fresh weight), respectively. For the adult population of Catalonia,
250 the estimated dietary intake of PBDEs from the group of meat and meat products was
251 20.2 ng/day, which means a 20.8% of the total daily dietary intake of PBDEs. In addition
252 to the sum tetra- to octaBDEs, the following six tetra-through heptabrominated congeners
253 were also individually analyzed: PBDEs 47, 99, 100, 153, 154 and 183. The \sum PBDEs
254 (tetra to octa) for the samples of meat and meat products was 49.9 ng/kg of fresh weight,
255 with the lowest and highest concentrations found in hot dogs (87.6 ng/kg of fresh weight)
256 and pork sausage (64.7 ng/kg of fresh weight), and in veal steak (23.4 ng/kg of fresh
257 weight) and chicken breast (29.6 ng/kg of fresh weight), respectively (Domingo et al.,
258 2008). With respect to the individual congeners, the highest values corresponded to the
259 salami samples: 29.0 and 22.0 ng/kg for BDE-99 and BDE-47, respectively. High values

260 of these two congeners were also found in the samples of hot dogs (16.0 and 21.0 ng/kg)
261 and pork sausages (12.5 and 14.0 ng/kg). In the samples of all analyzed meat and meat
262 products, the concentration of the congeners ranged between 1.6 (BDE-100 and BDE-
263 154) and 9.0 ng/kg (BDE-99). The estimated dietary intake of PBDEs from the
264 consumption of meat and meat products by a standard adult man living in Catalonia was
265 6.8 ng/day. PBDEs were not analyzed in the BF3 survey (Domingo, 2012a).

266

267 3.6. *Hexachlorobenzene (HCB)*

268

269 In the BF1 survey, the concentrations of HCB in composite samples of meat and
270 meat products purchased in Catalonia, ranged between 0.353 (pork sausages) and 0.319
271 ng/g fresh weight (hot dogs) in the upper part of the range, and 0.007 (breast chicken) and
272 0.023 ng/g fresh weight (boiled ham) in the lower part of the range. The mean
273 concentration was 0.173 ng/g fresh weight (Falcó et al., 2004). The estimated dietary
274 intake of HCB derived from the consumption of meat and meat products was 31.98 ng/day
275 for an adult male (19% of the total daily dietary intake of HCB), being only surpassed by
276 the group of dairy products (55%), and close to the group of fish and other seafood (14%).
277 In the BF2 survey, the HCB levels ranged between 0.305 (salami) and 0.210 ng/g fresh
278 weight (hot dogs) in the upper part of the range, and 0.012 (loin of pork) and 0.027-0.029
279 ng/g fresh weight (boiled ham and breast chicken) in the lower part of the range. The
280 mean concentration was 0.112 ng/g fresh weight (Martí-Cid et al., 2008b). The estimated
281 dietary intake of HCB derived from the consumption of meat and meat products was
282 12.83 ng/day for an adult male (18% of the total). In our last survey (BF3), the HCB levels
283 ranged between 0.265 (hot dogs) and 0.140 ng/g fresh weight in the upper part of the
284 range, and 0.015 (boiled ham) and 0.005 ng/g fresh weight (breast chicken) in the lower
285 part of the range. The mean concentration was 0.0083 ng/g fresh weight (Perelló et al.,
286 2012). The estimated dietary intake of HCB derived from the consumption of meat and
287 meat products was 9.97 ng/day for an adult male (26% of the total), being this food group
288 that showing the greatest contribution (followed by the dairy products) to the total daily
289 dietary intake of HCB.

290

291 3.7. *Polychlorinated naphthalenes (PCNs)*

292

293 In the BF1 survey, the concentrations of tetra-, penta-, hexa-, and hepta-CN_s, those
294 of octachloronaphthalene, and the mean sum of PCN_s were determined in composite
295 samples of meat and meat products (Domingo et al, 2003). The mean concentration of the
296 Σ PCN_s (tetra-octa) was 18 pg/g fresh weight, with a range between 0.3 (octaCN) and 10
297 pg/g fresh weight (Σ tetraCN_s). For an adult male, the dietary exposure to PCN_s through
298 the consumption of meat and meat products was 3.25 ng/day, meaning 7% of the total, a
299 percentage similar to that of fish and shellfish and dairy products, and notably lower than
300 that of cereals. In the BF2 survey (Martí-Cid et al., 2008c), the mean concentration of the
301 Σ PCN_s (tetra-octa) was 2.8 pg/g fresh weight with a range between 0.2 (Σ hexaCN_s,
302 Σ heptaCN_s and octaCN) and 1.7 Σ tetraCN_s. The highest levels of the Σ PCN_s were
303 detected in salami (5.8 pg/g fresh weight) and hot dog (3.8 pg/g fresh weight), while the
304 lowest concentrations were found in chicken (1.7 pg/g fresh weight). For an adult male,
305 the dietary exposure to PCN_s through the consumption of meat and meat products was
306 0.42 ng/day, meaning 5.8% of the total, a percentage notably lower than those of the food
307 groups showing the highest contribution to the total intake of PCN_s: fish and seafood
308 (26.9%) and cereals (26.5%). No data regarding the BF3 survey are currently available.

309

310 3.8. Polychlorinated diphenyl ethers (PCDEs)

311

312 In our first survey (BF1), the concentrations of tetra-, penta, hexa-, hepta- and
313 octaCDEs, and the mean sum concentration of PCDEs were determined in composite
314 samples of meat and meat products (Bocio et al, 2003). The concentrations of PCDEs
315 were, for all homologues (tetra- to octaCDE), under the respective detection limits. In
316 fact, PCDEs were only detected in samples of fish and shellfish (fresh and tinned).
317 Therefore, the daily dietary intake of PCDEs could be estimated only very roughly. For
318 it, we assigned to the non-detected (ND) concentrations of PCDEs in the samples of meat
319 and meat products, values of ND = 1/2 LOD. The dietary exposure to PCN_s through the
320 consumption of meat and meat products was estimated 0.3 ng/day vs. a total intake of 45
321 ng/day, for which fish and other seafood contributed with 38 ng/day. In the BF2 survey
322 (Martí-Cid et al., 2008c), the mean concentration of PCDEs could be only detected in the
323 fish and other seafood samples. Using the same criteria than that used in the BF1, for an
324 adult male, the dietary exposure to PCDEs through the consumption of meat and meat
325 products was 0.18 ng/day vs. a total intake of 51.68 ng/day, from which 50.24 ng/day
326 came from the consumption of fish and shellfish. As for other environmental pollutants

327 measured in the BF1 and BF2 surveys, no data regarding the levels of meat and meat
328 products in BF3 survey are available.

329

330 3.9. *Polycyclic aromatic hydrocarbons (PAHs)*

331

332 In our BF1 survey, we determined in 11 food groups the concentrations of 16 PAHs
333 (naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene,
334 fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene,
335 benzo[k]fluoranthene, benzo[a]pyrene, dibenzo[a,h]anthracene, benzo[g,h,i]perylene,
336 and indeno[1,2,3-c,d]pyrene) (Falcó et al., 2003). In meat and meat products, the
337 concentrations of the analyzed PAHs ranged between 0.038 and 0.042 $\mu\text{g}/\text{kg}$ fresh weight
338 for dibenzo[a,h]anthracene and indeno[1,2,3-c,d]pyrene, respectively, and 4.638 and
339 2.437 $\mu\text{g}/\text{kg}$ fresh weight for phenanthrene and naphthalene, respectively. The total PAH
340 concentration in that food group was 13.4 $\mu\text{g}/\text{kg}$ fresh weight, being only overwhelmed
341 by the group of cereals (14.5 $\mu\text{g}/\text{kg}$ fresh weight). Regarding the intake of PAHs through
342 the consumption of meat and meat products by an adult male, amounts of 0.018, 0.331
343 and 2.48 $\mu\text{g}/\text{day}$ were estimated for benzo[a]pyrene, the sum of the 7 probable human
344 carcinogens according to the US EPA, and the sum of the 16 analyzed PAHs. Among the
345 11 food groups, meat and meat products ranked the third one for the contribution of
346 benzo[a]pyrene, and the second for both the sum of the 7 probable human carcinogens
347 and the sum of the 16 PAHs. In all cases the first contribution corresponded to the group
348 of cereals.

349 The concentrations of the same 16 PAHs were again determined in our BF2 survey
350 (Martí-Cid et al., 2008d). In that survey, and according to the food groups, the highest
351 levels of total PAHs were detected in meat and meat products, 25.56 $\mu\text{g}/\text{kg}$ fresh weight,
352 being cereals (20.44 $\mu\text{g}/\text{kg}$) in second place. The highest contribution to total PAHs was
353 found in the samples of salami (189.28 $\mu\text{g}/\text{kg}$), followed at a great distance by hot dogs
354 (13.57 $\mu\text{g}/\text{kg}$). In contrast, the samples of loin of pork (1.12 $\mu\text{g}/\text{kg}$) and those of boiled
355 ham (1.44 $\mu\text{g}/\text{kg}$) were the lowest contributors. The concentrations of the individual
356 PAHs ranged between 0.09 $\mu\text{g}/\text{kg}$ fresh weight for indeno[1,2,3-c,d]pyrene and
357 benzo[g,h,i]perylene (both), and 9.42 $\mu\text{g}/\text{kg}$ fresh weight for phenanthrene. With respect
358 to the exposure to PAHs through the consumption of meat and meat products by an adult
359 male, values of 0.026, 0.285 and 3.282 $\mu\text{g}/\text{day}$ were estimated for benzo[a]pyrene, the
360 sum of the 7 probable human carcinogens according to the US EPA, and the sum of the

361 16 PAHs. Among the 12 food groups included in that survey, meat and meat products
362 ranked the first one for the contribution of benzo[a]pyrene and the sum of the 7 probable
363 human carcinogens, and the second one for the sum of the 16 PAHs, with cereals being
364 the first one.

365 In our BF3 survey, the highest levels of total PAHs were again detected in meat
366 and meat products, 38.99 $\mu\text{g}/\text{kg}$ fresh weight, followed by the group of oils and fats (18.75
367 $\mu\text{g}/\text{kg}$) (Martorell et al., 2010). The highest contribution to total PAHs was also found in
368 the samples of salami (364.91 $\mu\text{g}/\text{kg}$), followed again at a great distance by the samples
369 of hot dogs (13.86 $\mu\text{g}/\text{kg}$). In contrast, the samples of loin of pork (1.12 $\mu\text{g}/\text{kg}$) and those
370 of boiled ham (1.44 $\mu\text{g}/\text{kg}$) were the lowest contributors. The concentrations of the
371 individual PAHs for the mean samples of meat and meat products ranged between 0.03
372 $\mu\text{g}/\text{kg}$ fresh weight, for dibenzo[a,h]anthracene, and 9.42 $\mu\text{g}/\text{kg}$ fresh weight, for
373 phenanthrene. The exposure to PAHs through the consumption of meat and meat products
374 by an adult male was 0.019, 0.209 and 4.75 $\mu\text{g}/\text{day}$, estimated for benzo[a]pyrene, the
375 sum of the 7 probable human carcinogens (according to the US EPA), and the sum of the
376 16 PAHs, respectively. The group of meat and meat products was again in the first place
377 for the contribution of benzo[a]pyrene, the sum of the 7 probable human carcinogens, as
378 well as the sum of the 16 PAHs (with cereals in the second place).

379

380 *3.10. Perfluoroalkyl substances (PFASs)*

381

382 Recently, the available scientific information on the levels of PFASs in food, and
383 about the health risks of the dietary exposure to these compounds, was extensively
384 reviewed (Domingo, 2012b). In our laboratory (Ericson et al., 2008), we determined the
385 levels of 11 PFASs in composite samples constituted of the most frequently consumed
386 foodstuffs by the population of Tarragona County (Catalonia, Spain). We also estimated
387 the dietary intake of those PFASs by that population. In the group of meat and meats
388 products, the following samples were included: veal (steak, hamburger), pork (sausage,
389 hot dogs, steak, hamburger, ham), chicken (breast, thighs, sausages) and lamb (steak).
390 Perfluorooctane sulfonate (PFOS) was the only PFAS that could be detected in these
391 samples, with mean values of 0.045, 0.021, 0.028, and 0.040 ng/g fresh weight for pork,
392 chicken, veal and lamb, respectively. For an adult male living in Catalonia, the dietary
393 intake of PFOS was 1.07 $\text{ng}/\text{kg}/\text{day}$, being fish and shellfish the group with the highest

394 contribution to the total dietary intake, followed by the groups of dairy products, and the
395 group of meat and meat products.

396

397 **4. Other recent data on human exposure to chemical contaminants through** 398 **consumption of meat and meat products**

399

400 In 1996-1998, as a part of a surveillance program on the health risks for the
401 population living in the neighborhood of the only hazardous waste incinerator (HWI) in
402 Spain, our laboratory analyzed (baseline or background study) the concentrations of
403 PCDD/Fs in a number of the most consumed foods by the population living in the zone
404 (Tarragona County, Catalonia) under potential direct influence of the emissions of
405 pollutants from the stack. The daily intake of PCDD/Fs through the diet by that population
406 was also estimated (Domingo et al., 1999). Composite samples of the following meats
407 were analyzed: beef (hamburger, steak, liver), pork (sausage, hot dogs, steak, liver,
408 hamburger), chicken (liver, breast, sausage) and lamb (steak). The intake of PCDD/Fs
409 through meat consumption was estimated to be 20.76 pg I-TEQ, which was equivalent to
410 9.88% of the total daily dietary intake of PCDD/Fs. The highest PCDD/F concentrations
411 in meats were found in beef and lamb samples. The dietary intake of PCDD/Fs by that
412 population was again assessed in 2002 (Bocio and Domingo, 2005), 2006 (Martí-Cid et
413 al., 2008e) and 2012 (Domingo et al., 2012). In those studies, the kind of analyzed meats
414 was basically the same, although composite samples of some meat products (salami and
415 boiled ham) were also included (Domingo et al., 2012). The intakes of PCDD/Fs through
416 the consumption of meat and meat products were 5.4, 2.26 and 3.18 pg WHO-TEQ/day,
417 for the 2002, 2006 and 2012 studies, respectively, which mean contributions to the total
418 dietary intake of PCDD/Fs of 7.8%, 8.0% and 9.6% (Bocio and Domingo, 2005; Domingo
419 et al., 2012; Martí-Cid et al., 2008e). In general terms, in these 3 studies, the highest
420 values of PCDD/Fs in meats were detected in lamb (0.040 ng WHO-TEQ/kg fresh weight,
421 2002 study) and beef (0.030 ng WHO-TEQ/kg fresh weight, in the 2002 and 2012
422 studies), being the lowest levels found in chicken (0.011 and 0.008 ng WHO-TEQ/kg
423 fresh weight, in the 2008 and 2012 studies, respectively).

424 The levels in foods of the toxic metals As, Cd, Hg, Pb, as well as the trace elements
425 beryllium (Be), chromium (Cr), manganese (Mn), nickel (Ni), tin (Sn), thallium (Tl), and
426 vanadium (V), were also determined during the same surveillance program, being the
427 exposure to these elements by the population living near the HWI also estimated. Some

428 of these elements are also potentially carcinogenic in humans. A baseline (background)
429 study was performed in 1996-1998 (Llobet et al., 1998), followed by surveys carried out
430 in 2003 (Bocio et al., 2005), 2006 (Martí-Cid et al., 2009) and 2013 (Perelló et al., 2015).
431 Analyzed meats included composite samples of veal, lamb, pork and chicken. The results
432 varied notably depending on the year of sampling, the specific samples, as well as the
433 respective metal. All that information is summarized in Perelló et al. (2015).

434 The levels of contamination with POPs and its relationship with dietary habits have
435 been also studied in the population from the Canary Islands, another Spanish region.
436 Boada et al. (2014) assessed the role of the dietary intake of animal products as a
437 probability factor for increased serum POPs. Regarding to meat, it was found that while
438 poultry and rabbit consumption increased the probability of having high levels of non-
439 DDT-derivative pesticides, sausage, lard and bacon consumption decreased the
440 probability of having high levels of these pesticides. In turn, poultry and rabbit
441 consumption increased also the probability of having detectable levels of markers PCBs,
442 while sausage consumption increased the probability of having detectable levels of
443 dioxin-like PCBs (DL-PCBs). In another recent study of the same research group, the
444 concentrations of PAHs, organochlorine pesticides, and dioxin-like PCBs were
445 determined in 100 samples of meat and charcuterie (Rodríguez-Hernandez et al., 2015a).
446 The results indicated that the consumption of beef, pork, lamb, chicken, and "chorizo",
447 represents a relevant carcinogenic risk for consumers (carcinogenic risk quotient between
448 1.33 and 13.98). In order to reduce carcinogenic risk, it was suggested not to surpassing
449 the number of 5 servings of beef/pork/chicken (considered together) (Rodríguez-
450 Hernandez et al., 2015a). These authors also showed that the consumption of organic
451 meat does not diminish the carcinogenic potential associated with the intake of POPs.
452 Seventy-six samples of meat (beef, chicken, and lamb) of two modes of production
453 (organic and conventional) were acquired and the levels of 33 carcinogenic POPs were
454 quantified. The results showed that there was not any sample completely free of
455 carcinogenic contaminants, being minimal the differences between organically and
456 conventionally produced meats. The pattern of meat consumption exceeded the maximum
457 limits, being, according to the levels of contaminants associated with a relevant
458 carcinogenic risk. The consumption of organically produced meat did not reduce this
459 carcinogenic risk. It was even higher in the case of lamb consumption (Rodríguez-
460 Hernandez et al., 2015b).

461 Recently, Kim (2012) reviewed the origins, occurrence, transfer through the food
462 chain, and the significance for human health of a number of contaminants and residues
463 (PCDD/Fs, PCBs, PBDEs, PFOS and perfluorooctanoic acid (PFOA), pesticides, toxic
464 metals, and veterinary drugs) in red meat. In agreement with the results of our case-study
465 (Catalonia, Spain), it was concluded that prevention and reduction of the release of
466 chemical contaminants into the environment were important steps to reduce the levels of
467 these pollutants in red meats, and consequently, to reduce the health risks for the
468 consumers (Kim, 2012).

469 In recent years, we have extensively reviewed the available scientific literature
470 concerning human daily dietary exposure to the following environmental contaminants:
471 PCDD/Fs (Bocio and Domingo, 2005; Domingo and Bocio, 2007), PCBs (Domingo, and
472 Bocio, 2007), PBDEs (Domingo, 2004a, 2012a; Domingo et al., 2008), PCNs (Domingo,
473 2004b), PCDEs (Domingo, 2006), PFASs (Domingo, 2012b) and PAHs (Domingo and
474 Nadal, 2015). Meat and meat products were in all the reviews. Taking together the
475 information summarized in these papers, as well the experimental data obtained in our
476 case-study (Catalonia, Spain), in general terms, it can be stated that this food group is not
477 the main responsible of the daily dietary exposure to carcinogenic, or probably
478 carcinogenic, environmental pollutants such as As, Cd and Pb, PCDD/Fs (2,3,7,8-TCDD,
479 which is classified into the Group 1), various DL-PCBs, benzo[a]pyrene and other PAHs,
480 or hexachlorobenzene (probable human carcinogen group B2, US EPA). On the other
481 hand, it has not been established yet whether PCNs, PCDEs, PBDEs, or PFAAs such as
482 PFOS, can cause cancer in humans. Anyhow, the group of meat and meat products does
483 not occupy for most of these contaminants, the first place among the different food groups
484 with respect to its contribution to the dietary exposure to these environmental pollutants.
485 Fish and shellfish is usually in the first position (Domingo, 2015).

486

487 **5. Influence of cooking on the levels of environmental pollutants in meat and meat** 488 **products**

489

490 The potential toxicants in foods, including meat and meat products, are derived
491 from natural or industrial sources. In addition to natural toxins and toxins present in
492 animals for human consumption, another group of potentially toxic compounds in food
493 are environmental pollutants, while a third group are those organic chemicals produced
494 when food is cooked and/or processed, and include mainly PAHs, HAAs and NOCs

495 (Engel et al., 2015; Peshin et al., 2002). In 2008, we initiated in our laboratory a study
496 aimed at evaluating the effects of traditional cooking processes in Catalonia (fried, grilled,
497 roast and boiled) on the concentrations of various inorganic and organic environmental
498 pollutants in a number of foods. Veal steak, loin of pork, breast and thigh of chicken, and
499 steak and rib of lamb, were selected as meat samples (Perelló et al., 2008, 2009, 2010).
500 The levels of As, Cd, Hg, Pb, PCDD/Fs, PCBs, PCDEs, PBDEs, 16 PAHs and HCB were
501 determined in raw and cooked samples. In general terms, the cooking process influenced
502 only very slightly the content of toxic metals in food, while cooking reduced PCDD/F
503 levels in veal and pork samples. (Perelló et al., 2008). In contrast to PCDD/Fs, all cooking
504 processes (excepting grilled chicken) enhanced PCB concentrations and those of the
505 Σ PCDEs (excepting roasting for chicken) (Perelló et al., 2010). We also determined the
506 levels of 11 PFASs in composite samples of veal steak (raw, grilled, and fried), pork loin
507 (raw, grilled, and fried), chicken breast (raw, grilled, and fried), black pudding
508 (uncooked), liver lamb (raw), pate of pork liver, foie gras of duck, hot dogs and chicken
509 nuggets (fried). PFOS was the compound most frequently detected, being found in grilled
510 pork, grilled and fried chicken, and lamb liver, while perfluorohexanoic acid (PFHxA)
511 was detected in samples of raw veal, chicken nuggets and hot dogs. The results were not
512 sufficiently clear to establish if cooking with non-stick cookware could contribute to a
513 higher human exposure to PFASs (Ericson-Jogsten et al., 2009).

514 According to these results, as well as other data from the scientific literature
515 recently reviewed by Domingo (2011), it was concluded that although certain cooking
516 processes could reduce (or increase) the levels of chemical contaminants in food, it seems
517 that the influence of cooking on the concentration of these environmental pollutants
518 depends not only on the particular cooking process, but even more on the contents of the
519 contaminants in specific food item before being cooked. In general terms, cooking
520 procedures that release or remove fat from the product should tend to reduce the total
521 concentrations of the organic contaminants in the cooked food. This might be of special
522 relevance in the current context on the carcinogenicity of consumption of meat and meat
523 products, at least, with respect to the most widespread environmental pollutants.

524 The influence of cooking on the presence of NOCs and HAAs in meats was not
525 included in the present review. However, because of the potential carcinogenicity of these
526 undesirable compounds when consuming cooked meats, we would like to highlight some
527 recent reviews on that important issue (Kim et al., 2013; Abid et al., 2014; Behsnilian et

528 al., 2014; Trafialek and Kolanowski, 2014). In turn, the human dietary exposure to PAHs
529 (including meat and meat products) was recently reviewed by Domingo and Nadal (2015).

530

531 **6. Conclusions**

532

533 Because of the great socioeconomic consequences of the recent decision of the
534 IARC (2015) on the carcinogenicity of consumption of red and processed meat, the main
535 goal of the present article was adding information on that relevant issue. The press release
536 of the IARC has raised a considerable concern, not only in the consumers, but also in the
537 meat and related industries, as well as in multiple businesses related to the consumption
538 of meat and meat products. Logically, we quite agree with the IARC on its classification
539 of consumption of red meat and processed meat in the Groups 2A and 1, respectively, as
540 this classification is based on an important number of scientific studies supporting the
541 statements (Bouvard et al., 2015). However, and according to the information reviewed
542 in our current article, we would like to add some conclusions that we feel may be useful
543 for establishing the specific risks for the consumers.

544 The IARC have noted that meat processing such as curing and smoking, could result
545 in formation of the carcinogenic chemicals NOCs and PAHs, while cooking could also
546 produce HAAs and PAHs. However, and based on the information contained in the report
547 by Bouvard et al. (2015), the IARC did not consider the influence of environmental
548 pollutants on the carcinogenicity of consumption of meats, which may be already found
549 in the own raw/unprocessed meat. This would be the case of, at least, As, Cd, Pb,
550 PCDD/Fs, DL-PCBs, and some other PAHs. The results of our studies on that subject,
551 together with those of other researchers over the world, suggest that although certain
552 cooking processes could modify (either reducing or increasing) the levels of chemical
553 contaminants in food, it seems that the influence of cooking on the concentrations of these
554 contaminants depends not only on the particular cooking process, but even more on their
555 original contents in each specific food item. As most of these environmental pollutants
556 are organic, cooking procedures that release or remove fat from the meat should tend to
557 reduce the total concentrations of these contaminants in the cooked meat (Domingo,
558 2011; Perelló et al., 2009, 2010). Anyhow, we have noted that, in general terms, chicken
559 contains less organic contaminants than red meats. Once again, and as with most foods,
560 to reduce the daily intake of fats through the consumption of meat and meat products will
561 be useful for a healthy diet. This reduction may prevent cardiovascular risks and also a

562 part of the carcinogenic risks, at least those derived from dietary exposure to certain
563 carcinogenic environmental contaminants. On the other hand, in order to calm down the
564 consumers, we miss more information on the generation of NOCs and HAAs in the
565 different processes in which meats are involved and their prevention. Some tool that
566 allows balancing the health benefits and risks of a regular consumption of meat and meat
567 products could be very useful for the general population. In relation to this, an interesting
568 precedent is related with the regular fish and other seafood consumption. Thus, it was
569 concluded that although a regular consumption of most fish and shellfish species should
570 not mean adverse health effects for the consumers, the specific fish and shellfish species
571 consumed, the frequency of consumption, as well as the meal size, are essential issues for
572 adequately balancing the health benefits and risks of regular fish consumption (Domingo,
573 2015). This could be also valid for meat and meat products.

574

575 **References**

576

- 577 Abid Z, Cross AJ, Sinha R. Meat, dairy, and cancer. *Am J Clin Nutr.* 2014, 100 Suppl 1:386S-
578 393S.
- 579 Alaejos MS, González V, Afonso AM. Exposure to heterocyclic aromatic amines from the
580 consumption of cooked red meat and its effect on human cancer risk: a review. *Food Addit*
581 *Contam Part A Chem Anal Control Expo Risk Assess.* 2008, 25, 2-24.
- 582 Behnlian D, Butz P, Greiner R, Lautenschlaeger R. Process-induced undesirable compounds:
583 chances of non-thermal approaches. *Meat Sci.* 2014, 98, 392-403.
- 584 Boada LD, Sangil M, Alvarez-León EE, Hernández-Rodríguez G, Henríquez-Hernández LA,
585 Camacho M, Zumbado M, Serra-Majem L, Luzardo OP. Consumption of foods of animal origin
586 as determinant of contamination by organochlorine pesticides and polychlorobiphenyls: results
587 from a population-based study in Spain. *Chemosphere* 2014, 114, 121-128.
- 588 Bocio A, Llobet JM, Domingo JL, Corbella J, Teixidó A, Casas C. Polybrominated diphenyl
589 ethers (PBDEs) in foodstuffs: human exposure through the diet. *J Agric Food Chem.* 2003, 51,
590 3191-3195.
- 591 Bocio A, Llobet JM, Domingo JL. Human exposure to polychlorinated diphenyl ethers through
592 the diet in Catalonia, Spain. *J Agric Food Chem.* 2004, 52, 1769-1772.
- 593 Bocio A, Domingo JL. Daily intake of polychlorinated dibenzo-p-dioxins/polychlorinated
594 dibenzofurans (PCDD/PCDFs) in foodstuffs consumed in Tarragona, Spain: a review of recent

595 studies (2001-2003) on human PCDD/PCDF exposure through the diet. *Environ Res.* 2005, 97,
596 1-9.

597 Bocio A, Nadal M, Domingo JL. Human exposure to metals through the diet in Tarragona, Spain:
598 temporal trend. *Biol Trace Elem Res.* 2005, 104, 193-201.

599 Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi FE, Benbrahim-Tallaa L, Guha N,
600 Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group.
601 Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 2015 (in press).

602 De Mey E, De Maere H, Paelinck H, Fraeye I. Volatile N-nitrosamines in Meat Products: Potential
603 Precursors, Influence of Processing and Mitigation Strategies. *Crit Rev Food Sci Nutr.* 2015 (in
604 press).

605 Domingo JL, Bocio A. Levels of PCDD/PCDFs and PCBs in edible marine species and human
606 intake: a literature review. *Environ Int.* 2007, 33, 397-405.

607 Domingo JL, Nadal M. Human dietary exposure to polycyclic aromatic hydrocarbons: A review
608 of the scientific literature. *Food Chem Toxicol.* 2015, 86, 144-153.

609 Domingo JL, Schuhmacher M, Granero S, Llobet JM. PCDDs and PCDFs in food samples from
610 Catalonia, Spain. An assessment of dietary intake. *Chemosphere.* 1999, 38, 3517-3528.

611 Domingo JL, Falcó G, Llobet JM, Casas C, Teixidó A, Müller L. Polychlorinated naphthalenes
612 in foods: estimated dietary intake by the population of Catalonia, Spain. *Environ Sci Technol.*
613 2003, 37, 2332-2335.

614 Domingo JL, Martí-Cid R, Castell V, Llobet JM. Human exposure to PBDEs through the diet in
615 Catalonia, Spain: temporal trend. A review of recent literature on dietary PBDE intake.
616 *Toxicology.* 2008, 248, 25-32.

617 Domingo JL, Perelló G, Nadal M, Schuhmacher M. Dietary intake of polychlorinated dibenzo-p-
618 dioxins and dibenzofurans (PCDD/Fs) by a population living in the vicinity of a hazardous waste
619 incinerator: assessment of the temporal trend. *Environ Int.* 2012, 50, 22-30.

620 Domingo JL. Human exposure to polybrominated diphenyl ethers through the diet. *J Chromatogr*
621 *A.* 2004a, 1054, 321-326.

622 Domingo JL. Polychlorinated naphthalenes in animal aquatic species and human exposure
623 through the diet: a review. *J Chromatogr A.* 2004b, 1054, 327-334.

624 Domingo JL. Polychlorinated diphenyl ethers (PCDEs): environmental levels, toxicity and human
625 exposure: a review of the published literature. *Environ Int.* 2006, 32, 121-127.

626 Domingo JL. Influence of cooking processes on the concentrations of toxic metals and various
627 organic environmental pollutants in food: a review of the published literature. *Crit Rev Food Sci*
628 *Nutr.* 2011, 51, 29-37.

629 Domingo JL. Polybrominated diphenyl ethers in food and human dietary exposure: a review of
630 the recent scientific literature. *Food Chem Toxicol.* 2012a, 50, 238-249.

631 Domingo JL. Health risks of dietary exposure to perfluorinated compounds. *Environ Int.* 2012b,
632 40, 187-195.

633 Domingo JL. Nutrients and Chemical Pollutants in Fish and Shellfish. *Balancing Health Benefits*
634 *and Risks of Regular Fish Consumption.* *Crit Rev Food Sci Nutr.* 2015 (in press).

635 Engel E, Ratel J, Bouhlel J, Planche C, Meurillon M. Novel approaches to improving the chemical
636 safety of the meat chain towards toxicants. *Meat Sci.* 2015, 109, 75-85.

637 Ericson I, Martí-Cid R, Nadal M, Van Bavel B, Lindström G, Domingo JL. Human exposure to
638 perfluorinated chemicals through the diet: intake of perfluorinated compounds in foods from the
639 Catalan (Spain) market. *J Agric Food Chem.* 2008, 56, 1787-1794.

640 Ericson-Jogsten I, Perelló G, Llebaria X, Bigas E, Martí-Cid R, Kärrman A, Domingo JL.
641 Exposure to perfluorinated compounds in Catalonia, Spain, through consumption of various raw
642 and cooked foodstuffs, including packaged food. *Food Chem Toxicol.* 2009, 47, 1577-1583.

643 Falcó G, Domingo JL, Llobet JM, Teixidó A, Casas C, Müller L. Polycyclic aromatic
644 hydrocarbons in foods: human exposure through the diet in Catalonia, Spain. *J Food Prot.* 2003,
645 66, 2325-2331.

646 Falcó G, Bocio A, Llobet JM, Domingo JL, Casas C, Teixidó A. Dietary intake of
647 hexachlorobenzene in Catalonia, Spain. *Sci Total Environ.* 2004, 322, 63-70.

648 Herrmann SS, Duedahl-Olesen L, Christensen T, Olesen PT, Granby K. Dietary exposure to
649 volatile and non-volatile N-nitrosamines from processed meat products in Denmark. *Food Chem*
650 *Toxicol.* 2015, 80, 137-143.

651 IARC, International Agency for Reserach on Cancer, Press release No. 240, October 26, 2015:
652 Monographs evaluate consumption of red meat and processed meat,
653 https://www.iarc.fr/en/media-centre/pr/2015/pdfs/pr240_E.pdf (accessed November 10, 2015).

654 Kim E, Coelho D, Blachier F. Review of the association between meat consumption and risk of
655 colorectal cancer. *Nutr Res.* 2013, 33, 983-994.

656 Kim M. *Chemical contamination of red meat.* In: *Chemical Contaminants in Residues and Food.*
657 Schrenk D (ed.), Woodhead Publishing Series in Food Science, Technology and Nutrition, No.
658 235, Woodhead Publishing Limited, Philadelphia, USA, 2012, pp.447-468.

659 Klurfeld DM. Research gaps in evaluating the relationship of meat and health. *Meat Sci.* 2015,
660 109, 86-95.

661 Larsson BK Formation of polycyclic aromatic hydrocarbons during the smoking and grilling of
662 food. *Prog Clin Biol Res.* 1986, 206, 169-80.

663 Llobet JM, Granero S, Schuhmacher M, Corbella J, Domingo JL. Biological monitoring of
664 environmental pollution and human exposure to metals in Tarragona, Spain. IV. Estimation of the
665 dietary intake. *Trace Elem Electrolytes* 1998, 15, 76-80.

666 Llobet JM, Falcó G, Casas C, Teixidó A, Domingo JL. Concentrations of arsenic, cadmium,
667 mercury, and lead in common foods and estimated daily intake by children, adolescents, adults,
668 and seniors of Catalonia, Spain. *J Agric Food Chem*. 2003a, 51, 838-842.

669 Llobet JM, Domingo JL, Bocio A, Casas C, Teixidó A, Müller L. Human exposure to dioxins
670 through the diet in Catalonia, Spain: carcinogenic and non-carcinogenic risk. *Chemosphere*.
671 2003b, 50, 1193-1200.

672 Llobet JM, Bocio A, Domingo JL, Teixidó A, Casas C, Müller L. Levels of polychlorinated
673 biphenyls in foods from Catalonia, Spain: estimated dietary intake. *J Food Prot*. 2003c, 66, 479-
674 484.

675 Llobet JM, Martí-Cid R, Castell V, Domingo JL. Significant decreasing trend in human dietary
676 exposure to PCDD/PCDFs and PCBs in Catalonia, Spain. *Toxicol Lett*. 2008, 178, 117-126.

677 Martí-Cid R, Llobet JM, Castell V, Domingo JL. Dietary intake of arsenic, cadmium, mercury,
678 and lead by the population of Catalonia, Spain. *Biol Trace Elem Res*. 2008a, 125, 120-132.

679 Martí-Cid R, Llobet JM, Castell V, Domingo JL. Human dietary exposure to hexachlorobenzene
680 in Catalonia, Spain. *J Food Prot*. 2008b, 71, 2148-2152.

681 Martí-Cid R, Llobet JM, Castell V, Domingo JL. Human exposure to polychlorinated
682 naphthalenes and polychlorinated diphenyl ethers from foods in Catalonia, Spain: temporal trend.
683 *Environ Sci Technol*. 2008c, 42, 4195-4201.

684 Martí-Cid R, Llobet JM, Castell V, Domingo JL. Evolution of the dietary exposure to polycyclic
685 aromatic hydrocarbons in Catalonia, Spain. *Food Chem Toxicol*. 2008d, 46, 3163-3171.

686 Martí-Cid R, Bocio A, Domingo JL. Dietary exposure to PCDD/PCDFs by individuals living near
687 a hazardous waste incinerator in Catalonia, Spain: temporal trend. *Chemosphere*. 2008e, 70,
688 1588-1595.

689 Martí-Cid R, Perelló G, Domingo JL. Dietary exposure to metals by individuals living near a
690 hazardous waste incinerator in Catalonia, Spain: temporal trend. *Biol Trace Elem Res*. 2009, 131,
691 245-254.

692 Martorell I, Perelló G, Martí-Cid R, Castell V, Llobet JM, Domingo JL. Polycyclic aromatic
693 hydrocarbons (PAH) in foods and estimated PAH intake by the population of Catalonia, Spain:
694 Temporal trend. *Environ Int*. 2010, 36, 424-432.

695 Martorell I, Perelló G, Martí-Cid R, Llobet JM, Castell V, Domingo JL. Human exposure to
696 arsenic, cadmium, mercury, and lead from foods in Catalonia, Spain: temporal trend. *Biol Trace
697 Elem Res*. 2011, 142, 309-322.

698 McAfee AJ, McSorley EM, Cuskelly GJ, Moss BW, Wallace JM, Bonham MP, Fearon AM. Red
699 meat consumption: an overview of the risks and benefits. *Meat Sci*. 2010, 84, 1-13.

700 Murphy MM, Spungen JH, Bi X, Barraj LM. Fresh and fresh lean pork are substantial sources of
701 key nutrients when these products are consumed by adults in the United States. *Nutr Res*. 2011,
702 31, 776-783.

703 Pereira PM, Vicente AF. Meat nutritional composition and nutritive role in the human diet. *Meat*
704 *Sci.* 2013, 93, 586-592.

705 Perelló G, Martí-Cid R, Llobet JM, Domingo JL. Effects of various cooking processes on the
706 concentrations of arsenic, cadmium, mercury, and lead in foods. *J Agric Food Chem.* 2008, 56,
707 11262-11269.

708 Perelló G, Martí-Cid R, Castell V, Llobet JM, Domingo JL. Concentrations of polybrominated
709 diphenyl ethers, hexachlorobenzene and polycyclic aromatic hydrocarbons in various foodstuffs
710 before and after cooking. *Food Chem Toxicol.* 2009, 47, 709-715

711 Perelló G, Martí-Cid R, Castell V, Llobet JM, Domingo JL. Influence of various cooking
712 processes on the concentrations of PCDD/PCDFs, PCBs and PCDEs in foods. *Food Control* 2010,
713 21, 178-185.

714 Perelló G, Gómez-Catalán J, Castell V, Llobet JM, Domingo JL. Assessment of the temporal
715 trend of the dietary exposure to PCDD/Fs and PCBs in Catalonia, over Spain: health risks. *Food*
716 *Chem Toxicol.* 2012, 50, 399-408.

717 Perelló G, Vicente E, Castell V, Llobet JM, Nadal M, Domingo JL. Dietary intake of trace
718 elements by the population of Catalonia (Spain): results from a total diet study. *Food Addit*
719 *Contam Part A Chem Anal Control Expo Risk Assess.* 2015, 32, 748-755.

720 Peshin SS, Lall SB, Gupta SK. Potential food contaminants and associated health risks. *Acta*
721 *Pharmacol Sin.* 2002, 23, 193-202

722 Rodríguez-Hernández A, Boada LD, Almeida-González M, Mendoza Z, Ruiz-Suárez N, Valeron
723 PF, Camacho M, Zumbado M, Henríquez-Hernández LA, Luzardo OP. An estimation of the
724 carcinogenic risk associated with the intake of multiple relevant carcinogens found in meat and
725 charcuterie products. *Sci Total Environ* 2015a, 514, 33-41.

726 Rodríguez-Hernández AR, Boada LD, Mendoza Z, Ruiz-Suárez N, Valerón PF, Camacho M,
727 Zumbado M, Almeida-González M, Henríquez-Hernández LA, Luzardo OP. Consumption of
728 organic meat does not diminish the carcinogenic potential associated with the intake of persistent
729 organic pollutants (POPs). *Environ Sci Pollut Res Int.* 2015b (in press).

730 Trafialek J, Kolanowski W. Dietary exposure to meat-related carcinogenic substances: is there a
731 way to estimate the risk? *Int J Food Sci Nutr.* 2014, 65, 774-780.

732 Zanovec M, O'Neil CE, Keast DR, Fulgoni VL 3rd, Nicklas TA. Lean beef contributes significant
733 amounts of key nutrients to the diets of US adults: National Health and Nutrition Examination
734 Survey 1999-2004. *Nutr Res.* 2010, 30, 375-381.

735 Zhang W, Xiao S, Samaraweera H, Lee EJ, Ahn DU. Improving functional value of meat
736 products. *Meat Sci.* 2010, 86, 15-31.

737

738