MEDICINA y SEGURIDAD del trabajo

Revisiones

PBDEs exposure and biological effects on e-waste recycling workers: a systematic review

Efectos biológicos derivados de la exposición a PBDEs en trabajadores del reciclaje de e-waste: revisión sistemática

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Abstract

Introduction: PBDEs are potentially dangerous substances released during the e-waste recycling processes. Scientific evidence relates PBDEs with adverse health outcomes like cancer, endocrine disruptions and problems in the offspring. A high concentration of PBDEs has been found on biological samples (serum, hair, breast milk and umbilical cord) from exposed workers, so their exposure could imply a potential risk on workers health.

Aim: To summarize the evidence between exposure to PBDEs contained in e-waste and adverse health outcomes on recycling industry workers.

Materials and methods: A systematic review was done among the scientific literature published between 2003 and 2013 in seven data bases using Medical Subject Headings (MeSH) terms.

Results: 301 articles were evaluated and 20 were included in the review. 65% were from China, 80% had a cross-sectional design. We assessed evidence of association between exposure to e-waste and levels of PBDEs in several biological samples. Workers showed high levels in the DNA damage markers. The effects from the exposure to PBDEs on the thyroid function were not consistent.

Conclusions: Findings from most studies shows a correlation between the exposure to PBDEs and the alteration of the biological parameters on the recycling industry workers, but our ability to assess temporality associations was limited by the small number of prospective and longitudinal studies. Conventional industrial hygiene improvements in e-waste recycling facilities may reduce the exposure on workers to PBDEs.

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Key words: *PBDEs, e-waste, occupational exposure.*

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Resumen

Introducción: Los PBDEs son sustancias potencialmente peligrosas liberadas del reciclaje de e-waste. La evidencia científica implica a los PBDEs en alteraciones en la salud como cáncer, alteraciones endocrinas y problemas en la descendencia. Se han encontrado elevadas concentraciones en muestras biológicas (suero, pelo, leche materna y cordón umbilical) de los trabajadores expuestos, por lo que su exposición implicaría un potencial riesgo para la salud para los trabajadores y su descendencia.

Objetivo: Identificar la evidencia existente entre exposición a PBDEs contenidos en e-waste y los daños sobre la salud en trabajadores de la industria del reciclaje.

Material y métodos: Se realizó una revisión sistemática de la literatura científica publicada entre 2003 y 2013, en siete bases de datos mediante términos MeSH. Las referencias se cribaron en función de los objetivos.

Resultados: Se recuperaron 301 artículos y se incluyeron en la revisión 20. El 65% fueron realizados en China, el 80% respondían a un diseño transversal. Los estudios evidencian una asociación entre exposición a PBDEs y los niveles de PBDEs en distintas muestras biológicas. Los trabajadores presentaron mayores niveles de marcadores de daño al DNA. Los efectos de la exposición a PBDEs sobre la función tiroidea no fueron consistentes.

Conclusiones: La literatura revisada evidencia una asociación entre exposición a PBDEs y alteración de parámetros biológicos en trabajadores de la industria del reciclaje. No puede establecerse una relación de causalidad por el tipo de diseño empleado. Los estudios de intervención evidencian la eficacia de las medidas de mejora para disminuir la exposición a PBDEs.

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Palabras clave: *PBDEs, basura electrónica, exposición ocupacional.*

INTRODUCTION

E-Waste (electronic waste) or WEEE (Waste Electrical and Electronic Equipment –in Spanish: residuos de aparatos electrónicos) are terms used to refer to those electronic devices that are in the end of their useful life and are discarded, such as computers, televisions, mobile telephones or printers, all of them made of combinations of plastic and metals. The boom of technology makes people demand newer and more efficient devices, so the life of these products is becoming shorter. Between 20 and 50 tons of e-waste[1] are generated each year, which contain 182,000kg of PBDEs[2].

PBDEs (Polybrominated Diphenyl Ethers) are compounds widely produced and used since 1970, after the prohibition of PCBs as flame retardants. They are added to polymers in order to obtain fire-resistant materials. They are mainly used in thermoplastics to manufacture electronic products such as computer and television cases, electric components and cables. PBDEs are very stable and highly lipophilic compounds, so they can remain into the environment for a long time, with a high potential of long distance transportation and bioaccumulation in humans and other species.

PBDE´s structure consists of two brominated aromatic rings bonded by other group. Each ring contains up to 5 brominated substitutes, from monobrominated to the decabrominated derivatives, reaching a total amount of 209 congeners.

Commercial PBDEs mixtures are obtained by mixing several congeners mainly from the following three types: pentaBDEs, octaBDEs and decaBDEs.

Stockholm Convention has listed penta-BDE and octa-BDE commercial mixtures as persistent organic pollutants (POP substances) due to their persistence, potential bioaccumulation and toxicity for fauna and human beings.

It has been proved that DecaBDE is degraded into other less brominated congeners (penta- and octa- BDE), which have more bioavailability, toxicity and persistency[3] and for that reason is not a POP substance and, consequently, can be used as flame retardant.

European Union banned the use of penta- and octa-PBDE in August 2004[4] and The Stockholm Convention listed them as POPs in May 2009[5].

Deca-BDE was registered under the UE’s REACH Regulation at the end of August 2010. It has been banned in Europe for electric and electronic devices[6], although is allowed in textile, cars and construction (specific exemptions in Regulation (EU) 757/2010). In May 2013, Norway submitted a proposal to list Deca-BDE as a POP under the Stockholm Convention. The European Chemical Agency (ECHA) proposed in August a restriction for deca-BDE, which is expected to be submitted on the 1st of August 2014, although this would be the first step of a process that could last several years.

USA voluntarily stopped producing penta- and octa-BDEs in 2004. The main deca-BDE producers announced the end of production, import and sale by 31st December 2012[7].

PBDEs will be in the flow of waste for many years as a consequence of the previous wide use on the production of electric and electronic devices and given their life cycle (with a 10 years half life in some cases). 50% to 80% of electronic waste is moved to recycling plants located in China, India, Pakistan, Vietnam or The Philippines, due to a cheaper labor cost and to the lack of specific regulations existing in these countries.

This is an important threaten for the occupational and environmental health, which is increased by the rudimentary recycling techniques frequently used, such as extraction of metals using open-air acid baths, removal of electronic components of circuit cards by heating them up over grills and opened air burning to recover metals[8,9]. This is usually done in not fully prepared places (open-air or places without the proper ventilation) such as small family workshops, without enough and adequate protective equipments for workers. People working under rudimentary e-waste recycling techniques are particularly exposed to high levels of PBDEs.

Absorption can be caused by inhalation, dermal absorption or digestion (by ingestion of food)[10]. Many studies have found high levels of PBDEs on air, soil, vegetation, dust and food, showing that e-waste workers are highly exposed to toxics. Nevertheless, their presence in the environment cannot be directly associated to adverse effect on human health.

Population working in jobs related to e-waste recycling, had a higher frecuency of adverse health effects. Some studies in animals suggest that high concentrations of PBDEs may cause alterations on health, such as cancer[11], delays on puberty[12], decrease in the number of spermatozoids[13], fetal malformations[14], endocrine disruption[15], permanent defects on learning skills, memory and behavior changes[16, 17].

PBDEs have been detected in e-waste recycling workers and in residents of nearby areas. It is especially concerning that hundred thousands of children work and live at e-waste recycling places. PBDEs have also been found in breastmilk, placenta and hair of childbearing-aged women in Taizhou (Zhejiang, China) - an important recycling center[19] and in blood samples from the umbilical cord of mother in Guiyu, showing that prenatal exposure to PBDEs may potentially affect newborns.

Occupational PBDE exposure is increasing due to the evolution of electronic market and the inadequated protective measures used in recycling activities.

The aim of this report is to provide an updated review of the evidence linking the exposure to PBDEs contained on e-waste and the different damages or effects on e-waste recycling workers.

MATERIAL AND METHODS

We searched seven of the main biomedical databases: Medline (through PudMed), LILACS, SciELO, SCOPUS, OSH Update, THE WEB OF KNOWLEDGE and The Cochrane Library.

In order to establish the search strategy, MeSH terms appearing on table I were used. We choose key words based on the following terms: “e-waste”, “PBDE”, “enfermedad profesional” and “exposición ocupacional”, with different combinations.

Table I. List of the search terms used in the different databases

DESCRIPTORS
E waste +occupational exposure + PBDES
(Electronic Waste) AND Occupational Exposure
Electronic waste
Electronic garbage
PBDE
Polibromodifeniléteres
Flame retardants
Waste AND Occupational diseases
E Waste
Flame retardants
Electronic waste
Electric waste
E- Waste AND Workers
WEEE
WEEE AND Polybrominated diphenyl ethers
WEEE AND PBDE
WEEE AND Occupational exposure
WEEE AND Occupational health

We then supplemented this material with reports from European and American occupational and health institutions: Occupational Safety and Health Administration (OSHA Europe), OSHA USA, International Labour Organization (ILO), Occupational Safety and Health Administration (NIOSH), Instituto Nacional de Seguridad y Salud en el Trabajo (INSHT), international agencies (EPA, PNUMA, UNESCO) and other entities such as CNRCOP (Centro Nacional de Referencia sobre Contaminantes Orgánicos Persistentes), BSEF (Bromine Science and Environmental Forum) and social agents such as Instituto Sindical de Trabajo, Ambiente y Salud (ISTAS).

Full text articles obtained from the search strategy were included. Inclusion and exclusion criteria showed in Table II were applied to these articles.

Table II. Inclusion and exclusion criterias

Inclusion criteria	Exclusion criteria
• Original articles and articles following a systematic review methodology or meta-analysis addressed to the study of risks in the exposure to PBDES on e-waste recycling companies and possible alterations derived from this exposure. • Articles studying the exposure to PBDEs in locations close to e-waste recycling plants or electronic waste dumps. • Studies published in Spanish, English, French and Portuguese.	• Duplicated articles. • Articles focused on environmental exposure. • Articles whose study aim was a waste different than PBDEs. • Exposure to PBDEs studied address solely to inhabitants outside work environment. • Articles studying the exposure to PBDEs derived from manufacturing processes. • Studies on environmental impact (plants, animals or in-vivo or in-vitro). • Articles whose study aim was the non-work related exposure to PBDEs on pregnant women and during breastfeeding period. • Articles studying work exposure to PBDEs in regular garbage dumps.

The level of evidence was established based on the criteria found on the Scottish Intercollegiate Guidelines (SIGN)[21].

Titles of papers were studied, duplicates and obviously irrelevant references were eliminated, and the remaining abstracts were read independently by two researchers to decide on the papers to be retrieved. The remaining papers were evaluated and finally reviewed.

From each paper that was finally reviewed, we abstracted a standard set of information including: author and year of publication, publication reference, aim of the study, type of design, population and simple size, factor and effect variables, data recovery methods, bias control, epidemiologic markers, association measures, statistical tests, conclusions, limitations and knowledge advances. We summarized this information in one table.

RESULTS

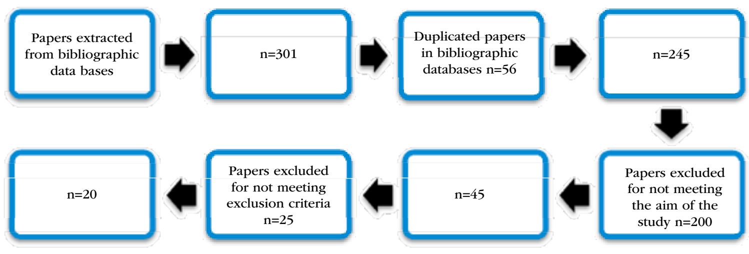
Beginning on the established search strategy, 301 references of published articles were extracted (Table III).

Table III. Search terms used in the different databases and number of articles extracted

DATABASE	DESCRIPTORS	LIMITS	No. OF ARTICLES
MEDLINE	E waste +occupational exposure + PBDES Electronic waste and occupational exposure	10 years 10 years	3 33
LILACS	Electronic waste PBDE (Electronic waste) and ("Electronic waste" OR "Reciclagem" OR "halogenated pipheny ethers" OR "Flame retardants"	10 years 10 years 10 years	1 2 39
WOK	e waste and occupational and pbdes Enquiry:Topic=(Occupational Exposure) and Topic=(Electronic Waste) and Topic=(polybrominated diphenyl ethers)	10 years	23
SCOPUS	e waste and occupational exposure and PBDEs	10 years	154
IBECS	PBDE	10 years	1
SCIELO	Flame retardants	10 years	1
OSH UPDATE	PBDE	10 years	44
TOTAL PAPERS			301

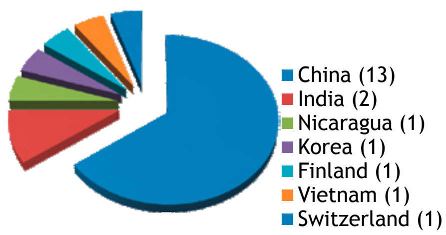
Once applying the above described filters and the inclusion and exclusion criteria, 20 articles were selected for full text review (Figure 2).

Figure 2. Papers selection strategy

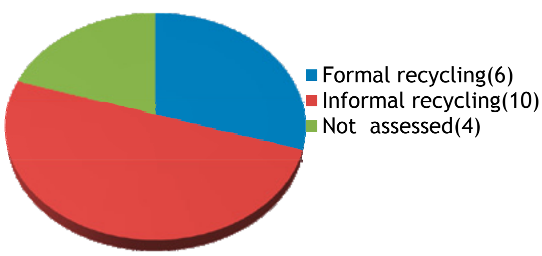


China is the country which holds the highest number of publications (n=13). Most of the reports were from informal e-waste recycling sector.

Graphic 1. Countries with publications on PBDEs



Graphic 2. Type of recycling



According to the type of design, the most prevalent studies were cross-sectional studies with control group (n=16). Also two cross sectional articles (without control group), two follow up studies, one evidence validation study and one systematic review were reviewed.

Most of articles studied PBDEs serum levels and congener patterns[22-29] and PBDEs hair levels [30-33] on e-waste recycling workers.

Four studies examined the association between e-waste exposure on workers and health outcomes, such as thyroid function[34-36] or DNA oxidative damage markers (micronucleated binucleated cells in peripheral blood or 8-OHdG)[31,36].

We found four studies that researched the presence of PBDEs metabolites in blood [22,24,25,37]

Two articles about the presence of PBDEs in breast milk[19,38] and in placenta[19] were reviewed. Two publications[28,39] evaluated the impact of the improvement measure on industrial hygienic implemented in an e-waste company, measuring the changes in the levels of exposure and in the PBDEs congeners pattern.

The systematic review done by Grant, K., *et al.* (2013)[40] analyzes 23 epidemiologic cross-sectional studies from South Eastern China, following PRISMA guidelines. For studies reports the evidence for the association between the exposure to PBDEs in electronic waste processes and adverse health outcomes.

They recorded plausible outcomes associated with exposure to potentially dangerous substances as a consequence of informal destruction and recycling of e-waste.

Adverse health effects reported were changes on thyroid function, changes on cellular expression and function, reduced birthweights, changes in behavior and decreased lung function (Table IV).

In the two follow-up studies (Rosenberg C, 2011, and Thuresson K, 2006), assess the impact of work environment changes on the PBDEs occupational exposure (Table IV).

Table IV. Main systematic review characteristics, intervention essays and evidence assessment study

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Grant K,[40] 2013	Health consequences of exposure to e-waste: a systematic review	Systematic review following PRISMA guide	n=23	(+)	Exposure to PBDEs 1-Levels registered in population in e-waste areas: In China; Guiyu – Blood: Range 77-8452 ng/g l.w.(lipid weight), umbilical cord blood: Range 1.14-504.97 ng/g pl, BDE 209 in blood: max 3100 ng/g l.w. Taizhou – Breast milk: Range 8.89-457 ng/g l.w, Placenta: Range 1.28-72.1 ng/g l.w., Hair: Range 8.47-486 ng/g d.w. Guangdong – BDE 209 blood: max 3436 ng/g l.w. In Korea: Seoul – Blood: Range 8.61-46.05 ng/g p.l. 2-Effects on health and alteration of action mechanisms: Potential carcinogenic, genotoxic, endocrine disruptor, DM type 2, metabolic Sd, low weight at birth, psychomotor and mental alterations, neuroconductual alteration, infertility	2++
Thuresson K [28] 2006	Polybrominated diphenil ether exposure to electronics recycling workers: A follow up study	Intervention essay	Cross-sectional study: n=19 (before improvement measures) y n=27 (after improvement measures). Longitudinal study: n=12	(-)	Significant reduction of the most abundant PBDEs after improvement measures: BDE 183 (p 0.05) and BDE 209(p'0.001). Concentrations of BDE47 (p'0,25) and BDE153 (p'0.25) did not vary significantly. Octa and Nona BDE (determined in 2000) presented higher concentrations than the referenced group.	1-
Rosenberg, C.[39] 2011	Exposure to flame retardants in electronics recycling sites	Intervention essay	n=34	(-)	1- Air concentrations of PBDEs (ng/m3) Σ PBDES 2008 A: Median=295. Range (17-500) vs B: 2000 range (450-5200) vs C: 42 Range (4,6-58) vs D: 31 range (26-62) Σ PBDES 2009 A: Median =65, range (42-360) vs B: 630 range (240-3200) vs C: 28 range (18-66) vs D: 10 range (6,8-51) 2-Concentrations of PBDEs congeners. The pattern was similar in A, B and D, with a mean of BDE 209 of 81% in 2008 and 91 % in 2009 of the total PBDEs. The pattern differed in site C, BDE 209 was 66% (2008) and 62 % (2009)	1-

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Zheng J [33]. 2011	Levels and sources of brominated flame retardants in human hair from urban, e-waste, and rural areas in South China	Validation sudy	n=173	(-)	Median PBDE (in dust): E-waste workers 11500 ng/g (2700-28000) vs Non-occupational exposure 1900 ng/g (825-5890) vs Urban population 5210(540-41400) vs rural population 836(251-1890) Median PBDE(in hair): E-waste workers 126 ng/g (12,4-845) vs Non-occupational exposure 43,2 ng/g (7,40-219) vs urban areas residents 16,55 ng/g (4,17-69,5) vs rural areas residents 9,95 ng/g(2,55-75,2) Correlation between human hair and dust for PBDEs: r 0,23 (p 0,77). Median BDE209 in hair (e-waste workers vs urban population: 41,6 vs 9,42.	3

Rosenberg C. *et al.* (2011)[39] evaluated the concentration of PBDEs on air using portable auto samplers on workers in different areas of a recycling plant in Finland in 2008 and after intervention in 2009. Zone A: plastic fractions grinding n=6 in 2008 and n=6 in 2009. Zone B: separation of materials with laser techniques and mechanic separation of metals n=7 in 2008 and n=5 in 2009. Zone C: manual dismantling and classification of waste and selective destruction of dangerous and valuable components n=5 in 2008 and n=4 in 2009. Zone D: batteries and dry accumulators by means of a dry and closed process of product grinding n=6 in 2008 and n=6 in 2009.

Dust samples were collected in the four areas and 46 air samples were taken with portable auto samplers during the first and second day, after the weekend and for a period of 191 to 408 minutes, in order to analyze the presence of PBDEs.

Industrial hygiene measures implemented were: improvements in ventilation systems by installing filters in the air pipes in order to prevent polluted air recirculate in working areas; in one of the areas a floor covering was installed in order to facilitate the cleaning and the cleaning service was intensified; a new grinding machine was installed, thus reducing the amount of dust released by this process and four of the workers used air purifiers breathing protection equipments.

After all these improvements, reduction in PBDE levels and deca-BDE 209 on air in all the recycling areas was observed. Congeners pattern was similar in areas A, B and D, where BDE 209 represents an average of 81% in 2008 and 91% in 2009 of the total PBDEs. In area C, BDE 209 was 66% (2008) and 62% (2009) of the total concentration of PBDEs.

Thuresson, K. *et al.* (2006)[28] evaluated the impact of industrial hygiene improvements on the occupational exposure in an e-waste recycling company in Switzerland. The shredder (considered the main PBDEs polluting focus) located in the dismantling room was placed outside the building. A specific ventilation system was installed, forcing the airflow from ceiling to floor in order to remove particles and dust from the air. Brooms were replaced by vacuum cleaners and the surface of working benches began to be cleaned with wet rags. All the improvement measures were totally installed by November 1999.

In 1997, a sample of 19 workers was studied and in 2000, once all the improvement measures were installed, 27 workers were studied. Those workers were classified in two groups: “Blue collar workers” (waste dismantling workers) and “White collar workers” (office workers separated from the dismantling area). A control group of 17 workers from an abattoir in the South of Sweden with little or no computer contact was established.

Non-parametric test were used for comparisons (Wilcoxon, U- Mann Whitney, Spearman). Bias control and confounding variables were not detailed. Samples were analyzed in two different laboratories.

Results show that, BDE 183 ($p<0,05$) and BDE 209 ($p<0,001$) serum levels have a significant reduction after the adoption of industrial hygiene improvements. Nevertheless, BDE 47 ($p>0,25$) and BDE153 ($p>0,25$) did not have a significantly reduction before and after the intervention, noticing a significant increase of BDE 153 in intra individual comparisons.

Octa- and nona-BDE levels in serum measured after the changes implemented in the company were significantly higher ($p<0.01$) than those obtained in the control group.

Zheng J *et al.* (2011)[33] studied PBDE levels and congener profiles in hair and dust in order to find out if dust was the main exposure route and to validate hair as specimen to evaluate the exposure to PBDEs (Table IV).

Two groups involved in e-waste dismantling were randomly chosen as exposure groups: First group was formed by 30 occupationally exposed e-waste recycling workers and the second group by 82 non-occupational exposed residents wich live in an e-waste recycling area. As control group, 29 urban residents and 32 rural residents were selected.

Socio-demographic information was collected through a questionnaire. Inclusion and exclusion criteria were not described enough.

Statistical analyses included ANOVA and Pearson correlation test.

PBDEs hair levels and PBDEs levels of dust collected in workshops were higher on e-waste workers than on the other groups. BDE209 was the most abundant congener for all samples, although highest levels were found on e-waste recycling workers.

No correlation was found between levels on dust and hair ($r=0,23$; $p=0,77$). Occupational exposure has a positive correlation with hair PBDEs levels. Congener profile on hair is different than one on dust.

Table V summarizes the results of the analyzed studies following a cross-sectional design.

Table V. Main characteristics of cross-sectional studies analyzed in our review

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Kim B.H [26] 2005	Concentrations of polybrominated diphenyl ethers, polychlorinated dibenzo-p-dioxins and dibenzofurans, and polychlorinated biphenyls in human blood samples from Korea	Cross-sectional with control group.	n=35	(-)	1-PBDEs levels (median): Exposed 19,33(8,61-46,05 ng/g l.w.) vs non-exposed 17,16 (8,53-28,9 ng/g l.w). For men and 13,32(7,24-20,00 ng/g l.w.) for women ($p<0,05$ e IC 95%) 2-BDE 47 is the most frequent congener: 33% of the total concentration of PBDEs. Correlation ($r= 0,912$, $p<0,05$) 3-BDE -183 (median): Exposed workers 4,12 (0,13-0,59 ng/g l.w.) vs non-exposed men 2,04 (0,51-4,86 ng/g l.w.) and non-exposed women 2,10 (0,59-5,85 ng/g l.w.) ($p = 0,01$) 4-No correlation between concentration of PBDEs and age ($r = 0.002$, $p \leq 0.05$) or BMI ($r = 0,086$, $p \leq 0,05$)	3
Bi, X. [23] 2007	Exposure of electronics dismantling workers to polybrominated diphenyl ethers, polychlorinated biphenyls, and qrganochlorine pesticides in South China	Cross- sectional with control group.	n=47	(-)	Σ PBDES exposed: Median 600 ng/g lipidic weight (140-8500) vs non-exposed 170 ng/g (16-490) Concentration BDE-209: Median exposed 600 ng/g l.w. (range 340-3100) vs non-exposed 86 ng/g l.w. (scope 170-490). Concentration BDE 197(octa): Median 27 vs 8,3 ng/g.l.w BDE-207 (nona): Median 73 vs 43 ng/g.l.w	3
Qu W 2007[27]	Exposure to polybrominated diphenyl ethers among workers at an electronic waste dismantling region in Guangdong, China	Cross-sectional with control group.	n=55	(-)	Mean BDE-209: Workers 83,5 ng g^{-1} lw (Non-detected -3436) vs residents 18,5 (Non-detected-377) vs control 5,7 (Non-detected -63,2). Percentage of BDE209 in each group: 75, 75,6 y 55,5%, respectively.	3

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Athanasiadou, M.[22] 2008	Polybrominated diphenyl ethers (PBDEs) and bioaccumulative hydroxylated PBDE metabolites in young humans from Managua, Nicaragua	Cross- sectional with control group.	n=162 children n=32 women	(+)	Concentrations of PBDEs (pmol/g p.l.): (Median; sample 1 and sample 2) Group 1 ΣPBDE 1250/1160 and Group 2 ΣPBDE 144/145 vs Group 3ΣPBDE 72/60 Group 4 ΣPBDE 30/42 vs group 5 ΣPBDE 40/40 Concentrations of OH-PBDES (pmol/g l.w.): Group 1 ΣOH-PBDE 120/100 and Group 2 ΣOH-PBDE 11 vs Group 3ΣOH-PBDE 5,6 and Group 4 ΣOH-PBDE 1 vs Group 5 ΣOH-PBDE 3,4 In women: Group CΣPBDE 142 vs Group D ΣPBDE 114/135 vs Group A ΣPBDE47 and Group B ΣPBDE 31 (pmol/g l.w.)	3
Wen S.[31] 2008	Elevated levels of urinary 8-hydroxy-2'-deoxyguanosine in male electrical and electronic equipment dismantling workers exposed to high concentrations of polychlorinated dibenzo-p-dioxins and dibenzofurans, polybrominated diphenyl ethers, and polychlorinated biphenyls.	Cross-sectional	n=64	(-)	8- OH dG urine levels: Pre & postworkshift (6,40± 1,64 vs 24,55 ±5,96 mmol/mol creatinnine), p<0,05. Concentration of PBDEs in dust: (27,5±5,8) x 10^6 Concentration of PBDEs in hair: (870.8±205,4)x 10^6 pg/g dw	3
Yuan J.[36] 2008	Elevated serum polybrominated diphenyl ethers and thyroid-stimulating hormone associated with lymphocytic micronuclei in Chinese workers from an e-waste dismantling site	Cross-sectional with control group.	n=49	(-)	PBDE (in serum): Median; 382 vs 158 ng/g l.w. (p 0,045). TSH (Serum): 1,7 microIU/mL vs 1.1 mIU/L (p<0,01).Binucleated cells: 5%o (range 0-96$‰_0$) vs 0,00$‰_0$ (range 0-5%o), p<0,01. 8-OHdG urinary: 156,3 mmol/ creatinine mol (13,52-733,70) vs 82,06 (6,54-1057,03) with p>0,05	3

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Zhao G.[32] 2008	PBBs, PBDEs, and PCBs levels in hair of residents around e-waste disassembly sites in Zhejiang Province, China, and their potential sources	Cross- sectional with control group.	total n=58	(-)	1-Electronic samples (stuffing powder)ΣPBDES 29,71 ng g-1 dw and PBDE 209: 4,19 x 103 ng g^{-1}dw(dry weight) 2-Concentrations of PBDEs in soil samples ΣPBDES (median): Exposed area 42,42 vs non-exposed area 3.32 ng g^{-1}dw. BDE 209 (mean): 192,38 ng g^{-1} dw vs (undetectable) 3-Concentrations of PBDEs in hair samples: ΣPBDES in exposed (mean) A: 29,64 ng g^{-1} , vs B:7.41 ng g^{-1} vs C: 4.73 ng g- 1dw vs D: 11,10 ng g^{-1} dw vs E (control area) 4.49 ng g^{-1} dw Concentrations of PBDE209 in B,C and D with means of 10,8; 5,42; 3,10; vs A and E undetectable.	2-
Eguchi, A.[24] 2010	Organohalogen and metabolite contaminants in human serum samples from Indian E-waste recycling workers.	Cross- sectional with control group.	n=10	(-)	1-Mean concentrations of total PBDEs were 240 pg /g in workers vs 100 pg / g in the control group $p<0,05$ 2-Mean concentrations of total OH-PBDEwre 1.5 pg/g in workers vs 25 pg / g in the control group $p<0,05$ 3-MeO- PBDE (median): Control group 8,4 pg/g vs exposure group (undetectable, except for one sample 0,97 pg/g)	3
Leung A.[19] 2010	Body burdens of polybrominated diphenyl ethers in childbearing-aged women at an intensive electronic-waste recycling site in China.	Cross-sectional with control group.	n=10	(-)	Levels of PBDEs in women living in the e-waste area vs control group (mean): Breast milk117±191(8,89-457) vs 2,06±0,94(1,00-3,56)ng/g fat; placenta 19,5±29,9(1,28-72,1) vs 1,02±0,36(0,59-1,42) ng/g fat, hair 110±210(8,47-486) vs 3,57±2,03(1,56-5,61) ng/g fat. Positive association between body burden of PBDEs and fish and seafood consumption	3

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Tue,N.M.[38] 2010	Accumulation of polychlorinated biphenyls and brominated flame retardants in breast milk from women living in Vietnamese e-waste recycling sites	Cross- sectional with control group.	n=33	(+)	1. Σ PBDEs(ng g^{-1} l.w) in breast milk (median): Zone 4: 0,73 (0,26-1,1) and zone 1:0,57(0,24-0,8) vs zone 2: 2,3(0,55-13) vs zone 3: 84(20-250) p<0,05 (Σ PBDEs(ng g^{-1} l.w) zone 3 A: 84(20-250) vs zone 3 B:3,2 (2,0-4,0)) 2-BDE 47 (median): zone 4: 0.13 (0.070–0.25) vs zona1: 0.097 (0.041–0.20) vs zone 2: 0.40(0.11–1.8) vs zona 3B: 0.81(0.63–1.0) vs zone 3A: 4.8 (3.5–32) BDE -153 Zone 4: 0.098(0.062–0.14) vs zone 1: 0.10 (0.061–0.25) vs zone 2: 0.40 (0.021–1.5) vs zone 3(non-occupational exposure): 0.65 (0.27–1.0) vs zone 3(occupational exposure) 4.4 (2.1–23) BDE-209 zone 4: ND vs zone 1: 0.17 (0.069–0.50) vs zone 2: 0.42 (0.12–7.3) vs zone 3B: 0.11(n.d.–0.16)vs zone 3 A: 4.1(0.87–96)	3
Wang H.[37] 2010	Examining the relationship between Brominated flame retardants (BFR) exposure and changes of thyroid hormone levels around E-Waste dismantling sites.	Cross- sectional with control group.	n=442	(+)	Occupational exposure group vs control group: lower TSH (1,26 vs 1,57 Micro IU/ml), T3 (1,06 ng/ml vs 1,18 ng/ml), and T3 libre (2,72 vs 2,86 pmol/L).All p<0,001. No differences in T4. Levels of PBDEs in occupational exposure groups vs control group: 189.79 vs 122,37 ng/g lipid weight.	3
Yu Z.[37] 2010	Identification of hydroxylated octa- and nona-bromodiphenyl ethers in human serum from electronic waste dismantling workers	Case serie	n=6	(-)	Isolated in serum samples: 6-OH-BDE199, 6-OH-BDE196 and 6-OH-BDE206.	3
Han G.[34] 2011	Correlations of PCBs, DIOXIN, and PBDE with TSH in Children's Blood in Areas of Computer E-waste Recycling*	Cross- sectional with control group.	n= 369	(+)	1-Total concentration of PBDE: Exposed 664,28 ± 262,38 ng / g vs control group (375,81 ± 262,43 ng / g 3-Levels TSH: Exposed 1,88 ± 0,42 UI / mL vs control 3,31 ± 1,04 UI / mL, 2- PBDE and TSH: Positive correlation (exposed area 0.39 vs control area 0.783)	3

Author/Year	Title	Type of Study	Sample size	Confounding factor control	Results	SIGN evidence level
Ma J.[30] 2011	Elevated concentrations of polychlorinated dibenzo-p-dioxins and polychlorinated and polybrominated diphenyl ethers in hair from workers at an electronic waste recycling facility in Eastern China.	Cross- sectional with control group.	n=38	(-)	Mean PBDEs: 157 (21,5-1020) vs 40,3 (12,6- 127) ng/g dw. Mean BDE 209: 132(6,52-963) vs 19,3 (4,47-74,8). Mean BDE 47: 11,4 (ND-29,7) vs 15,0 (2,70- 32,6)	3
Eguchi A.[25] 2012	Different profiles of anthropogenic and naturally produced organohalogen compounds in serum from residents living near a coastal area and e-waste recycling workers in India	Cross- sectional with control group.	n=45	(-)	Mean of PBDE (in serum): 340 vs 330 pg g^{-1}w.w., p<0,05. Octa to Nona-BDE (in blood): Mean47 pg g vs 27 pg g^{-1}w.w., (p<0,05). OH-PBDEs (blood): 16 vs 35 pg g^{-1}w.w., (p<0,05) MeO-PBDEs (in blood): 0,92 vs 7,7 pg g^{-1}w.w. MeO- PBDEs(Marine fish vs sweet water fish): 8,7 vs 0,54 ng g^{-1} lw (p <0,05)	3
Yang Q [29] 2013	Exposure to typical persistent organic pollutants from an electronic waste recycling site in Northern China	Cross- sectional with control group.	n=56	(+)	PBDEs in this study are grouped in three categories according to the main congeners of the commercial compounds Penta-, Octa- and Deca BDE, respectively. Median in the exposure group was 5,73 (1.80-12.3), 2.67 (1.77-4.21) y 12.3(7.49-17.2) ng/g lipid weight, respectively. And in the control group: 5.87(0.64-25.9), 0.97(0.59-1.52) and 5.77(4.10-8.18) ng/g lipid weight.	3

Kim B-H *et al.* (2005)[26], a cross-sectional study with reference group, studied PBDEs levels and congeners on 13 workers serum samples from an e-waste incineration plant in Seoul, Korea, with a reference group of 22 people.

PBDEs levels in the exposed population were significantly higher than in the reference group ($p<0.05$). BDE 183 was significantly higher on workers than in general population ($p=0,01$). No significant correlation between the concentration of PBDEs and age was found, although it was found between PBDEs and BMI. The study uses Principal Component Analysis (PCA) and the t-Student test.

Confounding variables and bias control is not properly described in the article.

With similar design, a cross-sectional study with control group, Bi X *et al.* (2007)[23] studied PBDEs exposure and health outcomes in China. They measure the concentrations and congeners profile on 26 serum samples from e-waste workers (Guiyu) and a control group formed by 21 people (Haojiang). Members of both samples were volunteers aged 18 to 81, 64% women and 36% men.

Confounding variables and bias control is not properly described. In the statistical analysis, Pearson correlation coefficient and U-Mann-Whitney were used.

PBDEs levels were three fold higher on occupational exposed group than in control group, difference which was statistically significant ($p<0,00$). No correlation was found between PBDEs serum levels and age. In the control group, no correlation between highly brominated PBDE congeners (BDE -197, -207, -209) and age was found.

They concluded that concentrations of PBDEs and highly brominated PBDEs detected on the exposed workers group in Guiyu were higher than those reported in European and American cities. Levels of PBDEs in the control group are possibly due to the recycling activity in Guiyu as a result of the atmospheric transport.

Qu W *et al.* (2007)[27] prepared a cross-sectional study with reference group. They investigate the association between the exposure to PBDEs on e-waste dismantling workers and the concentration of PBDEs in blood. Two exposure groups formed by volunteers were studied.

The first group was formed by 20 e-waste dismantling workers and the second group (non occupational) was formed by 15 farmers living 50km away from the dismantling region. The control group was formed by 20 women from a city in the South of China.

Levels of PBDEs on e-waste workers for significantly higher ($p<0.05$) than those on the other two groups, especially the levels of highly brominated congeners (hepta- to deca-BDEs), which were 11 to 20 times higher, but no for BDE-196, 203 and 206. In all groups, BDE 209 was the dominant congener. No correlation was found between serum levels of PBDEs and age, height or weight.

These results concluded that work exposure to PBDEs is associated with high levels of PBDEs in blood, especially for highly brominated congeners.

The cross-sectional study (with control group) of Athanasiadou, M. *et al.* (2008)[22] examined PBDEs levels, congeners pattern and the presence of hydroxylated metabolites (OH-PBDEs) in serum samples on 162 garbage dump working children in Nicaragua. The sample was stratified in 5 groups, according to labour experience on dumps, place of residence and fish consumption: two groups with 64 children with occupational exposure (groups 1 and 2), two groups with 80 children with non-occupational exposure (groups 3 and 4) and a control group with 18 children (group 5), located in an area at 20 km.

The study included 32 women divided in four groups depending on the residence area (rural-fishing area –groups A and B– and urban area –groups C and D). The aim of the study was explore an association between PBDEs serum levels and fish consumption.

Confounding variables and bias were controlled by structured interviews, taking socio-demographic information, age, gender, fish consumption, place of residence, dietetic habits, work history and economic and cultural level. Statistical analysis was not described.

Ten PBDEs congeners were quantified. BDE-47 was he dominant congener and BDE-209 the less frequent. Occupational exposed children had higher serum levels of PBDEs and OH-PBDE metabolites than other groups. Women with low fish consumption had higher PBDEs levels than those living in fishing areas and consuming more fish.

Those authors found, PBDEs hidroxylated metabolites bioaccumulated in human serum. They finally concluded that serum levels of PBDEs and OH-PBDEs metabolites in occupational exposure children were significantly higher than those in serum samples from children living in urban áreas (althought they have high levels in serum, as well). It indicates that dust would be an important source of exposure to PBDEs in this populated area.

The oxidative damage to DNA has been studied by Wen S. *et al.* (2008)31 in a randomized cross-sectional study. Their aim was investigate the association between occupational exposure to PBDEs and oxidative damage to DNA, by measuring the levels of 8-OHdG (8-hydroxy-2-desoxyguanosine) in urine. 64 men aged 18 to 60 working for at least one year in two different industries devoted to e-waste dismantling were recruited.

64 urine and hair samples, pre and post work exposure, and 3 environmental samples of dust in workshops were analyzed.

Levels of 80HdG in urine were higher ($p<0.05$) at the end of the working day tan at the beginning. The more abundant PBDEs congeners were PBDE209> 47> 99> 183> 153, being deca-BDE the most abundant in all the samples (48.5-81.9%).

The aim of Yuan J *et al.* (2008)[36] was to analyze, by a cross-sectional study with control group, the association between the exposure to e-waste and thyroid alterations as possible inductors of genotoxic damage estimated through the measurement of micronucleated binucleated cells. They also determined the levels of 8-OHdG in urine, as biomarker of oxidative stress in exposed workers.

23 informal recycling workers with exposure to PBDEs were selected and a control group formed by 26 farmers.

The levels of workers PBDEs and TSH in serum were significantly higher than in the control group, with $p<0.045$ y $p<0.01$, respectively. Nevertheless, no significant differences were observed on the levels of urinary 8-OHdG in both groups. The authors state that this can be due to the study's low statistic power. The results show that working with e-waste is associated to high levels of TSH and higher presence of micronucleated binucleated cells.

Working with e-waste turned out to be a predictable variable of the concentration of TSH (OR 28, 95%, CI 5.90-132.83; $p<0.000$).

They reject the existence of association between PBDEs and oxidative stress. Methodologically, bias study and confounding factors is appropriate. The statistical analysis used t-Student, Pearson and U Mann-Whitney tests.

In other cross section study with control group, Zhao G. & col (2008)[32] explored the exposure to PBDEs in e-waste recycling areas, studying the levels of congeners and OBDEs in hair samples of 44 workers implied in very rudimentary recycling processes, taking as control group 4 residents, from five different areas. Six soil samples were collected coming from 4 recycling activity areas, 3 soil samples from the control area and one e-waste sample (formed by cable coating, stuffing powder and chipped circuit boards).

These measures detected high levels of PBDE and BDE 209 (BDE 209 was the most often found congener) in all electronic waste samples, but specially in stuffing powder.

PBDEs concentrations on soil were significantly higher in e-waste areas than in the control areas.

Levels of PBDEs in hair samples were significantly higher in the exposed areas than in control areas ($p<0.05$).

The general conclusion was that the average levels of PBDEs measured in the hair samples were coherent with the ones detected in the soil.

Confounding variables and bias controls are not well described. For statistic analysis they use the non–parametric U-Mann Whitney test.

Eguchi A. *et al.* (2010)[24] studied the presence of PBDEs' OH-BDE hidroxilated metabolites in serum on 5 e-waste recycling workers in India, aged 26 to 33, compared to a control group formed by 5 rural area inhabitants, aged 25 to 35.

Confounding variables and bias controls are not well described, as well as the statistic study.

Results showed that concentrations of PBDEs and BDE 209 in exposed workers were higher, although they were significantly higher only for BDE 209. The OH-PBDEs in the control group were significantly higher ($p<0.05$) than in the exposed workers.

BDE 209 was the dominant congener in all the samples.

The effect of the exposure to PBDEs on reproductive health is studied by Leung A. *et al.* (2010)[19], who investigated the levels and pattern of PBDEs congeners in samples belonging to three types of specimens (breast milk, placenta and hair) from pregnant women and the potential risks on their children's health.

The exposure group was formed by 5 pregnant women living in Taizhou (e-waste recycling area), one of them working in the recycling industry. Participants were randomly selected. The control group was formed by 5 women living in a place located 245 km away from Taizhou.

Sociodemographic information, eating habits and over exposure to other substances were collected by means of a questionnaire.

X2, ANOVA, U-Mann-Whitney and Spearman correlations tests were used for the statistic analysis. Confounding variables control is not properly defined in the article.

Concentracions of PBDEs in the three samples (breast milk, placenta and hair) in the group of women living in the recycling area were much higher than those in the non-exposed group ($p<0.05$), specially in hair and breast milk.

Women working in the e-waste recycling had the second highest level of PBDEs.

There was a positive correlation between the concentrations of total PBDEs and low brominated PBDEs in the different types of samples gathered from the exposure group: hair and breast milk ($r=0.998$, $p<0.0001$), hair and placenta ($r=0.995$, $p<0.0001$) and breast milk and placenta ($r=0.999$ y $p<0.0001$). The congeners profile was the same in all samples. The dominant congener was BDE47.

A positive correlation was also found between body burden of PBDEs in women living in the e-waste recycling area and animal-origin food consumption (especially fish and seafood).

The estimated daily intake of PBDEs of a 6-month-old breastfed infant living in the e-waste recycling area was 572+-839 ng/kg body wt/day.

Concentrations of PBDEs in breast milk is studied by Tue, N.M. *et al.* (2010)[38] through a cross-sectional study with control group. They compared the exposure to PBDEs in women with levels of PBDEs in women breast milk (working or not) living in three places dedicated to electronic waste recycling: site 1 (batteries recycling), sites 2 and 3 (e-waste dismantling) and site 4 (typical urban area).

A questionnaire was conducted in 2007 to obtain information about sociodemographic variables (age, height, weight, number of childbirths, length of rest periods, occupation (working or not in the recycling industry), period of participation on recycling activities and food habits. These variables were statistically analyzed through the analysis of main components and multiple linear regression analysis. Data were transformed in order to achieve a normal distribution. Wilcoxon test was also used.

Levels of PBDEs in the e-waste recycling areas were significantly higher than in the batteries recycling area and in the control group. Congener profile was very similar in sites 1 and 2, with high levels of octa-, nona- and deca-BDE. Concentrations of BDE 209 were 50%. The profile of PBDEs was different in the reference area, where low brominated congeners were predominant, such as BDE-47 and BDE-153. BDE-209 was undetectable. There was a significantly correlation between levels of PBDEs and the development of recycling activities.

Wang H. *et al.* (2010)[35] studied with a cross-sectional design with control group, the effect of PBDEs released during e-waste recycling activities on the thyroid function. Three groups of workers were selected, each one with a different type of exposure. The first group (occupational exposure) was formed by 236 e-waste workers living in three different sites and randomly selected. The second group (non-occupational exposure) was formed by 89 people living around recycling sites. The control group was formed by 117 people working in a green plantation town.

Socio-demographic and health information were self reported by each participant.

TSH levels were significantly lower ($p<0.001$) in the e-waste workers group than in the non-exposed group. Nevertheless, no differences were found between e-waste workers and the people living around the recycling plants.

Age, race or smoking were not associated ($p>0.05$) with thyroid hormones levels. There was a strong positive correlation between levels of BDE126 and T4 concentrations (beta= 0.25, SE=0.10, p=0.0181) and BDE 205 and T4 (beta=3.27, S=0.97, p=0.001).

Authors also found that factors such as duration of exposure time, years of occupational dismantling and occupational mode of incineration had a strong positive correlation with the levels of PBDE ($p<0.01$). The respiratory protection presented a negative correlation ($p<0.05$) with the levels of PBDEs.

Methodologically, two independent sample-t-tests, covariance analyses were and linear regression analysis. Possible confounding factors, such as total lipids in plasma, sex, alcohol intake and age, were monitored.

Yu Z *et al.* (2010)[37] studied the presence of OH-PBDEs in blood of six e-waste dismantling workers as a possible indicator of highly brominated PBDEs metabolization.

The results identify 6-OH-BDE199, 6-OH-BDE196 and 6-OH-BDE206 in blood samples, concluding that highly brominated PBDEs can be oxidatively metabolized in OH-octa-BDE and OH-nona-BDE in human serum following a continuous long-term exposure to high concentrations of BDE-209.

There were no bias control measures or confounding potential variables described. Inclusion and exclusion criteria were not either detailed.

The association between exposure to PBDEs and levels of thyroid hormones is studied by Han G *et al.* (2011)[34] through a cross-sectional study with control group. A sample of 195 children with non-occupational exposure was collected from a site close to an e-waste recycling area and 174 children as control group from a further location.

It was statistically analyzed through a comparison of averages, using T-Student and linear regression tests

Levels of PBDEs of the exposed children were significantly higher than in the control group. In both groups a positive correlation between the concentration of PBDEs and the levels of TSH was found, being significantly higher in the control group. The health of children in the control area was better than in the polluted area, because PBDEs lead to increase the concentrations of these substances in serum, affecting the levels of thyroid hormones in children.

The link between occupational exposure to PCDD/Fs and PBDEs and the levels of these substances in hair was studied by Ma J *et al.* (2011)[30] by means of cross-sectional study with control group. Hair samples collected from 27 e-waste recycling workers were analyzed, all of them working in the industry for more than one year. The control group was formed by 27 people living in Shanghai, with no occupational exposure.

The information about their work history, health and hair characteristics (color, treatments) was surveyed.

Concentrations of PBDEs in e-waste recycling workers hair were three times higher than in the control group. The dominant congener in hair samples for both groups was PBDE 209. The control group had higher levels of BDE47 than the reference group.

An association was found between the congeners profile in hair and the congeners profile in the atmosphere within the recycling plant premises, concluding that hair samples could show exposures to PBDEs released from e-waste recycling operations.

Presence of metabolites of PBDEs is studied by Eguchi A *et al.* (2012)[25] through a cross-sectional design. They assessed the link between the exposure to PBDEs in e-waste recycling workers and levels of PBDEs and their metabolites (MeO-PBDEs -methoxylated PBDEs- and OH-PBDEs) in blood. They also analyzed the concentration of MeO-PBDEs in fish samples from marine and freshwater environments in order to find a potential association between fish intake and levels of MeO-PBDEs in blood.

Serum samples were collected from 25 e-waste recycling workers and 20 residents near a coastal area. By means of a personal interview they gathered the demographic information and everything related to their health and homes.

Concentrations of OH-PBDE and MeO-PBDE in serum from residents living near the coastal area were were significantly higher ($p<0.05$) than those in serum from e-waste recycling workers. Nevertheless, cocentrations of octa- to nona-BDEs anda octa-brominated OH-PBDEs were significantly higher in e-waste recycling workers than those in coastal population ($p<0.05$).

Concentrations of MeO-PBDEs in marine fish were significantly higher than those in freshwater fish ($p<0.05$). BDE-209 was the dominant congener identified in all samples (80%).

The result of the study shows that there is an association between occupational exposure and levels of PBDEs in blood, while higher levels of OH-PBDEs and MeO-PBDEs in the coastal population would be due to higher fish consumption.

Statistically, non parametric tests of association were used. Inclusion and exclusion criteria, together with bias control, are not described enough.

Yang Q. *et al.* (2013)[29] investigate levels of exposure to typical pollutants relates to e-waste dismantling and recycling processes, including PBDEs by measuring their concentrations in serum samples of a population (e-waste workers and local residents).

It is a cross-sectional study with two exposure groups and a control group. The first one was formed by 17 occupational exposed workers at a small dismantling workshops with rudimentary techniques. The second group included 18 local residents. The control group was formed by 21 people living 40 km away.

Participants were randomly recruited. Demographic information was obtained through questionnaire surveys.

Regarding the statistical analysis, concentration data of all the chemicals were logarithmically transformed to obtain normal distribution, confirmed by Kolmogorov-

Smirnov test. Differences between groups were examined by independent-samples t-test. Multivariate linear regresion analysis was performed to exclude potencial confounding factors.

Serum levels of PBDEs of the exposure group were significantly higher ($p<0.001$) than those of the control group, but this was not the case for BDE-209 ($p=0.83$).

In the logistic regression test, the main positive correlation ($p<0.05$) shows that concentrations in serum in the exposed population was significantly higher than in the control group. No significant correlation was found between serum pollutants concentrations and age, BMI, years of working as e-waste worker and sampling season.

Living or working at e-waste recycling areas was associated to higher concentration of PBDEs in serum, except for BDE-209.

DISCUSSION AND CONCLUSIONS

Epidemiologic information about the link between exposure to PBDEs in e-waste workers and the effect on human health is not very prolific.

The lack of coincidence among all the studies included in this review may be conditioned by the variability of the populations studied and the epidemiologic design used, since 16 out of the 20 studies have cross-sectional design, which limits our ability to assess temporality. Only two studies have a longitudinal design.

A major limitation is that only in four studies, population is randomly selected introducing a potential bias. In 14 studies, investigators did not adjust for the effects of confounders and no other possible exposure ways to PBDEs have been taken into account.

E-waste recycling process implies an exposure to many chemicals, so it is very difficult to assess the effects of the exposure to PBDEs separately.

We conclude that evidence is suggestive to infer association between serum PBDEs levels and working in e-waste recycling facilities. This evidence is consistent, with no studies showing different results, and it is repeated regardless the geographic area in which the study is carried out, although the magnitudes are different, ranging from 26 ng/g lipid in Sweden to 600 ng/g lipid in China, where the highest concentration is found (3436 ng g-1 l.w.),[27] which is probably due to the fact that in this study e-waste workers use very primitive techniques with very little protection measures, which would lead to a higher exposure. The level of evidence for this result, according to SIGN criteria is 3.

In eleven studies[22-29,34,36,37], high levels of PBDEs in serum were found among the population of e-waste surrounding areas and even in far away towns selected as control group. This result clearly indicates that general population without occupational exposure is somehow exposed to these chemicals. In any case, concentrations of PBDEs in e-waste recycling workers are still significantly higher than those in the control group. Two studies are coincident in this regard: Guiyu, China[23], PBDEs median levels in e-waste workers were 3.5 fold higher than those in population of a region located 50km away, and China[27], where the PBDEs total levels in blood in e-waste workers were 3.6 fold higher than in the population of a different Chinese town without PBDEs exposure known. The level of evidence, according to SIGN criteria was 3.

Concentration of PBDEs in blood is associated with exposure time, working procedures and protection measures (level of evidence 3). Age or BMI had no correlation.

An evidence was found (level 1-) about the efficiency of the improvement measures in industrial hygiene in order to reduce an exposure pathway to PBDEs on e-waste recycling activity[28, 39].

All the studies reviewed[19,30-33], investigating the connection between work exposure to PBDEs and levels of PBDEs in hair, showed that levels of PBDEs in hair in the exposed population were significantly higher than those in control population (level of evidence 3).

It is interesting, despite the fact that levels of PBDEs in hair in people living close to recycling areas were higher than in the people living in the cities, concentrations of PBDEs found in the dust collected from the houses closed to the recycling plants were lower than those found in the city houses. This suggest that PBDEs exposure in the reference population arises from sources such as diet and house dust ingestion[44].

While comparing levels of PBDEs in hair and dust, they observed that the proportion of deca- BDE decreases in expense of nona-BDE, compared to concentrations detected in dust, which suggest that metabólico debromination of BDE-209 into nona-BDE may occur.

Other studies[30-32,44] also report higher concentrations of PBDEs in hair in e-waste workers than in control groups. They are not identical each other depending on the technology used on e-waste dismantling, characteristics of the sample population and PBDEs pattern studied. In all reports, the major congener was BDE-209, which is approximately 97% of the deca-BDE mixture, which has been one of the most used in the last years.

Although BDE-209 has low bioavailability and short half-life (15 days), it was found that BDE-209 can be accumulated in human blood and milk. Higher brominated diphenyl ethers would be oxidatively metabolized into low brominated PBDEs, including penta- and nona-BDEs[23,27,44,45].

Biomonitoring not necessarily to identifies the source of PBDEs, since it may occur in places different than the workplace[19,46]. Nevertheless, biomonitoring studies are useful to identify and characterize the exposure and show us the need of implementing exposure control measures[28].

It has been lately documented in laboratory studies that hydroxilated PBDEs (OH-PBDEs) and MeO-PBDEs produce thyroid toxicity[47] and disruption of ovarian steroidogenesis[48].

In studies in-vivo, OH-PBDEs have been detected in rats and mice blood after being exposed to mixtures of PBDEs o BDE-209[20,49]. Nevertheless, in another in vitro study, OH-PBDEs were not detected after the exposure of human hepatocytes to BDE-209[51].

In our review, we found several studies with level of evidence 3, which studies the presence of these metabolytes in workers serum. Levels of OH-PBDEs metabolytes[25,37] and MeO-PBDEs[24,25] were higher in the reference population than in e-waste workers.

Eguchi associates higher levels of MeO-PBDEs with marine fish intake. Yu[37] found OH-octa-BDEs and OH-nona- BDEs in serum samples from e-waste workers. In both studies, BDE-209 was the predominant congener in all the samples.

Nevertheless, Athanasiadou *et al.*[22] studied child labour in Nicaragua dumps. Children in contact with e-waste showed higher levels of PBDEs and OH-PBDEs than children living 20km away. The major congener was BDE-47 and the less frequent BDE-209.

Yang[29] does not find significant differences in levels of BDE-209 among e-waste recycling workers and the control group. This suggests that there are diferentes pathways of exposur such as domestic, or low-brominated-BDE formed by debromination of BDE-209.

The highest concentrations in serum (octa- to nona- BDE) in e-waste workers compared with the reference population[25] would be explained by the BDE-209 debromination theory.

The measurement of the levels of octa- to nona-BDE and PBDEs metabolytes (OH and MeO-PBDEs) could be used to show long term work exposure, while the presence of BDE-209 would be used to assess recent exposure.

TSH is an important parameter of thyroid functions, because it may affect the levels of other hormones by acting on the hypothalamic hypophyseal axis.

Studies in rats show that a short-term exposure to some commercial PBDEs mixtures interfered with the thyroid hormone system via uridinediphosphate-glucuronosyltransferase (UGTs)[52,53].

Reported effects on TSH are not consistent. Wang H.[35] reports decreased concentrations associated with e-waste exposure. Nevertheless, Han G and Yuan[34,36] reports increased concentrations in the exposed population. Also, Han[34] found an association between levels of PBDEs and TSH concentrations.

Findings from several studies shows that free radicals released from PBDEs may cause irreversible oxidative damage in DNA molecules[54]. It plays an important role in various diseases, such as pulmonary diseases, cardiovascular diseases and cancer[55,56].

The cytogenetic essay for micronucleus detection (CBMN: cytokinesis-block micronucleus) is a globally validated and technologically accessible study. It is useful to assess genetic inestability induced by genotoxic agents. Micronucleus are cytoplasmic bodies with nuclear nature that correspond to genetic material non properly incorporated to the daughter cells during cell division, they show chromosomic aberrations and have their origin in chromosomic breakages, in errors during replication or further DNA cell division and/or exposure to genotoxic agents.

In vitro studies[57,58] suggest that PBDEs may damage DNA, producing an increase in the number of micronucleated cells. In several studies[36], the authors found a higher presence of micronucleated cells in e-waste exposed population than in non-exposed population. This shows that PBDEs can be a genotoxic substance and that e-waste recycling workers may have a higher risk of diseases. In fact, the IARC (International Agency for Research on Cancer) classifies PBDEs as “possible carcinogenic substance”.

8-Hidroxi-2´-deoxyguanosine (8-OHdG) is often used to asses oxidative damage[59]. Results found in our review are not conclusive. Zhang G.F.[31] reports that levels of 8-OHdG in urine after the workday were higher than at the beginning of it, showing a positive association between exposure to PBDEs and DNA oxydative damage.

Recent studies in human suggest that high levels of PBDEs in breast milk are related with cryptorchidism in newborns[60], low weight at birth and reduction in length and breast circumference in newborns[61]. It has been found a negative correlation between concentration of PBDEs in serum and the sperm count in young men[62].

Results of studies are coincident, with a level of evidence 3. Noting an association between exposure to PBDEs in working women and the increase in levels of PBDEs in breastmilk and placenta.

One of the studies[19] which analyzes levels of PBDEs in breast milk, placenta and hair samples from a group of childbearing-aged women working in a recycling site in order to relate them to possible health risk showed. Concentrations of PBDEs found in all samples were significantly higher in the exposure group than in non-exposed group.

This result matches with Tue N.M.’s study[38] in which levels of PBDEs in breast milk of women from three e-waste exposure areas (work exposure or not) were not higher than those found in urban area women.

In this study, BDE-209 was the predominant congener in the exposure group while BDE47 and BDE 153 were in the control group.

In Leung’s study, the dominant congener in all samples was BDE 47. Levels of BDE-209 were not analyzed.

High body burden would not only cause problems in worker’s health but also implies a potencial health risk in future generations. The estimate intake of PBDEs for a 6-month-old baby living in an e-waste area and being breastfed would be 572±839 ng/kg body wt/day, 57 times higher than in children in the reference area [19].

Studies in animals and in vitro show association between levels of PBDEs and adverse health effects.

The reviewed studies are coincident to establish an association between exposure to PBDEs and biological parameters alterations but due to the design of the reviewed studies, our ability to assess temporality of associations between exposure to PBDEs in e-waste workers and health effects is limited.

It seems reasonable to implement industrial hygiene measures to reduce levels of emission into the air and levels of exposure to PBDEs from recycling processes, also to implement personal and health protection measures.

Despite all efforts done during last years by different organizations, both in legislative tasks and in programs to determine adverse health effects of PBDEs, the focus is mainly environmental. Nevertheless, evolution in electronic market makes that e-waste represent an emergent work health problem. Further research should be conducted on epidemiologic studies on health impacts caused by e-waste recycling operations, that allow the establishment of causal relations. Regulatory and public health interventions must be developed and implemented to prevent and reduce PBDEs occupational exposure on e-waste workers.

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REFERENCES

1. Chen, A.M., Dietrich, K.N., Huo, X., Ho, S.M. Developmental neurotoxicants in e-waste: an emerging health concern. *Environ. Health Perspect* 2010; 119: 431–438.
2. Ni HG, Zeng H, Tao S, Zeng EY. Environmental and human exposure to persistent halogenated compounds derived from e-waste in China. *Environ. Toxicol. Chem* 2010; 29: 1237–1247.
3. United Nations Environment Programme (UNEP). Stockholm convention on persistent organic pollutants. 2001. Available on: http://www.pops.int/documents/convtext-en.pdf (accessed Dec 20, 2013).
4. Council of the European Parliament. Directive 2002/96/EC of the European Parliament and of the Council of 27 January 2003 on waste electrical and electronic equipment (WEEE). March 13, 2003. *OJEU* 2003; 37: 24-38.
5. United Nations Environment Programme (UNEP). Stockholm Convention on Persistent Organic Pollutants (POPs). Press release: Governments Unite to step-up reduction on global DDT Reliance and add nine new chemicals under international treaty,2009. Available on: http://www.unep.org/Documents.Multilingual/Default.asp?DocumentID=585&ArticleID=6158&RoHS- Directiva de Restricción de Sustancias Peligrosas-, Julio 2008 (accessed Jan 4,2014).
6. Bromine Science and Enviromental Forum (BSEF). Available on www.bsef.com/our-substances/deca-bde/scientific-studies (accessed Jan 4, 2014).
7. US Environmental Protection Agency (EPA). DecaBDE phase-out initiative (last updated on 25th of July 2012). Available on: http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/deccadbe.html (accessed Jan 4, 2014).
8. Leung AOW, Luksemburg WJ, Wong AS, Wong MH. Spatial distribution of polybrominated diphenyl ethers and polychlorinated dibenzo-p-dioxins and dibenzofurans in soil and combusted residue at guiyu, an electronic waste recycling site in Southeast China. *Environ. Sci. Technol* 2007; 41: 2730-2737.
9. Shen CF, Huang SB, Wang ZJ, Qiao M, Tang XJ, Yu CN, Shi DZ, Zhu YF, Shi JY, Chen XC, Setty K, Chen YX, Identification of Ah receptor agonists in soil of E-waste recycling sites from Taizhou area in China, *Environ. Sci. Technol* 2008; 42: 49–55.
10. Allen JG, Mcclean MD, Stapleton HM, Webster TF. Linking PBDEs in house dust to consumer products using X-ray fluorescence. *Environ. Sci. Technol* 2008; 42: 4222–4228.

11. National Toxicology program. Carcinogenesis studies of Decabromodiphenyl Oxide (CAS No. 1163-19-5) in F344/N Rats and B6C3F 1 Mice (Feed studies). *NTP Technical Report Series*. Research Triangle Park, NC: National Toxicology Program; 1986.

12. Laws SC. The effects of DE-71, a comercial polybrominated diphenyl ether mixture, on female pubertal development and thyroid function. *Toxicologist*. 2003; 72:137.

13. Kuriyama S. Maternal exposure to low dose 2,2´4,4´,5 pentabromodiphenyl ether (PBDE 99)impairs male reproductive performance in adult male offspring. *Organohalogen Compd*. 2003; 61:92-95.

14. Breslin WJ. Teratogenic evaluation of a polybromodiphenyl oxide mixture in New Zealand White rabbits following oral exposure. *Fundam Appl Toxicol*. 1989; 12:151-157.

15. Zhou T. Developmental exposure to brominated diphenyl ethers results in thyroid hormone disruption. *Toxicol Sci*. 2002; 66: 105-116.

16. Branchi I. Effects of perinatal exposure to a polybrominated diphenyl ether (PBDE 99) on mouse neurobehavioural development. *Neurotoxicology*. 2002; 23:375-384.

17. Viberg H. Neurobehavioral derangements in adult mice receiving decabrominated diphenyl ether (PBDE 209) during a defined period of neonatal brain development. *Toxicol Sci*. 2003; 76:112-120.

18. Sjödin *et al*. Flame retardant exposure: Polybrominated diphenyl ethers in blood from Swedish workers. *Environ. Health Perspect*. 1999; 107:643-48.

19. Leung A. *et al*. Body burdens of polybrominated diphenyl ethers in childbearing-aged women at an intensive electronic- waste recycling site in China. *Environ. Sci. Pollut. Res*. 2010; 17: 1300-13.

20. Wu K. *et al*. Polybrominated diphenyl ethers in umbilical cord blood and relevant factors in neonates from Guiyu, China. *Environ. Sci. Technol*. 2010; 44: 813-19.

21. Harbour R, Miller J, for the Scottish Intercollegiate Guidelines Network Grading Review Group. A new System for grading recomendations in evidence based guidelines. *BMJ* 2001; 323: 334-6.

22. Athanasiadou M, Cuadra SN, Marsh G, Bergman Å, Jakobsson K. Polybrominated diphenyl ethers (PBDEs) and bioaccumulative hydroxylated PBDE metabolites in young humans from Managua, Nicaragua. *Environmental Health Perspectives* 2008;116 (3): 400-408.

23. Bi X, Thomas GO, Jones KC, Qu W, Sheng G, Martin FL *et al*. Exposure of electronics dismantling workers to polybrominated diphenyl ethers, polychlorinated biphenyls, and organochlorine pesticides in South China. *Environmental Science and Technology* 2007; 41 (16): 5647-5653.

24. Eguchi A, Nomiyama K, Devanathan G, Subramanian A, Bulbule KA, Parthasarathy P *et al*. Organohalogen and metabolite contaminants in human serum samples from Indian E-waste recycling workers. *Interdisciplinary Studies on Environmental Chemistry*. [Revista on-line]. 2010. Vol.4. pp. 167–174. Available in www.terrapub.com (accessed Dec 20, 2013).

25. Eguchi A, Nomiyama K, Devanathan G, Subramanian A, Bulbule KA, Parthasarathy P, Takahashi. Different profiles of anthropogenic and naturally produced organohalogen compounds in serum from residents living near a coastal area and e-waste recycling workers in India. *Environment International*, 2012; 47: 8-16.

26. Kim B-H, Ikonomou MG, Lee S-J, Kim H-S, Chang Y-S. Concentrations of polybrominated diphenyl ethers, polychlorinated dibenzo-p-dioxins and dibenzofurans, and polychlorinated biphenyls in human blood samples from Korea. *Science of the Total Environment*, 2005; 336 (1-3): 45-56.

27. Qu W, Bi X., Sheng G, Lu S, Fu J, Yuan J *et al*. Exposure to polybrominated diphenyl ethers among workers at an electronic waste dismantling region in Guangdong, China. *Environment International* 2007; 33 (8): 1029-1034.

28. Thuresson K, Bergman Å, Rothenbacher K, Herrmann T, Sjölin S, Hagmar L, *et al*. Polybrominated diphenyl ether exposure to electronics recycling workers - a follow up study. *Chemosphere* 2006; 64 (11):1855-1861.

29. Yang Q, Qiu X, Li R, Liu S, Li K, Wang F, *et al*. Exposure to typical persistent organic pollutants from an electronic waste recycling site in Northern China. *Chemosphere* 2013; 91 (2): 205-211.

30. Ma J, Cheng J, Wang W, Kunisue T, Wu M, Kannan K. Elevated concentrations of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans and polybrominated diphenyl ethers in hair from workers at an electronic waste recycling facility in eastern China. *J Hazard Mater*. 2011. 86:1966-1971.

31. Wen S, Yang FX, Gong Y, Zhang XL, Hui Y, Li JG, Liu AL, Wu YN, Lu WQ, Xu Y. Elevated levels of urinary 8-hydroxy-2'-deoxyguanosine in male electrical and electronic equipment dismantling workers exposed to high concentrations of polychlorinated dibenzo-p-dioxins and dibenzofurans, polybrominated diphenyl ethers, and polychlorinated biphenyls. *Environ Sci Techno*l 2008; 42 (11): 4202-4207.

32. Zhao GF, Wang ZJ, Dong MH, Rao KF, Luo JP, Wang DH, Zha JM, Huang SB, Xu YP, Ma M. 2008. PBBs, PBDEs, and PCBs levels in hair of residents around e-waste disassembly sites in Zhejiang Province, China, and their potential sources. *Sci. Total. Environ*. 397: 46-57.

33. Zheng J, Luo XJ, Yuan JG, Wang J, Wang YT, Chen SJ, *et al.* Levels and sources of brominated flame retardants in human hair from urban, e-waste, and rural areas in South China. *Environmental Pollution* 2011; 159 (12): 706-3713.

34. Han G, Ding G, Lou X, Wang X, Han J, Shen H, Zhou Y, Du L. Correlations of PCBs, DIOXIN, and PBDE with TSH in children's blood in areas of computer E-waste recycling. *Biomed Environ Sci* 2011; 24(2): 112-116.

35. Wang H, Zhang Y, Liu Q, Wang F, Nie J, Qian Y. Examining the relationship between brominated flame retardants (BFR) exposure and changes of thyroid hormone levels around e-waste dismantling sites. *International Journal of Hygiene and Environmental Health* 2010; 213 (5): 369-380.

36. Yuan J, Chen L, Chen D, Guo H, Bi X, Ju Y, *et al.* Elevated serum polybrominated diphenyl ethers and thyroid-stimulating hormone associated with lymphocytic micronuclei in Chinese workers from an e-waste dismantling site. *Environmental Science and Technology* 2008; 42 (6): 2195-2200.

37. Yu Z, Zheng K, Ren G, Zheng Y, Ma S, Peng P, *et al.* Identification of hydroxylated octa- and nona-bromodiphenyl ethers in human serum from electronic waste dismantling workers. *Environmental Science and Technology* 2010; 44 (10): 3979-3985.

38. Tue NM, Takahashi S, Suzuki G, Isobe T, Viet PH, Kobara Y, Seike N, *et al.* Contamination of indoor dust and air by polychlorinated biphenyls and brominated flame retardants and relevance of non-dietary exposure in Vietnamese informal e-waste recycling sites. *Environment International* 2013; 51: 160-167.

39. Rosenberg C, Hämeilä M, Tornaeus J, Säkkinen K, Puttonen K, Korpi A, *et al.* Exposure to flame retardants in electronics recycling sites. Annals of Occupational Hygiene 2011; 55 (6): 658-665.

40. Grant K, Goldizen F, Sly P, Brune MN, Neira M, Van den Berg M, *et al.* Health consequences of exposure to e-waste: a systematic review. *The Lancet Global Health*, In Press, Corrected Proof, Available online 30 October 2013.

41. Sjodin A, Hagmar L, Klasson-Wehler E, Kronholm- Diab K, Jakobsson E, Bergaman A. Flame retardant exposure: polybrominated diphenyl ethers in blood from Swedish workers. Environ Health Perspect. 1999; 107:643-648.

42. Jones-Otazo H, Clarke JP, Diamond ML, Archbold JA, Ferguson G, Harner T, Richardson GM, Ryan JJ, Wilford B. Is house dust the missing exposure pathway for PBDEs? An analysis of the urban fate and human exposure to PBDEs. *Environ. Sci. Technol.* 2005; 39: 5121-5130.

43. Luo XJ, Liu J, Luo Y, Zhang XL, Wu JP, Lin Z, Chen SJ, Mai BX, Yang ZY. Polybrominated diphenyl ethers (PBDEs) in free-range domestic fowl from an e-waste recycling site in South China: levels, profile and human dietary exposure. Environ. Int. 2009; 35: 253-258.

44. Sjödin A, Patterson DG, Bergman Å. Brominated flame retardants in serum from U.S. blood donors. *Environ. Sci. Technol.* 2001; 35: 3830-3833.

45. La Guardia MJ, Hale RC, Harvey E. Detailed polybrominated diphenyl ether (PBDE) congener composition of the widely used penta-, octa-, and deca- PBDE technical flame retardant mixtures. *Environ. Sci. Technol* 2006: 40; 6247-6254.

46. Paustenbach D. Biomonitoring and biomarkers: exposure assessment will never be the same. *Environ Health Perspect.* 2006; 114: 1143-1149.

47. Darnerud PO, Aune M, Larsson L, Hallgren S. Plasma PBDE and thyroxine levels in rats exposed to Bromkal or BDE-47. *Chemosphere* 2007;67: 386-392.

48. Canto´n RF. Inhibition of human placental aromatase activity by hydroxylated polybrominated diphenyl ethers (OH-PBDEs). *Toxicol. Appl. Pharmacol.* 2008; 227: 68-75.

49. Chen LJ, Lebetkin EH, Sanders JM, Burka LT. Metabolism and disposition of 2,2,4,4,5 pentabromodiphenyl ether (BDE99) following a single or repeated administration to rats or mice. *Xenobiotica* 2006; 36: 515-534.

50. Sandholm A, Emanuelsson BM, Klasson Wehler E. Bioavailability and half-life of decabromodiphenyl ether (BDE- 209) in rats. *Xenobiotica* 2003; 33: 1149-1158.

51. Stapleton HM, Kelly SM, Pei R, Letcher R.J, Gunsch C. Metabolism of polybrominated diphenyl ethers (PBDEs) by human hepatocytes in vitro. *Environ. Health Perspect.* 2009; 117: 197-202.

52. Zhou, T. Effects of short-term in vivo exposure to polybrominated diphenyl ethers on thyroid hormones and hepatic enzyme activities in weanling rats. *Toxicol. Sci.* 2001; 61: 76-82.

53. Zhou R. Study on the relation between iodine nutrition of pregnant women in different occasions and thyroid function of their neonates. *Zhonghua Liu Xing Bing Xue Za Zhi* 2002; 23: 356-359.

54. He P. PBDE-47-induced oxidative stress, DNA damage and apoptosis in primary cultured rat hippocampal neurons. *NeuroToxicology* 2008; 29 (1): 124-129.

55. Beckman KB. The free radical theory of aging matures. *Physiol. Rev.* 1998, 78 (2), 547-581.

56. Hwang ES, Kim GH. Biomarkers for oxidative stress status of DNA, lipids, and proteins in vitro and in vivo cancer research. *Toxicology* 2007; 229: 1-10.

57. Hu XZ. Apoptosis induction on human hepatoma cells Hep G2 of decabrominated diphenyl ether (PBDE-209). *Toxicol. Lett.* 2007; 171: 19-28.

58. Wang JJ. Cyto- and genotoxicity of ultrafine TiO2 particles in cultured human lymphoblastoid cells. *Mutat. Res.* 2007; 628: 99-106.

59. Kasai H. Analysis of a form of oxidative DNA damage, 8-hydroxy-2-deoxyguanosine, as a marker of cellular oxidative stress during carcinogenesis. *Mutat. Res. Genet. Toxicol. Environ. Mutagen.* 1997; 387 (3): 147-163.

60. Main KM. Flame retardants in placenta and breast milk and cryptorchidism in newborn boys. *Environm Health Perspec*t. 2007; 115: 1519-1526.

61. Chao HR. Levels of PBDEs in breast milk from central Taiwan and their relation to infant birth outcome and maternal menstruation effects. *Environ Int.* 2007; 33: 239-245.

62. Akutsu K. Polybrominated diphenyl ethers in human serum and sperm quality. *Bull Environ Contam Toxicol.* 2008; 80: 345-350.