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Mini review

# Hair analysis for biomonitoring of environmental and occupational exposure to organic pollutants: State of the art, critical review and future needs

Brice M.R. Appenzeller[a,*], Aristidis M. Tsatsakis[b]

[a] Laboratory of Analytical Human Biomonitoring – CRP-Sante, Université du Luxembourg, 162A avenue de la Faïencerie, L-1511 Luxembourg
[b] Centre of Toxicology Sciences and Research, Division of Morphology, Medical School, University of Crete, Voutes, Heraklion 71003, Crete, Greece

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ABSTRACT

This paper presents the current state of the art in human hair analysis for the detection of organic pollutants associated with environmental and occupational exposure. The different chemical classes are reviewed with a special focus set on compounds that were only recently investigated. The importance of methods sensitivity and particularly the influence of this parameter on the results presented in previous publications is highlighted. This report also investigates the relevance of hair analysis as an indicator of subjects' level of exposure and underlines limitations that are still associated with this matrix. This study also presents a critical assessment of some specific aspects presented in the literature as well as future needs to strengthen the position of hair as a relevant biomarker of exposure to be used in epidemiological studies.



**Contents**



*Abbreviations:* PAH, polycyclic aromatic hydrocarbons; PBC, polychlorinated biphenyls; PBDE, polybrominated diphenyl ethers; PCDD, polychlorinated dibenzo-p-dioxins; PCDF, dibenzofurans; GC–MS, gas chromatography–mass spectrometry; ECD, electron capture detector; HRGC, high resolution gas chromatography; HRMS, high resolution mass spectrometry; DDT, dichlorodiphenyltrichloroethane; DDE, dichlorodiphenyldichloroethylene; DDD, dichlorodiphenyldichloroethane; ERC, easily removable chemicals; HCH, hexachlorohexane; SPME, solid phase microextraction; LOD, limit of detection; LOQ, limit of quantification; HCB, hexachlorobenzene; DMP, dimethylphosphate; DEP, diethylphosphate; DMTP, dimethylthiophosphate; DETP, diethylthiophosphate; DEDTP, diethydithiophosphate; MMA, malathion monocarboxylic acid; 3-PBA, 3-phenoxybenzoic acid.

* Corresponding author. Tel.: +352 46 66 44 67 27; fax: +352 22 13 31.
*E-mail address:* brice.appenzeller@crp-sante.lu (B.M.R. Appenzeller).

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## 1. Introduction

The widespread use of hair as a biological matrix for toxicological analysis is about to make it move from the "alternative matrices" to the "classical matrices" category, on the same account as blood or urine (Esteban and Castaño, 2009). Hair has actually become a natural matrix in numerous domains such as forensic and clinical analysis for the detection of medical drugs or drugs of abuse (Tsatsakis et al., 1997, 2000; Nakahara, 1999; Psillakis et al., 1999; Mieczkowski et al., 2001; Mantzouranis et al., 2004; Boumba et al., 2006; Pragst and Balikova, 2006; Kintz, 2007), assessment of trace element deficiency (Rodrigues et al., 2008; Li et al., 2011) or biomonitoring of the exposure to inorganic compounds (*e.g.* metals) (Yasutake et al., 2004; Gault et al., 2008; Kehagia et al., 2011; Shah et al., 2011). The increasing interest shown in hair analysis is explained by the several advantages associated with this matrix, and primarily its easiness of sampling and storage which does not require restricted measures such as presence of medical staff, adapted settings, or refrigerated conditions. The memory-effect of hair due to accumulation of chemicals in this matrix and possibility of retrospective analysis also amounted for its success in several contexts such as drug-facilitated crime evidence or assessment of the history of drug consumption in addiction treatment. The extended window of detection, compared with biological fluids, has also contributed to consider hair analysis a most relevant biomarker in the assessment of chronic consumption/exposure. The stability of both the matrix itself and the compounds contained therein also accounted for the use of hair in some history-related cases (Kintz et al., 2007; Musshof et al., 2009) and for the increased use of hair in post-mortem analysis in general (Kronstrand and Druid, 2006).

Compared with the forensic and clinical fields, the literature dealing with human hair analysis for the detection of organic pollutants is rather poor. In fact, to the best of our knowledge, about 40 publications only presented experimental results describing the detection of organic pollutants in hair in relation to environmental and/or occupational exposure. These publications concern only few chemical categories namely pesticides (including different chemical classes such as organochlorines, organophosphates, pyrethroids and others), polybrominated diphenyl ethers (PBDEs), polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and dioxins.

The present publication reviews the current state-of-the art of the literature dealing with the detection of organic pollutants in human hair, with a special focus on chemicals which were only recently investigated. The importance of method sensitivity was also highlighted, insofar as it may significantly influence the results, particularly in the biomonitoring of low-level exposure. The relevance and reliability of hair analysis as an indicator of humans' level of exposure was also investigated. Attention was also paid to the limitations that are still associated with the hair matrix. Finally, studies on organic pollutants in hair were critically reviewed in order to underline possible improvements and future needs to consolidate the use of hair as a biomarker of exposure in epidemiological studies.

## 2. State of the art

### 2.1. "Classical" compounds

Dioxins, *i.e.* polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF), which are by-products of industrial and combustion process or direct industrial compounds, were among the first organic pollutants detected in human hair (Schramm et al., 1992). PCDDs and PCDFs are typically analyzed using high resolution gas chromatography coupled with high resolution mass spectrometry (HRGC-HRMS) and limits of detection of the methods presented in the different works are close to 0.1 pg/g; which appears sufficient to allow high rates of positive detection (number of samples with concentration above the limit of detection divided by the total number of samples analyzed) (Table 8). These compounds are the ones for which the lowest levels of concentration in hair are generally reported (around 1 pg/g or below), even though congeners with the highest molecular mass (hepta- and octa-chlorinated congeners) can reach levels of nearly 1 and 27 ng/g for octa-CDF and octa-CDD respectively (Fig. 1). Studies investigating dioxins in hair generally included a limited number of subjects (from 1 to 6) with the exception of the study of Nakao et al. (2005) that compared dioxin levels in hair collected from 68 incineration workers with 64 subjects from the general population. The highest concentrations were observed in samples from Nakao's study (Japan) as well as in a pooled hair sample collected from a contaminated area close to a pentachlorophenol production plant in the region of Tianjin, China (Luksemburg et al., 1997).

PCBs were also among the first organic pollutants analyzed in human hair (Zupancic-Kralj et al., 1992). The different techniques used to detect PCBs in hair included HRGC with electron capture detector (ECD), HRGC-HRMS, GC-ECD and GC–MS, and the reported limits of detection ranged from 0.3 to 320 pg/g (Table 7). The rate of positive detection is generally high but may decrease below 10% for some congeners. The concentration levels described in the different studies covered several orders of magnitude but the median values were generally below 10,000 pg/g. Particularly high concentrations were however reported in hair samples obtained from children living in the urban region of Beijing (Zhang et al., 2007), China, and in hair of residents around e-waste disassembly sites in China (Zhao et al., 2008). Several studies involved populations composed of 10 subjects and more, but comparisons remain difficult as only few PCB congeners were common to the different works.

Pesticides and particularly organochlorine pesticides are by far the organic pollutants which have been the most investigated in human hair. These chemicals also are record-holders of the highest concentrations since all the categories listed in Tables 1–8 (organochlorines, organophosphates, pyrethroids and other pesticides) have already been detected at levels above 1000 pg/mg. Surprisingly, the highest concentration levels were not necessarily detected in hair of subjects with occupational exposure. For instance, the highest concentration of both o,p′-DDT and p,p′-DDT was observed in hair of Romanian adolescents (Covaci et al., 2008) (Fig. 1). The highest concentration of organophosphates (malathion and chlorpyrifos) and pyrethroids (bioallethrin) was observed in hair samples of pregnant women in Philippines (Ostrea et al., 2009). The studies which investigated pesticides in human hair often involved populations composed of hundreds of subjects. Nevertheless, with the exception of some organochlorines, few pesticides were common to several studies. Pesticides were mainly analyzed with GC–MS and GC-ECD and the limits of detection presented in the different publications ranged from below 1 pg/mg up to nearly 500 pg/mg. As a result, the rate of positive detection was significantly different between the studies. The latter aspect is more in depth detailed in the Section 3, with a special focus on organochlorine pesticides.

### 2.2. Compounds recently investigated

#### 2.2.1. Polybrominated diphenyl ethers (PBDEs)

PBDEs have been used worldwide as flame retardants, added to many products such as textiles, plastics (particularly hard plastics used in electronics) and products containing polyurethane foam (*e.g.* mattresses, carpets) (Alaee et al., 2003). Estimations of the exposure to PBDEs suggested that ingestion and dermal absorption of house dust were the major pathways of exposure to these indoor

**Table 1**
Concentration of organochlorine pesticides in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/ quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| α-HCH | *n* = 42, ado[d] | 100 | [1.0–99.5] 13.3 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [n.d.–5.2] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 74, 2–9y | 100 | [3.0–17] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 222 | 31 | [n.d.–687] 40.4 | LOD: 2.5; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 24.2 | [n.d.–50.3] 7.2 | LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 14, 23–60y | 79 | [n.d.–0.6] 0.11 | LOD: 0.01; LOQ: 0.05 | Luxembourg | (Salquebre et al., 2011) |
| β-HCH | *n* = 42, ado[d] | 100 | [4.3–264] 54.9 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [n.d.–16.3] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 74, 2–9y | 94.6 | [n.d.–50] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 14, 23–60y | 100 | [0.3–10.3] 2.3 | LOD: 0.02; LOQ: 0.1 | Luxembourg | (Salquebre et al., 2011) |
| γ-HCH | *n* = 193, 5–6y | 3 | [n.d.–>400] n.a. | LOQ: 200 | Germany | (Neuber et al., 1999) |
| | *n* = 42, ado[d] | 100 | [7.5–236] 78.9 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | 100 | [2.7–73.7] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–488 | Philippines | (Ostrea et al., 2008) |
| | *n* = 74, 2–9y | 100 | [8.0–59] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 222 | 33 | [n.d.–905.9] 124.2 | LOD: 2.5; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 51.5 | [n.d.–174.7] 70.2 | LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 14, 23–60y | 100 | [0.3–8.9] 2.1 | LOD: 0.02; LOQ: 0.1 | Luxembourg | (Salquebre et al., 2011) |
| | *n* = 282 | 0 | n.d. | LOD: 245 | Philippines | (Posecion et al., 2006) |
| δ-HCH | *n* = 42, ado[d] | 95 | [0.3–23.5] 5.8 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 74, 2–9y | 76 | [n.d.–10] n.a. | LOD: 0.01-0.06[j] | China | (Zhang et al., 2007) |
| $\sum$α–γ-HCH | *n* = 222 | 51 | [n.d.–938.2] 117.8 | LOD: 2.5; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| $\sum$α–β–γ-HCH | *n* = 14, 26–68y | 100 | [8.8–95.2] 51.4 | LOD: 1 | Europe[g] | (Covaci and Schepens, 2001) |
| | *n* = 47[e] | 100 | [6.0–95.2] n.a. | LOD: 0.3-2 | Europe[f] | (Covaci et al., 2002b) |
| $\sum$α–β–γ–δ-HCH | *n* = 42, ado[d] | 100 | [12.8–463] 172 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| o,p′-DDT | *n* = 42, ado[d] | 100 | [3.0–1280] 73.5 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [n.d.–14.4] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 222 | 10[s] | [n.d.–21.6] 8.0[h] | LOD: 1.0; LOQ: 2.5 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 42.4[h] | [n.d.–2135] 2.6[h] | LOQ: 2.5 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.68 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| | *n* = 14, 23–60y | 64 | [n.d.–3.7] 1.6 | LOD: 0.2; LOQ: 1.0 | Luxembourg | (Salquebre et al., 2011) |
| p,p′-DDT | *n* = 193, 5–6y | 9 | [n.d.–>400] n.a. | LOQ: 160 | Germany | (Neuber et al., 1999) |
| | *n* = 42, ado[d] | 100 | [7.0–3920] 192 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | 100 | [2.4–43.6] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 74, 2–9y | 81 | [n.d.–20] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 222 | 7 | [n.d.–222.6] 5.7 | LOD: 2.5; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 9.1 | [n.d.–158.7] 23.2 | LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 10, 25–53y | 100 | [n.a.] 2.26 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| | *n* = 14, 23–60y | 71 | [n.d.–5.6] 5.1 | LOD: 0.2; LOQ: 1.0 | Luxembourg | (Salquebre et al., 2011) |
| | *n* = 282 | 0 | n.a. | LOD: 31 | Philippines | (Posecion et al., 2006) |
| | *n* = 449 | 0.4/0.7[i] | 0.98/2.11[i] | LOD: 30.5–488 | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5 | Philippines | (Ostrea et al., 2008) |
| | *n* = 597 | 0.8 | [400–1160] 650 | LOD: 30.5 | Philippines | (Ostrea et al., 2009) |
| o,p′-DDE | *n* = 42, ado[d] | 100 | [0.5–61.3] 7.1 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [n.d.–453.1] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 222 | 3 | [n.d.–18.4] 6.2 | LOD: 1.0; LOQ: 2.5 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 45.5 | [n.d.–571] 2.7 | LOQ: 2.5 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.82 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| | *n* = 14, 23–60y | 50 | [n.d.–0.40] 0.30 | LOD: 0.02; LOQ: 0.1 | Luxembourg | (Salquebre et al., 2011) |
| p,p′-DDE | *n* = 42, ado[d] | 100 | [7.4–946] 127 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [2.1–278.7] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 449 | 0 | n.d. | LOD: 30.5–488 | Philippines | (Ostrea et al., 2006) |
| | *n* = 74, 2–9y | 100 | [2.6–22] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 222 | 13.5 | [n.d.–80.4] 7.8 | LOD: 2.0; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 15.2 | [n.d.–58] 5.7 | LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 10, 25–53y | 100 | [n.a.] 4.58 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| | *n* = 14, 23–60y | 100 | [0.3–4.2] 1.5 | LOD: 0.02: LOQ: 0.1 | Luxembourg | (Salquebre et al., 2011) |

Table 1 (*Continued*)

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/ quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| | *n* = 3 | 100 | [1.1–1.5] | n.a. | Luxembourg | (Dauberschmidt and Wennig, 1998) |
| o,p′-DDD | *n* = 42, ado[d] | 88 | [0.4–138] 26.4 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | 0 | n.d. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 222 | 9 | [n.d.–363.7] 73.1 | LOD: 0.5; LOQ: 2.5 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 57.6 | [n.d.–6.8] 3.1 | LOQ: 2.5 | Greece | (Tsatsakis et al., 2008a) |
| p,p′-DDD | *n* = 42, ado[d] | 100 | [0.8–528] 18.2 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | n.a. | [n.d.-17.3] n.a. | LOD: 0.3-2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.112 | LOD: 0.01-0.32 | USA | (Altshul et al., 2004) |
| | *n* = 74, 2–9y | 68 | [n.d.–3.7] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| ∑DDTs,DDEs, DDDs | *n* = 14, 26–68y | 100 | [12.7–754.2] 126.3 | LOD: 1 | Europe[g] | (Covaci and Schepens, 2001) |
| | *n* = 42, ado[d] | 100 | [20.1–6550] 394 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 47[e] | 100 | [8.7–754.2] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 222 | 32 | [n.d.–389.4] 9.4 | LOQ: 2.5–5.0 | Greece | (Tsatsakis et al., 2008b) |
| Chlordane | *n* = 74, 2–9y | 67 | [n.d.–12] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| Oxychlordane | *n* = 42, ado[d] | 50 | [0.4–9.5] 2.5 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| *trans*-nonachlor | *n* = 42, ado[d] | 93 | [0.6–690] 89.1 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.72 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| Aldrin | *n* = 74, 2–9y | 30 | [n.d. –5.8] n.a. | LOD: 0.01–0.06[j] | China | (Zhang et al., 2007) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.24 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| Dieldrin | *n* = 10, 25–53y | 0 | n.d. | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| HCB | *n* = 42, ado[d] | 48 | [0.3–4.1] 0.8 | LOD: 0.1–0.2 | Romania | (Covaci et al., 2008) |
| | *n* = 1[j], 37y | 100 | [1.385–1.553] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 47[e] | n.a. | [n.d.–3.3] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| | *n* = 222 | 27 | [n.d.–323.2] 19.7 | LOD: 2.5; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008b) |
| | *n* = 211[c] | 21.2 | [n.d.–15.9] 2.2 | LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 10, 25–53y | 100 | [n.a.] 0.56 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| Heptachlor | *n* = 10, 25–53y | 100 | [n.a.] 0.42 | LOD: 0.01–0.32 | USA | (Altshul et al., 2004) |
| α-Endosulfan | *n* = 14, 23–60y | 43 | [n.d.–1.3] 1.2 | LOD: 0.2; LOQ: 1.0 | Luxembourg | (Salquebre et al., 2011) |

n.d., not detected (below the limit of detection); n.a., not available.

[a] Median is calculated for positive samples only (concentration above the limit used for quantification).

[b] Country where samples have been collected.

[c] Reported occupational or specific exposure.

[d] Adolescents.

[e] 30 out of the 47 people had a history of occupational exposure.

[f] 35 people from Greece, 2 from Romania and 10 from Belgium.

[g] 2 people from Romania, 4 people from Belgium, 8 people from Greece.

[h] Sum p,p′-DDD + o,p′-DDT.

[i] Values obtained from maternal hair (positive sample only) at midgestation and at birth.

[j] LOD not detailed for each molecule.

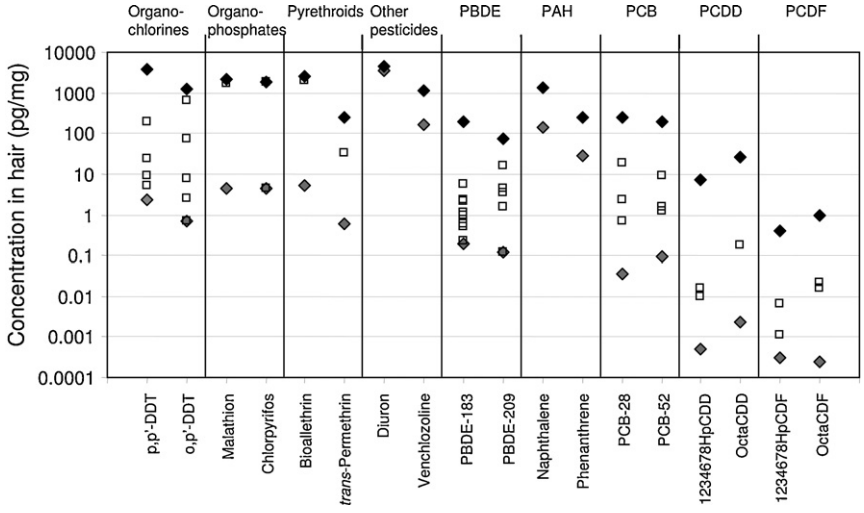


**Fig. 1.** Concentrations in hair reported for the two chemicals displaying the highest concentration in each of the categories presented in Tables 1–8. "◆" lowest value measured, "black ♦" highest value measured, "□"median values reported in different publications.

**Table 2**
Concentration of organophosphate pesticides in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| Dichlorvos | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.5; LOQ: 2.0 | Luxembourg | (Salquebre et al., 2011) |
| Malathion | *n* = 449 | 1.8/0.0[d] | 4.60/0.0[d] | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2008) |
| | *n* = 597 | 1.3 | [1620–2120] 1720 | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2009) |
| | *n* = 211[c] | 0 | n.d. | LOD: 2.0; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 282 | 2.84 | 4.85 ± 1.23[e] | LOD: 123 | Philippines | (Posecion et al., 2006) |
| Methyl parathion | *n* = 211[c] | 0 | n.d. | LOD: 2.0; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| MMA[f] | *n* = 449 | 0/0.2[d] | 0/0.44[d] | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2006) |
| Chlorpyrifos | *n* = 449 | 0.0/0.4[d] | 0.0/4.48[d] | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0.2 | n.a. | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2008) |
| | *n* = 597 | 0.3 | [1770–1830] 1800 | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2009) |
| | *n* = 282 | 0.35 | 4.58 | LOD: 245 | Philippines | (Posecion et al., 2006) |
| Fenthion | *n* = 211[c] | 0 | n.d. | LOD: 2.0; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| Diazinon | *n* = 449 | 0 | n.d. | LOD: 30.5–48 [h] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5 | Philippines | (Ostrea et al., 2008) |
| | *n* = 211[c] | 5 | 2.8[e] | LOD: 2.0; LOQ: 5.0 | Greece | (Tsatsakis et al., 2008a) |
| | *n* = 282 | 0 | n.d. | LOD: 31 | Philippines | (Posecion et al., 2006) |
| Oxadiazon | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.1; LOQ: 0.5 | Luxembourg | (Salquebre et al., 2011) |
| DMP[g] | *n* = 27 | 63 | [n.a.] 165.0 | LOD: 6; LOQ: 20 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 6[c] | 100 | [n.a.] 181.7 | LOD: 6; LOQ: 20 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 30[c] | 40 | [100–460] 240[e] | LOD: 100; LOQ: 330 | Greece | (Margariti and Tsatsakis, 2009) |
| DEP[g] | *n* = 27 | 96.3 | [n.a.] 51.2 | LOD: 5; LOQ: 10 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 6[c] | 100 | [n.a.] 812.9 | LOD: 5; LOQ: 10 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 30[c] | 70 | [320–440] 360[e] | LOD: 20; LOQ: 60 | Greece | (Margariti and Tsatsakis, 2009) |
| DMTP[g] | *n* = 30[c] | 20 | [320–410] 360[e] | LOD: 100; LOQ: 340 | Greece | (Margariti and Tsatsakis, 2009) |
| DETP[g] | *n* = 27 | 66.7 | [n.a.] 54.0 | LOD: 5; LOQ: 10 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 6[c] | 100 | [n.a.] 660.1 | LOD: 5; LOQ: 10 | Greece | (Tsatsakis et al., 2010) |
| DEDTP[g] | *n* = 27 | 70.4 | [n.a.] 40.0 | LOD: 3; LOQ: 5 | Greece | (Tsatsakis et al., 2010) |
| | *n* = 6[c] | 100 | [n.a.] 60.6 | LOD: 3; LOQ: 5 | Greece | (Tsatsakis et al., 2010) |

n.d., not detected (below the limit of detection); n.a., not available.
[a] Median is calculated for positive samples only (concentration above the limit used for quantification).
[b] Country where samples have been collected.
[c] Reported occupational or specific exposure.
[d] Values obtained from maternal hair (positive sample only) at midgestation and at birth
[e] mean.
[f] Malathion monocarboxylic acid.
[g] DMP: dimethylphosphate; DEP: diethylphosphate; DMTP: dimethylthiophate; DETP: diethyltiophosphate; DEDTP: diethyldithiophosphate.
[h] LOD not detailed for each molecule.

contaminants for all the age groups, except infants who were considered being by far the most exposed category mainly due to breast feeding (Johnson-Restrepo and Kannan, 2009). The latter consideration is in line with the exponential increase in the concentration of PBDEs in human milk that has been observed since the seventies (Solomon and Huddle, 2006). The structural similarities between PBDEs and thyroid hormones are thought to be responsible for their possible endocrine disruptor properties and the subsequent associated biological effects (Kodavandi et al., 2005; Zhang et al., 2010). Before being detected in hair, PBDEs have been analyzed in other human matrices such as milk (Fangstrom et al., 2005), blood (Karlsson et al., 2007) and adipose tissue (She et al., 2002). So far, the detection of PBDEs in human hair has been reported in 5 published works carried out in China (3 studies), Italy and Canada and focused on a limited number of congeners (13 or less) excepted the study of Leung et al. (2011) that investigated 36 out of the 209 different possible congeners. The highest concentration detected in an individual's hair was observed for PBDE-47 (188 pg/mg) in a child bearing-aged women from the region of Taizhou, China, an area with e-waste recycling activities. PBDE-209 displayed the highest median concentration reported in all the works except the Canadian study (Fig. 1) and the study from Leung et al. (2011), in which BDE-209 was not tested. The comparison on the 5 congeners (47, 99, 100, 183 and 209) that were common to the different

**Table 3**
Concentration of pyrethroid pesticides in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| Pyrethroids | | | | | | |
| Bioallethrin | *n* = 449 | 11.9/7.8[d] | 5.20/2.40[d] | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 488 | Philippines | (Ostrea et al., 2008) |
| | *n* = 597 | 14.5 | [600–2490] 2050 | LOD: 488 | Philippines | (Ostrea et al., 2009) |
| | *n* = 282 | 16.67 | 6.78 ± 2.10 | LOD: 488 | Philippines | (Posecion et al., 2006) |
| λ-Cyhalothrin | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.2; LOQ: 1.0 | Luxembourg | (Salquebre et al., 2011) |
| Cyfluthrin | *n* = 449 | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–488 | Philippines | (Ostrea et al., 2008) |
| Cypermethrin | *n* = 449 | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2008) |
| | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.1; LOQ: 0.5 | Luxembourg | (Salquebre et al., 2011) |
| Deltamethrin | *n* = 14, 23–60y | 0 | n.d. | LOD: 1.0; LOQ: 5.0 | Luxembourg | (Salquebre et al., 2011) |
| Fenvalerate | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.2; LOQ: 2 | Luxembourg | (Salquebre et al., 2011) |
| Transflutrin | *n* = 449 | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2008) |
| | *n* = 282 | 0 | n.d. | LOD: 245 | Philippines | (Posecion et al., 2006) |
| *trans*-permethrin | *n* = 14, 23–60y | 100 | [0.6–250] 34 | LOQ: n.d. | Luxembourg | (Salquebre et al., 2011) |
| 3-PBA | *n* = 449 | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |

n.d., not detected (below the limit of detection); n.a., not available.
[a] Median is calculated for positive samples only (concentration above the limit used for quantification).
[b] Country where samples have been collected.
[d] Values obtained from maternal hair (positive sample only) at midgestation and at birth.
[e] LOD not detailed for each molecule.

**Table 4**
Concentration of pesticides from different chemical classes in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| Diuron | *n* = 5[c] | n.a. | [3460–4610] n.a. | n.a. | France | (Cirimele et al., 1999) |
| Aldrin | *n* = 14, 23–60y | 0 | n.d. | LOD: 0.05; LOQ:0.2 | Luxembourg | (Salquebre et al., 2011) |
| Dieldrin | *n* = 14, 23–60y | 0 | n.d. | LOD: 1; LOQ: 5 | Luxembourg | (Salquebre et al., 2011) |
| Vinchlozolin | *n* = 5[c] | n.a. | [170–1120] n.a. | n.a. | France | (Cirimele et al., 1999) |
| Propoxur | *n* = 449 | 10.5/11.8[d] | 2.67/0.58[d] | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5 | Philippines | (Ostrea et al., 2008) |
| | *n* = 597 | 21.6 | [220–420] 250 | LOD: 30.5 | Philippines | (Ostrea et al., 2009) |
| | *n* = 282 | 13.1 | 2.80 ± 0.05[f] | LOD: 31 | Philippines | (Posecion et al., 2006) |
| Pretilachlor | *n* = 449 | 0.2 | 2.68/2.55[d] | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2006) |
| | *n* = 638, newborns | 0 | n.d. | LOD: 30.5–488[e] | Philippines | (Ostrea et al., 2008) |
| | *n* = 282 | 0.35 | 2.68 | LOD: 61 | Philippines | (Posecion et al., 2006) |
| Trifluralin | *n* = 14, 23–60y | 36 | [0.1–0.8] 0.22 | LOD: 0.01; LOQ: 0.05 | Luxembourg | (Salquebre et al., 2011) |
| Pentachlorophenol | *n* = 14, 23–60y | 21 | [18.1–244] 30.2 | LOD: 2; LOQ: 10 | Luxembourg | (Salquebre et al., 2011) |
| Tebuconazole | *n* = 14, 23–60y | 14 | [20.0–65.6] 42.8 | LOD: 0.2; LOQ: 2 | Luxembourg | (Salquebre et al., 2011) |
| Diflufenican | *n* = 14, 23–60y | 7 | 1.9 | LOD: 0.05; LOQ: 0.2 | Luxembourg | (Salquebre et al., 2011) |

n.d., not detected (below the limit of detection); n.a., not available.
[a] Median is calculated for positive samples only (concentration above the limit used for quantification).
[b] Country where samples have been collected.
[c] Reported occupational or specific exposure.
[d] Values obtained from maternal hair (positive sample only) at midgestation and at birth.
[e] LOD not detailed for each molecule.
[f] Mean.

**Table 5**
Concentration of polybrominated diphenyl ethers (PBDEs) in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| PBDE-3, -15 | *n* = 36[c], *n* = 4 | 0 | n.d. | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008)[d] |
| PBDE-17 | *n* = 36[c] | 18–80[e] | [n.d.–5.97] n.a.–3.70[e] | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 25 | n.a. | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| PBDE-28 | *n* = 36[c] | 91–100[e] | [0.10–7.59] 1.03–5.19[e] | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 100 | [0.53–1.14] 0.84 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 33 | [n.d.–0.117] 0.068 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.402–33.4] 0.569 | n.a. | China | (Leung et al., 2011)[g] |
| PBDE-47 | *n* = 18, 22–42y | 100 | [0.86–5.24] 2.25 | LOD: 0.5–4 | China | (Kang et al., 2011) |
| | *n* = 9, 24–44y | 100 | [0.31–3.9] 0.60 | LOD: 0.10; LOQ: 0.30 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 100 | [0.31–0.65] 0.51 | LOD: 0.10; LOQ: 0.30 | Spain | (Tadeo et al., 2009) |
| | *n* = 36[c] | 100 | [0.20–9.65] 1.0–5.49[e] | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 100 | [1.07–1.57] 1.17 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 67 | [n.d.–0.842] 0.231 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.343–188] 2.08 | n.a. | China | (Leung et al., 2011) |
| PBDE-66 | *n* = 36[c], *n* = 4 | 9–38[e] | n.a. | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| PBDE-100 | *n* = 18, 22–42y | 100 | [0.13–0.49] 0.25 | LOD: 0.5–4 | China | (Kang et al., 2011) |
| | *n* = 9, 24–44y | 100 | [0.30–1.34] 0.50 | LOD: 0.08; LOQ: 0.27 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 100 | [0.30–0.58] 0.33 | LOD: 0.08; LOQ: 0.27 | Spain | (Tadeo et al., 2009) |
| | *n* = 36[c] | 13–33[e] | n.a | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 100 | [0.25–1.81] 1.09 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 67 | [n.d.–0.454] 0.07 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.078–5.07] 0.201 | n.a. | China | (Leung et al., 2011) |
| PBDE-99 | *n* = 18, 22–42y | 100 | [0.22–1.47] 0.54 | LOD: 0.5–4 | China | (Kang et al., 2011) |
| | *n* = 9, 24–44y | 100 | [0.30–2.1] 0.85 | LOD: 0.10; LOQ: 0.30 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 100 | [0.33–1.22] 0.80 | LOD: 0.10; LOQ: 0.30 | Spain | (Tadeo et al., 2009) |
| | *n* = 36[c] | 0–38[e] | n.a. | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 50 | [0.25–0.45] 0.33 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 75 | [n.d.–1.18] 0.21 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.151–76.4] 1.18 | n.a. | China | (Leung et al., 2011) |
| PBDE-153 | *n* = 36[c] | 46–89[e] | [n.d.–12.04] n.a.–4.84 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 75 | [n.d.–1.39] 1.10 | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 92 | [n.d.–0.51] 0.035 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.044–60.6] 0.515 | n.a. | China | (Leung et al., 2011) |
| PBDE-154 | *n* = 36[c] | 11–50[e] | [n.d.–1.38] n.a.–0.63[e] | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 0 | n.d | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 46 | [n.d.–0.27] 0.08 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.015–8.54] 0.147 | n.a. | China | (Leung et al., 2011) |
| PBDE-183 | *n* = 18, 22–42y | 100 | [0.08–1.01] 0.27 | LOD: 0.5–4 | China | (Kang et al., 2011) |
| | *n* = 9, 24–44y | 0 | n.d. | LOQ: 0.60 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 43 | [n.d.–0.28] n.d. | LOQ: 0.60 | Spain | (Tadeo et al., 2009) |
| | *n* = 36[c] | 50–100[e] | [0.32–24.28] 0.32–5.06[e] | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |
| | *n* = 4 | 0 | n.d. | LOD: 0.08–0.32[f] | China | (Zhao et al., 2008) |

Table 5 (*Continued*)

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| | *n* = 24, 0–15y | 21 | [n.d.–0.23] 0.09 | LOD:0.025; LOQ:0.06 | Canada | (Aleksa et al., 2011) |
| | *n* = 8[c] | 100 | [0.077–3.97] 1.26 | n.a. | China | (Leung et al., 2011) |
| PBDE-190 | *n* = 9, 24–44y | 100 | [0.4–1.21] 0.60 | LOD: 0.12; LOQ: 0.40 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 100 | [0.34–0.7] 0.50 | LOD: 0.12; LOQ: 0.40 | Spain | (Tadeo et al., 2009) |
| PBDE-209 | *n* = 9, 24–44y | 100 | [3.4–12.9] 4.50 | LOD: 0.9; LOQ: 3.0 | Spain | (Tadeo et al., 2009) |
| | *n* = 7, 1–11y | 57 | [n.d.–5.1] 4.20 | LOD: 0.9; LOQ: 3.0 | Spain | (Tadeo et al., 2009) |
| | *n* = 36[c] | 20–88[e] | [n.d.–73.1] 1.50–15.46[e] | LOD: 1.0 | China | (Zhao et al., 2008) |
| | *n* = 4 | 25 | n.a. | LOD: 1.0 | China | (Zhao et al., 2008) |
| | *n* = 24, 0–15y | 37 | [n.d.–0.46] 0.12 | LOD:2.5; LOQ:6.5 | Canada | (Aleksa et al., 2011) |

n.d., not detected (below the limit of detection); n.a., not available.

[a] Median is calculated for positive samples only (concentration above the limit used for quantification).

[b] Country where samples have been collected.

[c] Reported occupational or specific exposure.

[d] Data from Zhao *et al*., were presented separately for people with specific exposure (*n* = 36) and for the control group (*n* = 4) except for BDE-3 and -15.

[e] Range of values for the different sites investigated.

[f] LOD not detailed for each molecule.

[g] Only 7 out of the 36 PBDE investigated by Leung et al. (2011) were detailed here.

studies demonstrated concentrations in the same range for the 3 countries. However, the highest concentrations were generally observed in the Chinese and in the Spanish populations and the lowest were detected in the population of Canada (*n* = 24) and in the sub-population (*n* = 4) from Yandang, a remote mountainous area of West China (Table 5). The two studies that compared children (1–11 years old) vs adults (Tadeo et al., 2009) and newborns vs children (1–15 years old) (Aleksa et al., 2011) respectively, reported higher concentrations in the older groups, which contradicts the above-mentioned estimations of higher exposure for younger individuals and particularly for infants (Johnson-Restrepo and Kannan, 2009).

#### 2.2.2. Polycyclic aromatic hydrocarbons (PAHs) metabolites

Polycyclic aromatic hydrocarbons (PAHs) are by-products of incomplete combustion of organic material. Particularly high exposure has been reported for specific populations such as workers in PAH-releasing industries (such as road pavement, aluminium production, transports, fossil fuel combustion. . .) (Perera et al., 1988; Strickland and Kang, 1999; Väänänen et al., 2003, 2006; Elovaara et al., 2006), smokers (Strickland and Kang, 1999), and populations with high intake of grilled food (Nwaneshiudu et al., 2007). To a greater extent, PAHs released into the atmosphere (mainly from human activities) and subsequent contamination of human surroundings result in the exposure at environmental levels of the entire population through diet and inhalation, at least in densely-populated industrialized countries. The most documented adverse health effects associated with exposure to PAHs are related to their carcinogenic properties (Loew et al., 1979; Cavalieri and Rogan, 1985; Dipple et al., 1999; Binková and Šrám, 2004; Xue and Warshawsky, 2005) and their neurotoxicity (Jedrychowski et al., 2003; Choi et al., 2006; Tang et al., 2006). Although the biomonitoring of human exposure to PAH is generally achieved through the determination of urinary metabolites (Chetiyanukornkul et al., 2006; Elovaara et al., 2006) or the detection of PAH DNA-adducts in white blood cells (Godschalk et al., 2003), hair has also been investigated for the detection of parent molecules (Toriba et al., 2003) as well as for their mono-hydroxy metabolites (Schummer et al., 2009). The highest concentrations were observed for naphthalene (range: 136–1370 pg/mg), phenanthrene (28.9–255 pg/mg) and fluorene (range: 6.7–42.9 pg/mg) (Toriba et al., 2003) and their respective metabolites (3499 and 14,198 pg/mg for 1- and 2-naphthols respectively; 1998 pg/mg for 9OH-phenanthrene and 679 pg/mg for 9OH-fluorene) (Schummer et al., 2009), and significantly higher concentrations were detected in smokers' hair for anthracene, chrysene and benzo[k]fluoranthene (Toriba et al., 2003).

## 3. Importance of method sensitivity in human biomonitoring of low-level exposure

When assessing environmental exposure by the quantification of chemicals in a biological matrix, analytical sensitivity is a fundamental parameter since contrary to cases of acute exposure (*e.g.* intoxication), levels of concentration resulting from environmental exposure are relatively low. For instance, serum concentration reported in cases of acute poisoning with pesticides range from 20 μg/L (for bifenthrin) up to 1.5 and 6.5 mg/L (for carbofuran and endosulfan respectively) (Lacassie et al., 2001). In comparison, levels of pesticide concentration detected in serum collected from raw population is generally about 10 ng/L or lower (Barr et al., 2002; Berman et al., 2011), which is between one thousand and one million times inferior. Sensitivity is particularly relevant in the case of hair analysis in that the weight of material used is often limited to 50–200 mg compared to other matrices such as urine, blood/serum or meconium in the case of which the amount used for the detection of organic pollutants is commonly 2–5 mL (Barr et al., 2002, 2005; Baker et al., 2004; Conka et al., 2005; Zhao et al., 2007) and 10 mL or more for breast milk (Damgaard et al., 2006; Cok et al., 2011). Of course, given that human biomonitoring has to be comprehended as a diagnosis tool, reaching high sensitivity only makes sense as far as the associated selectivity is quite high (virtually 100%). High selectivity is ensured by detection techniques such as mass spectrometry, tandem mass spectrometry or high resolution mass spectrometry that limit the risk of false positive results.

The lack of highly sensitive methods has probably been among the main limitations to the use of hair for the biomonitoring of human exposure to organic pollutants. As a result, no reference values have yet been provided in public health authorities reports regarding organic pollutants concentration in hair, and it appears that urine and blood remain the reference matrices (CDC, 2009). The lack of sufficiently sensitive analytical methods has also probably contributed to supporting erroneous statements concerning

**Table 6**
Concentration of polycyclic aromatic hydrocarbons (plus hydroxy-PAH and nitro-PAH) in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (ng/g)[a] | Limit of detection/quantification (ng/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| Naphthalene | *n* = 20 | n.a. | [136–1370] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Fluorene | *n* = 20 | n.a. | [2.6–32.5] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Phenanthrene | *n* = 20 | n.a. | [28.9–255] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Anthracene | *n* = 20 | n.a. | [0.8–22.6] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Fluoranthene | *n* = 20 | n.a. | [6.7–42.9] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Pyrene | *n* = 20 | n.a. | [5.6–36.1] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Benzo[a]anthracene | *n* = 20 | n.a. | [0.2–5.0] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Chrysene | *n* = 20 | n.a. | [0.7–5.8] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Benzo[k]fluoranthene | *n* = 20 | n.a. | [0.1–2.9] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| Benzo[a]pyrene | *n* = 20 | n.a. | [0.4–2.2] n.a. | LOD: 1.6–24 pg/inj[d] | Japan | (Toriba et al., 2003) |
| 1OH-naphthalene | *n* = 30 | 17 | [207.4–3499] 1473 | LOD: 5.5; LOQ: 18.0 | Luxembourg | (Schummer et al., 2009) |
| 2OH-Naphthalene | *n* = 30 | 100 | [<15–14198] 1063 | LOD: 4.5; LOQ: 15.0 | Luxembourg | (Schummer et al., 2009) |
| 9OH-Fluorene | *n* = 30 | 23 | [<54.6–679] 679 | LOD: 54.6; LOQ: 191 | Luxembourg | (Schummer et al., 2009) |
| 2OH-Fluorene | *n* = 30 | 7 | [<4.2–20] 20 | LOD: 4.2; LOQ: 13.7 | Luxembourg | (Schummer et al., 2009) |
| 4OH-Phenanthrene | *n* = 30 | 3 | [<27.7] n.a. | LOD: 8.3; LOQ: 27.7 | Luxembourg | (Schummer et al., 2009) |
| 3OH-Phenanthrene | *n* = 30 | 10 | [<31.0] n.a. | LOD: 9.3; LOQ: 31.0 | Luxembourg | (Schummer et al., 2009) |
| 9OH-Phenanthrene | *n* = 30 | 27 | [<36.9–1998] 436 | LOD: 11.1; LOQ: 36.9 | Luxembourg | (Schummer et al., 2009) |
| 1OH-Phenanthrene | *n* = 30 | 7 | [19.4–215] 19.4 | LOD: 3.9; LOQ: 12.8 | Luxembourg | (Schummer et al., 2009) |
| 2OH-Phenanthrene | *n* = 30 | 7 | [<16.7–17.4] n.a. | LOD: 5.0; LOQ: 16.7 | Luxembourg | (Schummer et al., 2009) |
| 1OH-Pyrene | *n* = 30 | 3 | [<16.8] n.a. | LOD: 16.8; LOQ: 56.2 | Luxembourg | (Schummer et al., 2009) |
| 2OH-Benzo[c]phen | *n* = 30 | 3 | [<251] n.a. | LOD: 75.9; LOQ: 251 | Luxembourg | (Schummer et al., 2009) |
| 6OH-Chrys | *n* = 30 | 3 | [<89.3] n.a. | LOD: 26.6; LOQ: 89.3 | Luxembourg | (Schummer et al., 2009) |
| 3,6-DNBeP | *n* = 8 | 100 | [0.011–0.121] 30 | LOQ: 0.2 pg | Japan | (Hasei et al., 2011) |

n.d., not detected (below the limit of detection); n.a., not available.
[a] Median is calculated for positive samples only (concentration above the limit used for quantification).
[b] Country where samples have been collected.
[d] Picogram per injection.

hair analysis, such as the common idea that hair analysis could not be a reliable indicator of environmental exposure or internal body burden and should only be viewed as a supportive tool (Harkins and Susten, 2003). Although similar doubts had first called into question the use of hair analysis for clinical or forensic purposes (Wennig, 2000), the current widespread use of this matrix in this field definitely demonstrates its relevance (Nakahara, 1999; Boumba et al., 2006; Pragst and Balikova, 2006). The rise in the use of hair for the biomonitoring of human exposure to organic pollutants that we are currently noticing has been delayed because their concentration is significantly lower (typically picograms per milligram of hair down to below picograms per gram for polychlorinated biphenyls (PCBs) and dioxins) (Tables 1–8) than those of medical drugs and drugs of abuse, that are mostly present at concentration levels of nanograms per mg (Pragst and Balikova, 2006).

The difficulty to evaluate whether a method is sensitive enough to demonstrate human exposure has been highlighted through several studies. Although the ultimate proof of method remains positive detection in field samples, results below the limit of detection may be interpreted in different ways. On the one hand, negative results may indicate that the method is not sensitive enough; on the other hand, it may lead to think that examined people are not exposed to the target compounds or are exposed at lower levels than initially expected (Fig. 2). However, the question that remains is: what is the expected level of exposure? For drugs, the concentration in a biological matrix corresponds to a "typical" intake (to reach the therapeutic zone for medical drugs or the amount corresponding to a classical dose for drugs of abuse) (Pragst and Balikova, 2006). Even if the concentration can vary, on the whole, there is limited need to reach limits of detection far below the expected concentration. In the field of environmental/occupational exposure, there is no such "therapeutic zone" below which sensitivity would not be relevant, in that the level of exposure can vary in several orders of magnitude between people. Moreover, history demonstrates that levels of exposure previously believed safe may actually be harmful, as shown for PCBs and dioxins, for which the

**Table 7**
Concentration of polychlorinated biphenyls (PCBs) in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (pg/g)[a] | Limit of detection/quantification (pg/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| ∑PCBs (99, 118, 138, 149, 153, 170, 180) | *n* = 14, 26–68y | 79 | [<2000–44700] 1050 | LOD: 500 | Europe[n] | (Covaci and Schepens, 2001) |
| | *n* = 47[d] | n.a. | [n.d.–44.7] n.a. | LOD: 0.3–2 | Europe[f] | (Covaci et al., 2002b) |
| ∑PCBs (*n* = 48) | *n* = 10, 25–53y | 100 | [n.a.] 72400 | LOD: 0.01–0.32[k] | USA | (Altshul et al., 2004) |
| ∑PCBs (*n* = 27) | *n* = 40 | 100 | [12300–736000] n.a. | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 8 | *n* = 40 | 95 | [20–11630] 20–4070[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 15 | *n* = 74, 2–9y | 3 | [n.d.–94000] n.a | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB 18 | *n* = 40 | 0 | n.d. | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 28, 52, 101 | *n* = 14, 26–68y | 0 | n.a. | LOD: 500 | Europe[g] | (Covaci and Schepens, 2001) |
| PCB 28, 101 | *n* = 47[d] | 0 | n.d. | LOD: 0.3–2[k] | Europe[f] | (Covaci et al., 2002b) |
| PCB28 | *n* = 5[h], 20–40y | 100 | [36–666] n.a | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 10, 25–53y | n.a. | [n.a.] 720 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| | *n* = 40 | 100 | [650–247090] 2350–18760[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 44 | *n* = 10, 25–53y | n.a. | [n.a.] 1080 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| | *n* = 40 | 50 | [n.d.–27910] n.d.–9000[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB52 | *n* = 5[h], 20–40y | 100 | [96–755] n.a. | n.a | Italy | (Tirler et al., 2006) |
| | *n* = 74, 2–9y | 99 | [n.d.–190000] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| | *n* = 10, 25–53y | n.a. | [n.a.] 1540 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| | *n* = 40 | 100 | [200–53980] 1230–9350[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB60 | *n* = 74, 2–9y | 69 | [n.d.–6800] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| | *n* = 10, 25–53y | n.a. | [n.a.] 400 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| PCB 66 | *n* = 10, 25–53y | n.a. | [n.a.] 1120 | LOD: 10–320 | USA | (Altshul et al., 2004) |
| | *n* = 40 | 100 | [170–74650] 590–13780[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 70 | *n* = 10, 25–53y | n.a. | [n.a.] 1300 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| PCB77 | *n* = 64, 38y[f] | n.d. | [4.27–314] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44y[c,f] | n.d. | [20.5–2630] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 1[j], 37y | 100 | [22.7–25.5] n.a. | n.a | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [3.1–35.4] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [17.2–46.1] 35.2 | LOD: 3.9–5.0[k] | Japan | (Nakao et al., 2002) |
| | *n* = 40 | 90 | [60–17590] 150–11420[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 77/110 | *n* = 10, 25–53y | n.a. | [n.a.] 2720 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| PCB81 | *n* = 1[j], 37y | 0 | <1 | LOD: 1 | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 0 | <1 | LOD: 1 | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [1.22–3.29] 2.34 | LOD: 3.9–5.0[k] | Japan | (Nakao et al., 2002) |
| | *n* = 40 | 60 | [60–8590] 170–3900[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 84 | *n* = 10, 25–53y | n.a. | [n.a.] 1340 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| PCB 95 | *n* = 10, 25–53y | n.a. | [n.a.] 1700 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| PCB101 | *n* = 5[h], 20–40y | 100 | [387–1348] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 10, 25–53y | n.a. | [n.a.] 2720 | LOD: 10–320[k] | USA | (Altshul et al., 2004) |
| | *n* = 40 | 100 | [470–68870] 690–9070[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB103 | *n* = 74, 2–9y | 58 | [n.d.–20000] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB105 | *n* = 1[j], 37y | 100 | [249–305.8] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [29.3–249.0] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 74, 2–9y | 27 | [n.d.–6900] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| | *n* = 40 | 82 | [70–52890] 150–10220[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB114 | *n* = 1[j], 37y | 100 | [32.1–39.1] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 86 | [<1–35.9] n.a. | LOD: 1 | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 80 | [70–7180] 130–3130[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB118 | *n* = 42, ado[e] | 100 | [400–10000] 1700 | LOD: 100–200[k] | Romania | (Covaci et al., 2008) |
| | *n* = 1[j], 37y | n.d. | [896.4–1253] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [127.6–896.4] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 70 | [n.d.–7010] 160–1710[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB123 | *n* = 1[j], 37y | 100 | [9.5–20.3] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 86 | [<1–9.5] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 72 | [n.d.–18890] n.a.–1960[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB126 | *n* = 64, 38y[f] | n.d. | [<0.30–34.3] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44y[c,f] | n.d. | [<0.30–27.9] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 1[j], 37y | 100 | [3.6–4.8] n.a. | LOD: 1 | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 57 | [<1–3.6] n.a. | n.a. | Italy | (Tirler et al., 2006) |

Table 7 (*Continued*)

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (pg/g)[a] | Limit of detection/quantification (pg/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| | *n* = 6, 23–40y | 100 | [2.69–4.41] 3.33 | LOD: 3.9–5.0[k] | Japan | (Nakao et al., 2002) |
| | *n* = 40 | 20 | n.a. | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB128 | *n* = 74, 2–9y | 13 | [n.d.–5500] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| | *n* = 40 | 95 | [60–16800] 290–3670[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB138 | *n* = 42, ado[e] | 86 | [200–7300] 900 | LOD: 100–200[k] | Romania | (Covaci et al., 2008) |
| | *n* = 5[h], 20–40y | 100 | [374–2102] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 100 | [490–82650] 1460–12410[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| | *n* = 3 | 100 | [1.1–3.2] | n.a. | Luxembourg | (Dauberschmidt and Wennig, 1998) |
| PCB143 | *n* = 74, 2–9y | 1.4 | [n.d.–1200] n.a. | LOD: 2–60 | China | (Zhang et al., 2007) |
| PCB153 | *n* = 42, ado[e] | 100 | [200–20500] 2100 | LOD: 100–200[k] | Romania | (Covaci et al., 2008) |
| | *n* = 5[h], 20–40y | 100 | [332–2174] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 97 | [80–3200] 390–1790[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| | *n* = 3 | 100 | [1.8–4.9] | n.a. | Luxembourg | (Dauberschmidt and Wennig, 1998) |
| PCB154 | *n* = 74, 2–9y | 7 | [n.d.–1400] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB156 | *n* = 1[j], 37y | 100 | [247.1–388] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [43.3–247.2] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 20 | [n.d.–11070] n.a.–3150 | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB157 | *n* = 1[j], 37y | 100 | [44.6–65.7] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [5.2–46.8] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 20 | [n.d.–9410] n.a.–2720[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB167 | *n* = 1[j], 37y | 100 | [75.4–123.2] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [14.7–75.4] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 95 | [80–2260] 380–1730[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB169 | *n* = 64, 38y[f] | n.d. | [<0.38–12.8] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44y[c,f] | n.d. | [<0.38–9.55] n.a. | LOD: 0.25–0.38[k] | Japan | (Nakao et al., 2005) |
| | *n* = 1[j], 37y | 100 | [1.3–1.5] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 28 | [<1–2.1] | LOD: 1 | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [0.374–1.09] 0.762 | LOD: 3.9–5.0[k] | Japan | (Nakao et al., 2002) |
| | *n* = 40 | 55 | [n.d.–1190] n.a.–780[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB170 | *n* = 42, ado[e] | 76 | [200–3600] 400 | LOD: 100–200[k] | Romania | (Covaci et al., 2008) |
| | *n* = 40 | 100 | [250–16020] 400–5420[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB173 | *n* = 74, 2–9y | 43 | [n.d.–2300] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB180 | *n* = 42, ado[e] | 81 | [200–10700] 1400 | LOD: 100–200[k] | Romania | (Covaci et al., 2008) |
| | *n* = 5[h], 20–40y | 100 | [206–623] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 92 | [100–9240] 160–2770[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| | *n* = 3 | 100 | [0.5–1.3] | n.a. | Luxembourg | (Dauberschmidt and Wennig, 1998) |
| PCB182 | *n* = 74, 2–9y | 16 | [n.d.–3200] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB 187 | *n* = 40 | 95 | [80–10070] 310–1690[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB189 | *n* = 1[j], 37y | 100 | [21.8–45.9] n.a. | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 6[i], 20–40y | 100 | [6.8–25.9] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 40 | 87 | [60–14200] 160–2290[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB 195 | *n* = 40 | 100 | [180–2870] 490–1960[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB202 | *n* = 74, 2–9y | 19 | [n.d.–8100] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB205 | *n* = 74, 2–9y | 11 | [n.d.–930] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB 206 | *n* = 40 | 100 | [250–2650] 400–1880[l] | LOD: 20–120[k] | China | (Zhao et al., 2008) |
| PCB207 | *n* = 74, 2–9y | 4 | [n.d.–10100] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB208 | *n* = 74, 2–9y | 13 | [n.d.–3700] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |
| PCB209 | *n* = 74, 2–9y | 20 | [n.d.–5100] n.a. | LOD: 2–60[k] | China | (Zhang et al., 2007) |

n.d., not detected (below the limit of detection); n.a., not available.

[a] Median is calculated for positive samples only (concentration above the limit used for quantification).
[b] Country where samples have been collected.
[c] Reported occupational or specific exposure.
[d] 30 out of the 47 people had a history of occupational exposure.
[e] adolescents.
[f] 35 people from Greece, 2 from Romania and 10 from Belgium.
[g] 2 people from Romania, 4 people from Belgium, 8 people from Greece.
[h] Three persons providing 1 sample plus 1 person providing 2 samples collected at different years.
[i] Three persons providing 1 sample plus 1 person providing 3 samples collected at different years.
[j] Hair from the same person collected at 3 different times.
[k] LOD not detailed for each molecule.
[l] Range of values for the different sites investigated.

current "no observable adverse effect level" (NOAEL) is nearly one million-fold lower than it initially was (Solomon and Huddle, 2006).

In the absence of other indications, one possible way to assess whether a method is sensitive enough is to compare its sensitivity with previously published values. This approach is of course limited to chemicals that have previously been investigated. Moreover, as presented here for lindane and DDT (Fig. 2), published values may concern different countries or regions with different levels of exposure of people, which limits direct transposition. This was demonstrated for DDT and DDE, which are detected in human

**Table 8**
Concentration of dioxins (PCDD and PCDF) in human hair, rate of positive detection, population, limit of detection/quantification of the method and country where samples were collected, reported by previous studies.

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (pg/g)[a] | Limit of detection/quantification (pg/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| $\sum$PCDDs[i] | *n* = 6, 23–40y | n.d. | | | | |
| 2378-TCDD | *n* = 64, 38[d] | n.d. | [<0.088–4.08] 0.467[h] | LOD: 0.088 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.088–11.7] 1.45[h] | | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [n.d.–0.87] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [1.98–2.93] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y[j] | – | <0.2 | LOD: 0.2 | Italy | (Tirler et al., 2001) |
| | *n* = 5[f], 20–40y | 20 | [<0.02–0.04] n.a. | LOD: 0.02 | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [0.164–1.05] 0.42 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total TCDD | *n* = 2[e,c] | n.d. | [5.2–17] | n.a. | China | (Luksemburg et al., 1997) |
| 12378-PeCDD | *n* = 64, 38[d] | n.d. | [<0.100–0.830] 0.094[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,a] | n.d. | [<0.100–9.94] 0.707[h] | | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [n.d.–7.4] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [4.22–4.95] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | 0.3 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 5[f], 20–40y | 80 | [<0.02–0.28] n.a. | LOD: 0.02 | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [0.123–0.878] 0.44 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total PeCDD | *n* = 2[e,c] | n.d. | [11–49] | n.a. | China | (Luksemburg et al., 1997) |
| 123478-HxCDD | *n* = 64, 38[d] | n.d. | [<0.100–2.79] 0.372[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–16.1] 1.55[h] | | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [3–31] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [1.77–2.04] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 5[f], 20–40y | 100 | [0.07–0.29] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 83 | [n.d.–1.96] 1.47 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 123578-HxCDD | *n* = 2[e,c] | n.d. | [15–130] | n.a. | China | (Luksemburg et al., 1997) |
| 123678-HxCDD | *n* = 64, 38[d] | n.d. | [<0.100–22.9] 1.10[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–18.3] 1.38[h] | | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [4.71–5.24] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 5[f], 20–40y | 100 | [0.09–0.32] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [0.536–1.10] 0.79 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 123789-HxCDD | *n* = 2[e,c] | n.d. | [7.5–73] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [3.12–3.30] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 5[f], 20–40y | 100 | [0.05–0.22] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 50 | [n.d.–0.376] 0.29 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total HxCDD | *n* = 2[e,c] | n.d. | [72–650] | n.a. | China | (Luksemburg et al., 1997) |
| 1234678-HpCDD | *n* = 64, 38[d] | n.d. | [<0.120–62.6] 9.48[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.120–70.2] 15.5[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [320–6900] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [15.7–16.8] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | 3.2 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* =6[g], 20–40y | 100 | [0.48–3.2] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [2.74–6.78] 4.03 | LOD: 0.12 | Japan | (Nakao et al., 2002) |
| Total HpCDD | *n* = 2[e,c] | n.d. | [450–4000] | n.a. | China | (Luksemburg et al., 1997) |
| OctaCDD | *n* = 64, 38[d] | n.d. | [17.4–446] 182[h] | LOD: 0.25 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44 [d c] | n.d. | [15.4–465] 178[h] | | Japan | (Nakao et al., 2005) |
| | *n* = 2[e,c] | n.d. | [2800–27000] | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | n.d. | [24.0–87.7] | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 1, 37y | – | 22.5 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* =6[g], 20–40y | 100 | [2.32–22.5] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 6, 23–40y | 100 | [17.4–97.7] 34.1 | LOD: 0.25 | Japan | (Nakao et al., 2002) |
| 2378 TCDF | *n* = 1, 37y | 100 | 0.4 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.088–1.42] 0.454[h] | LOD: 0.088 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.088–14.8] 0.932[h] | LOD: 0.088 | Japan | (Nakao et al., 2005) |
| | *n* =6[g], 20–40y | 100 | [0.03–0.4] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [0.99–4.6] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [12.6–24.9] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.289–1.03] 0.55 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total TCDF | *n* = 2[e,c] | 100 | [29–80] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| 12378 PCDF | *n* = 1, 37y | 100 | 0.2 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–1.40] 0.156[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–2.76] 0.466[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |

Table 8 (*Continued*)

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (pg/g)[a] | Limit of detection/quantification (pg/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| | *n* =6[g], 20–40y | 100 | [0.06–0.23] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | 11 | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [13.0–23.7] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.221–1.11] 0.51 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 23478 PCDF | *n* = 1, 37y | 100 | 0.5 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–0.450] 0.129[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [0.100–4.68] 0.540[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* =6[g], 20–40y | 100 | [0.11–0.52] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [1.9–10] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [10.0–18.8] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.356–1.67] 0.52 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total PCDF | *n* = 2[e,c] | 100 | [27–120] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| 123478 HxCDF | *n* = 1, 37y | 0 | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–0.600] 0.085[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–7.03] 0.538[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 5[f], 20–40y | 100 | [0.13–0.53] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [14–150] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [7.05–12.02] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.163–0.971] 0.69 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 123678 HxCDF | *n* = 1, 37y | 0 | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–0.680] 0.125[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–5.40] 0.533[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 5[f], 20–40y | 100 | [0.08–0.37] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [3.1–29] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [6.62–10.7] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 50 | [n.d.–0.617] 0.24 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 234678 HxCDF | *n* = 1, 37y | 0 | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–0.730] 0.059[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.100–0.280] 0.020[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 5[f], 20–40y | 100 | [0.15–0.63] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [1.8–10] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [5.54–8.43] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.387–0.971] 0.68 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| 123789 HxCDF | *n* = 1, 37y | 0 | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.100–0.810] 0.167[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44 [d c] | n.d. | [<0.100–7.22] 0.694[h] | LOD: 0.100 | Japan | (Nakao et al., 2005) |
| | *n* = 5[f], 20–40y | 100 | [0.02–0.06] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [1.9–21] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [1.47–2.44] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.158–1.06] 0.59 | LOD: 0.088–0.10 | Japan | (Nakao et al., 2002) |
| Total HxCDF | *n* = 2[e,c] | 100 | [42–400] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| 1234678 HpCDF | *n* = 1, 37y | 100 | 1.3 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.120–6.66] 1.10[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44 [d c] | n.d. | [<120–43.3] 6.73[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* =6[g], 20–40y | 100 | [0.32–1.65] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [31–400] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [12.1–17.7] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.753–24.4] 1.42 | LOD: 0.12 | Japan | (Nakao et al., 2002) |
| 1234789 HpCDF | *n* = 1, 37y | 0 | <0.5 | 0.5 | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.120–0.860] 0.043[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44 [d c] | n.d. | [<0.120–1.64] 0.145[h] | LOD: 0.12 | Japan | (Nakao et al., 2005) |
| | *n* = 5[f], 20–40y | 100 | [0.06–0.30] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [6.9–68] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| | *n* = 2[e,c] | 100 | [n.d.–21.3] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 83 | [n.d.–0.81] 0.24 | LOD: 0.12 | Japan | (Nakao et al., 2002) |
| Total HpCDF | *n* = 2[e,c] | 100 | [55–640] n.a. | n.a. | China | (Luksemburg et al., 1997) |
| OCDF | *n* = 1, 37y | 100 | 3.2 | n.a. | Italy | (Tirler et al., 2001) |
| | *n* = 64, 38[d] | n.d. | [<0.25–193] 16.0 | LOD: 0.25 | Japan | (Nakao et al., 2005) |
| | *n* = 68, 44[d,c] | n.d. | [<0.25–145] 22.0 | LOD: 0.25 | Japan | (Nakao et al., 2005) |
| | *n* =6[g], 20–40y | 100 | [0.24–3.2] n.a. | n.a. | Italy | (Tirler et al., 2006) |
| | *n* = 2[e,c] | 100 | [80–960] n.a. | n.a. | China | (Luksemburg et al., 1997) |

Table 8 (*Continued*)

| Compounds (parents and metabolites) | Population (*n*), age | Positive detection (%) | Level of concentration (range) median (pg/g)[a] | Limit of detection/quantification (pg/g) | Country[b] | Reference |
|---|---|---|---|---|---|---|
| | *n* = 2[e,c] | 100 | [7.63–9.10] n.a. | n.a. | China | (Luksemburg et al., 2002) |
| | *n* = 6, 23–40y | 100 | [0.728–65.5] 2.5 | LOD: 0.25 | Japan | (Nakao et al., 2002) |

n.d., not detected (below the limit of detection); n.a., not available.

[a] Median is calculated for positive samples only (concentration above the limit used for quantification).

[b] Country where samples have been collected.

[c] Reported occupational or specific exposure.

[d] Median age.

[e] Collected from 2 barbers, number of donors unknown.

[f] Three persons providing 1 sample plus 1 person providing 2 samples collected at different years.

[g] Three persons providing 1 sample plus 1 person providing 3 samples collected at different years.

[h] mean.

[i] Sum of 2,3,7,8-Tetra Chlorinated Dibenzo-p-Dioxin; 1,2,3,7,8-PentaCDD; 1,2,3,4,7,8-HexaCDD; 1,2,3,6,7,8-HexaCDD; 1,2,3,7,8,9-HexaCDD; 1,2,3,4,6,7,8-HeptaCDD; OctaCDD.

[j] Hair from the same person collected at 3 different times.

tissues at highly-varying concentration levels depending on the country where samples were collected (Jaga and Dharmani, 2003). In that regard, the possibility to obtain values from different areas corresponding to populations with different lifestyles (diet, industrialization, agriculture, etc) can gain lot of knowledge.

The example of lindane and p,p′-DDT, two organochlorine pesticides both categorized as persistent organic pollutants (POPs), which we are presenting here (Fig. 2 and Fig. 3) is a good illustration of the aforementioned issue. Since the first reports describing their detection in hair were published in 1998-1999 (Dauberschmidt and Wennig, 1998; Neuber et al., 1999), the sensitivity of the methods has been increased by 100 to 1000 (Fig. 3), mainly due to technical progresses in general, and more recently to the use of solid phase microextraction associated with GC–MS/MS (Salquebre et al., 2011). In the process, the rate of positive detection has increased from values close to zero to 100% in most of the recent publications (Table 1). In line with previous reports concerning other matrices (*e.g.* adipose tissue, breast milk, serum) (Jaga and Dharmani, 2003), the range of concentrations may vary significantly in the different countries, resulting in the fact that a limit of detection enabling a 100% positive detection rate in a region may be insufficient in another one

## 4. Relevance of hair analysis for the biomonitoring of exposure to organic pollutants

"Biomonitoring", which is the contraction of "biological monitoring", is generally defined as the assessment of human exposure to chemicals by measuring the chemicals, their metabolites or reaction products in biological matrices. These measurements can be used to assess the internal dose (biomarker of exposure) or the biological response of the body to the exposure (biomarker of effect) (Needham et al., 2007; Stahl et al., 2010). Although no study has hitherto investigated hair analysis as a possible biomarker of effect, several published datasets may be used to discuss its relevance as a biomarker of exposure. In that regard, the main question that has to be addressed when assessing the usefulness of this biomarker is: are values obtained from analyses purely random and meaningless or can they be interpreted in relation to logical considerations? In other words, is hair analysis sensitive enough to demonstrate inter-individual differences that make sense? Is it sufficiently repeatable? Can it be used to highlight trends, define reference levels and identify specific exposure? Ultimately, can it be used to assess the dose that enters the body or any corresponding concentration in target organs?

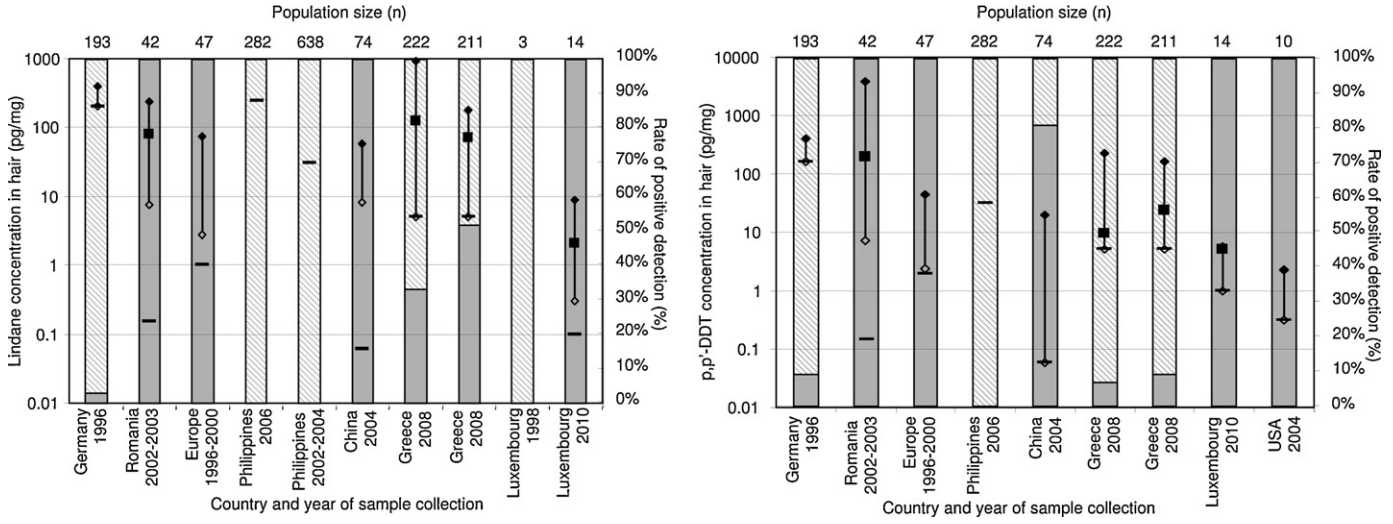


**Fig. 2.** Concentration of lindane (left chart) and p,p′-DDT (right chart) in human hair and rate of positive detection reported for different countries. "◇" lower value detected, "♦" higher value detected, "■" median value, "–" limit of detection/quantification of the method. Dark bars represent the percentage of positive detection; bright bars represent the percentage of samples with concentration below the LOD or LOQ.

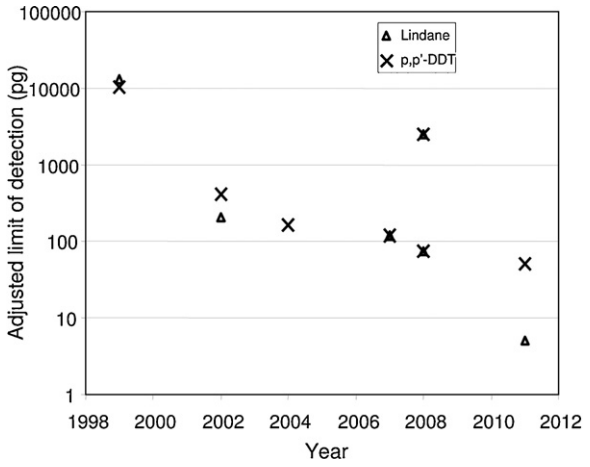


**Fig. 3.** Evolution of the sensitivity of analytical methods for the detection of lindane "△" and p,p′-DDT "×" during the last 12 years. Limits of detection collected from the literature are adjusted to the amount of hair used for analysis in each study (*i.e.* adjusted limit equals to the limit expressed in pg/mg, multiplied by the weight of hair (mg) used).

Although differences in chemical concentration in hair may be observed between countries, as highlighted for lindane and DDT in Fig. 2 and for other pollutants in general (Tables 1–8), geographical comparison remains difficult to interpret because of the heterogeneousness of the populations under study and the generally limited number of participants which does not allow adequate statistical analysis; especially when considering that the concentration range of a chemical within a population can cover several orders of magnitude. Nevertheless, in several studies, significant differences have already been observed between sub-groups in that higher concentration of chemicals was detected in hair from people suspected to undergo higher exposure compared to the control group. For instance, Japanese incineration workers displayed significantly increased concentration of PCDDs, PCDFs and PCBs than the general population (up to 7.4 times more for penta-PCDD) (Nakao et al., 2005). In another work conducted in Japan, smokers were shown to have higher levels of polycyclic aromatic hydrocarbons in hair than non-smokers (Toriba et al., 2003). More recently, levels of PBDEs, PBBS and PCBs were found to be significantly higher in hair of residents around e-waste disassembly sites in China in comparison with residents from a control site (Zhao et al., 2008).

Correlations were also observed between chemical concentration in hair and their presence in human surroundings. For instance, Kang et al. (2011), reported a positive significant correlation between the concentration of PBDE-183 in hair and in dust home in China. These findings are in line with those of a previous study conducted in the USA, which demonstrated that PBDE-47 concentrations in human milk and in dust were correlated (Wu et al., 2007). Concerning organochlorines and PCBs, Covaci et al. (2008), suggested that concentration detected in hair of Romanian adolescents would be in line with elevated concentration detected in soil and food in the same area (Covaci et al., 2001; Dragan et al., 2006). Hair analysis also enabled highlighting more subtle and unexpected differences between sub-populations such as the significantly higher concentration of organochlorines and PCBs detected in females' hair compared to males (Altshul et al., 2004; Zhang et al., 2007; Covaci et al., 2008). In particular, Covaci et al. (2008), demonstrated that the mean concentration of p,p′-DDT and p,p′-DDE were 25 and 10 times higher for girls respectively, which confirms previous findings describing higher concentration of OC in female serum compared with males (Dirtu et al., 2006).

The relationships observed between the concentration of chemicals in hair and in other matrices (fluids and tissues) also demonstrate that hair is representative of the internal dose. One of the best illustrations was provided by Covaci and Schepens (Covaci and Schepens, 2001) who reported that the profiles of PCB concentration in hair and in other matrices (serum, milk and adipose tissue) were similar. Correlations were also observed between hair and serum concentration for hexachloro dibenzo-p-dioxin (HxCDD), pentachloro dibenzofuran (PeCDF), pentachloro biphenyl (PeCB) and hexachloro biphenyl (HxCB) (Nakao et al., 2002) and p,p′-DDE (Altshul et al., 2004). In addition, Nakao et al. (2002), who investigated 21 organic pollutants (PCDDs, PCDFs and PCBs) in hair and serum samples collected from 6 donors, reported that a higher rate of positive detection was obtained by means of hair analysis compared with serum, in the process highlighting the superiority of hair over serum analysis for identifying exposure. Comparing the two matrices demonstrated that analyzing hair only would have resulted in 5% of "false negative assessment" (absence of a chemical that was however detected in the other matrix) whereas analyzing serum only would have led to 30% of false negative assessment. Similarly, the study conducted by Ostrea et al. (2006) on 449 pregnant women in the Philippines allowed detecting 6 among 11 target pesticides, in proportion ranging from 0.2% to 11.9% of positive detection for pretilachlor and bioallethrin respectively. On the contrary, serum analysis only enabled the detection of one (propoxur) in the proportion of 0.7% compared to 10.5% obtained with hair analysis.

Information on possible relationships between hair and tissues may also be obtained from studies on animals, which contrary to studies on human, allow easier analysis of any possible matrix (*e.g.* muscle, fat, brain, and organs) (Covaci et al., 2004). In a study carried out on hedgehogs from Belgium and The Netherlands, significant correlation was observed between concentrations in hair and liver, kidney and muscle tissues for PBDEs (D'Havé et al., 2005).

Although proportional relationships between intake and hair concentration have already been described in humans for some drugs (*e.g.* ethanol) (Appenzeller et al., 2007a), such a relationship is unlikely to be demonstrated for organic pollutants in as much as the dose to which people are chronically exposed is unknown. Once again, studies on animals under controlled exposure remains the only possibility of comparing hair concentration of chemicals with the dose administrated. It also provides the opportunity of extrapolating data obtained from animals to human (Table 9). As calculated in Table 9, some subjects with particularly high concentration of pesticides in hair would undergo significant level of exposure (*e.g.* 4 g/year for diazinon). Of course, precautions have to be taken regarding such an extrapolation. For instance, contrary to animals under controlled exposure, human may be exposed through several pathways (ingestion, inhalation, dermal contact) that may contribute to different extents to the total exposure. Inter-species differences in metabolism and elimination of chemicals also have to be taken into account. Nevertheless, extrapolation to human provides at least rough indication on the amount of pollutant people have been exposed to, which is more useful than a matrix concentration only as it can be compared to levels of exposure that are known to induce biological effects. Conversely, the calculated level of exposure of human can be applied to animals to investigate possible affections associated with realistic environmental or occupational levels of exposure.

## 5. Limitations still associated with hair matrix

### 5.1. External deposition of chemicals on hair surface

One of the most recurrent criticisms concerning hair analysis for the biomonitoring of human exposure to pollutants lies in the possibility of external deposition of chemicals on the hair surface.

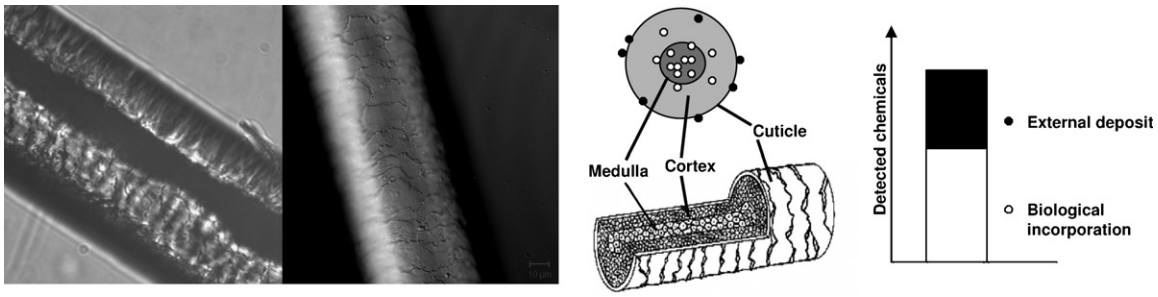


**Fig. 4.** First picture (transmitted light microscopy) shows inner hair (cortex and medulla). Second picture (confocal microscopy) shows scales composing hair surface (cuticle). Figure: left part represents hair shaft cross-section with theoretical distribution of molecules ● due to external deposition (*i.e.* contamination), and ○ incorporated from biological pathway (after exposure and diffusion in the body) among cuticle, cortex and medulla; Right part presents the corresponding theoretical representation of the total amount of chemicals detected in hair (determined in unwashed hair) and composed of both external contamination (possibly removed by hair washing) and incorporated molecules (not removed by washing).

As discussed above, chemical concentration in hair is interpreted as representative of the internal dose that people have undergone during the period in which the hair sample has grown. Although the biological mechanisms of chemical incorporation in hair are still debated, it is admitted that they are mainly incorporated from blood into living cells in the hair bulb (Pragst and Balikova, 2006). Besides incorporation from blood, chemicals can also be alternatively incorporated from deep skin compartments, and deposited from sweat and sebum, the respective contribution of the latter mechanisms being dependent on the chemical and physical properties of the compounds (Harkey, 1993; Henderson, 1993; Cone, 1996). On the whole, it is generally admitted that biologically incorporated molecules are located inside hair shafts (cortex and medulla) while external contamination is likely to remain on the surface of hair scales (*i.e.* cuticle) (Fig. 4).

In forensic toxicology, distinguishing external deposition from internally incorporated drugs is mainly used for the identification of adulterated specimens (*e.g.* by voluntary or involuntary application on hair) and to differentiate consumers from people exposed to indirect contamination (typically smoke of cannabis cigarettes) (Stout et al., 2006; Tsanaclis and Wicks, 2008). In environmental exposure, external deposition roughly concerns any possible pollutant insofar as it is likely to be present in the air and dust surrounding people. In any case, the aim of decontamination is to remove externally deposited molecules that accumulate on hair surface without removing internal chemicals which correspond to the average level of exposure of subjects.

The decontamination of hair before testing it for drugs is generally performed with organic solvents (*e.g.* dichloromethane, methanol, acetone) (Pragst and Balikova, 2006). Although organic solvents also have been used in studies investigating the presence of organic pollutants in hair (Cirimele et al., 1999; Toriba et al., 2003; Margariti and Tsatsakis, 2009; Salquebre et al., 2011), most of the studies reported the use of more gentle decontamination procedures such as deionized water (Luksemburg et al., 2002; Covaci et al., 2008; Schummer et al., 2009), or water with shampoo (Nakao et al., 2002; Altshul et al., 2004; Tirler et al., 2006; Zhao et al., 2008; Tadeo et al., 2009; Kang et al., 2011). In some studies, hair was even analyzed without being decontaminated, the authors considering that external deposition also represents chemicals to which the subjects have been exposed, and should not be removed before analysis (Ostrea et al., 2009). Nevertheless, no standardized "universal" procedure for the decontamination of hair before analysis has been set up to date and in most studies, the efficiency of the washing procedure was not assessed.

However, the few studies which investigated the effect of the washing procedure used to clean hair before analysis highlighted its relevance. Comparing unwashed hair and hair washed with shampoo just before analysis, Schramm et al. (1992) observed a significant but not uniform decrease in the concentration of PCDD/Fs congeners. Octa-CDD/Fs were reduced by 50% but the hexachlorinated congeners were removed by a factor of nearly 100. These results led to the conclusion that the PCDD/F burden could not be mainly attributed to particle deposition on hair surface. Later on, Nakao et al. (2002) demonstrated that washing hair with common surfactant decreased the levels of PCDDs and PDCFs in hair samples by 50% and 64% respectively. They also observed that washing once more had no further effect on the elimination of either chemical and that both the unwashed and washed samples contained similar composition of PCDDs and PCDFs. They concluded that PCDD/Fs were mainly deposited on hair surface via atmospheric transfer and are completely removed by the first wash. The residual amounts of these compounds were thought to be contained in the inner part of the hair. Altshul et al. (2004) reported similar observation when comparing the concentration of PCBs and organochlorine pesticides in hair washed with hot water only and hair washed with shampoo once and twice. In fact, washing with shampoo once decreased the levels of PCBs, pesticides and lipids by 25–33% on average. For the less-chlorinated congeners (PCB-8 and PCB-18), the decrease was even larger (48% and 62%). The study also demonstrated that most of the decrease occurred after the first shampoo washing: 82% of the total loss for $\sum$PCBs, 88% for p,p′-DDE. More recently, Ostrea et al. (2006) reported that washing hair with shampoo prior to analysis had no influence on the concentration of propoxur, but significantly decreased the concentration of bioallethrin.

The effect of washing hair with organic solvents was tested by Toriba et al. (2003) who analyzed polycyclic aromatic hydrocarbons (PAHs) in hair. Three different solvents were tested (methanol, n-hexane and dichloromethane), each within a cycle of three successive washings. Although different results were obtained for both the different molecules analyzed and the different solvents, the results were in line with the studies that used shampoo, in that a part of the target molecules was removed by washing (most likely the external chemicals) and a remaining part seemed to be unaffected by washing (most likely the inner chemicals). Although the most significant part of the removable chemicals was removed during the first washing, chemicals were sometimes also removed during the second and the third washing. This might be explained by the fact that washing was carried out without agitation, contrary to studies using shampoo.

Although the aforementioned experiments demonstrate that a part of the target chemicals are removed by washing while another part remains unaffected, it has to be acknowledged that none of them allows conclusive demonstration that (i) externally deposited chemicals were completely removed, and (ii) absolutely no internally incorporated chemicals were removed by washing. This uncertainty should however not be considered a limitation to

the use of hair as a biomarker of exposure. On the one hand, if a part of the externally deposited molecules becomes "unremovable", it can be considered as representative of the history of exposure of the subject. On the other hand, the removal of a limited part of internal molecules should not dramatically influence the final result, as far as it is repeatable. In this regard, considering the "easily removable chemicals" (ERC) instead of the strictly externally deposited chemicals would be more relevant.

Chemicals deposited on hair surface are not problematic themselves, keeping in mind that personal exposure may also be assessed using techniques that mainly provide information on pollutants present in air and/or dust (*e.g* wearable samplers or wiping hand with swabs) (Scherer et al., 2000; Besaratinia et al., 2002; Bouvier et al., 2006). The risk of misinterpretation lies in that chemicals deposited on hair surface are likely to be easily removed during subjects' self-washing, which may induce significant variability in chemical concentration depending on the time elapsed between hair sampling and subjects' last washing. In that regard, hair washing before analysis appears to be a necessary precaution. On the basis of the considerations presented above, some criteria may be proposed to ensure that a washing procedure is suitable to remove the ERC:

1) The hair total ERC is significantly decreased by the first hair washing
2) A steady-state is reached, *i.e*. no more chemicals (or a significantly lower amount) are removed by additional washings
3) The non-ERC that is extracted after hair destructuration (pulverization or digestion) is not affected by washing

Another approach to avoid misinterpretation due to external contamination is to analyze chemical metabolites, which are produced in the body and are unlikely to be deposited on hair surface from air or dust. In that regard, Schummer et al. (2009) investigated human exposure to PAHs by determining the concentration of monohydroxy-PAHs (PAH metabolites) in hair. As expected, the concentration of metabolites was not significantly decreased by washings performed before hair analysis. The approach is of course limited to metabolites which are unlikely to be present in the environment due to their use as active compounds themselves (*e.g*. dieldrin is both produced from the metabolization of aldrin and directly used as an active compound) or due to environmental degradation (*e.g*. DDE is produced from both metabolization and environmental degradation of DDT).

### 5.2. Influence of hair pigmentation and hair treatment

The influence of hair pigmentation (*i.e*. the melanin content of hair) has also been quoted among the possible limitations to the use of hair as a biomarker of exposure. Although this parameter has been little investigated for organic pollutants so far, the influence of melanin on drug incorporation in hair has been described for several medical drugs and drugs of abuse in studies conducted on humans (Rothe et al., 1997; Kronstrand et al., 1999, 2001; Rollins et al., 2003; Appenzeller et al., 2007b), animals (Green and Wilson, 1996; Pötsch et al., 1997; Slawson et al., 1998) or trough *in vitro* experiments (Claffey et al., 2001; Borges et al., 2003). Different results have been reported, depending on the molecules under study.

Investigating bicolor Lister-hooded rats administered with methadone in their drinking water, Green and Wilson (Green and Wilson, 1996) observed that black hair incorporated larger quantities of methadone than white hair in the ratio 21.3:1. Later on, a study conducted on tricolor guinea pigs drinking 1 mg/mL codeine solution in water, reported that codeine concentration in reddish-brown and in white hair amounted for only 50% and 25% respectively of the concentration detected in black hair (Pötsch et al., 1997). In another study carried out on rats and mice, Slawson et al. (1998) also observed significantly higher concentration of phencyclidine in black hair than yellow or non-pigmented hair, and suggested normalizing phencyclidine concentration using the ratio eumelanin to pheomelanin.

Concerning human, Rothe et al. (1997), investigating several drugs in grey hair from patients and post-mortem cases, observed that drug concentration was generally lower in white hair, although the white:pigmented ratio was different depending on the drugs (from 0.09 for metochlopramide to 1.22 for nortryptiline) and also between subjects for the same compound (white:pigmented ratio from 0.18 to 0.88 for amitriptiline). In two studies conducted on volunteers with controlled administration of codeine and selegenine respectively, Kronstrand et al. (1999, 2001) demonstrated strong exponential correlation between drug concentration in hair and melanin content. The exponential correlation between codeine concentration in hair and melanin was confirmed by Rollins et al. (2003). More recently, positive linear relationship was observed between melanin and codeine, cocaine and cocaine metabolites concentration in hair of volunteers under controlled administration. On the contrary, the absence of influence of melanin on the concentration of analytes in hair was also observed by Appenzeller et al. (2007a,b) who analyzed ethyl glucuronide concentration in hair of chronic alcohol-abusing patients enrolled in a withdrawal program. These results were rapidly confirmed on animals under controlled feeding with alcohol (Kharbouche et al., 2010).

The general conclusions suggest that the incorporation of basic drugs (positively charged at physiological pH) from blood would be enhanced by electrostatic interactions with the carboxylic groups of melanin while neutral drugs would be less affected by hair pigmentation.

Recently, the effect of hair pigmentation on the incorporation of pesticide metabolites in hair was also investigated by Margariti and Tsatsakis (2009) who analyzed metabolites of dimethoate (an organophosphate used as an insecticide) in hair of two-colored rabbits after controlled exposure (Margariti and Tsatsakis, 2009). Dimethoate was provided in drinking water at two different levels (12 and 24 mg/kg) and hair was collected after 4 and 6 months of exposure. The results demonstrated significant differences between pigmented and white hair only for one of the two metabolites that were analyzed. Dimethylphosphate (DMP) concentration was higher in pigmented hair after both 4 and 6 months and for both levels of exposure, although the pigmented:white ratio did not exceed 1.8. No influence of hair pigmentation was observed for the other metabolites analyzed (dimethylthiophosphate, DMTP).

Finally, although the concentration of some chemicals in hair is likely to be influenced by hair pigmentation, a possible effect of melanin on chemicals incorporation in hair should affect results interpretation in the case of biomonitoring of environmental exposure less than in the forensic field. Since pollutants (unlike drugs) concentration in human hair may vary in several orders of magnitude between subjects (Tables 1–8), limited modification of the concentration of organic pollutants in hair due to melanin will not change the significance of the results. Although further research is needed to investigate the question of how hair pigmentation should be taken into account in the determination of organic pollutants in hair, one may keep in mind that similar problem may exist in the conventional samples too, such as the influence of creatinine in the urine matrix.

One last possible limitation to the use of hair for the biomonitoring of environmental and occupational exposure concerns hair-care treatment. Once again, although this aspect is currently highly investigated for drugs of abuse (Baeck et al., 2011; Gareri et al., 2011), information regarding organic pollutants is scarce. The only

study that compared the concentration of PCBs, HCHs and DDTs in artificially-colored hair versus non-colored hair observed slight but not significant differences between the two categories (Covaci et al., 2002a). Here again, although this parameter might not significantly affect results interpretation (at least for the more stable chemicals) further research is necessary to accurately assess to what extent hair treatment might be integrated in the results. Meanwhile, gathering information on hair treatment by means of questionnaires filled in parallel to hair collection, as suggested by Schramm (Schramm, 2008), appears highly relevant.

## 6. Critical evaluation of the current literature about the use of hair as a biomarker of exposure in epidemiological studies

Biomonitoring aims at assessing subjects' level of exposure in order to correlate it to diseases onset and to biological effects in general. In that regard, hair presents the advantage of providing wider windows of detection than urine or blood, and being less affected by short-term variations in the exposure and therefore more representative of the average level of exposure. As a result, values obtained from hair analysis might be more relevant with the aim of investigating possible correlation with biological effects in epidemiological studies involving extended population. Nevertheless, several aspects have to be considered to preserve the advantages associated with hair and to consolidate its position alongside the more classical matrices.

### 6.1. Amount of hair sampled

The first aspect directly concerns sampling. As often mentioned, one of the main advantages of hair over other biological matrices lies in its easiness of sampling that does not require medical staff, causes no pain, is non-invasive and can be performed without specific measures to preserve a subject's intimacy (as is the case for urine). As a consequence, hair sampling allows reaching a high level of compliance from volunteers and can be asked to sensitive population such as children or pregnant women (Pichini et al., 2003; Woodruff et al., 2003). However, methods presented in some studies require a substantial amount of hair (*e.g.* up to 5 or 10 g) (Tirler et al., 2001; Nakao et al., 2005; Tirler et al., 2006; Zhao et al., 2008). Although using such a significant amount of hair allows increasing the sensitivity of the method and may be conceivable on limited population for method development, it may represent a heavy limitation to its use in epidemiological studies involving extended population as (i) volunteers' compliance may dramatically decrease as the amount of hair requested increases and (ii) collecting a significant amount of hair may not be possible from some subjects (infants and young children) (Aleksa et al., 2011). In that regard, priority has to be given to analytical methods requiring limited amounts of hair and new methods have to be developed bearing in mind this aspect (Aleksa et al., 2011; Salquebre et al., 2011).

### 6.2. Multi-class methods

Another observation concerning previously published works on hair analysis is that most of them focused on specific compounds or on one chemical class only (Tables 1–8), contrary to studies using other biological matrices (blood, urine or milk) or environmental matrices or food where multi-class methods are more common (Barr et al., 2002; Mage et al., 2004; González-Rodríguez et al., 2005; Fernandez-Alvarez et al., 2008). For instance, the most investigated pesticides in hair are by far organochlorines and only few studies investigated other pesticide classes. Cirimele et al. (1999)

**Table 9**
Human daily and annual dose of pesticides extrapolated from animals under controlled chronic exposure.

| Pesticide | p,p'-DDT | | Aldrin | | Diazinon | |
|---|---|---|---|---|---|---|
| Animal | Rats Sprague-Dawley | | | | Rabbits New Zealand | |
| Controlled exposure | 0.01 mg/L in drinking water; 4 weeks | | | | In drinking water; 4 months | |
| Daily dose (μg/kg) | 1[a] | | | | 8000 | 15000 |
| Hair concentration (pg/mg) | 7900 | 2800 | | | 170 | 230 |
| Reference | (Shin et al., 2004) | | | | (Tutudaki et al., 2003) | |
| Human | Typical range | Highest detected | Median value (USA) | Highest detected | Mean value in 5 positive subjects | |
| Hair concentration (pg/mg) | 10 | 3920 | 0.24 | 5.8 | 2.8 | |
| Reference | Fig. 2 | (Covaci et al., 2008) | (Altshul et al., 2004) | (Zhang et al., 2007) | (Tsatsakis et al., 2008a) | |
| Extrapolated Daily dose (ng/kg) | 1.26 | 496 | 0.0857 | 2.07 | 131,765 | 182,609 |
| Annual dose for a 70 kg adult (μg) | 32 | 12,677,974 (12.7 mg) | 2.2 | 53 | 3,366,588 (3.37 g) | 4,665,652 (4.66 g) |

[a] Considering a daily water intake of 10 mL/100 g.

were probably the first to simultaneously analyze several agricultural pesticides from different chemical classes in hair collected from farm workers. Later on, the team of Ostrea (Ostrea et al., 2006, 2008, 2009; Posecion et al., 2006) used a method including organochlorines, carbamate, organophosphates, pyrethroids and chloroacetaniline applied to populations composed of hundreds of subjects without occupational exposure. Although the high limits of detection only allowed a limited number of positive cases detected, these studies clearly demonstrated that a high level of concentration of non-organochlorine pesticides could be detected in hair in the general population. A common problem associated with multi-class methods lies in the fact that analytical sensitivity is directly affected by the specificity of the method. As a result, sensitivity generally decreases with an increasing number of molecules from different chemical classes (with different physic-chemical properties) that are simultaneously analyzed in one run. On the other hand, priority lists defined by authorities are based on the risks associated with molecules and generally include compounds from different chemical classes without taking into account technical feasibility (Pitarch et al., 2007; Sorensen et al., 2010). Moreover, the importance of cumulative exposure to chemical mixtures, even at low levels, is increasingly pointed out (Boobis et al., 2008; Reffstrup et al., 2010). These considerations highlight the need to develop multi-class methods with high sensitivity for the biomonitoring of human exposure to pesticides based on hair analysis. As quoted above, recently-developed methods based on SPME coupled with GC-MS/MS enabled researchers to reach high sensitivity while analyzing several different classes of pesticides simultaneously (Salquebre et al., 2011). Efforts should be continued in this direction, to the benefit of studies investigating the consequences of chronic exposure to low levels of chemicals.

### 6.3. Limit of detection and limit of quantification

An overview of the literature dealing with the analysis of organic pollutants in hair also underlines differences between studies regarding the validation parameters of the methods used. As described in works focusing on the validation of bioanalytical methods, there is a great deal of confusion over the terms related to the ability to detect low concentrations, and the limit of detection (LOD) must be differentiated from the limit of quantification (LOQ) (Bressolle et al., 1996; Peters et al., 2007). LOD is the lowest concentration that can be differentiated from the noise level. Typically, a value corresponding to the signal-to-noise ratio of 3 is considered to correspond to LOD ("signal" being defined as height of the analyte peak and "noise" as the amplitude of the baseline around the peak). The specificity of the method can be determined by the analysis of a blank matrix at the retention time of the analyte of interest. LOQ (or LLOQ, for lower limit of quantification) corresponds to the lower concentration at which quantification is possible with acceptable precision and accuracy (typically within ±20%). Another approach consists in defining LOQ as corresponding to a S/N ratio of 10. In theory, concentrations below LOQ should not be quantitatively reported and should only be considered semiquantitative or qualitative data (Bressolle et al., 1996; Peters et al., 2007). As observed in Tables 1–8, most publications however seemed to use equally LOD and LOQ, which may be confusing and question the reliability of the data presented. On the other hand, should one really avoid providing values below LOQ only because the associated variability stands at 21% instead of 20%, especially when keeping in mind that concentrations can vary in several orders of magnitude between people? The issue is definitely different from what is expected in analysis of medical drugs or drugs of abuse, where a 20% variation may significantly influence the interpretation (*e.g.* going out of the therapeutic range or exceeding a cutoff value). Although efforts should be made on method validation, the differences between forensic sciences and biomonitoring of human exposure in the use of data especially having to be considered.

## 7. Conclusions

Hair analysis is a promising biomarker for the biomonitoring of human exposure to environmental chemicals.

Both parent molecules and metabolites of several chemical classes were proven to be detectable in hair, mainly due to technical progress that allowed improving methods sensitivity to reach levels compatible with chemical concentration in hair.

Moreover, the reliability of results obtained from hair analysis is supported by an increasing number of datasets which demonstrate that chemical concentration in hair may be representative of both the level of exposure and the chemical concentration in other compartments of the body.

Although possible sources of results misinterpretation deserve further investigation, one has to bear in mind that interfering factors may not dramatically influence the significance of the results in the perspective of assessing human exposure.

In that regard, hair may be considered a reliable matrix that will be increasingly used in epidemiological studies investigating relationships between exposure and biological effects. In addition to the intrinsic advantages associated with hair such as easiness of sampling, storage and extended windows of detection, the relevance of this matrix shall be strengthen by the development of methods requiring limited amounts of matrix to ensure high level of compliance among volunteers, the focus on multi-class methods to enable investigation of cumulative exposure and the standardization of method validation.

## Conflicts of interest

The authors declare that there are no conflicts of interest.

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