EXTERNAL SCIENTIFIC REPORT

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Extensive literature search, selection for relevance and data extraction of studies related to the toxicity of PCDD/Fs and DL-PCBs in humans

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Abstract

To enable the hazard identification and characterisation in the risk assessment for humans related to the seventeen 2,3,7,8-substituted dioxins (PCCDs) and furans (PCDFs) and the twelve dioxin-like polychlorinated biphenyls (DL-PCBs), EFSA outsourced an extensive literature search (ELS), followed by selection for relevance and extraction of relevant data for consideration in the risk assessment. Two tailored search strategies for Web of Science (WoS) and PubMed for identifying relevant human studies were developed in discussion with EFSA and used to carry out two ELSs. The outcome of the ELSs were exported into EndNote files, with a total of 4,549 studies identified in WoS and a total of 3,677 studies identified in PubMed. The EndNote files were combined and duplicates were removed, which left 6,699 studies in total. The combined EndNote file was imported into DistillerSR®, the duplication detection tool in DistillerSR® was used and additional 598 duplicates were identified and moved to quarantine in DistillerSR®. Level 1 and Level 2 relevance templates were created in DistillerSR® using the eligibility criteria (inclusion/exclusion criteria) provided by EFSA in the Technical Specifications and these were discussed with EFSA. Following the discussions and a relevance pilot test the remaining 6,101 studies were checked for relevance. When the selection for relevance had been complete, 257 studies proceeded to Level 3 data extraction. The data extraction templates were created in DistillerSR® using the criteria provided by EFSA. Following discussions with EFSA and a data extraction pilot test, the project team performed the data extraction on these studies with the relevant information added to the data extraction forms in DistillerSR®.

Key words: extensive literature search, dioxins, human studies

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Summary

To enable the hazard identification and characterisation in the risk assessment for humans related to the seventeen 2,3,7,8-substituted dioxins (PCCDs) and furans (PCDFs) and the twelve dioxin-like polychlorinated biphenyls (DL-PCBs), EFSA outsourced an extensive literature search (ELS), followed by selection for relevance and extraction of relevant data for consideration in the risk assessment.

Due to their biopersistence in the environment (Persistent Organic Pollutants – POPs), PCDDs and PCDFs are listed in Annex C of the Stockholm Convention which requires users to reduce or eliminate releases from unintentional production. The use of DL-PCBs is banned under the Convention.

The toxicity of PCDD/Fs and DL-PCBs and their effects on humans has been the subject of a large number of studies in the published literature. Human exposure to dioxins and dioxin-like compounds primarily occurs through dietary sources of fatty foods of animal origin (e.g. dairy products and fish) or breast-milk.

This Final Report provides an overview of the work conducted by the project team for the extensive literature search, selection for relevance and data extraction of studies related to the toxicity of PCDD/Fs and DL-PCBs in humans.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

This contract was awarded by EFSA to:

Contractor:	Risk & Policy Analysts Ltd
Contract title:	Extensive literature search, selection for relevance and data extraction of studies related to the toxicity of PCDD/Fs and DL-PCBs in humans
Contract number:	NP/EFSA/BIOCONTAM/2016/06

1.1.1. Background as provided by EFSA

The Unit on Biological Hazard and Contaminants (BIOCONTAM Unit) supports the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel), which provides scientific advice on contaminants in the food chain and undesirable substances such as natural toxicants, mycotoxins and residues of unauthorised substances.

In January 2015 EFSA received a mandate from the European Commission for a scientific opinion on the risks for human and animal health related to the presence of dioxins and dioxin-like polychlorinated biphenyls (DL-PCBs) in food and feed. The mandate was allocated to the CONTAM Panel. A Working Group was established to develop the draft opinion.

To support preparatory work for the hazard identification and characterization steps in the human risk assessment, EFSA wishes to outsource an extensive literature search (ELS) followed by a full relevance assessment (selection of relevant studies), and subsequent data extraction of relevant studies, related to the toxicity of the seventeen 2,3,7,8-substituted dioxins (PCDDs) and furans (PCDFs) and twelve DL-PCBs in experimental animals.

Preliminary keywords and the bibliographic databases to be interrogated, eligibility criteria for selection of relevant studies (inclusion/exclusion criteria), and the outlines of data extraction forms will be provided and will have to be tailored and implemented by the contractor.

The contractor should ensure that all the steps for conducting the ELS, study selection and data extraction are properly documented and reported.

A collaboration model with EFSA with progress meetings during the duration of the project is envisaged to ensure fit-for-purpose results.

The present Call is based on EFSA's 2016 Work Programme for grants and operational procurements as presented in Annex II of the EFSA Programming Document 2016 – 2018, available on the EFSA's website (http://www.efsa.europa.eu/sites/default/files/mb151203-a2.pdf).

As stated in the specifications for this study, the Final report contains the following:

- The final protocol including the project plan implemented by the contractor to carry out the project
- The results of the ELSs
- The results of the selection for relevance
- The results of the data extraction process

1.2. Additional information

The results of the selection for relevance and data extraction processes are present within DistillerSR®.

2. Data and Methodologies

2.1. Data

Data for this study has been drawn from published literature contained within the Web of Science (WoS) (including: Web of Science™ Core Collection, BIOSIS Citation Index℠, CABI: CAB Abstracts®, Current Contents Connect®, Data Citation Index SM, FSTA®–the food science resource, MEDLINE®, SciELO Citation Index, Zoological Record®) and PubMed databases.

2.2. Methodologies

The study involved the development of methodologies, these methodologies included:

- Development of two search strategies to carry out an ELS through interrogation of WoS and PubMed databases. This is described further in Section 4.1
- Development of tools to enable the selection of identified titles and abstracts, and full text. This is described in Section 4.2.
- Development of a tool to allow data extraction from identified studies. This is described in Section 4.3.

3. Commentary on Dioxins

3.1. Overview of Dioxins

The term 'dioxins' is used to refer to a family of 210 structurally and chemically related polychlorinated dibenzo-*p*-dioxins (PCDD, 75 congeners) and polychlorinated dibenzofurans (PCDFs, 135 congeners). PCDD and PCDFs are triclinic, planar aromatic compounds. In addition, other groups of chemicals have similar properties to PCDDs and PCDFs in terms of their toxicity profiles and persistence, including 12 polychlorinated biphenyls which are non-*ortho* or mono-*ortho* PCBs with at least four chlorine atoms, often referred to as 'dioxin-like' PCBs (DL-PCBs).

PCDDs and PCDFs are widely distributed in the environment, being formed as by-products during combustion processes including waste incineration, forest fires and volcanic eruptions, and during a number of industrial processes including smelting, chlorine bleaching of paper pulp and the manufacturing of some chlorinated organic chemicals such as pesticides and herbicides. Historically, DL-PCBs were manufactured and used on a global scale, however their manufacture was banned under the Stockholm Convention on Persistent Organic Pollutants in 2001. Despite this ban, DL-PCBs continue to be released into the environment through disposal of largescale electrical equipment and waste, in which they were used as dielectric fluids.

DL-PCBs were historically manufactured for use as coolants and lubricants in transformers, capacitors and other electrical equipment. There are no known natural sources of DL-PCBs (ATSDR, 2014a). DL-PCBs have been banned in over 150 countries under the Stockholm Protocol as being Persistent Organic Pollutants (POPs); however, release to the environment can still occur through the disposal of electrical waste.

Levels of dioxins and DL-PCBs are generally low in air and drinking and source water. However, releases to the air and from waste sites can lead to contamination in the food chain where dioxins typically bioaccumulate. Dioxins and DL-PCBs possess good chemical stability, thereby persisting longer in the environment. In addition, due to their hydrophobic nature the compounds are absorbed by fat tissue of humans and animals where they are stored (INSERM, 2000). This may lead to accumulation in fatty foods such as dairy products, some fish, meat and shellfish. Their half-life is typically 7-11 years in humans, with concentrations increasing up the food chain (WHO, 2014).

There have been 419 types of dioxin-related compounds identified to date, with around 30 of these considered to have significant toxicity. Of these 30 compounds, 17 congeners with chlorine atoms at the 2,3,7,8 positions are relatively resistant to metabolic degradation and are considered to have potential adverse effects in humans and animals. The potency of these compounds varies greatly which has led to the development of 'Toxic Equivalency Factors' (TEFs) to compare the toxicity of individual compounds, and allow the combined effect of all dioxins and DL-PCBs to be assessed. TEFs are set by the World Health Organisation (WHO) and express the concentrations of other dioxins and DL-PCBs as a concentration equivalent to the most toxic and well-studied dioxin 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). The weighted concentrations are then summed to give a single value, termed a Toxic Equivalent (TEQ) (EFSA, 2015; US EPA, 2016).

TCDD was pre-registered under the REACH regulations between the 1st June and 1st December 2008 although there is no further information on progression to full registration. The substance is classified and labelled as being fatal if swallowed, causing serious eye irritation, very toxic to aquatic life, and very toxic to aquatic life with long lasting effects.

3.2. Exposure to dioxins and DL-PCBs

The exposure of humans to dioxins and DL-PCBs primarily occurs through dietary sources, although additional exposure can occur through dermal, inhalation and transplacental routes. A tolerable weekly limit of 14 pg WHO-TEQ/g fat was set by the Scientific Committee on Food in 2001. The US Environmental Production Agency (US EPA) has proposed a reference dose for chronic oral exposure of 0.7 pg/kg body weight (bw) per day (US EPA, 2012), which is equivalent to 4.9 pg/kg bw per week.

The highest concentrations of dioxins and DL-PCBs are found in meat, some fish, eggs and dairy products with cereals, fats and oil also contributing (Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, COT, 2001; Codex Committee, 2003). In Europe, milk and dairy products (16-39%) and meat and meat products (6-32%) are the two main sources of dioxin exposure in the diet (Codex Committee, 2003).

Contamination of the food chain with dioxins was first reported in the 1950s in the US, when thousands of chickens became diseased and died through consuming dioxin-contaminated feed. In 1999, dioxins in hen feed resulted in contamination of the food chain in Belgium (Hoogenboom et al., 2015), and in Ireland in 2008, levels of dioxin and DL-PCBs of up to 200 pg WHO-TEQ/g fat were reported in pork. EFSA investigated the incident and concluded that daily consumption of 10% Irish pork contaminated to the highest level for 90 days would increase the body burden by approximately 10% and therefore a single consumption was not considered of concern (EFSA, 2008). The presence of high levels of dioxin and DL-PCBs in sheep and deer liver was also investigated by EFSA (EFSA CONTAM Panel, 2011) and it was concluded that the regular consumption of sheep liver results in an increase of approximately 20% in the median background exposure to dioxin and dioxin-like compounds and that frequent consumption may result in health concerns.

3.3. PCDDs and PCDFs

PCDDs and PCDFs are listed in Annex C of the Stockholm Convention on Persistent Organic Pollutants meaning that measures must be taken to avoid unintentional release. There is potential for 75 PCDDs and 135 PCDFs through the possible chlorination of up to eight ring positions in the structure. Seventeen PCDDs and PCDFs with 2,3,7,8 substitution pattern have been assigned a toxic equivalency factor (TEF) by WHO related to the most toxic congener, 2,3,7,8-TCDD (Table 1).

Table 1: Seventeen PCDDs and PCDFs and their toxic equivalent factors (TEF) (Van den Berg et al., 2006)

Compound	World Health Organization Toxic Equivalent Factor (WHO-TEF)
PCDDs	
2,3,7,8-TCDD	1
1,2,3,7,8-PeCDD	1
1,2,3,4,7,8-HxCDD	0.1
1,2,3,6,7,8-HxCDD	0.1
1,2,3,7,8,9-HxCDD	0.1
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.0003
PCDFs	
2,3,7,8-TCDF	0.1
1,2,3,7,8-PeCDF	0.03
2,3,4,7,8-PeCDF	0.3
1,2,3,4,7,8-HxCDF	0.1
1,2,3,6,7,8-HxCDF	0.1
1,2,3,7,8,9-HxCDF	0.1
2,3,4,6,7,8-HxCDF	0.1
1,2,3,4,6,7,8-HpCDF	0.01
1,2,3,4,7,8,9-HpCDF	0.01
OCDF	0.0003

3.4. Toxicity of PCDDs and PCDFs

Exposure to PCDDs, PCDDFs and DL-PCBs are associated with a number of adverse effects in humans and animals, considered to be mediated through the arylhydrocarbon (Ah) receptor which is ubiquitous in all organisms. Binding of dioxin or dioxin-like compounds to the Ah receptor results in an expression change of certain genes, including those encoding biotransformation enzymes. Effects on the immune and reproductive system are often observed, together with effects on brain development and learning ability. The effects of the compounds can also create a specific complex of atypical enzymes and the receptor also disrupts the endocrine signalling routes of steroid hormones and the endocrine system (Tavakoly Sany et al., 2015). The higher toxicity of TCDD may be due to its high affinity binding and long term occupancy of the receptor (COT, 2001).

Short-term exposure to high levels of dioxins in humans, such as might be encountered in occupational settings or following accidental spills, have been associated with skin lesions (chloracne and patchy darkening of the skin). However, longer-term low-level (environmental) exposures are associated with a number of adverse effects in humans including impairment of the immune system, the developing nervous system, the endocrine system (thyroid and steroid hormones) and reproductive function. The developing foetus and neonates have been identified as being particularly sensitive to exposure to dioxins as these can affect the developing organ systems (WHO, 2014). It is noted that compared to animal studies, there is less information available regarding the toxicity for TCDD in humans. IARC (1997) have classified TCDD as Group 1 – '*carcinogenic to humans*' - with some other dioxins classified as Group 3 – '*not classifiable as to their carcinogenicity to humans*'. In addition, IARC recently classified 2,3,4,7,8-pentachlorodibenzofuran and 3,3',4,4',5-pentachlorobiphenyl in Group 1. Dioxins are non-genotoxic carcinogens, and it is considered that a threshold for carcinogenicity exists, possibly involving the Ah receptor. In addition, tolerable intake guidance that is based on non-cancer endpoints is considered to also be protective for carcinogenicity (WHO, 2002).

The strongest evidence for TCDD carcinogenicity is for all cancers combined, whilst TCDD exposure has also been linked to soft-tissue sarcoma, non-Hodgkin lymphoma and cancer of the lung (IARC, 2012).

The COT (2001) have summarised the main effects of dioxin exposure and the available data which is presented in Table 2.

Table 2: Effects associated with dioxin exposure according to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2001)

Effect	Epidemiological evidence
Chloracne	Proven association No clear dose relationship
Gastrointestinal effects and liver enzymes	Transient increases in some liver enzymes
Cardiovascular diseases	Positive association in occupational studies, but not in air force veterans exposed to herbicides in Vietnam (Operation Ranch Hand). Dose-response in some studies
Changes in lipid levels	Results not consistent
Diabetes	Overall results not consistent Increased risks of morbidity in Seveso and Ranch Hand study
Reproductive hormones	Inconsistent results
Reproductive outcomes	Change in sex ratio of offspring with highly exposed fathers in Seveso. Increased risk of infertility and a longer time to pregnancy and a non-significant increased risk of endometriosis with exposed women in Seveso.
Thyroid function	Results not entirely consistent. Some small differences reported in thyroid hormone uptake levels
Neurological/psychological effects	Inconsistent findings. Some effects reported in Ranch Hand study and Seveso (polyneuropathies, abnormal co-ordination) No association with depression
Respiratory system	Inconsistent evidence Irritative effects and reduced lung function in some studies
Urinary system	No major renal or bladder dysfunctions observed
Immunological effects	Inconsistent findings
Neurobehavioral development effects	Some observed differences in Dutch cohort studies
Cancer	Regarded as a probable human carcinogen (based on human, animal and mechanistic data)
Chloracne	Proven association No clear dose relationship
Gastrointestinal effects and liver enzymes	Transient increases in some liver enzymes
Cardiovascular diseases	Positive association in occupational studies, but not in air force veterans exposed to herbicides in Vietnam (Operation Ranch Hand). Dose-response in some studies
Changes in lipid levels	Results not consistent

3.5. Toxicity of DL-PCBs

There are twelve DL-PCBs of interest, as summarised in Table 3. These contain at least four chlorine atoms in their structure.

Exposure to DL-PCBs in humans can result in chloracne and other dermal lesions, increased levels of some liver enzymes including possible hepatic liver damage and respiratory issues (ATSDR, 2014b).

Table 3: The twelve DL-PCBs

PCB	IUPAC Name
PCB-77	3,3′,4,4′-TetraCB
PCB-81	3,4,4′,5-TetraCB
PCB-105	2,3,3′,4,4′-PentaCB
PCB-114	2,3,4,4′,5-PentaCB
PCB-118	2,3′,4,4′,5-PentaCB
PCB-123	2,3′,4,4′,5-PentaCB
PCB-126	3,3′,4,4′,5-PentaCB
PCB-156	2,3,3′,4,4′,5-HexaCB
PCB-157	2,3,3′,4,4′,5′-HexaCB
PCB-167	2,3′,4,4′,5,5′-HexaCB
PCB-169	3,3′,4,4′,5,5′-HexaCB
PCB-189	2,3,3′,4,4′,5,5′-HeptaCB

DL-PCBs interact with the Ah receptor in a similar manner to TCDD which causes the toxic effects of the DL-PCBs and have similar toxicity effects as dioxins which are described in Section 3.4. DL-PCBs have been associated with both cancers of the lung and breast and also with malignant melanoma. PCBs can also cross through the placenta and accumulate in breast milk, resulting in a potentially greater accumulation of PCBs in children than adults (IARC, 2016). DL-PCBs have also recently been upgraded to group 1 carcinogens by IARC.

3.6. Concluding remarks

The toxicity of the seventeen 2,3,7,8-substitued dioxins and furans and the twelve DL-PCBs in humans has been the subject of many case studies in the literature (for example Mocarelli et al., 2008; and Wittsiepe et al, 2007; Scialli et al., 2015). The US EPA, the Scientific Committee on Food (SCF) and the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee have used different approaches in risk assessments for dioxin and dioxin-like compounds which had an effect on the final health-based guidance value. Whilst the US EPA has used human studies and pharmacokinetic modelling of blood levels (estimated from epidemiological studies), FAO/WHO and SCF have used animal studies and a body-burden one-compartment kinetics approach (EFSA, 2015). In view of these differences, EFSA plans to undertake a risk assessment related to the presence of these compounds in food and feed. To assist in the hazard identification and characterisation steps for a human risk assessment, the relevant data (i.e. toxicity) is to be extracted and documented from the extensive literature available.

4. Development of methodologies

The project plan and steps that were undertaken by the project team are outlined in the following sections.

4.1. Search strategies

The methodology that was developed for the ELS of studies related to the toxicity of the 17 2,3,7,8-substituted PCDD/Fs and the 12 DL-PCBs in humans. The search criteria were developed using the preliminary keywords and some of the eligibility criteria as identified in the tender specification (see Table 4 for the preliminary words and Table 7 for the eligibility criteria). These extensive searches focussed on scientific literature published in peer-reviewed journals during the period 1998 – present date. All searches were carried out in English. The search terms were developed by an Information

Scientist and Senior Key Expert using a sensitivity analysis (detailed in Appendix A). The initial search terms developed were discussed with EFSA. However, it became apparent that some key studies, as identified by EFSA, were not being identified using the search strategy initially developed. The search terms where then redeveloped and more studies were identified, where these included the key studies identified by EFSA. Subsequently, the revised search criteria were discussed and agreed with EFSA. The final search terms are outlined in more detail below.

Table 4: Preliminary keywords

Preliminary Keywords	Dioxins, Tetrachlorodibenzodioxin, TCDD, Dioxin-like, TEQ, Coplanar, Polychlorinated biphenyls, PCBs **AND** Epidemiology, Cohort Studies, Case-Control Studies, adverse effects, Observational Study, Cross-Sectional Studies, Case series/Case reports

4.1.1. Web of Science

Broad search terms were used that are appropriate to the database being interrogated, namely Web of Science. A number of Web of Science databases were used as part of the search, these included the Web of Science™ Core Collection, BIOSIS Citation Index℠, CABI: CAB Abstracts®, Current Contents Connect®, Data Citation Index℠, FSTA®–the food science resource, MEDLINE®, SciELO Citation Index and Zoological Record®. All searches were carried out in English and over a time span of 1998 to 5 July 2016.

As indicated above, the criteria were initially developed and discussed with EFSA and then were updated. The final WoS search terms and the number of papers identified appear in Table 5.

Table 5: Web of Science search strategy

Information source	Search string
Web of Science (including: Web of Science™ Core Collection, BIOSIS Citation Index℠, CABI: CAB Abstracts®, Current Contents Connect®, Data Citation Index SM, FSTA®–the food science resource, MEDLINE®, SciELO Citation Index, Zoological Record®)	Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar OR PCDD$ OR PCDF$ OR "Polychlorinated dibenzofuran" OR Polychlorinated dibenzodioxin) AND TOPIC: (epidemiolog* OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*" OR urine OR serum OR plasma OR haema* OR hema* OR blood OR sperm OR semen OR hormone* OR reproduct*) AND TOPIC: (human OR women OR men OR child*) *Timespan=1998-2016* *Search language=Auto* Refined by: [excluding] DOCUMENT TYPES: (MEETING ABSTRACT OR LETTER OR EDITORIAL MATERIAL OR BOOK CHAPTER OR NEWS ITEM OR OTHER OR BIOGRAPHY) AND [excluding] LANGUAGES: (PORTUGUESE OR SPANISH OR CZECH OR FRENCH OR ITALIAN OR RUSSIAN OR CROATIAN OR GERMAN OR POLISH OR JAPANESE OR HUNGARIAN OR CHINESE OR FINNISH OR DANISH OR NORWEGIAN OR SWEDISH OR KOREAN OR DUTCH):
Numbers of papers retrieved	**4,549**

4.1.2. PubMed

Broad search terms were used that are appropriate to the database being interrogated, namely PubMed. All searches were carried out in English and over a time span of 1998 to 5 July 2016.

As indicated above, the criteria were initially developed and discussed with EFSA and then were updated. The final PubMed search terms and numbers of papers appear in Table 6.

Table 6: PubMed search strategy

Information source	Search string
Pub med	((((((((("journal article"[Publication Type]) OR "review"[Publication Type]) OR "scientific integrity review"[Publication Type]) OR "meta analysis"[Publication Type]) OR research[Publication Type]) OR review, systematic[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ((((((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD*[Title/Abstract]) OR PCDD*[Title/Abstract]) OR PCDF*[Title/Abstract]) OR "Polychlorinated dibenzofuran"[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract] OR "Polychlorinated dibenzodioxin"[Title/Abstract])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh]))))) AND (((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms] OR blood [MeSH Terms] OR hormones [MeSH Terms] OR serum [MeSH Terms] OR urine [MeSH Terms] OR semen[MeSH Terms])) OR (epidemiolog*[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case reports"[Title/Abstract] OR urine[Title/Abstract] OR serum[Title/Abstract] OR plasma [Title/Abstract] OR haema*[Title/Abstract] OR hema [Title/Abstract] OR blood [Title/Abstract] OR sperm [Title/Abstract] OR semen[Title/Abstract] OR hormone*[Title/Abstract] OR reproduct*[Title/Abstract]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])))):
Number of studies retrieved	**3,677**

4.1.3. Combined data set

The ELS identified a combined total of 8,226 studies through the interrogation of Web of Science (4,549) and PubMed (3,677) databases, as described above. The studies from these searches were

combined (8,226) in EndNote and exact duplicates (1,527) were removed using EndNote; this left 6,699 studies to go forward to the next stage, i.e. the relevance checking.

4.2. Selection for relevance

As part of the selection of relevance, two levels of relevance checks were performed by the project team, these were; Level 1, screening of title and abstract, and Level 2, screening of full article.

Prior to the selection of relevance taking place, the project team performed a pilot test and the results of the pilot test were discussed with EFSA.

4.2.1. Pilot test for the selection for relevance

A pilot test of Level 1 (Title and abstract screening) and Level 2 (Full text screening) relevance checks was performed. The forms for each of the Level 1 and Level 2 relevance checks were designed based on the eligibility criteria that appeared in the tendered specification, Table 7.

As part of the pilot test, reviewers from the project team reviewed 200 studies in total, the answer options selected by each reviewer were analysed and suggested changes to both Level 1 and Level 2 forms were suggested. These forms were discussed with EFSA and the appropriate changes were then made within DistillerSR®. A sample of studies deemed not relevant during Level 1 screening and for which divergences and doubts were raised during Level 2 were provided to EFSA.

The details of the pilot test and studies deemed not relevant during Level 1 screening and for which divergences and doubts were raised are detailed in Appendix B.

Table 7: Eligibility criteria for the selection of studies in humans

Eligibility criteria	Inclusion	Exclusion
Study design	Cross-sectional studies Cohort studies Case-control studies (retrospective and nested) Case series/Case reports[a]	Animal studies *In vitro* studies
Study characteristics	Any study duration Any number of subjects	-
Population	All populations groups, all ages, males and females Study location: all countries	-
Exposure/ intervention	All routes of exposure (dietary, dermal, inhalation, transplacental exposure) Studies in which levels of the following target compounds have been measured in human tissues (including by bioassays), OR Studies in which the total dietary exposure to the following target compounds has been estimated, - 17 PCDD/Fs and 12 DL-PCBs - 17 PCDD/Fs - 12 DL-PCBs - 17 PCDD/Fs plus non-*ortho* PCBs, at least one PCB being PCB-126 - TCDD (when dominates the TEQs, as in the Seveso incident) or any of the individual target congeners that	Studies on mono-*ortho* PCBs only Studies on non dioxin-like (indicator) PCBs[b] Studies on mixtures in which the contribution from the target compounds does not allow the calculation of TEQs

Eligibility criteria	Inclusion	Exclusion
	dominates the TEQs	
Specific outcome of interest	All endpoints, including hormone levels	Studies on gene expression only Studies on drug metabolising enzyme activity/levels only
Language	English	-
Time	From 1998 onwards	-
Publication type	Peer-reviewed primary research studies (i.e. studies generating new data) Systematic reviews, reviews and meta-analysis(c)	Expert opinions, editorials, and letters to the editor PhD Theses Extended abstracts, conference proceedings

(a): Case series/case report studies will not go through the data extraction process.
(b): Indicator PCBs: PCB-28, -52, -101, -138, -153, and -180.
(c): Systematic reviews, reviews and meta-analysis will be included and used as background information. These types of publications will not go through the data extraction process

4.2.2. Duplicate removal

Once the pilot test had been complete and the forms had been updated the studies and answer options provided were deleted by the project team. The project team then added the 6,699 studies from the combined EndNote file to DistillerSR®. Once the 6,699 studies had been imported, the duplicate detection tool within DistillerSR® was used to detect duplicate studies. Those were moved into the quarantine within DistillerSR®. The project team used the *Check By Title & Author* duplicate detection option and minimum word lengths from three to seven words were used. In total 598 studies were moved into quarantine, this left 6,101 studies after the duplicates were removed.

4.2.3. Level 1 – Title and abstract screening

The updated and final Level 1 relevance form is shown below. The form consisted of one question and five answer options as per below.

Screening of title and abstract (Level 1 in DistillerSR®)

Is the study reporting on **human health** due to intervention/exposure to **any of the target compounds**?

- Target compounds (below):

17 PCDD/Fs:

Polychlorinated dioxins (PCDD)

2,3,7,8-TCDD
1,2,3,7,8-PeCDD
1,2,3,4,7,8-HxCDD
1,2,3,6,7,8-HxCDD
1,2,3,7,8,9-HxCDD
1,2,3,4,6,7,8-HpCDD
OCDD

Polychlorinated dibenzofurans (PCDF)
2,3,7,8-TCDF
1,2,3,7,8-PeCDF
2,3,4,7,8-PeCDF

1,2,3,4,7,8-HxCDF
1,2,3,6,7,8-HxCDF
1,2,3,7,8,9-HxCDF
2,3,4,6,7,8-HxCDF
1,2,3,4,6,7,8-HpCDF
1,2,3,4,7,8,9-HpCDF
OCDF

12 DL-PCBs:

Non-*ortho* DL-PCBs
3,3',4,4'-TCB (PCB-77)
3,4,4',5-TCB (PCB-81)
3,3',4,4',5-PeCB (PCB-126)
3,3',4,4',5,5'-HxCB (PCB-169)

Mono-*ortho* DL-PCBs
2,3,3',4,4'-PeCB (PCB-105)
2,3,4,4',5-PeCB (PCB-114)
2,3',4,4',5-PeCB (PCB-118)
2',3,4,4',5-PeCB (PCB-123)
2,3,3',4,4',5-HxCB (PCB-156)
2,3,3',4,4',5'-HxCB (PCB-157)
2,3',4,4',5,5'-HxCB (PCB-167)
2,3,3',4,4',5,5'-HpCB (PCB-189)

Possible Answers (Radio type used):

- Yes,
- no (it refers to occurrence, analytical methods, other OR it refers to non-target compounds, e.g. Aroclor, BFRs),
- no (it refers to animal studies),
- no (it refers to the target compounds BUT it refers to *in vitro* studies, gene expression only, enzyme induction only) and
- unclear (e.g. target compounds not specifically identified in the abstract, but may be identified in the full text)

The total number of studies was divided into two and each study was reviewed by two separate reviewers, one being a senior scientist with experience in epidemiology. As part of the Level 1 screening process there were conflicts between reviewers. Each of these conflicts were checked by another reviewer prior to an answer option being updated.

Out of the 6,101 studies screened during Level 1 screening, 3,883 studies were excluded. For example, this included studies which were about printed circuit boards (PCB) and related to the Swedish prostate cancer database (PcBaSe).

4.2.4. Level 2 – Full text screening

The updated and final Level 2 relevance form is shown below. The form consisted of seven questions and a comments box. The type of study and information contained meant that different answers options were selected and some studies were excluded.

Screening of full text (Level 2 in DistillerSR®)

1) Is the study a **peer-reviewed primary research study/systematic review/review/meta-analysis of interest of the target compounds in humans**?

   Possible Answers (Radio type used):

- No (expert opinion, editorials, letters to the editor),
- No (PhD Theses),
- No (Extended abstract, conference proceeding),
- Yes - a systematic review/review/meta-analysis,
- Yes - primary research

2) Is the study (full text) in **English**?

Possible Answers (Radio type used): Yes (included), No (excluded)

3) Is the study a **cross-sectional/cohort/case-control study or case series/case report of the target compounds in humans?**

Possible Answers (Radio type used):

- Cross-sectional study,
- Cohort study,
- Case-control study (retrospective and nested),
- Case series/Case reports,
- No (study on animals OR In vitro study)

4) Is the study on the target compounds? Target compounds:

17 PCDD/Fs:

2,3,7,8-**TCDD**
1,2,3,7,8-**PeCDD**
1,2,3,4,7,8-**HxCDD**
1,2,3,6,7,8-**HxCDD**
1,2,3,7,8,9-**HxCDD**
1,2,3,4,6,7,8-**HpCDD**
OCDD
2,3,7,8-**TCDF**
1,2,3,7,8-**PeCDF**
2,3,4,7,8-**PeCDF**
1,2,3,4,7,8-**HxCDF**
1,2,3,6,7,8-**HxCDF**
1,2,3,7,8,9-**HxCDF**
2,3,4,6,7,8-**HxCDF**
1,2,3,4,6,7,8-**HpCDF**
1,2,3,4,7,8,9-**HpCDF**
OCDF

12 DL-PCBs:

3,3',4,4'-TCB (**PCB-77**)
3,4,4',5-TCB (**PCB-81**)
3,3',4,4',5-PeCB (**PCB-126**)
3,3',4,4',5,5'-HxCB (**PCB-169**)
2,3,3',4,4'-PeCB (**PCB-105**)
2,3,4,4',5-PeCB (**PCB-114**)
2,3',4,4',5-PeCB (**PCB-118**)
2',3,4,4',5-PeCB (**PCB-123**)
2,3,3',4,4',5-HxCB (**PCB-156**)
2,3,3',4,4',5'-HxCB (**PCB-157**)

2,3',4,4',5,5'-HxCB (**PCB-167**)
2,3,3',4,4',5,5'-HpCB (**PCB-189**)

Possible Answers (Radio type used): Yes, No

5) Have the target compounds been measured in **tissue** OR is the **total dietary exposure** estimated?

Possible Answers (Radio type used): Yes, No

6) Which target compounds (see question 4) were results reported on?

(PCB studies must analyse and report on PCB-126 to be considered relevant. Studies which report on TEQs or results of the total 17 PCDD/F or total 12 DL-PCBs are relevant)

Possible answers (checkbox used):

- All 17 PCDD/Fs AND all 12 DL-PCBs,
- Any of the 17 PCDD/Fs,
- Any of the 12 DL-PCBs (must include PCB-126),
- TEQs, total PCDD-Fs and
- Only full PCDD/F and/or full PCB data is reported and/or specific PCB levels (excluding PCB-126) (results include none relevant compounds)

7) **Specific outcome of interest** (End-point health categories include; developmental effects, reproductive organs/effects, hepatotoxicity/gastrointestinal effects, immunotoxicity, cardiovascular effects, behavioural effects, carcinogenicity, metabolic effects (diabetes, thyroid function, obesity), effects on other hormone levels, other)

Possible Answers (Checkbox used):

- All endpoints, including hormone levels and categories indicated above
- study on gene expression only,
- study on drug metabolising enzyme activity/levels only,
- No health end-point

8) **Comments** (if necessary)

As part of the Level 2 screening, a total of 2,218 studies were reviewed, each study was reviewed by two separate reviewers, being one of the reviewers a senior scientist with experience in epidemiology. As part of the Level 2 screening process there were conflicts between reviewers. Each of these conflicts were checked by another reviewer and based on the reviewers opinion, the study was included to Level 3 or excluded at Level 2.

Out of the 2,218 studies screened, 1,961 studies were excluded. These included studies that were excluded because they did not meet the eligibility. This included studies that did not identify and measure the target compounds, and studies where the target compounds were measured but the study did not discuss human health effects or endpoints, according to the eligibility criteria. Excluded

studies also included studies that were not required to have data extracted, these were systematic reviews, reviews and meta-analysis.

As part of the level 2 screening process, 257 studies proceeded to Level 3 data extraction (see Appendix C for the list of references).

4.2.5. Selection for Relevance Outcome

The results of the Level 1 and Level 2 screening were as follows:

Table 8: Outcome of Level 1 and Level 2 screening

Inclusion/Exclusion	Number of studies
Number of studies imported into DistillerSR®	6,699
Number of duplicates removed	598
Number of studies included in Level 1 Screening	6,101
Number of studies excluded	3,883 (63.6%)
Number of studies that proceeded to Level 2 Screening	2,218 (36.4%)
Number of full studies assessed for relevance	2,218
Number of full studies excluded	1,961 (88.4%)
Number of studies proceeding to Level 3 screening	257 (11.6%)

A PRISMA flowchart is shown in Figure 1.

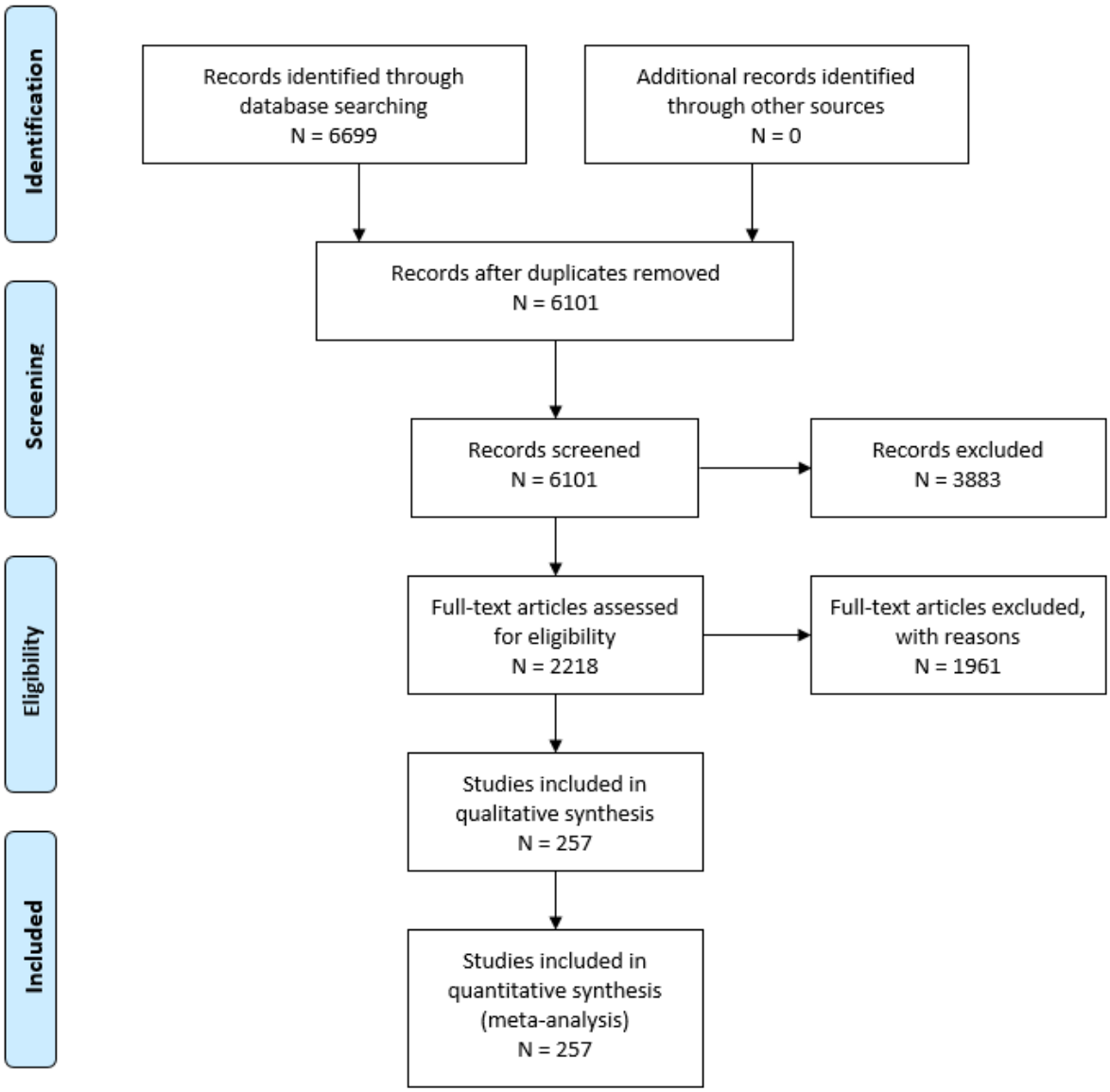

Figure 1: PRISMA flowchart for the extensive literature search, selection for relevance and data extraction[1] of studies related to the toxicity of PCDD/Fs and DL-PCBs in humans

[1] The term 'full-text excluded, with reasons' in the PRISMA flow diagram refer to the reasons as in the relevance eligibility criteria from the tender specifications (screening level 2).

4.3. Data extraction

The last stage of the project was data extraction. Prior to data extraction taking place the project team conducted a pilot test. The project team created a data extraction form using the updated data extraction outline provided by EFSA as shown in Table 9.

Table 9: Outline of the data extraction form for studies in humans

Study ID	Reference[(a)]:
	Trial/study name and acronym (if applicable):
	Total number of subjects:
Funding	Funding source(s):
Study design	Cross-sectional studies Cohort studies Case control studies Meta-analysis
	Type of blinding:
	Year the study was conducted (start):
	Duration/length of follow-up:
	Dates of sampling (when relevant):
	Dates of analysis of the target compounds in the samples:
Subjects	Number of participants in the present study: Participation rates (%): Number of subject with measured levels:
	Number of subjects per group: Follow-up rates by group (%):
	Sex (male/female):
	Geography (country, region, state, etc.):
	Race and ethnicity, socioeconomic background, other variables (e.g. age, BMI, parity) as reported:
	Age at exposure and outcome assessment (e.g. mean, median, measures of variance as presented in paper such as SD, SEM, 75th/90th/95th percentile, minimum/maximum):
	Inclusion and exclusion criteria:
Intervention/ exposure	Compounds (e.g. PCDD/Fs and/or DL-PCBs): Exposure: - Measured levels in tissues (e.g. breast milk, blood, fat): - Lipid adjusted: - Estimated dietary exposure: Method for assessing the dietary exposure: Validation of the method:
	Levels measured in human tissues:
	Dietary intake (pg WHO-TEQ/kg bw per day):
	TEF scheme (NATO, WHO_{1998}, WHO_{2005}, other, no TEF scheme applied):
Methods: health outcome assessment	End-point health category[(b)]:
	Parameters measured:
	Diagnostic or method to measure health outcome (including self-reporting):
	Were sub-groups analyses predefined (yes/no, if not, how was it justified?):
	Confounders (other exposures), modifying factors, or other potential sources of bias considered in the analysis, and how they were considered:
Results: Main findings as reported by the authors and statistically significant findings	Measures of effect and confidence interval at each exposure level as reported in the paper, and for each sub-group when applicable:
	Statistical test used:
	How were the variables treated (continuous or transformed or categorical):
	Shape of dose-response if reported by the authors (e.g. description of whether shape appears to be monotonic, non-monotonic, *p* value, according to the study authors):

(a): Relevant information on the particular study/trial not provided in the paper can be retrieved from the references provided
(b): Reproductive effects (including organs), hepatotoxicity/gastrointestinal effects, immunotoxicity, cardiovascular effects, behavioural effects, neurotoxicity, carcinogenicity, metabolic effects (diabetes, thyroid function, obesity), effects on other hormone levels, teeth, musculoskeletal/bones, other (more than one option should be possible).

4.3.1. Pilot test for the data extraction

A pilot test of Level 3 (Data extraction) was performed. For the pilot study data were extracted from 10 studies. The outcome of the pilot study was discussed with EFSA. Clarification was requested from EFSA about what specific information they were seeking for particular questions and EFSA provided this information. Two minor amendments were made to the data extraction form following the pilot test.

More detail about the data extraction pilot test is provided in Appendix D.

4.3.2. Level 3 – Data Extraction

The updated and final Level 1 relevance form is shown below. The form consisted of one question and five answer options.

Study ID

1. Trial/study name and acronym (if applicable)

   Possible Answers – (textbox)

2. Total number of subjects

   Possible Answers – (textbox)

Funding

3. Funding source(s)

   Possible Answers – (textbox)

Study design

4. Was the study a:

   Possible Answers –

   - Cohort study
   - Case control study
   - Cross sectional study
   - Longitudinal study
   - Meta-analysis

5. Type of blinding used in the study

   Possible Answers – (textbox)

6. Year the study was conducted (start)

   if not reported insert: 0000

   Possible Answers – (textbox)

7. Duration/length of follow-up

   Possible Answers – (textbox)

8. Dates of sampling (when relevant)

Possible Answers – (textbox)

9. Dates of analysis of the target compounds in the samples

Possible Answers – (textbox)

Subjects

10. Number of participants in the present study

Possible Answers – (textbox)

11. Subject participation rates (%)

Possible Answers – (textbox)

12. Number of subjects per group

Possible Answers – (textbox)

13. Follow-up rates by group (%)

Possible Answers – (textbox)

14. Sex (male/female)

Possible Answers (checkbox) – Male, Female

15. Geography (country, region, state, etc.)

Possible Answers – (textbox)

16. Race and ethnicity, socioeconomic background, other variables (e.g. age, BMI, parity) as reported

Possible Answers – (textbox)

17. Age at exposure and outcome assessment (e.g. mean, median, measures of variance as presented in paper such as SD, SEM, 75th/90th/95th percentile, minimum/maximum)

Possible Answers – (textbox)

18. Inclusion criteria

Possible Answers – (textbox)

19. Exclusion criteria

Possible Answers – (textbox)

Intervention/exposure

20. Compounds (e.g. PCDD/Fs and/or DL-PCBs)

Possible Answers – (textbox)

21. Exposure:

- (a) Measured levels in tissues (e.g. breast milk, blood, fat):
- (b) Lipid adjusted:
- (c) Estimated dietary exposure:
  Method for assessing the dietary exposure:
  Validation of the method:

Possible Answers – (textbox)

22. Levels measured in human tissues

Possible Answers – (textbox)

23. Dietary intake (pg WHO-TEQ/kg bw per day)

Possible Answers – (textbox)

24. TEF scheme (NATO, WHO_{1998}, WHO_{2005}, other, no TEF scheme applied)

Possible Answers (radio option) –

- NATO
- WHO1998
- WHO_{2005}
- Other (e.g. WHO unclear)
- Unclear
- N/A

Methods and health outcome assessment

25. End-point health category

Possible Answers (Checkboxes) –

- Reproductive effects (including organs)
- hepatoxicity/gastrointestinal effects
- immunotoxicity
- cardiovascular effects
- behavioural effects
- neurotoxicity
- carcinogenicity
- metabolic effects (diabetes, thyroid function, obesity)
- effects on other hormone levels
- teeth
- musculoskeletical/bones
- other

26. Parameters measured

Possible Answers – (textbox)

27. Diagnostic or method to measure health outcome (including self-reporting)

Possible Answers – (textbox)

28. Were sub-groups analyses predefined (yes/no, if not, how was it justified?)

Possible Answers (radio option) –

- Yes
- No

30. Confounders (other exposures), modifying factors, or other potential sources of bias considered in the analysis, and how they were considered

Possible Answers – (textbox)

Results: Main findings as reported by the authors and statistically significant findings

31. Measures of effect and confidence interval at each exposure level as reported in the paper, and for each sub-group when applicable

    Possible Answers – (textbox)

32. Statistical test(s) used

    Possible Answers – (textbox)

33. How were the variables treated (continuous or transformed or categorical)

    Possible Answers (radio option) –

    - continuous
    - transformed
    - categorical

34. Shape of dose-response if reported by the authors (e.g. description of whether shape appears to be monotonic, non-monotonic, p value, according to the study authors)

    Possible Answers – (textbox)

Additional Information (Optional)

35. Insert here any comments or additional information you would like to add about the study

    Possible Answers – (textbox)

The data extraction was carried out by two reviewers, with one of the reviewers being a senior scientist with experience in epidemiology. The first reviewer prefilled a table with information about the study and the senior scientist reviewed the information and completed the table. Once the tables had been completed, the relevant information was then added to DistillerSR® for each relevant study.

4.4. Results and discussion

The project team conducted two ELS, searching WoS and PubMed to identify relevant human studies related to exposure to PCDDs/PCDFs/DL-PCBs. A total of 4,549 studies were identified in WoS and 3,677 studies in PubMed, which, following the removal of duplicates, provided a combined set of 6,699 studies for evaluation. The studies were imported into DistillerSR® and 598 further duplicates were removed using the duplicate detection tool within DistillerSR®.

Following a pilot test, screening of studies for relevance was carried out at two levels, with level 1 assessing relevance from the title and abstract, and level 2 from the full text. Following level 1 and level 2 screening, 257 studies were identified for data extraction (see Appendix C). Following a pilot test, data were extracted for the 257 studies.

References

ATSDR (Agency for Toxic Substances and Disease Registry), 2014a. Toxic Substances Portal-Polychlorinated Biphenyls (PCBs). Dated July 2014. Available online: http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=140&tid=26 [Accessed: 15 April 2016].

ATSDR (Agency for Toxic Substances and Disease Registry), 2014b. ATSDR Case Studies in Environmental Medicine Polychlorinated Biphenyls (PCBs) Toxicity. Dated May 14, 2014. Available online: http://www.atsdr.cdc.gov/csem/pcb/docs/pcb.pdf

COT (Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment), 2001. Statement on the Tolerable Daily Intake for Dioxin and Dioxin-like Polychlorinated Biphenyls. COT/2001/07.

Codex Committee, 2003. Position Paper on Dioxins and Dioxin-like PCBs.

EFSA (European Food Safety Authority), 2008. Statement of EFSA on the risks for public health due to the presence of dioxins in pork from Ireland. EFSA Journal 2008;6(12):911, 15 pp. doi: 10.2903/j.efsa.2008.911

EFSA (European Food Safety Authority), 2015. Scientific statement on the health-based guidance value for dioxins and dioxin-like PCBs. EFSA Journal 2015;13(5):4124, 14 pp. doi: 10.2903/j.efsa.2015.4124

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2011. Scientific Opinion on the risk to public health related to the presence of high levels of dioxins and dioxin-like PCBs in liver from sheep and deer. EFSA Journal 2011;9(7):2297, 71 pp. doi: 10.2903/j.efsa.2011.2297

Hoogenboom R, Traag W, Fernandes A and Rose M, 2015. European developments following incidents with dioxins and PCBs in the food and feed chain. Food Control, 50, 670-683.

IARC (International Agenvcy for Research on Cancer), 1997. Polychlorinated dibenzo-para-dioxins and Polychlorinated dibenzofurans. Monograph 69. http://monographs.iarc.fr/ENG/Monographs/vol69/

IARC (International Agenvcy for Research on Cancer), 2016. Polychlorinated biphenyls. Monograph Volume 107. Available online: http://monographs.iarc.fr/ENG/Monographs/vol107/

IARC (International Agenvcy for Research on Cancer), 2012. 2,3,7,8-Tetrachlorodibenzo-para-dioxin, 2,3,4,7,8-Pentachlorodibenzofuran and 3,3', 4,4', 5-Pentachlorobiphenyl. IARC Monograph 100F. Available at http://monographs.iarc.fr/ENG/Monographs/vol100F/mono100F-27.pdf.

INSERM, 2000. Collective Experts Report Dioxins in the environment: What are the health risks? Available online: http://www.ncbi.nlm.nih.gov/books/NBK7128/

Mocarelli P, Gerthoux PM, Patterson DG Jr, Milani S, Limonta G, Bertona M, Signorini S, Tramacere P, Colombo L, Crespi C, Brambilla P, Sarto C, Carreri V, Sampson EJ, Turner WE and Needham LL, 2008. Dioxin exposure, from infancy through puberty, produces endocrine disruption and affects human semen quality. Environmental Health Perspectives, 116, 70-77.

SCF (Scientific Committee on Food), 2001. Opinion of the Scientific Committee on Food on the Risk Assessment of Dioxins and Dioxin-like PCBs in Food. Adopted on 30 May 2001. European Commission, Brussels. Available online: http://europa.eu.int/comm/food/fs/sc/scf/outcome_en.html.

Scialli AR, Watkins DK and Ginevan ME, 2015. Agent Orange Exposure and 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) in human milk. Birth Defects Research. Part B Developmental and Reproductive Toxicology, 104(3), 129-139.

Tavakoly Sany SB, Hashim R, Salleh A, Rezayi M, Karlen DJ, Razavizadeh BB and Abouzari-Lotf E, 2015. Dioxin risk assessment: mechanisms of action and possible toxicity in human health. Environmental Science and Pollution Research, 22, 19434-19450.

US EPA (US Environmental Protection Agency), 2012. EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments, Volume 1. EPA/600/R-10/038F. Available online: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/supdocs/dioxinv1sup.pdf

Van den Berg M, Birnbaum LS, Denison M, De Vito M, Farland W, Feeley M, Fiedler H, Hakansson H, Hanberg A, Haws L, Rose M, Safe S, Schrenk D, Tohyama C, Tritscher A, Tuomisto J, Tysklind M, Walker N and Peterson RE, 2006, The 2005 World Health Organisation Reevaluation of Human and Mammalian Toxic Equivalency Factors for Dioxins and Dioxin-Like Compounds. Toxicological Sciences, 93(2), 223-241.

WHO (World Health Organization), 2002. Polychlorinated dibenzodioxins, polychlorinated dibenzofurans, and coplanar polychlorinated biphenyls. In: Safety evaluation of certain food additives and contaminants. Geneva, World Health Organization (WHO Food Additives Series, No. 48). Available online: http://www.inchem.org/documents/jecfa/jecmono/v48je20.htm

WHO (World Health Organization), 2014. Dioxins and their effects on human health. Fact Sheet No 225. June 2014. Available online: http://www.who.int/mediacentre/factsheets/fs225/en/ on 15th April 2016.

Wittsiepe J, Fürst P, Schrey P, Lemm F, Kraft M, Eberwein G, Winneke G and Wilhelm M, 2007. PCDD/F and dioxin-like PCB in human blood and milk from German mothers. Chemosphere, 67, S286-S294.

Abbreviations

Ah	arylhydrocarbon
COT	The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
DL-PCBs	Dioxin-like polychlorinated biphenyls
ELS	extensive literature search
FAO	Food and Agriculture Organization of the United Nations
PCDDs	Polychlorinated dibenzo-*p*-dioxins
PCDFs	Polychlorinated dibenzofurans
POP	Persistent Organic Pollutant
SCF	Scientific Committee on Food
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
TEFs	Toxic Equivalency Factors
TEQ	Toxic Equivalent
WHO	World Health Organization
WoS	Web of Science

Appendix A – Development of the search strategy

1. Development of search strategy - sensitivity analysis

Methodology has been developed for the extensive literature search for studies related to the toxicity of PCDD/Fs and DL-PCBs in humans. The search criteria have been developed for Web of Science (WoS, including Web of ScienceTM Core Collection, BIOSIS Citation IndexSM, CABI: CAB Abstracts®, Current Contents Connect®, Data Citation Index SM, FSTA®–the food science resource, MEDLINE®, SciELO Citation Index, Zoological Record®) and PubMed, using the preliminary keywords and some of the eligibility criteria as identified in the tender specification as the starting point (Appendix A). These extensive searches will focus on material published in the public domain during the period 1998 – present. All searches will be carried out in English.

The search terms have been developed using a sensitivity analysis as outlined in more detail below.

1.1. Web of Science

Following consultation with an Information Scientist, it was agreed that the initial search terms presented in the Tender Document would need to be amended to ensure that terms would be picked up if the MeSH terms had not been added. In addition to allow feedback given at the kick-off meeting to be incorporated, an initial search was performed using the following terms:

TOPIC: (Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD OR PCDD OR "Polychlorinated dibenzodioxin*"OR PCDF OR "polychlorinated dibenzofuran*" OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar) *AND* **TOPIC:** (epidemiology OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*")

Timespan=1998-2016

Search language=Auto

Number of papers retrieved – 7,129

Following amendment to restrict results to human studies only, the search terms became:

TOPIC: (Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD OR PCDD OR "Polychlorinated dibenzodioxin*"OR PCDF OR "polychlorinated dibenzofuran*" OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar) *AND* **TOPIC:** (epidemiology OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*") *AND* **TOPIC:** human)

Timespan=1998-2016

Search language=Auto

Number of papers retrieved – 3,301

Following amendment to restrict results to human studies published in the English language only, the search terms became:

TOPIC: (Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD OR PCDD OR "Polychlorinated dibenzodioxin*"OR PCDF OR "polychlorinated dibenzofuran*" OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar) *AND* **TOPIC:** (epidemiology OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*") *AND* **TOPIC:** human)

Refined by: [excluding] **LANGUAGES:** (GERMAN OR FINNISH OR CZECH OR JAPANESE OR CHINESE OR DANISH OR CROATIAN OR ITALIAN OR POLISH OR NORWEGIAN OR SWEDISH OR FRENCH OR SPANISH OR KOREAN OR PORTUGUESE OR RUSSIAN OR HUNGARIAN OR DUTCH)

Number of papers retrieved – 3,062

Following (1) amendment to restrict results to human studies published in the English language only within peer-reviewed research studies, systematic reviews, reviews and meta-analysis, (2) amendment of epidemiology to epidemiolog* to ensure widest capture, (3) inclusion of $ to all abbreviations to ensure only 1 character is picked up after the abbreviation (e.g. TCDDs) the search terms became:

TOPIC: (Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD$ OR PCDD$ OR "Polychlorinated dibenzodioxin*"OR PCDF$ OR "polychlorinated dibenzofuran*" OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar) *AND* **TOPIC:** (epidemiolog* OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*") *AND* **TOPIC:** human)

Refined by: [excluding] **LANGUAGES:** (GERMAN OR FINNISH OR CZECH OR JAPANESE OR CHINESE OR DANISH OR CROATIAN OR ITALIAN OR POLISH OR NORWEGIAN OR SWEDISH OR FRENCH OR SPANISH OR KOREAN OR PORTUGUESE OR RUSSIAN OR HUNGARIAN OR DUTCH)

AND [excluding] **DOCUMENT TYPES:** (MEETING OR NEWS OR BOOK OR OTHER OR LETTER OR UNSPECIFIED OR EDITORIAL OR BIOGRAPHY)

Number of papers retrieved – 1,850

Following consultation with EFSA it became apparent that some key studies were not being identified using the above search strategy; these included:

Warner et al 2007. **SERUM DIOXIN CONCENTRATIONS AND QUALITY OF OVARIAN FUNCTION IN WOMEN IN SEVESO** (key words: endocrine disruptor, hormones, ovary, TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin).

Mocarelli et al 2008. **DIOXIN EXPOSURE, FROM INFANCY THROUGH PUBERTY, PRODUCES ENDOCRINE DISRUPTION AND AFFECTS HUMAN SEMEN QUALITY** (key words: dioxin, endocrine disruption, environmental contaminants, human sperm quality, reproductive hormones, TCDD).

Mocarelli et al 2011. **PERINATAL EXPOSURE TO LOW DOSES OF DIOXIN CAN PERMANENTLY IMPAIR HUMAN SEMEN QUALITY** (breast-feeding, dioxin, environmental endocrine disrupters, human sperm impairment, human sperm quality, perinatal exposure, reproductive hormones, TCDD)**.**

Eskenazi et al 2007**. SERUM DIOXIN CONCENTRATIONS AND RISK OF UTERINE LEIOMYOMA IN THE SEVESO WOMEN'S HEALTH STUDY** (endocrine disruptors; leiomyoma; tetrachlorodibenzodioxin; uterus)**.**

Leijs et al 2009**. EFFECTS OF DIOXINS, PCBs AND PBDEs ON IMMUNOLOGY AND HEMATOLOGY IN ADOLESCENTS** (No keywords)**.**

Delvaux et al 2014. **PRENATAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS AND BODY COMPOSITION AT AGE 7-9 YEARS** (Children Body composition Endocrine disruptors Growth Prenatal exposure).

This is because the papers do not meet the criteria *AND* **TOPIC:** (epidemiolog* OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*").

The following strategy is therefore proposed – this is a less specific search and so a greater number of irrelevant papers are likely to be identified. Numbers have been restricted as far as possible by restricting the search to specific research areas with WoS.

TOPIC: (Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD$ OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar OR PCDD$ OR PCDF$ OR "Polychlorinated dibenzofuran" OR "polychlorinated dibenzodioxin") AND TOPIC:(human)

Timespan=1998-2016

Search language=Auto

Refined by: [excluding] **LANGUAGES:** (GERMAN OR FINNISH OR CZECH OR JAPANESE OR CHINESE OR DANISH OR CROATIAN OR ITALIAN OR POLISH OR NORWEGIAN OR SWEDISH OR FRENCH OR SPANISH OR KOREAN OR PORTUGUESE OR RUSSIAN OR HUNGARIAN OR DUTCH)

AND [excluding] **DOCUMENT TYPES:** (MEETING OR NEWS OR BOOK OR OTHER OR LETTER OR UNSPECIFIED OR EDITORIAL OR BIOGRAPHY)

Number of papers retrieved – 16,957

Refined by: [excluding] **RESEARCH AREAS:** PHARMACOLOGY PHARMACY OR GENETICS HEREDITY OR SCIENCE TECHNOLOGY OTHER TOPICS OR ENGINEERING OR GASTROENTEROLOGY HEPATOLOGY OR MARINE FRESHWATER BIOLOGY OR RADIOLOGY NUCLEAR MEDICINE MEDICAL IMAGING OR MEDICAL LABORATORY TECHNOLOGY OR GERIATRICS GERONTOLOGY OR ZOOLOGY OR MATHEMATICS OR AGRICULTURE OR SURGERY OR INFECTIOUS DISEASES OR DERMATOLOGY OR BEHAVIORAL SCIENCES OR HEALTH CARE SCIENCES SERVICES OR ANATOMY MORPHOLOGY OR HEMATOLOGY OR BIOTECHNOLOGY APPLIED MICROBIOLOGY OR INSTRUMENTS INSTRUMENTATIO OR PSYCHOLOGY OR BIOPHYSICS OR PHYSICS OR DENTISTRY ORAL SURGERY MEDICINE OR PSYCHIATRY OR ENTOMOLOGY OR BIODIVERSITY CONSERVATION OR METEOROLOGY ATMOSPHERIC SCIENCES OR PLANT SCIENCES OR WATER RESOURCES OR FISHERIES OR COMPUTER SCIENCE OR GEOLOGY OR OPHTHALMOLOGY OR HISTORY OR MICROBIOLOGY OR GOVERNMENT LAW OR BUSINESS ECONOMICS OR MATERIALS SCIENCE OR ANTHROPOLOGY OR OTORHINOLARYNGOLOGY OR GEOGRAPHY OR SPECTROSCOPY OR ANESTHESIOLOGY OR EDUCATION EDUCATIONAL RESEARCH OR MICROSCOPY OR INFORMATION SCIENCE LIBRARY SCIENCE OR TELECOMMUNICATIONS OR TRANSPLANTATION OR NUCLEAR SCIENCE TECHNOLOGY OR ENERGY FUELS OR ELECTROCHEMISTRY OR OCEANOGRAPHY OR COMMUNICATION OR IMAGING SCIENCE PHOTOGRAPHIC TECHNOLOGY OR AUTOMATION CONTROL SYSTEMS OR OPTICS OR PARASITOLOGY OR NURSING OR EVOLUTIONARY BIOLOGY OR CRYSTALLOGRAPHY

Number of papers retrieved – 9,303

This is a large number of papers to evaluate and restricting research areas is difficult to do accurately – therefore the inclusion of keywords from the missing key studies listed above was explored. The inclusion of the key words to address biological sample type, adverse effect and gender/age group was considered appropriate by the Information Scientist. Although likely to narrow the numbers of papers identified from the general strategy above, these are still generic terms which will pick up irrelevant titles.

The following revised strategy is therefore proposed:

Tetrachlorodibenzodioxin OR "2,3,7,8-Tetrachlorodibenzo-p-dioxin" OR TCDD OR dioxin* OR "polychlorinated biphenyl*" OR PCB$ OR TEQ OR "total equivalen*" OR coplanar OR PCDD$ OR PCDF$ OR "Polychlorinated dibenzofuran" OR Polychlorinated dibenzodioxin) ANDTOPIC: (epidemiolog* OR "cohort stud*" OR "case control stud* " OR "adverse effect*" OR "observational stud*" OR "case serie*" OR "case report*" OR "cross sectional stud*" OR urine OR serum OR plasma OR haema* OR hema* OR blood OR sperm OR semen OR hormone* OR reproduct*) AND TOPIC: (human OR women OR men OR child*)

Timespan=1998-2016

Search language=Auto

Refined by: [excluding] DOCUMENT TYPES: (MEETING ABSTRACT OR LETTER OR EDITORIAL MATERIAL OR BOOK CHAPTER OR NEWS ITEM OR OTHER OR BIOGRAPHY) AND [excluding] LANGUAGES: (PORTUGUESE OR SPANISH OR CZECH OR FRENCH OR ITALIAN OR RUSSIAN OR CROATIAN OR GERMAN OR POLISH OR JAPANESE OR HUNGARIAN OR CHINESE OR FINNISH OR DANISH OR NORWEGIAN OR SWEDISH OR KOREAN OR DUTCH):

Number of papers retrieved – 4,549

1.2. PubMed

Following consultation with an Information Scientist, it was agreed that the initial search terms presented in the Tender Document would need to be amended to ensure that search terms were restricted to Title/Abstract or MeSH terms. An initial search was performed using the following terms:

((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND (((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms]) OR (epidemiology[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case serie"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case reports"[Title/Abstract])):

Numbers of papers retrieved – 2,262

Following amendment to restrict results to human studies only, the search terms became:

((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND (((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms]) OR (epidemiology[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case serie"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case

reports"[Title/Abstract])) Sort by: Relevance Filters: Publication date from 1998/01/01 to 2016/12/31; Humans:

Numbers of papers retrieved – 1,717

Following amendment to restrict results to human studies published in the English language only, the search terms became:

((((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract]) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]))) AND (((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms]) OR (epidemiology[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case serie"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case reports"[Title/Abstract]))) AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]) AND Humans[Mesh])) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/12/31"[PDat]) Sort by: Relevance Filters: Publication date from 1998/01/01 to 2016/12/31; Humans:

Numbers of papers retrieved – 1,647

Following (1) amendment to restrict results to human studies published in the English language only within peer-reviewed research studies, systematic reviews, reviews and meta-analysis, and (2) amendment of epidemiology to epidemiolog* to ensure widest the search terms became:

(((((((("journal article"[Publication Type]) OR "review"[Publication Type]) OR "scientific integrity review"[Publication Type]) OR "meta analysis"[Publication Type]) OR research[Publication Type]) OR review, systematic[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ((((((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD*[Title/Abstract]) OR PCDD*[Title/Abstract]) OR "Polychlorinated dibenzodioxin"[Title/Abstract]) OR PCDF*[Title/Abstract]) OR "Polychlorinated dibenzofuran"[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND (((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms]) OR (epidemiolog*[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case serie"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case reports"[Title/Abstract]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh]))

AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh]))

Number of papers retrieved – 1,869

As for the WoS search described above, the same key studies were not identified using the above search strategy in PubMed. The following changes are therefore proposed, however, this is a less specific search and so a greater number of irrelevant papers will be identified:

(((((((("journal article"[Publication Type]) OR "review"[Publication Type]) OR "scientific integrity review"[Publication Type]) OR "meta analysis"[Publication Type]) OR research[Publication Type]) OR review, systematic[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/11"[PDat]) AND Humans[Mesh])) AND ((((((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/11"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD*[Title/Abstract]) OR PCDD*[Title/Abstract]) OR "Polychlorinated dibenzodioxin"[Title/Abstract]) OR PCDF*[Title/Abstract]) OR "Polychlorinated dibenzofuran"[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract]) AND Humans[Mesh])) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/11"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/11"[PDat]) AND Humans[Mesh]))

Number of studies retrieved – 7,482

As for the WoS search strategy, this is a large number of papers to evaluate and restricting research areas is difficult to do accurately – therefore the inclusion of keywords from the missing key studies as detailed above for the revised WoS search was explored.

The following revised strategy is therefore proposed:

(((((((((("journal article"[Publication Type]) OR "review"[Publication Type]) OR "scientific integrity review"[Publication Type]) OR "meta analysis"[Publication Type]) OR research[Publication Type]) OR review, systematic[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ((((((((((((((tetrachlorodibenzodioxin[MeSH Terms]) OR 2,3,7,8 tetrachlorodibenzo p dioxin[MeSH Terms]) OR tcdd[MeSH Terms]) OR dioxins[MeSH Terms]) OR polychlorinated biphenyls[MeSH Terms]) OR pcbs[MeSH Terms]) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) OR (((((((((Tetrachlorodibenzodioxin[Title/Abstract]) OR "2,3,7,8 tetrachlorodibenzo p dioxin"[Title/Abstract]) OR TCDD*[Title/Abstract]) OR PCDD*[Title/Abstract]) OR PCDF*[Title/Abstract]) OR "Polychlorinated dibenzofuran"[Title/Abstract]) OR dioxin*[Title/Abstract]) OR "polychlorinated biphenyl*"[Title/Abstract]) OR PCB*[Title/Abstract]) OR (TEQ[Title/Abstract] OR "total equivalen*"[Title/Abstract])) OR coplanar[Title/Abstract] OR "Polychlorinated dibenzodioxin"[Title/Abstract])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]))) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh]))))) AND ((((((((cohort study OR cohort studies[MeSH Terms])) OR (case control study OR case control studies[MeSH Terms])) OR adverse effects[MeSH Terms]) OR (cross sectional study OR cross sectional studies[MeSH Terms])) OR case reports[MeSH Terms] OR blood [MeSH Terms] OR hormones [MeSH Terms] OR serum [MeSH Terms] OR urine [MeSH Terms] OR semen[MeSH Terms])) OR (epidemiolog*[Title/Abstract] OR "cohort study"[Title/Abstract] OR "cohort studies"[Title/Abstract] OR "case control study"[Title/Abstract] OR "case control studies"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "observational study"[Title/Abstract] OR "observational studies"[Title/Abstract] OR "case series"[Title/Abstract] OR "cross sectional study"[Title/Abstract] OR "cross sectional studies"[Title/Abstract] OR "case report"[Title/Abstract]OR "case reports"[Title/Abstract] OR urine[Title/Abstract] OR serum[Title/Abstract] OR plasma [Title/Abstract] OR haema*[Title/Abstract] OR hema [Title/Abstract] OR blood [Title/Abstract] OR sperm [Title/Abstract] OR semen[Title/Abstract] OR hormone*[Title/Abstract] OR

reproduct*[Title/Abstract]))) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND (english[Language] AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh])) AND ("1998/01/01"[PDat] : "2016/07/05"[PDat]) AND Humans[Mesh]))):

Numbers of studies retrieved – 3,677

Appendix B – Selection for relevance pilot test

1. Overview

After agreement on the templates for the selection for Level 1 and Level 2 relevance with EFSA, a pilot test using these templates was carried out by members of the project team. Outcomes of the pilot test include a sample of studies deemed 'not relevant' after Level 1 (title and abstract) screening and a set of studies for which divergences/doubts were raised following Level 2 screening (full text).

Following agreement with EFSA, 200 studies were selected for the pilot test in total. Reviewers 1 and 2 reviewed 100 studies in duplicate and reviewers 3 and 4 reviewed the other 100 studies in duplicate.

The project team found that conflicts in Level 1 screening were reasonably easy to address. Reviewers found that it was not always clear from the titles and abstracts whether a paper was relevant and, in these cases, the reviewers would indicate the studies were 'unclear', this meant that at full screening the paper would be reviewed further for relevance. In some abstracts only the information for the congeners where the highest values in tissue were indicated and it was unclear whether any of the eligible PCDD/Fs or PCBs in scope were measured. Therefore, these types of studies were also taken forward for Level 2 screening.

In Level 2 screening, there were a number of conflicts which are summarised in Table B.1. The conflicts included a number of inclusion/exclusion conflicts. There were various reasons for the conflicts. One of the reasons for the inclusion/exclusion conflicts was the inclusion and exclusion criteria applied to some of the answer options. The number of answer options and the presence of text boxes were also other important factors.

Table B.1: Conflict types identified in Level 2 screening

Conflict type/Question stage	Number of conflicts
Q1. Study relevance	14
Q2. Study language	0
Q3. Study year	0
Q4. Type of study	51
Q5. Human tissues or dietary exposure	11
Q6. Exposure	2
Q7. Target compounds	See comment below
Q8. Specific outcome of interest	See comment below
Q9. Comments	N/A

The Level 1 and Level 2 conflicts were reviewed as part of a QC process, when reviewing the response, it was identified that a number of changes to the Level 1 and Level 2 forms should be undertaken. The outcome of the pilot study was discussed with EFSA.

As part of Level 1 relevance checks in the pilot study, it was agreed that additional information about the specific target compounds would be added to the question. As part of Level 2 relevance checks a number of changes to the questions were discussed with EFSA and changes to the relevance templates agreed. The changes consisted of the removal of questions, slight amendments to the wording of the questions and both changes in the wording of answer and the addition of additional answers. The changes included:

- As part of question 1 the answer options were updated so that it was clear that review papers would be captured here (along with other studies) and that only primary research studies would proceed.
- It was agreed that a question about the year that the study was published (≥1998) would be removed.
- It was also agreed that information about all of the specific target compounds would also be added to a question about the target compounds.
- The wording and answer options of a question about which of the target compounds were included in the study were updated.
- As part of a question asking about specific outcomes of interest, examples of outcomes of interest were included.

1.1. Selection of studies deemed not relevant in Level 1 screening

As part of the tender specifications, a sample of studies deemed not relevant after title and abstract screening were to be provided. A sample of these studies is described below in Table B.2.

Table B.2: Selection of samples deemed not relevant after title and abstract screening

Reference	Refid in DistillerSR®	Reason for exclusion
Wagner, M., Oehlmann, J. Endocrine disruptors in bottled mineral water: Estrogenic activity in the E-Screen.	6	Refers to *in vitro* studies, gene expression, enzyme induction
Mikula, P., Svobodova, Z. Brominated flame retardants in the environment: Their sources and effects (a review).	25	Refers to non-target compounds
Romano, Megan E., Webster, Glenys M., Vuong, Ann M., Zoeller, R. Thomas, Chen, Aimin, Hoofnagle, Andrew N., Calafat, Antonia M., Karagas, Margaret R., Yolton, Kimberly, Lanphear, Bruce P., Braun, Joseph M. Gestational urinary bisphenol A and maternal and newborn thyroid hormone concentrations: The HOME Study.	51	Refers to non-target compounds
Zwitterionic carboxybetaine polymer surfaces and their resistance to long-term biofilm formation	74	Refers to occurrence, analytical methods, other
Hubler, M., Planitz, M. C., Vicent, O. Early pharmacokinetic of ropivacaine without epinephrine after injection into the psoas compartment.	79	Refers to occurrence, analytical methods, others
Perkins, N. J., Schisterman, E. F., Vexler, A. Receiver operating characteristic curve inference from a sample with a limit of detection.	92	Refers to occurrence, analytical methods, others
Kopf, P. G., Huwe, J. K., Walker, M. K. Hypertension, Cardiac Hypertrophy, and Impaired Vascular Relaxation Induced by 2,3,7,8-Tetrachlorodibenzo-p-Dioxin are Associated with Increased Superoxide.	110	Refers to animal studies
Anas, M. K. I., Guillemette, C., Ayotte, P., Pereg, D., Giguere, F., Bailey, J. L. In utero and lactational exposure to an environmentally relevant organochlorine mixture disrupts reproductive development and function in male rats.	122	Refers to animal studies
Bermudez, Dieldrich S., Gray, Leon E., Jr., Wilson, Vickie S. Modeling the Interaction of Binary and Ternary Mixtures of Estradiol with Bisphenol A and Bisphenol AF in an *In Vitro* Estrogen-Mediated Transcriptional Activation Assay (T47D-KBluc).	147	Refers to *in vitro* studies, gene expression, enzyme induction
Xu, Y., Kashiwakura, I., Takahashi, T. A. High sensitivity of megakaryocytic progenitor cells contained in	167	Refers to occurrence, analytical methods, others

Reference	Refid in DistillerSR®	Reason for exclusion
placental/umbilical cord blood to the stresses during cryopreservation.		
Chevrier, J. Invited commentary: Maternal plasma polybrominated diphenyl ethers and thyroid hormones--challenges and opportunities.	173	Refers to non-target compounds

1.2. Level 2 Screening: Studies where divergence/doubts have been raised

As part of the tender specifications, a set of studies where divergence/doubts have been raised during full text screening were to be provided. A sample of these studies is described below in Table B.3:

Table B.3: Studies where divergence/doubts have been raised during full text screening

Reference	Refid in DistillerSR®	Reason for divergence/doubts	Outcome
Ruiz-Suarez, N., Rial, C., Boada, L. D., Henriquez-Hernandez, L. A., Valeron, P. F., Camacho, M., Zumbado, M., Gonzalez, M. A., Lara, P., Luzardo, O. P., Are pet dogs good sentinels of human exposure to environmental polycyclic aromatic hydrocarbons, organochlorine pesticides and polychlorinated biphenyls?	42	The study includes animals (dogs) and humans, furthermore no health endpoints are discussed, just concentrations. The project team anticipated that just human data will be screened and extracted.	Only human data will be extracted.
Bu, Q. W., MacLeod, M., Wong, F. N., Toms, L. M. L., Mueller, J. F., Yu, G., Historical intake and elimination of polychlorinated biphenyls and organochlorine pesticides by the Australian population reconstructed from biomonitoring data	46	No health endpoint, the study uses previous data to construct a pharmacokinetic model.	Not relevant
Eskenazi, Brenda, Warner, Marcella, Samuels, Steven, Young, Jessica, Gerthou, xPier Mario, Needham, Larry, Patterson, Donald, Olive, David, Gavoni, Nicoletta, Vercellini, Paolo, Mocarelli, Paolo, Serum dioxin concentrations and risk of uterine leiomyoma in the Seveso Women's Health Study	59	Enrolment began in March 1996 and was completed in July 1998. The project team anticipate that the study is in scope as the publication data and not study time is the eligibility factor.	Relevant
Poulstrup, A., Hansen, H. L., Use of GIS and exposure modeling as tools in a study of cancer incidence in a population exposed to airborne dioxin	62	This a mini-monograph which, it is suggested, are relatively quickly published compared with longer monographs but still undergo peer review. The inclusion of mini-monographs was discussed with EFSA.	Relevant
Colt, J. S., Rothman, N., Severson, R. K., Hartge, P., Cerhan, J. R., Chatterjee, N., Cozen, W., Morton, L. M., De Roos, A. J., Davis, S., Chanock, S., Wang, S. S., Organochlorine exposure, immune gene variation, and risk of non-Hodgkin lymphoma	75	Only limited information is reported on PCB-156 and PCB-169. As information on PCB-126 is not included this study will be excluded from data extraction.	Not relevant
Matsuzaka, Y., Kikuti, Y. Y., Goya, K., Suzuki, T., Cai, L. Y., Oka, A., Inoko, H., Kulski, J. K., Izumi, S., Kimura, M., Lack of an association	89	The study reviews around ten dioxin detoxification genes, therefore out of	Not relevant

Reference	Refid in DistillerSR®	Reason for divergence/doubts	Outcome
human dioxin detoxification gene polymorphisms with endometriosis in Japanese women: results of a pilot study		scope.	
Karmaus, W., DeKoning, E. P., Kruse, H., Witten, J., Osius, N., Early childhood determinants of organochlorine concentrations in school-aged children	159	The authors investigated whether early childhood factors such as breast-feeding, parity, and smoking contribute to the variation of organochlorine compounds (inc PCBs) at approximately 7 y of age. However, results report on total PCB measurements including PCBs that are not eligible.	Not relevant
Wolff, M. S., Zeleniuch-Jacquotte, A., Dubin, N., Toniolo, P., Risk of breast cancer and organochlorine exposure	170	Total PCBs measured but individual components not defined here.	Not relevant
Moysich, K. B., Shields, P. G., Freudenheim, J. L., Schisterman, E. F., Vena, J. E., Kostyniak, P., Greizerstein, H., Marshall, J. R., Graham, S., Ambrosone, C. B., Polychlorinated biphenyls, cytochrome P4501A1 polymorphism, and postmenopausal breast cancer risk	186	PCB-105 and -118 studied, amongst others, but information is only reported on total PCBs.	Not relevant
Su, P. H., Chen, J. Y., Chen, J. W., Wang, S. L, Growth and thyroid function in children with in utero exposure to dioxin: a 5-year follow-up study	193	Total PCB and PCDD/Fs levels reported. However, PCDD/Fs are expressed as TEQs, therefore this study will be included. Outcome – relevant	Relevant

The studies that appear in Tables B.2 and B.3 were discussed with EFSA. It was agreed that all of the studies in Table B.2 were not relevant. The studies in Table B.3 were discussed and it was agreed that some studies were not relevant and that others should proceed to Level 3 data extraction.

Appendix C – List of studies identified for data extraction (n=257)

Refid	Bibliography
12	Winneke, G.,Ranft, U.,Wittsiepe, J.,Kasper-Sonnenberg, M.,Furst, P.,Kramer, U.,Seitner, G.,Wilhelm, M. (2014). Behavioral Sexual Dimorphism in School-Age Children and Early Developmental Exposure to Dioxins and PCBs: A Follow-Up Study of the Duisburg Cohort. Environmental Health Perspectives 122(3): 292-298.
74	Kido, T.,Dao, T. V.,Ho, M. D.,Dang, N. D.,Pham, N. T.,Okamoto, R.,Pham, T. T.,Maruzeni, S.,Nishijo, M.,Nakagawa, H.,Honma, S.,Le, S. K.,Nguyen, H. N. (2014). High cortisol and cortisone levels are associated with breast milk dioxin concentrations in Vietnamese women. European Journal of Endocrinology 170(1): 131-139.
170	Park, W. H.,Jun, D. W.,Kim, J. T.,Jeong, J. H.,Park, H.,Chang, Y. S.,Park, K. S.,Lee, H. K.,Pak, Y. K. (2013). Novel cell-based assay reveals associations of circulating serum AhR-ligands with metabolic syndrome and mitochondrial dysfunction. Biofactors 39(4): 494-504.
259	Tsukimori, K.,Uchi, H.,Tokunaga, S.,Yasukawa, F.,Chiba, T.,Kajiwara, J.,Hirata, T.,Furue, M. (2013). Blood levels of PCDDs, PCDFs, and coplanar PCBs in Yusho mothers and their descendants: Association with fetal Yusho disease. Chemosphere 90(5): 1581-1588.
409	Leijs, M. M.,ten Tusscher, G. W.,Olie, K.,van Teunenbroek, T.,van Aalderen, W. M.,de Voogt, P.,Vulsma, T.,Bartonova, A.,von Krauss, M. K.,Mosoiu, C.,Riojas-Rodriguez, H.,Calamandrei, G.,Koppe, J. G. (2012). Thyroid hormone metabolism and environmental chemical exposure. Environmental Health 11(Suppl 1)): 1-7.
423	Virtanen, H. E.,Koskenniemi, J. J.,Sundqvist, E.,Main, K. M.,Kiviranta, H.,Tuomisto, J. T.,Tuomisto, J.,Viluksela, M.,Vartiainen, T.,Skakkebaek, N. E.,Toppari, J. (2012). Associations between congenital cryptorchidism in newborn boys and levels of dioxins and PCBs in placenta. International Journal of Andrology 35(3): 283-293.
424	Krysiak-Baltyn, K.,Toppari, J.,Skakkebaek, N. E.,Jensen, T. S.,Virtanen, H. E.,Schramm, K. W.,Shen, H.,Vartiainen, T.,Kiviranta, H.,Taboureau, O.,Audouze, K.,Brunak, S.,Main, K. M. (2012). Association between chemical pattern in breast milk and congenital cryptorchidism: modelling of complex human exposures. International Journal of Andrology 35(3): 294-302.
497	Su, P. H.,Huang, P. C.,Lin, C. Y.,Ying, T. H.,Chen, J. Y.,Wang, S. L. (2012). The effect of in utero exposure to dioxins and polychlorinated biphenyls on reproductive development in eight year-old children. Environment International 39(1): 181-187.
530	Tsukimori, K.,Uchi, H.,Mitoma, C.,Yasukawa, F.,Chiba, T.,Todaka, T.,Kajiwara, J.,Yoshimura, T.,Hirata, T.,Fukushima, K.,Wake, N.,Furue, M. (2012). Maternal exposure to high levels of dioxins in relation to birth weight in women affected by Yusho disease. Environment International 38(1): 79-86.
538	Louis, G. M. B.,Rios, L. I.,McLain, A.,Cooney, M. A.,Kostyniak, P. J.,Sundaram, R. (2011). Persistent organochlorine pollutants and menstrual cycle characteristics. Chemosphere 85(11): 1742-1748.
542	Warner, M.,Mocarelli, P.,Samuels, S.,Needham, L.,Brambilla, P.,Eskenazi, B. (2011). Dioxin Exposure and Cancer Risk in the Seveso Women's Health Study. Environmental Health Perspectives 119(12): 1700-1705.
564	Humblet, O.,Williams, P. L.,Korrick, S. A.,Sergeyev, O.,Emond, C.,Birnbaum, L. S.,Burns, J. S.,Altshul, L.,Patterson, D. G.,Turner, W. E.,Lee, M. M.,Revich, B.,Hauser, R. (2011). Dioxin and Polychlorinated Biphenyl Concentrations in Mother's Serum and the Timing of Pubertal Onset in Sons. Epidemiology 22(6): 827-835.
571	Ronn, M.,Lind, L.,van Bavel, B.,Salihovic, S.,Michaelsson, K.,Lind, P. M. (2011). Circulating levels of

	persistent organic pollutants associate in divergent ways to fat mass measured by DXA in humans. Chemosphere 85(3): 335-343.
599	Korrick, S. A.,Lee, M. M.,Williams, P. L.,Sergeyev, O.,Burns, J. S.,Patterson, D. G.,Turner, W. E.,Needham, L. L.,Altshul, L.,Revich, B.,Hauser, R. (2011). Dioxin Exposure and Age of Pubertal Onset among Russian Boys. Environmental Health Perspectives 119(9): 1339-1344.
654	Mocarelli, P.,Gerthoux, P. M.,Needham, L. L.,Patterson, D. G.,Limonta, G.,Falbo, R.,Signorini, S.,Bertona, M.,Crespi, C.,Sarto, C.,Scott, P. K.,Turner, W. E.,Brambilla, P. (2011). Perinatal Exposure to Low Doses of Dioxin Can Permanently Impair Human Semen Quality. Environmental Health Perspectives 119(5): 713-718.
655	Miyashita, C.,Sasaki, S.,Saijo, Y.,Washino, N.,Okada, E.,Kobayashi, S.,Konishi, K.,Kajiwara, J.,Todaka, T.,Kishi, R. (2011). Effects of prenatal exposure to dioxin-like compounds on allergies and infections during infancy. Environmental Research 111(4): 551-558.
693	Kim, M. J.,Marchand, P.,Henegar, C.,Antignac, J. P.,Alili, R.,Poitou, C.,Bouillot, J. L.,Basdevant, A.,Le Bizec, B.,Barouki, R.,Clement, K. (2011). Fate and Complex Pathogenic Effects of Dioxins and Polychlorinated Biphenyls in Obese Subjects before and after Drastic Weight Loss. Environmental Health Perspectives 119(3): 377-383.
719	Pelclova, D.,Navratil, T.,Fenclova, Z.,Vlckova, S.,Kupka, K.,Urban, P.,Ridzon, P.,Zikan, V.,Landova, L.,Syslova, K.,Kuzma, M.,Kacer, P. (2011). Increased oxidative/nitrosative stress markers measured non- invasively in patients with high 2,3,7,8-tetrachloro-dibenzo-p-dioxin plasma level. Neuroendocrinology Letters 32(Suppl 1): 71-76.
722	Nhu, D. D.,Kido, T.,Hung, N. N.,Le, T. H. T.,Naganuma, R.,Son, L. K.,Honma, S.,Maruzeni, S.,Nishijo, M.,Nakagawa, H. (2011). Dioxin levels in the breast milk and estradiol and androgen levels in the saliva of Vietnamese primiparae. Toxicological and Environmental Chemistry 93(4): 824-838.
994	Konishi, K.,Sasaki, S.,Kato, S.,Ban, S.,Washino, N.,Kajiwara, J.,Todaka, T.,Hirakawa, H.,Hori, T.,Yasutake, D.,Kishi, R. (2009). Prenatal exposure to PCDDs/PCDFs and dioxin-like PCBs in relation to birth weight. Environmental Research 109(7): 906-913.
998	Pesatori, A. C.,Consonni, D.,Rubagotti, M.,Grillo, P.,Bertazzi, P. A. (2009). Cancer incidence in the population exposed to dioxin after the "Seveso accident": twenty years of follow-up. Environmental Health 8(39): 1-11.
1193	Leijs, M. M.,Koppe, J. G.,Olie, K.,van Aalderen, W. M. C.,de Voogt, P.,Vulsma, T.,Westra, M.,Ten Tusscher, G. W. (2008). Delayed initiation of breast development in girls with higher prenatal dioxin exposure; a longitudinal cohort study. Chemosphere 73(6): 999-1004.
1251	Cok, I.,Donmez, M. K.,Satiroglu, M. H.,Aydinuraz, B.,Henkelmann, B.,Shen, H. Q.,Kotalik, J.,Schramm, K. W. (2008). Concentrations of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like PCBs in adipose tissue of infertile men. Archives of Environmental Contamination and Toxicology 55(1): 143-152.
1262	Baccarelli, A.,Giacomini, S. M.,Corbetta, C.,Landi, M. T.,Bonzini, M.,Consonni, D.,Grillo, P.,Patterson, D. G.,Pesatori, A. C.,Bertazzi, P. A. (2008). Neonatal thyroid function in seveso 25 years after maternal exposure to dioxin. Plos Medicine 5(7): 1133-1142.
1285	Tsukimori, K.,Tokunaga, S.,Shibata, S.,Uchi, H.,Nakayama, D.,Lshimam, T.,Nakano, H.,Wake, N.,Yoshimura, T.,Furue, M. (2008). Long-term effects of polychlorinated biphenyls and dioxins on pregnancy outcomes in women affected by the Yusho incident. Environmental Health Perspectives 116(5): 626-630.
1299	Consonni, D.,Pesatori, A. C.,Zocchetti, C.,Sindaco, R.,D'Oro, L. C.,Rubagotti, M.,Bertazzi, P. A. (2008). Mortality in a population exposed to dioxin after the Seveso, Italy, accident in 1976 : 25 years of follow-up. American Journal of Epidemiology 167(7): 847-858.

1330	Cao, Y. G.,Winneke, G.,Wilhelm, M.,Wittsiepe, J.,Lemm, F.,Furst, P.,Ranft, U.,Imohl, M.,Kraftg, M.,Oesch-Bartlomowicz, B.,Kramer, U. (2008). Environmental exposure to dioxins and polychlorinated biphenyls reduce levels of gonadal hormones in newborns: Results from the Duisburg cohort study. International Journal of Hygiene and Environmental Health 211(1-2): 30-39.
1381	Mocarelli, P.,Gerthoux, P. M.,Patterson, D. G.,Milani, S.,Limonta, G.,Bertona, M.,Signorini, S.,Tramacere, P.,Colombo, L.,Crespi, C.,Brambilla, P.,Sarto, C.,Carreri, V.,Sampson, E. J.,Turner, W. E.,Needham, L. L. (2008). Dioxin exposure, from infancy through puberty, produces endocrine disruption and affects human semen quality. Environmental Health Perspectives 116(1): 70-77.
1474	Turyk, M. E.,Anderson, H. A.,Persky, V. W. (2007). Relationships of thyroid hormones with polychlorinated biphenyls, dioxins, furans, and DDE in adults. Environmental Health Perspectives 115(8): 1197-1203.
1561	Warner, M.,Eskenazi, B.,Olive, D. L.,Samuels, S.,Quick-Miles, S.,Vercellini, P.,Gerthoux, P. M.,Needham, L.,Patterson, D. G.,Mocarelli, P. (2007). Serum dioxin concentrations and quality of ovarian function in women of seveso. Environmental Health Perspectives 115(3): 336-340.
1574	Chao, H. R.,Wang, S. L.,Lin, L. Y.,Lee, W. J.,Papke, O. (2007). Placental transfer of polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls in Taiwanese mothers in relation, to menstrual cycle characteristics. Food and Chemical Toxicology 45(2): 259-265.
1633	Dhooge, W.,van Larebeke, N.,Koppen, G.,Nelen, V.,Schoeters, G.,Vlietinck, R.,Kaufman, J. M.,Comhaire, F. (2006). Serum dioxin-like activity is associated with reproductive parameters in young men from the general Flemish population. Environmental Health Perspectives 114(11): 1670-1676.
1634	Fujiyoshi, P. T.,Michalek, J. E.,Matsumura, F. (2006). Molecular epidemiologic evidence for diabetogenic effects of dioxin exposure in US air force veterans of the Vietnam War. Environmental Health Perspectives 114(11): 1677-1683.
1699	Chen, H. L.,Su, H. J.,Guo, Y. L.,Liao, P. C.,Hung, C. F.,Lee, C. C. (2006). Biochemistry examinations and health disorder evaluation of Taiwanese living near incinerators and with low serum PCDD/Fs levels. Science of the Total Environment 366(2-3): 538-548.
1736	Wang, S. L.,Chang, Y. C.,Chao, H. R.,Li, C. M.,Li, L. A.,Lin, L. Y.,Papke, O. (2006). Body burdens of polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls and their relations to estrogen metabolism in pregnant women. Environmental Health Perspectives 114(5): 740-745.
1740	Bloom, M.,Vena, J.,Olson, J.,Moysich, K. (2006). Chronic exposure to dioxin-like compounds and thyroid function among New York anglers. Environmental Toxicology and Pharmacology 21(3): 260-267.
1775	Chen, H. L.,Su, H. J.,Wang, Y. J.,Guo, Y. L.,Liao, P. C.,Lee, C. C. (2006). Interactive effects between CYP1A1 genotypes and environmental polychlorinated dibenzo-p-dioxins and dibenzofurans exposures on liver function profile. Journal of Toxicology and Environmental Health-Part a-Current Issues 69(4): 269-281.
1787	Yoshida, J.,Kumagai, S.,Tabuchi, T.,Kosaka, H.,Akasaka, S.,Kasai, H.,Oda, H. (2006). Negative association between serum dioxin level and oxidative DNA damage markers in municipal waste incinerator workers. International Archives of Occupational and Environmental Health 79(2): 115-122.
1894	Kang, M. J.,Lee, D. Y.,Joo, W. A.,Kim, C. W. (2005). Plasma protein level changes in waste incineration workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Journal of Proteome Research 4(4): 1248-1255.
1932	Pavuk, M.,Michalek, J. E.,Schecter, A.,Ketchum, N. S.,Akhtar, F. Z.,Fox, K. A. (2005). Did TCDD exposure or service in southeast Asia increase the risk of cancer in air force Vietnam veterans who did not spray agent orange?. Journal of Occupational and Environmental Medicine 47(4): 335-342.
2044	Warner, M.,Samuels, S.,Mocarelli, P.,Gerthoux, P. M.,Needham, L.,Patterson, D. G.,Eskenazi, B. (2004).

	Serum dioxin concentrations and age at menarche. Environmental Health Perspectives 112(13): 1289-1292.
2045	Alaluusua, S.,Calderara, P.,Gerthoux, P. M.,Lukinmaa, P. L.,Kovero, O.,Needham, L.,Patterson, D. G.,Tuomisto, J.,Mocareili, P. (2004). Developmental dental aberrations after the dioxin accident in seveso. Environmental Health Perspectives 112(13): 1313-1318.
2093	Valic, E.,Jahn, O.,Papke, O.,Winker, R.,Wolf, C.,Rudiger, W. H. (2004). Transient increase in micronucleus frequency and DNA effects in the comet assay in two patients after intoxication with 2,3,7,8-tetrachlorodibenzo-p-dioxin. International Archives of Occupational and Environmental Health 77(5): 301-306.
2102	De Felip, E.,Porpora, M. G.,di Domenico, A.,Ingelido, A. M.,Cardelli, M.,Cosmi, E. V.,Donnez, J. (2004). Dioxin-like compounds and endometriosis: a study on Italian and Belgian women of reproductive age. Toxicology Letters 150(2): 203-209.
2114	Baccarelli, A.,Pesatori, A. C.,Masten, S. A.,Patterson, D. G.,Needham, L. L.,Mocarelli, P.,Caporaso, N. E.,Consonni, D.,Grassman, J. A.,Bertazzi, P. A.,Landi, M. T. (2004). Aryl-hydrocarbon receptor-dependent pathway and toxic effects of TCDD in humans: a population-based study in Seveso, Italy. Toxicology Letters 149(1-3): 287-293.
2122	Lim, Y.,Yang, J. Y.,Kim, Y.,Chang, Y. S.,Shin, D. C. (2004). Assessment of human health risk of dioxin in Korea. Environmental Monitoring and Assessment 92(1-3): 211-228.
2180	Fierens, S.,Mairesse, H.,Heilier, J. F.,De Burbure, C.,Focant, J. F.,Eppe, G.,De Pauw, E.,Bernard, A. (2003). Dioxin/polychlorinated biphenyl body burden, diabetes and endometriosis: findings in a population-based study in Belgium. Biomarkers 8(6): 529-534.
2198	Ogawa, T.,Asai, Y.,Yamashita, M.,Takasuga, T. (2003). Detectable dioxins in human saliva and their effects on gingival epithelial cells. Journal of Dental Research 82(10): 849-853.
2233	Leem, J. H.,Hong, Y. C.,Lee, K. H.,Kwon, H. J.,Chang, Y. S.,Jang, J. Y. (2003). Health survey on workers and residents near the municipal waste and industrial waste incinerators in Korea. Industrial Health 41(3): 181-188.
2239	Eskenazi, B.,Mocarelli, P.,Warner, M.,Chee, W. Y.,Gerthoux, P. M.,Samuels, S.,Needham, L. L.,Patterson, D. G. (2003). Maternal serum dioxin levels and birth outcomes in Women of Seveso, Italy. Environmental Health Perspectives 111(7): 947-953.
2262	Landi, M. T.,Bertazzi, P. A.,Baccarelli, A.,Consonni, D.,Masten, S.,Lucier, G.,Mocarelli, P.,Needham, L.,Caporaso, N.,Grassman, J. (2003). TCDD-mediated alterations in the AhR-dependent pathway in Seveso, Italy, 20 years after the accident. Carcinogenesis 24(4): 673-680.
2318	Baccarelli, A.,Mocarelli, P.,Patterson, D. G.,Bonzini, M.,Pesatori, A. C.,Caporaso, N.,Landi, M. T. (2002). Immunologic effects of dioxin: New results from Seveso and comparison with other studies. Environmental Health Perspectives 110(12): 1169-1173.
2329	Ryan, J. J.,Amirova, Z.,Carrier, G. (2002). Sex ratios of children of Russian pesticide producers exposed to dioxin. Environmental Health Perspectives 110(11): A699-A701.
2390	Warner, M.,Eskenazi, B.,Mocarelli, P.,Gerthoux, P. M.,Samuels, S.,Needham, L.,Patterson, D.,Brambilla, P. (2002). Serum dioxin concentrations and breast cancer risk in the Seveso Women's Health Study. Environmental Health Perspectives 110(7): 625-628.
2391	Eskenazi, B.,Mocarelli, P.,Warner, M.,Samuels, S.,Vercellini, P.,Olive, D.,Needham, L. L.,Patterson, D. G.,Brambilla, P.,Gavoni, N.,Casalini, S.,Panazza, S.,Turner, W.,Gerthoux, P. M. (2002). Serum dioxin concentrations and endometriosis: A cohort study in Seveso, Italy. Environmental Health Perspectives 110(7): 629-634.
2545	Bertazzi, P. A.,Consonni, D.,Bachetti, S.,Rubagotti, M.,Baccarelli, A.,Zocchetti, C.,Pesatori, A. C. (2001). Health effects of dioxin exposure: A 20-year mortality study. American Journal of Epidemiology

	153(11): 1031-1044.
2561	Masuda, Y. (2001). Fate of PCDF/PCB congeners and change of clinical symptoms in patients with Yusho PCB poisoning for 30 years. Chemosphere 43(4-7): 925-930.
2563	Revich, B.,Aksel, E.,Ushakova, T.,Ivanova, I.,Zhuchenko, N.,Klyuev, N.,Brodsky, B.,Sotskov, Y. (2001). Dioxin exposure and public health in Chapaevsk, Russia. Chemosphere 43(4-7): 951-966.
2566	Ingel, F.,Platonova, V.,Katosova, L. (2001). Human emotional stress, dioxin blood content and genetic damage in Chapaevsk town. Chemosphere 43(4-7): 989-998.
2567	Revazova, J.,Yurchenko, V.,Katosova, L.,Platonova, V.,Sycheva, L.,Khripach, L.,Ingel, F.,Tsutsman, T.,Zhurkov, V. (2001). Cytogenetic investigation of women exposed to different levels of dioxins in Chapaevsk town. Chemosphere 43(4-7): 999-1004.
2576	Johnson, E. S.,Shorter, C.,Bestervelt, L. L.,Patterson, D. G.,Needham, L. L.,Piper, W. N.,Lucier, G.,Nolan, C. J. (2001). Serum hormone levels in humans with low serum concentrations of 2,3,7,8-TCDD. Toxicology and Industrial Health 17(4): 105-112.
2702	Mocarelli, P.,Gerthoux, P. M.,Ferrari, E.,Patterson, D. G.,Kieszak, S. M.,Brambilla, P.,Vincoli, N.,Signorini, S.,Tramacere, P.,Carreri, V.,Sampson, E. J.,Turner, W. E.,Needham, L. L. (2000). Paternal concentrations of dioxin and sex ratio of offspring. Lancet 355(9218): 1858-1863.
2711	Eskenazi, B.,Mocarelli, P.,Warner, M.,Samuels, S.,Vercellini, P.,Olive, D.,Needham, L.,Patterson, D.,Brambilla, P. (2000). Seveso Women's Health Study: a study of the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on reproductive health. Chemosphere 40(9-11): 1247-1253.
2720	Neubert, R.,Maskow, L.,Triebig, G.,Broding, H. C.,Jacob-Muller, U.,Helge, H.,Neubert, D. (2000). Chlorinated dibenzo-P-dioxins and dibenzofurans and the human immune system: 3. Plasma immunoglobulins and cytokines of workers with quantified moderately-increased body burdens. Life Sciences 66(22): 2123-2142.
2796	Coenraads, P. J.,Olie, K.,Tang, N. J. (1999). Blood lipid concentrations of dioxins and dibenzofurans causing chloracne. British Journal of Dermatology 141(4): 694-697.
2906	Nagayama, J.,Tsuji, H.,Iida, T.,Hirakawa, H.,Matsueda, T.,Okamura, K.,Hasegawa, M.,Sato, K.,Ma, H. Y.,Yanagawa, T.,Igarashi, H.,Fukushige, J.,Watanabe, T. (1998). Postnatal exposure to chlorinated dioxins and related chemicals on lymphocyte subsets in Japanese breast-fed infants. Chemosphere 37(9-12): 1781-1787.
2956	Calvert, G. M.,Wall, D. K.,Sweeney, M. H.,Fingerhut, M. A. (1998). Evaluation of cardiovascular outcomes among US workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Environmental Health Perspectives 106(Suppl 2): 635-643.
2959	Jung, D.,Berg, P. A.,Edler, L.,Ehrenthal, W.,Fenner, D.,Flesch-Janys, D.,Huber, C.,Klein, R.,Koitka, C.,Lucier, G.,Manz, A.,Muttray, A.,Needham, L.,Papke, O.,Pietsch, M.,Portier, C.,Patterson, D.,Prellwitz, W.,Rose, D. M.,Thews, A.,Konietzko, J. (1998). Immunologic findings in workers formerly exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin and its congeners. Environmental Health Perspectives 106(Suppl 2): 689-695.
2975	Lanting, C. I.,Patandin, S.,Fidler, V.,Weisglas-Kuperus, N.,Sauer, P. J. J.,Boersma, E. R.,Touwen, B. C. L. (1998). Neurological condition in 42-month-old children in relation to pre- and postnatal exposure to polychlorinated biphenyls and dioxins. Early Human Development 50(3): 283-292.
2983	Pesatori, A. C.,Zocchetti, C.,Guercilena, S.,Consonni, D.,Turrini, D.,Bertazzi, P. A. (1998). Dioxin exposure and non-malignant health effects: a mortality study. Occupational and Environmental Medicine 55(2): 126-131.
3038	Kahleova, H.,Tonstad, S.,Rosmus, J.,Fisar, P.,Mari, A.,Hill, M.,Pelikanova, T. (2016). The effect of a vegetarian versus conventional hypocaloric diet on serum concentrations of persistent organic pollutants in patients with type 2 diabetes. Nutrition Metabolism and Cardiovascular Diseases 26(5):

	430-438.
3046	Lignell, S.,Aune, M.,Darnerud, P. O.,Stridsberg, M.,Hanberg, A.,Larsson, S. C.,Glynn, A. (2016). Maternal body burdens of PCDD/Fs and PBDEs are associated with maternal serum levels of thyroid hormones in early pregnancy: a cross-sectional study. Environmental Health 15(55): 1-11.
3093	Fukushi, J.,Tokunaga, S.,Nakashima, Y.,Motomura, G.,Mitoma, C.,Uchi, H.,Furue, M.,Iwamoto, Y. (2016). Effects of dioxin-related compounds on bone mineral density in patients affected by the Yusho incident. Chemosphere 145: 25-33.
3102	Tran, N. N.,Pham, T. T.,Ozawa, K.,Nishijo, M.,Anh, T.,Nguyet, N.,Tran, T. Q.,Luong, V. H.,Tran, A. H.,Phan, V. H. A.,Nakai, A.,Nishino, Y.,Nishijo, H. (2016). Impacts of Perinatal Dioxin Exposure on Motor Coordination and Higher Cognitive Development in Vietnamese Preschool Children: A Five-Year Follow-Up. Plos One 11(1): 1-15.
3338	Yi, S. W.,Ryu, S. Y.,Ohrr, H.,Hong, J. S. (2014). Agent Orange exposure and risk of death in Korean Vietnam veterans: Korean Veterans Health Study. International Journal of Epidemiology 43(6): 1825-1834.
3383	Kumar, J.,Lind, L.,Salihovic, S.,Bavel, B. V.,Ingelsson, E.,Lind, P. M. (2014). Persistent organic pollutants and liver dysfunction biomarkers in a population-based human sample of men and women. Environmental Research 134: 251-256.
3388	Bechaux, C.,Zeilmaker, M.,Merlo, M.,Bokkers, B.,Crepet, A. (2014). An integrative risk assessment approach for persistent chemicals: A case study on dioxins, furans and dioxin-like PCBs in France. Regulatory Toxicology and Pharmacology 70(1): 261-269.
3393	Kumar, J.,Lind, P. M.,Salihovic, S.,van Bavel, B.,Ekdahl, K. N.,Nilsson, B.,Lind, L.,Ingelsson, E. (2014). Influence of persistent organic pollutants on the complement system in a population-based human sample. Environment International 71: 94-100.
3401	Chevrier, J.,Warner, M.,Gunier, R. B.,Brambilla, P.,Eskenazi, B.,Mocarelli, P. (2014). Serum Dioxin Concentrations and Thyroid Hormone Levels in the Seveso Women's Health Study. American Journal of Epidemiology 180(5): 490-498.
3402	Kumar, J.,Lind, M.,Salihovic, S.,van Bavel, B.,Ingelsson, E.,Lind, L. (2014). Persistent Organic Pollutants and Inflammatory Markers in a Cross-Sectional Study of Elderly Swedish People: The PIVUS Cohort. Environmental Health Perspectives 122(9): 977-983.
3408	Faure, A. C.,Viel, J. F.,Bailly, A.,Blagosklonov, O.,Amiot, C.,Roux, C. (2014). Evolution of sperm quality in men living in the vicinity of a municipal solid waste incinerator possibly correlated with decreasing dioxins emission levels. Andrologia 46(7): 744-752.
3414	ten Tusscher, G. W.,Leijs, M. M.,de Boer, L. C. C.,Legler, J.,Olie, K.,Spekreijse, H.,van Dijk, B. W.,Vulsma, T.,Briet, J.,Ilsen, A.,Koppe, J. G. (2014). Neurodevelopmental retardation, as assessed clinically and with magnetoencephalography and electroencephalography, associated with perinatal dioxin exposure. Science of the Total Environment 491-492: 235-239.
3431	Pestana, D.,Faria, G.,Sa, C.,Fernandes, V. C.,Teixeira, D.,Norberto, S.,Faria, A.,Meireles, M.,Marques, C.,Correia-Sa, L.,Cunha, A.,Guimaraes, J. T.,Taveira-Gomes, A.,Santos, A. C.,Domingues, V. F.,Delerue-Matos, C.,Monteiro, R.,Calhau, C. (2014). Persistent organic pollutant levels in human visceral and subcutaneous adipose tissue in obese individuals-Depot differences and dysmetabolism implications. Environmental Research 133: 170-177.
3447	Everett, C. J.,Thompson, O. M. (2014). Dioxins, furans and dioxin-like PCBs in human blood: Causes or Consequences of diabetic nephropathy?. Environmental Research 132: 126-131.
3477	Suzuki, H.,Kido, T.,Okamoto, R.,Nhu, D. D.,Nishijo, M.,Nakagawa, H.,Tawara, K.,Horikawa, H.,Sato, Y.,Dung, P. T.,Thom, L. H.,Hung, N. N. (2014). The Relationship between Dioxin Congeners in the Breast Milk of Vietnamese Women and Sister Chromatid Exchange. International Journal of Molecular

	Sciences 15(5): 7485-7499.
3485	Sun, X. L.,Kido, T.,Okamoto, R.,Manh, H. D.,Maruzeni, S.,Nishijo, M.,Nakagawa, H.,Honma, S.,Nakano, T.,Takasuga, T.,Nhu, D. D.,Hung, N. N.,Son, L. K. (2014). Relationship between dioxin and steroid hormones in sera of Vietnamese men. Biomarkers 19(3): 236-240.
3505	Wohlfahrt-Veje, C.,Audouze, K.,Brunak, S.,Antignac, J. P.,Bizec, B. I.,Juul, A.,Skakkebaek, N. E.,Main, K. M. (2014). Polychlorinated dibenzo-p-dioxins, furans, and biphenyls (PCDDs/PCDFs and PCBs) in breast milk and early childhood growth and IGF1. Reproduction 147(4): 391-399.
3544	Caspersen, I. H.,Haugen, M.,Schjolberg, S.,Vejrup, K.,Knutsen, H. K.,Brantster, A. L.,Meltzer, H. M.,Alexander, J.,Magnus, P.,Kvalem, H. E. (2016). Maternal dietary exposure to dioxins and polychlorinated biphenyls (PCBs) is associated with language delay in 3 year old Norwegian children. Environment international 91: 180-187.
3549	Chang, Jung-Wei,Chen, Hsiu-Ling,Su, Huey-Jen,Lee, Ching-Chang (2016). Abdominal Obesity and Insulin Resistance in People Exposed to Moderate-to-High Levels of Dioxin. Plos One 11(1): 1-14.
3562	Delvaux, Immle,Van Cauwenberghe, Jolijn,Den Hond, Elly,Schoeters, Greet,Govarts, Eva,Nelen, Vera,Baeyens, Willy,Van Larebeke, Nicolas,Sioen, Isabelle (2014). Prenatal exposure to environmental contaminants and body composition at age 7-9 years. Environmental research 132: 24-32.
3564	Dinse, Gregg E.,Jusko, Todd A.,Whitt, Irene Z.,Co, Caroll A.,Parks, Christine G.,Satoh, Minoru,Chan, Edward K. L.,Rose, Kathryn M.,Walker, Nigel J.,Birnbaum, Linda S.,Zeldin, Darryl C.,Weinberg, Clarice R.,Miller, Frederick W. (2016). Associations Between Selected Xenobiotics and Antinuclear Antibodies in the National Health and Nutrition Examination Survey, 1999-2004. Environmental health perspectives 124(4): 426-436.
3570	Eskenazi, Brenda,Warner, Marcella,Sirtori, Marcella,Fuerst, Thomas,Rauch, Stephen A.,Brambilla, Paolo,Mocarelli, Paolo,Rubinacci, Alessandro (2014). Serum Dioxin Concentrations and Bone Density and Structure in the Seveso Women's Health Study. Environmental health perspectives 122(1): 51-57.
3577	Galimova, E. F.,Amirova, Z. K.,Galimov, Sh N. (2015). Dioxins in the semen of men with infertility. Environmental Science and Pollution Research 22(19): 14566-14569.
3597	Henriquez-Hernandez, Luis A.,Luzardo, Octavio P.,Zumbado, Manuel,Camacho, Maria,Serra-Majem, Lluis,Alvarez-Leon, Eva E.,Boada, Luis D. (2014). Blood pressure in relation to contamination by polychlorobiphenyls and organochlorine pesticides: Results from a population-based study in the Canary Islands (Spain). Environmental research 135: 48-54.
3614	Kido, Teruhiko,Honma, Seijiro,Dang Duc, Nhu,Ho Dung, Manh,Dao Van, Tung,Sun Xian, Liang,Le Thai, Anh,Okamoto, Rie,Maruzeni, Shoko,Nakagawa, Hideaki,Nguyen Ngoc, Hung,Le Ke, Son (2016). Inverse association of highly chlorinated dioxin congeners in maternal breast milk with dehydroepiandrosterone levels in three-year-old Vietnamese children. Science of the Total Environment 550: 248-255.
3619	Koskenniemi, Jaakko J.,Virtanen, Helena E.,Kiviranta, Hannu,Damgaard, Ida N.,Matomaki, Jaakko,Thorup, Jorgen M.,Hurme, Timo,Skakkebaek, Niels E.,Main, Katharina M.,Toppari, Jorma (2015). Association between levels of persistent organic pollutants in adipose tissue and cryptorchidism in early childhood: a case-control study. Environmental Health 14(78): 1-10.
3628	Lee, Yu-Mi,Bae, Sang-Geun,Lee, Seon-Hwa,Jacobs, David R., Jr.,Lee, Duk-Hee (2013). Persistent organic pollutants and hyperuricemia in the US general population. Atherosclerosis 230(1): 1-5.
3629	Lee, Yu-Mi,Bae, Sang-Geun,Lee, Seon-Hwa,Jacobs, David R., Jr.,Lee, Duk-Hee (2013). Associations between Cigarette Smoking and Total Mortality Differ Depending on Serum Concentrations of Persistent Organic Pollutants among the Elderly. Journal of Korean medical science 28(8): 1122-U155.
3636	Lind, P. Monica,Penell, Johanna,Salihovic, Samira,van Bavel, Bert,Lind, Lars (2014). Circulating levels of p,p '-DDE are related to prevalent hypertension in the elderly. Environmental research 129: 27-31.
3645	Martinez-Zamora, M. A.,Mattioli, L.,Parera, J.,Abad, E.,Coloma, J. L.,van Babel, B.,Galceran, M.

	T.,Balasch, J.,Carmona, F. (2015). Increased levels of dioxin-like substances in adipose tissue in patients with deep infiltrating endometriosis. Human Reproduction 30(5): 1059-1068.
3652	Nakamoto, Mariko,Arisawa, Kokichi,Uemura, Hirokazu,Katsuura, Sakurako,Takami, Hidenobu,Sawachika, Fusakazu,Yamaguchi, Miwa,Juta, Tomoya,Sakai, Tohru,Toda, Eisaku,Mori, Kei,Hasegawa, Manabu,Tanto, Masaharu,Shima, Masayuki,Sumiyoshi, Yoshio,Morinaga, Kenji,Kodama, Kazunori,Suzuki, Takaichiro,Nagai, Masaki,Satoh, Hiroshi (2013). Association between blood levels of PCDDs/PCDFs/dioxin-like PCBs and history of allergic and other diseases in the Japanese population. International archives of occupational and environmental health 86(8): 849-859.
3654	Neugebauer, Julia,Wittsiepe, Juegen,Kasper-Sonnenberg, Monika,Schoeneck, Nina,Scholmerich, Axel,Wilhelm, Michael (2015). The influence of low level pre- and perinatal exposure to PCDD/Fs, PCBs, and lead on attention performance and attention-related behavior among German school-aged children: Results from the Duisburg Birth Cohort Study. International journal of hygiene and environmental health 218(1): 153-162.
3657	Nishijo, Muneko,Pham The, Tai,Nguyen Thi Nguyet, Anh,Tran Ngoc, Nghi,Nakagawa, Hideaki,Hoang Van, Luong,Tran Hai, Anh,Morikawa, Yuko,Waseda, Tomoo,Kido, Teruhiko,Nishijo, Hisao (2015). Urinary Amino Acid Alterations in 3-Year-Old Children with Neurodevelopmental Effects due to Perinatal Dioxin Exposure in Vietnam: A Nested Case-Control Study for Neurobiomarker Discovery. Plos One 10(1): 1-14.
3660	Nowack, Nikola,Wittsiepe, Juergen,Kasper-Sonnenberg, Monika,Wilhelm, Michael,Schoelmerich, Axel (2015). Influence of Low-Level Prenatal Exposure to PCDD/Fs and PCBs on Empathizing, Systemizing and Autistic Traits: Results from the Duisburg Birth Cohort Study. Plos One 10(6): 1-20.
3663	Papadopoulou, Eleni,Caspersen, Ida H.,Kvalem, Helen E.,Knutsen, Helle K.,Duarte-Salles, Talita,Alexander, Jan,Meltzer, Helle Margrete,Kogevinas, Manolis,Brantsaeter, Anne Lise,Haugen, Margaretha (2013). Maternal dietary intake of dioxins and polychlorinated biphenyls and birth size in the Norwegian Mother and Child Cohort Study (MoBa). Environment international 60: 209-216.
3664	Papadopoulou, Eleni,Kogevinas, Manolis,Botsivali, Maria,Pedersen, Marie,Besselink, Harrie,Mendez, Michelle A.,Fleming, Sarah,Hardie, Laura J.,Knudsen, Lisbeth E.,Wright, John,Agramunt, Silvia,Sunyer, Jordi,Granum, Berit,Gutzkow, Kristine B.,Brunborg, Gunnar,Alexander, Jan,Meltzer, Helle Margrete,Brantsaeter, Anne Lise,Sarri, Katerina,Chatzi, Leda,Merlo, Domenico F.,Kleinjans, Jos C.,Haugen, Margaretha (2014). Maternal diet, prenatal exposure to dioxin-like compounds and birth outcomes in a European prospective mother-child study (NewGeneris). Science of the Total Environment 484: 121-128.
3665	Papadopoulou, Eleni,Vafeiadi, Marina,Agramunt, Silvia,Mathianaki, Kleopatra,Karakosta, Polyxeni,Spanaki, Ariana,Besselink, Harrie,Kiviranta, Hannu,Rantakokko, Panu,KaterinaSarri,,Koutis, Antonis,Chatzi, Leda,Kogevinas, Manolis (2013). Maternal diet, prenatal exposure to dioxins and other persistent organic pollutants and anogenital distance in children. Science of the Total Environment 461: 222-229.
3704	Sun, Xian Liang,Kido, Teruhiko,Honma, Seijiro,Okamoto, Rie,Ho Dung, Manh,Maruzeni, Shoko,Nishijo, Muneko,Nakagawa, Hideaki,Nakano, Takeshi,Koh, Eitetsu,Takasuga, Takumi,Dang Duc, Nhu,Nguyen Ngoc, Hung,Le Ke, Son (2016). Influence of dioxin exposure upon levels of prostate-specific antigen and steroid hormones in Vietnamese men. Environmental Science and Pollution Research 23(8): 7807-7813.
3731	Warner, Marcella,Mocarelli, Paolo,Brambilla, Paolo,Wesselink, Amelia,Samuels, Steven,Signorini, Stefano,Eskenazi, Brenda (2013). Diabetes, Metabolic Syndrome, and Obesity in Relation to Serum Dioxin Concentrations: The Seveso Women's Health Study. Environmental health perspectives 121(8): 906-911.
3733	Wesselink, Amelia,Warner, Marcella,Samuels, Steven,Parigi, Aliza,Brambilla, Paolo,Mocarelli, Paolo,Eskenazi, Brenda (2014). Maternal dioxin exposure and pregnancy outcomes over 30 years of

	follow-up in Seveso. Environment international 63: 143-148.
3740	Xu, Peiwei,Lou, Xiaoming,Ding, Gangqiang,Shen, Haitao,Wu, Lizhi,Chen, Zhijian,Han, Jianlong,Han, Guangen,Wang, Xiaofeng (2014). Association of PCB, PBDE and PCDD/F body burdens with hormone levels for children in an e-waste dismantling area of Zhejiang Province, China. Science of the Total Environment 499: 55-61.
3785	Cai, L. Y.,Izumi, S.,Suzuki, T.,Goya, K.,Nakamura, E.,Sugiyama, T.,Kobayashi, H. (2011). Dioxins in ascites and serum of women with endometriosis: a pilot study. Human Reproduction 26(1): 117-126.
3791	Chang, Jung-Wei,Ou, Horng-Yih,Chen, Hsiu-Ling,Su, Huey-Jen,Lee, Ching-Chang (2013). Hyperuricemia After Exposure to Polychlorinated Dibenzo-P-Dioxins and Dibenzofurans Near a Highly Contaminated Area. Epidemiology 24(4): 582-589.
3813	Eskenazi, Brenda,Warner, Marcella,Marks, Amy R.,Samuels, Steven,Needham, Larry,Brambilla, Paolo,Mocarelli, Paolo (2010). Serum Dioxin Concentrations and Time to Pregnancy. Epidemiology 21(2): 224-231.
3844	Han, GuanGen,Ding, GangQiang,Lou, XiaoMing,Wang, XiaoFeng,Han, JianLong,Shen, HaiTao,Zhou, Yu,Du, LeYan (2011). Correlations of PCBs, DIOXIN, and PBDE with TSH in Children's Blood in Areas of Computer E-waste Recycling. Biomedical and Environmental Sciences 24(2): 112-116.
3853	Ho Dung, Manh,Kido, Teruhiko,Okamoto, Rie,Sun, XianLiang,Nguyen Hoang, Viet,Nakano, Madoca,Pham The, Tai,Maruzeni, Shoko,Nishijo, Muneko,Nakagawa, Hideaki,Suzuki, Hiroyuki,Honma, Seijiro,Dao Van, Tung,Dang Duc, Nhu,Nguyen Ngoc, Hung,Le Ke, Son (2013). The relationship between dioxins and salivary steroid hormones in Vietnamese primiparae. Environmental Health and Preventive Medicine 18(3): 221-229.
3884	Luzardo, Octavio P.,Alberto Henriquez-Hernandez, Luis,Valeron, Pilar F.,Lara, Pedro C.,Almeida-Gonzalez, Maira,Losada, Antonio,Zumbado, Manuel,Serra-Majem, Lluis,Elisa Alvarez-Leon, Eva,Boada, Luis D. (2012). The Relationship between Dioxin-Like Polychlorobiphenyls and IGF-I Serum Levels in Healthy Adults: Evidence from a Cross-Sectional Study. Plos One 7(5): 1-7.
3915	Rennert, Annette,Wittsiepe, Juergen,Kasper-Sonnenberg, Monika,Binder, Gerhard,Fuerst, Peter,Cramer, Claudia,Kraemer, Ursula,Wilhelm, Michael (2012). Prenatal and Early Life Exposure to Polychlorinated Dibenzo-P-Dioxins, Dibenzofurans and Biphenyls may Influence Dehydroepiandrosterone Sulfate Levels at Prepubertal Age: Results from the Duisburg Birth Cohort Study. Journal of Toxicology and Environmental Health-Part A-Current Issues 75(19-20): 1232-1240.
3924	Roos, Vendela,Ronn, Monika,Salihovic, Samira,Lind, Lars,van Bavel, Bert,Kullberg, Joel,Johansson, Lars,Ahlstrom, Hakan,Lind, P. Monica (2013). Circulating Levels of Persistent Organic Pollutants in Relation to Visceral and Subcutaneous Adipose Tissue by Abdominal MRI. Obesity 21(2): 413-418.
3936	Simsa, Peter,Mihalyi, Attila,Schoeters, Greet,Koppen, Gudrun,Kyama, Cleophas M.,Den Hond, Elly M.,Fueloep, Vilmos,D'Hooghe, Thomas M. (2010). Increased exposure to dioxin-like compounds is associated with endometriosis in a case-control study in women. Reproductive Biomedicine Online 20(5): 681-688.
3938	Stolevik, Solvor Berntsen,Nygaard, Unni Cecilie,Namork, Ellen,Haugen, Margaretha,Kvalem, Helen Engelstad,Meltzer, Helle Margrete,Alexander, Jan,van Delft, Joost H. M.,van Loveren, Henk,Lovik, Martinus,Granum, Berit (2011). Prenatal exposure to polychlorinated biphenyls and dioxins is associated with increased risk of wheeze and infections in infants. Food and Chemical Toxicology 49(8): 1843-1848.
3939	Stolevik, Solvor Berntsen,Nygaard, Unni Cecilie,Namork, Ellen,Haugen, Margaretha,Meltzer, Helle Margrete,Alexander, Jan,Knutsen, Helle Katrine,Aaberge, Ingeborg,Vainio, Kirsti,van Loveren, Henk,Lovik, Martinus,Granum, Berit (2013). Prenatal exposure to polychlorinated biphenyls and dioxins from the maternal diet may be associated with immunosuppressive effects that persist into early childhood. Food and Chemical Toxicology 51: 165-172.

3965	Vogt, Rainbow,Bennett, Deborah,Cassady, Diana,Frost, Joshua,Ritz, Beate,Hertz-Picciotto, Irva (2012). Cancer and non-cancer health effects from food contaminant exposures for children and adults in California: a risk assessment. Environmental Health 11(83): 1-14.
4015	Chen, Jein-Wen,Wang, Shu-Li,Liao, Po-Chi,Chen, Hsiao Yen,Ko, Ying-Ching,Lee, Ching-Chang (2008). Relationship between insulin sensitivity and exposure to dioxins and polychlorinated biphenyls in pregnant women. Environmental research 107(2): 245-253.
4031	Eskenazi, Brenda,Warner, Marcella,Samuels, Steven,Young, Jessica,Gerthoux, Pier Mario,Needham, Larry,Patterson, Donald,Olive, David,Gavoni, Nicoletta,Vercellini, Paolo,Mocarelli, Paolo (2007). Serum dioxin concentrations and risk of uterine leiomyoma in the Seveso Women's Health Study. American Journal of Epidemiology 166(1): 79-87.
4051	Gupta, Amit,Ketchum, Norma,Roehrborn, Claus G.,Schecter, Arnold,Aragaki, Corinne C.,Michalek, Joel E. (2006). Serum dioxin, testosterone, and subsequent risk of benign prostatic hyperplasia: A prospective cohort study of air force veterans. Environmental health perspectives 114(11): 1649-1654.
4052	Ha, M. H.,Lee, D. H.,Son, H. K.,Park, S. K.,Jacobs, D. R., Jr. (2009). Association between serum concentrations of persistent organic pollutants and prevalence of newly diagnosed hypertension: results from the National Health and Nutrition Examination Survey 1999-2002. Journal of human hypertension 23(4): 274-286.
4065	Imamura, Tomoaki,Kanagawa, Yoshiyuki,Matsumoto, Shinya,Tajima, Bunichi,Uenotsuchi, Takeshi,Shibata, Satoko,Furue, Masultaka (2007). Relationship between clinical features and blood levels of pentachlorodibenzofuran in patients with Yusho. Environmental toxicology 22(2): 124-131.
4069	Jackson, Leila W.,Lynch, Courtney D.,Kostyniak, Paul J.,McGuinness, Bridget M.,Louis, Germaine M. Buck (2010). Prenatal and postnatal exposure to polychlorinated biphenyls and child size at 24 months of age. Reproductive Toxicology 29(1): 25-31.
4091	Lee, Duk-Hee,Jacobs, David R.,Porta, Miquel (2007). Association of serum concentrations of persistent organic pollutants with the prevalence of learning disability and attention deficit disorder. Journal of epidemiology and community health 61(7): 591-596.
4092	Lee, Duk-Hee,Steffes, Michael,Jacobs, David R., Jr. (2007). Positive associations of serum concentration of polychlorinated biphenyls or organochlorine pesticides with self-reported arthritis, especially rheumatoid type, in women. Environmental health perspectives 115(6): 883-888.
4093	Leijs, Marike M.,Koppe, Jenne G.,Olie, Kees,van Aalderen, Wim M. C.,de Voogt, Pim,ten Tusscher, Gavin W. (2009). Effects of Dioxins, PCBs, and PBDEs on Immunology and Hematology in Adolescents. Environmental science & technology 43(20): 7946-7951.
4115	Niskar, Amanda S.,Needham, Larry L.,Rubin, Carol,Turner, Wayman E.,Martin, Colleen A.,Patterson, Donald G., Jr.,Hasty, Lisa,Wong, Lee-Yang,Marcus, Michele (2009). Serum dioxins, polychlorinated biphenyls, and endometriosis: A case-control study in Atlanta. Chemosphere 74(7): 944-949.
4121	Pelclova, Daniela,Fenclova, Zdenka,Urban, Pavel,Ridzon, Petr,Preiss, Jan,Kupka, Karel,Malik, Jan,Dubska, Zora,Navratil, Tomas (2009). Chronic health impairment due to 2,3,7,8-tetrachloro-dibenzo-p-dioxin exposure. Neuroendocrinology letters 30(Suppl 1): 219-224.
4122	Pelclova, Daniela,Prazny, Martin,Skrha, Jan,Fenclova, Zdenka,Kalousova, Marta,Urban, Pavel,Navratil, Tomas,Senholdova, Zdenka,Smerhovsky, Zdenek (2007). 2,3,7,8-TCDD exposure, endothelial dysfunction and impaired microvascular reactivity. Human & experimental toxicology 26(9): 705-713.
4162	Su, Pen-Hua,Chen, Jia-Yuh,Chen, Jein-Wen,Wang, Shu-Li (2010). Growth and Thyroid Function in Children With In Utero Exposure to Dioxin: A 5-Year Follow-Up Study. Pediatric research 67(2): 205-210.
4175	Urban, P.,Pelclova, D.,Lukas, E.,Kupka, K.,Preiss, J.,Fenclova, Z.,Smerhovsky, Z. (2007). Neurological and neurophysiological examinations on workers with chronic poisoning by 2,3,7,8-TCDD: follow-up 35

	years after exposure. European Journal of Neurology 14(2): 213-218.
4208	Baccarelli, A.,Pesatori, A. C.,Consonni, D.,Mocarelli, P.,Patterson, D. G.,Caporaso, N. E.,Bertazzi, P. A.,Landi, M. T. (2005). Health status and plasma dioxin levels in chloracne cases 20 years after the Seveso, Italy accident. British Journal of Dermatology 152(3): 459-465.
4244	Eskenazi, B.,Warner, M.,Mocarelli, P.,Samuels, S.,Needham, L. L.,Patterson, D. G.,Lippman, S.,Vercellini, P.,Gerthoux, P. M.,Brambilla, P.,Olive, D. (2002). Serum dioxin concentrations and menstrual cycle characteristics. American Journal of Epidemiology 156(4): 383-392.
4248	Foster, W. G.,Holloway, A. C.,Hughes, C. L. (2005). Dioxin-like activity and maternal thyroid hormone levels in second trimester maternal serum. American Journal of Obstetrics and Gynecology 193(6): 1900-1907.
4259	Gupta, Amit,Schecter, Arnold,Aragaki, Corinne C.,Roehrborn, Claus G. (2006). Dioxin exposure and Benign prostatic hyperplasia. Journal of Occupational and Environmental Medicine 48(7): 708-714.
4264	Heilier, J. F.,Nackers, F.,Verougstraete, V.,Tonglet, R.,Lison, D.,Donnez, J. (2005). Increased dioxin-like compounds in the serum of women with peritoneal endometriosis and deep endometriotic (adenomyotic) nodules. Fertility and sterility 84(2): 305-312.
4295	Lawson, C. C.,Schnorr, T. M.,Whelan, E. A.,Deddens, J. A.,Dankovic, D. A.,Piacitelli, L. A.,Sweeney, M. H.,Connally, L. B. (2004). Paternal occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin and birth outcomes of offspring: birth weight, preterm delivery, and birth defects. Environmental health perspectives 112(14): 1403-1408.
4332	Nakajima, S.,Saijo, Y.,Kato, S.,Sasaki, S.,Uno, K.,Kanagami, N.,Hirakawa, H.,Hori, T.,Tobiishi, K.,Todaka, T.,Nakamura, Y.,Yanagiya, S.,Sengoku, Y.,Iida, T.,Sata, F.,Kishi, R. (2006). Effects of prenatal exposure to polychlorinated biphenyls and dioxins on mental and motor development in Japanese children at 6 months of age. Environmental health perspectives 114(5): 773-778.
4333	Nakamura, T.,Miyazaki, W.,Ohnishi, Y.,Ishibashi, T.,Study Grp, Yusho (2005). Ophthalmic findings in Yusho. Journal of dermatological science: S57-S63.
4346	Pesatori, A. C.,Consonni, D.,Bachetti, S.,Zocchetti, C.,Bonzini, M.,Baccarelli, A.,Bertazzi, P. A. (2003). Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso accident". Industrial health 41(3): 127-138.
4358	Reynolds, P.,Hurley, S. E.,Petreas, M.,Goldberg, D. E.,Smith, D.,Gilliss, D.,Mahoney, M. E.,Jeffrey, S. S. (2005). Adipose levels of dioxins and risk of breast cancer. Cancer Causes & Control 16(5): 525-535.
4381	Schnorr, T. M.,Lawson, C. C.,Whelan, E. A.,Dankovic, D. A.,Deddens, J. A.,Piacitelli, L. A.,Reefhuis, J.,Sweeney, M. H.,Connally, L. B.,Fingerhut, M. A. (2001). Spontaneous abortion, sex ratio, and paternal occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Environmental health perspectives 109(11): 1127-1132.
4382	Schoenroth, L.,Chan, S.,Fritzler, M. (2004). Autoantibodies and levels of polychlorinated biphenyls in persons living near a hazardous waste treatment facility. Journal of Investigative Medicine 52(3): 170-176.
4408	Wang, S. L.,Chen, T. T.,Hsu, J. F.,Hsu, C. C.,Chang, L. W.,Ryan, J. J.,Guo, Y. L. L.,Lambert, G. H. (2003). Neonatal and childhood teeth in relation to perinatal exposure to polychlorinated biphenyls and dibenzofurans: observations of the Yucheng children in Taiwan. Environmental research 93(2): 131-137.
4409	Wang, S. L.,Su, P. H.,Jong, S. B.,Guo, Y. L.,Chou, W. L.,Papke, O. (2005). In utero exposure to dioxins and polychlorinated biphenyls and its relations to thyroid function and growth hormone in newborns. Environmental health perspectives 113(11): 1645-1650.
4490	Michalek, J. E.,Akhtar, F. Z.,Kiel, J. L. (1999). Serum dioxin, insulin, fasting glucose, and sex hormone-binding globulin in veterans of operation ranch hand. Journal of Clinical Endocrinology & Metabolism

	84(5): 1540-1543.
4491	Michalek, J. E.,Rahe, A. J.,Boyle, C. A. (1998). Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death. Epidemiology 9(2): 161-167.
4495	Nouwen, J.,Cornelis, C.,De Fre, R.,Wevers, M.,Viaene, P.,Mensink, C.,Patyn, J.,Verschaeve, L.,Hooghe, R.,Maes, A.,Collier, M.,Schoeters, G.,Van Cleuvenbergen, R.,Geuzens, P. (2001). Health risk assessment of dioxin emissions from municipal waste incinerators: the Neerlandquarter (Wilrijk, Belgium). Chemosphere 43(4-7): 909-923.
4535	Ward, E. M.,Schulte, P.,Grajewski, B.,Andersen, A.,Patterson, D. G.,Turner, W.,Jellum, E.,Deddens, J. A.,Friedland, J.,Roeleveld, N.,Waters, M.,Butler, M. A.,DiPietro, E.,Needham, L. L. (2000). Serum organochlorine levels and breast cancer: A nested case-control study of Norwegian women. Cancer Epidemiology Biomarkers & Prevention 9(12): 1357-1367.
4599	Akhtar, F. Z.,Garabrant, D. H.,Ketchum, N. S.,Michalek, J. E. (2004). Cancer in US Air Force veterans of the Vietnam War. J Occup Environ Med 46(2): 123-36.
4668	Aries, E.,Anderson, D. R.,Fisher, R. (2008). Exposure assessment of workers to airborne PCDD/Fs, PCBs and PAHs at an electric arc furnace steelmaking plant in the UK. Ann Occup Hyg 52(4): 213-25.
4737	Baccarelli, A.,Hirt, C.,Pesatori, A. C.,Consonni, D.,Patterson, D. G., Jr.,Bertazzi, P. A.,Dolken, G.,Landi, M. T. (2006). t(14;18) translocations in lymphocytes of healthy dioxin-exposed individuals from Seveso, Italy. Carcinogenesis 27(10): 2001-7.
4869	Boers, D.,Portengen, L.,Bueno-de-Mesquita, H. B.,Heederik, D.,Vermeulen, R. (2010). Cause-specific mortality of Dutch chlorophenoxy herbicide manufacturing workers. Occup Environ Med 67(1): 24-31.
4870	Boers, D.,Portengen, L.,Turner, W. E.,Bueno-de-Mesquita, H. B.,Heederik, D.,Vermeulen, R. (2012). Plasma dioxin levels and cause-specific mortality in an occupational cohort of workers exposed to chlorophenoxy herbicides, chlorophenols and contaminants. Occup Environ Med 69(2): 113-8.
4981	Calvert, G. M.,Sweeney, M. H.,Deddens, J.,Wall, D. K. (1999). Evaluation of diabetes mellitus, serum glucose, and thyroid function among United States workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Occup Environ Med 56(4): 270-6.
5025	Chang, J. W.,Chen, H. L.,Chang, C. C.,Su, H. J.,Liao, P. C.,Lee, C. C. (2011). Predicting the risk of cardiovascular disease in people exposed to moderate to high levels of dioxin. J Hazard Mater 198: 317-22.
5027	Chang, J. W.,Chen, H. L.,Su, H. J.,Liao, P. C.,Guo, H. R.,Lee, C. C. (2010). Dioxin exposure and insulin resistance in Taiwanese living near a highly contaminated area. Epidemiology 21(1): 56-61.
5028	Chang, J. W.,Chen, H. L.,Su, H. J.,Liao, P. C.,Guo, H. R.,Lee, C. C. (2011). Simultaneous exposure of non-diabetics to high levels of dioxins and mercury increases their risk of insulin resistance. J Hazard Mater 185(2-3): 749-55.
5029	Chang, J. W.,Chen, H. L.,Su, H. J.,Liao, P. C.,Lee, C. C. (2012). Biochemical study of retired pentachlorophenol workers with and without following dietary exposure to PCDD/Fs. Chemosphere 88(7): 813-9.
5030	Chang, J. W.,Ou, H. Y.,Chen, H. L.,Guo, H. R.,Liao, P. C.,Lee, C. C. (2010). Interrelationship between exposure to PCDD/Fs and hypertension in metabolic syndrome in Taiwanese living near a highly contaminated area. Chemosphere 81(8): 1027-32.
5047	Chen, H. L.,Hsu, C. Y.,Hung, D. Z.,Hu, M. L. (2006). Lipid peroxidation and antioxidant status in workers exposed to PCDD/Fs of metal recovery plants. Sci Total Environ 372(1): 12-9.
5078	Cheng, H.,Aylward, L.,Beall, C.,Starr, T. B.,Brunet, R. C.,Carrier, G.,Delzell, E. (2006). TCDD exposure-response analysis and risk assessment. Risk Anal 26(4): 1059-71.
5102	Cho, M. R.,Shin, J. Y.,Hwang, J. H.,Jacobs, D. R., Jr.,Kim, S. Y.,Lee, D. H. (2011). Associations of fat

	mass and lean mass with bone mineral density differ by levels of persistent organic pollutants: National Health and Nutrition Examination Survey 1999-2004. Chemosphere 82(9): 1268-76.
5116	Clemens, M. W.,Kochuba, A. L.,Carter, M. E.,Han, K.,Liu, J.,Evans, K. (2014). Association between Agent Orange exposure and nonmelanotic invasive skin cancer: a pilot study. Plast Reconstr Surg 133(2): 432-7.
5177	Cranmer, M.,Louie, S.,Kennedy, R. H.,Kern, P. A.,Fonseca, V. A. (2000). Exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is associated with hyperinsulinemia and insulin resistance. Toxicol Sci 56(2): 431-6.
5208	Danjou, A. M.,Fervers, B.,Boutron-Ruault, M. C.,Philip, T.,Clavel-Chapelon, F.,Dossus, L. (2015). Estimated dietary dioxin exposure and breast cancer risk among women from the French E3N prospective cohort. Breast Cancer Res 17(39): 1-10.
5233	De Roos, A. J.,Hartge, P.,Lubin, J. H.,Colt, J. S.,Davis, S.,Cerhan, J. R.,Severson, R. K.,Cozen, W.,Patterson, D. G., Jr.,Needham, L. L.,Rothman, N. (2005). Persistent organochlorine chemicals in plasma and risk of non-Hodgkin's lymphoma. Cancer Res 65(23): 11214-26.
5308	Donat-Vargas, C.,Gea, A.,Sayon-Orea, C.,Carlos, S.,Martinez-Gonzalez, M. A.,Bes-Rastrollo, M. (2014). Association between dietary intakes of PCBs and the risk of obesity: the SUN project. J Epidemiol Community Health 68(9): 834-41.
5309	Donat-Vargas, C.,Gea, A.,Sayon-Orea, C.,de la Fuente-Arrillaga, C.,Martinez-Gonzalez, M. A.,Bes-Rastrollo, M. (2015). Association between dietary intake of polychlorinated biphenyls and the incidence of hypertension in a Spanish cohort: the Seguimiento Universidad de Navarra project. Hypertension 65(4): 714-21.
5346	Elobeid, M. A.,Padilla, M. A.,Brock, D. W.,Ruden, D. M.,Allison, D. B. (2010). Endocrine disruptors and obesity: an examination of selected persistent organic pollutants in the NHANES 1999-2002 data. Int J Environ Res Public Health 7(7): 2988-3005.
5370	Eskenazi, B.,Warner, M.,Marks, A. R.,Samuels, S.,Gerthoux, P. M.,Vercellini, P.,Olive, D. L.,Needham, L.,Patterson, D., Jr.,Mocarelli, P. (2005). Serum dioxin concentrations and age at menopause. Environ Health Perspect 113(7): 858-62.
5376	Esser, A.,Gaum, P. M.,Schettgen, T.,Kraus, T.,Gube, M.,Lang, J. (2015). Effect of occupational polychlorinated biphenyls exposure on quality-adjusted life years over time at the HELPcB surveillance program. J Toxicol Environ Health A 78(2): 132-50.
5390	Everett, C. J.,Thompson, O. M. (2012). Associations of dioxins, furans and dioxin-like PCBs with diabetes and pre-diabetes: is the toxic equivalency approach useful?. Environ Res 118: 107-11.
5449	Flesch-Janys, D.,Steindorf, K.,Gurn, P.,Becher, H. (1998). Estimation of the cumulated exposure to polychlorinated dibenzo-p-dioxins/furans and standardized mortality ratio analysis of cancer mortality by dose in an occupationally exposed cohort. Environ Health Perspect 106(Suppl 2): 655-62.
5674	Ha, M. H.,Lee, D. H.,Jacobs, D. R. (2007). Association between serum concentrations of persistent organic pollutants and self-reported cardiovascular disease prevalence: results from the National Health and Nutrition Examination Survey, 1999-2002. Environ Health Perspect 115(8): 1204-9.
5692	Halldorsson, T. I.,Thorsdottir, I.,Meltzer, H. M.,Strom, M.,Olsen, S. F. (2009). Dioxin-like activity in plasma among Danish pregnant women: dietary predictors, birth weight and infant development. Environ Res 109(1): 22-8.
5694	Halperin, W.,Vogt, R.,Sweeney, M. H.,Shopp, G.,Fingerhut, M.,Petersen, M. (1998). Immunological markers among workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Occup Environ Med 55(11): 742-9.
5717	Hardell, L.,Lindstrom, G.,van Bavel, B.,Hardell, K.,Linde, A.,Carlberg, M.,Liljegren, G. (2001). Adipose tissue concentrations of dioxins and dibenzofurans, titers of antibodies to Epstein-Barr virus early

	antigen and the risk for non-Hodgkin lymphoma. Environ Res 87(2): 99-107.
5750	Heederik, D.,Hooiveld, M.,Bueno-de-Mesquita, H. B. (1998). Modelling of 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in a cohort of workers with exposure to phenoxy herbicides and chlorophenols. Chemosphere 37(9-12): 1743-54.
5819	Hooiveld, M.,Heederik, D. J.,Kogevinas, M.,Boffetta, P.,Needham, L. L.,Patterson, D. G., Jr.,Bueno-de-Mesquita, H. B. (1998). Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. Am J Epidemiol 147(9): 891-901.
5860	Hu, S. W.,Cheng, T. J.,ChangChien, G. P.,Chan, C. C. (2003). Association between dioxins/furans exposures and incinerator workers' hepatic function and blood lipids. J Occup Environ Med 45(6): 601-8.
5910	Inoue, H.,Mishima, K.,Yamamoto-Yoshida, S.,Ushikoshi-Nakayama, R.,Nakagawa, Y.,Yamamoto, K.,Ryo, K.,Ide, F.,Saito, I. (2012). Aryl hydrocarbon receptor-mediated induction of EBV reactivation as a risk factor for Sjogren's syndrome. J Immunol 188(9): 4654-62.
6019	Kang, H. K.,Dalager, N. A.,Needham, L. L.,Patterson, D. G., Jr.,Lees, P. S.,Yates, K.,Matanoski, G. M. (2006). Health status of Army Chemical Corps Vietnam veterans who sprayed defoliant in Vietnam. Am J Ind Med 49(11): 875-84.
6038	Karouna-Renier, N. K.,Rao, K. R.,Lanza, J. J.,Davis, D. A.,Wilson, P. A. (2007). Serum profiles of PCDDs and PCDFs, in individuals near the Escambia Wood Treating Company Superfund site in Pensacola, FL. Chemosphere 69(8): 1312-9.
6058	Kelly, K. J.,Connelly, E.,Reinhold, G. A.,Byrne, M.,Prezant, D. J. (2002). Assessment of health effects in New York City firefighters after exposure to polychlorinated biphenyls (PCBs) and polychlorinated dibenzofurans (PCDFs): the Staten Island Transformer Fire Health Surveillance Project. Arch Environ Health 57(4): 282-93.
6067	Kern, P. A.,Said, S.,Jackson, W. G., Jr.,Michalek, J. E. (2004). Insulin sensitivity following agent orange exposure in Vietnam veterans with high blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Clin Endocrinol Metab 89(9): 4665-72.
6073	Ketchum, N. S.,Michalek, J. E. (2005). Postservice mortality of Air Force veterans occupationally exposed to herbicides during the Vietnam War: 20-year follow-up results. Mil Med 170(5): 406-13.
6074	Ketchum, N. S.,Michalek, J. E.,Burton, J. E. (1999). Serum dioxin and cancer in veterans of Operation Ranch Hand. Am J Epidemiol 149(7): 630-9.
6101	Kim, J. S.,Lim, H. S.,Cho, S. I.,Cheong, H. K.,Lim, M. K. (2003). Impact of Agent Orange exposure among Korean Vietnam veterans. Ind Health 41(3): 149-57.
6129	Kitamura, K.,Kikuchi, Y.,Watanabe, S.,Waechter, G.,Sakurai, H.,Takada, T. (2000). Health effects of chronic exposure to polychlorinated dibenzo-P-dioxins (PCDD), dibenzofurans (PCDF) and coplanar PCB (Co-PCB) of municipal waste incinerator workers. J Epidemiol 10(4): 262-70.
6229	Kuwatsuka, Y.,Shimizu, K.,Akiyama, Y.,Koike, Y.,Ogawa, F.,Furue, M.,Utani, A. (2014). Yusho patients show increased serum IL-17, IL-23, IL-1beta, and TNFalpha levels more than 40 years after accidental polychlorinated biphenyl poisoning. J Immunotoxicol 11(3): 246-9.
6261	Landgren, O.,Shim, Y. K.,Michalek, J.,Costello, R.,Burton, D.,Ketchum, N.,Calvo, K. R.,Caporaso, N.,Raveche, E.,Middleton, D.,Marti, G.,Vogt, R. F., Jr. (2015). Agent Orange Exposure and Monoclonal Gammopathy of Undetermined Significance: An Operation Ranch Hand Veteran Cohort Study. JAMA Oncol 1(8): 1061-8.
6314	Lee, C. C.,Yao, Y. J.,Chen, H. L.,Guo, Y. L.,Su, H. J. (2006). Fatty liver and hepatic function for residents with markedly high serum PCDD/Fs levels in Taiwan. J Toxicol Environ Health A 69(5): 367-80.
6322	Lee, D. H.,Lee, I. K.,Jin, S. H.,Steffes, M.,Jacobs, D. R., Jr. (2007). Association between serum

	concentrations of persistent organic pollutants and insulin resistance among nondiabetic adults: results from the National Health and Nutrition Examination Survey 1999-2002. Diabetes Care 30(3): 622-8.
6323	Lee, D. H.,Lee, I. K.,Porta, M.,Steffes, M.,Jacobs, D. R., Jr. (2007). Relationship between serum concentrations of persistent organic pollutants and the prevalence of metabolic syndrome among non-diabetic adults: results from the National Health and Nutrition Examination Survey 1999-2002. Diabetologia 50(9): 1841-51.
6324	Lee, D. H.,Lee, I. K.,Song, K.,Steffes, M.,Toscano, W.,Baker, B. A.,Jacobs, D. R., Jr. (2006). A strong dose-response relation between serum concentrations of persistent organic pollutants and diabetes: results from the National Health and Examination Survey 1999-2002. Diabetes Care 29(7): 1638-44.
6380	Li, Q.,Lan, L.,Klaassen, Z.,Shah, S. R.,Moses, K. A.,Terris, M. K. (2013). High level of dioxin-TEQ in tissue is associated with Agent Orange exposure but not with biochemical recurrence after radical prostatectomy. Prostate Cancer Prostatic Dis 16(4): 376-81.
6411	Lin, Y. S.,Caffrey, J. L.,Hsu, P. C.,Chang, M. H.,Faramawi, M. F.,Lin, J. W. (2012). Environmental exposure to dioxin-like compounds and the mortality risk in the U.S. population. Int J Hyg Environ Health 215(6): 541-6.
6416	Lind, P. M.,Lee, D. H.,Jacobs, D. R.,Salihovic, S.,van Bavel, B.,Wolff, M. S.,Lind, L. (2013). Circulating levels of persistent organic pollutants are related to retrospective assessment of life-time weight change. Chemosphere 90(3): 998-1004.
6419	Lind, P. M.,van Bavel, B.,Salihovic, S.,Lind, L. (2012). Circulating levels of persistent organic pollutants (POPs) and carotid atherosclerosis in the elderly. Environ Health Perspect 120(1): 38-43.
6453	Long, M.,Deutch, B.,Bonefeld-Jorgensen, E. C. (2007). AhR transcriptional activity in serum of Inuits across Greenlandic districts. Environ Health 6(32): 1-17.
6463	Longnecker, M. P.,Michalek, J. E. (2000). Serum dioxin level in relation to diabetes mellitus among Air Force veterans with background levels of exposure. Epidemiology 11(1): 44-8.
6533	Manuwald, U.,Velasco Garrido, M.,Berger, J.,Manz, A.,Baur, X. (2012). Mortality study of chemical workers exposed to dioxins: follow-up 23 years after chemical plant closure. Occup Environ Med 69(9): 636-42.
6564	Matsumoto, S.,Akahane, M.,Kanagawa, Y.,Kajiwara, J.,Todaka, T.,Yasukawa, F.,Uchi, H.,Furue, M.,Imamura, T. (2013). Individuals' half-lives for 2,3,4,7,8-penta-chlorodibenzofuran (PeCDF) in blood: correlation with clinical manifestations and laboratory results in subjects with Yusho. Chemosphere 92(7): 772-7.
6622	Messerer, P.,Zober, A.,Becher, H. (1998). Blood lipid concentrations of dioxins and furans in a sample of BASF employees included in the IARC registry of workers exposed to phenoxy acid herbicides and/or chlorophenols. Environ Health Perspect 106(Suppl 2): 733-5.
6625	Michalek, J. E.,Akhtar, F. Z.,Arezzo, J. C.,Garabrant, D. H.,Albers, J. W. (2001). Serum dioxin and peripheral neuropathy in veterans of Operation Ranch Hand. Neurotoxicology 22(4): 479-90.
6627	Michalek, J. E.,Akhtar, F. Z.,Longnecker, M. P.,Burton, J. E. (2001). Relation of serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) level to hematological examination results in veterans of Operation Ranch Hand. Arch Environ Health 56(5): 396-405.
6628	Michalek, J. E.,Barrett, D. H.,Morris, R. D.,Jackson, W. G., Jr. (2003). Serum dioxin and psychological functioning in U.S. Air Force veterans of the Vietnam War. Mil Med 168(2): 153-9.
6630	Michalek, J. E.,Ketchum, N. S.,Check, I. J. (1999). Serum dioxin and immunologic response in veterans of Operation Ranch Hand. Am J Epidemiol 149(11): 1038-46.
6631	Michalek, J. E.,Ketchum, N. S.,Longnecker, M. P. (2001). Serum dioxin and hepatic abnormalities in veterans of Operation Ranch Hand. Ann Epidemiol 11(5): 304-11.

6632	Michalek, J. E.,Pavuk, M. (2008). Diabetes and cancer in veterans of Operation Ranch Hand after adjustment for calendar period, days of spraying, and time spent in Southeast Asia. J Occup Environ Med 50(3): 330-40.
6653	Mitoma, C.,Mine, Y.,Utani, A.,Imafuku, S.,Muto, M.,Akimoto, T.,Kanekura, T.,Furue, M.,Uchi, H. (2015). Current skin symptoms of Yusho patients exposed to high levels of 2,3,4,7,8-pentachlorinated dibenzofuran and polychlorinated biphenyls in 1968. Chemosphere 137: 45-51.
6739	Nagayama, J.,Nagayama, M.,Iida, T.,Hirakawa, H.,Matsueda, T.,Fukushige, J. (2003). Frequency of SCEs in Japanese infants exposed to dioxins and PCBs through the breast milk. Fukuoka Igaku Zasshi 94(5): 158-65.
6742	Nagayama, J.,Nagayama, M.,Iida, T.,Hirakawa, H.,Matsueda, T.,Yanagawa, T.,Fukushige, J. (2001). Effect of dioxins in mother's milk on sister chromatid exchange frequency in infant lymphocytes. Fukuoka Igaku Zasshi 92(5): 177-83.
6743	Nagayama, J.,Okamura, K.,Iida, T.,Hirakawa, H.,Matsueda, T.,Tsuji, H.,Hasegawa, M.,Sato, K.,Ma, H. Y.,Yanagawa, T.,Igarashi, H.,Fukushige, J.,Watanabe, T. (1998). Postnatal exposure to chlorinated dioxins and related chemicals on thyroid hormone status in Japanese breast-fed infants. Chemosphere 37(9-12): 1789-93.
6746	Nagayama, J.,Tsuji, H.,Iida, T.,Hirakawa, H.,Matsueda, T.,Ohki, M. (2001). Effects of contamination level of dioxins and related chemicals on thyroid hormone and immune response systems in patients with "Yusho". Chemosphere 43(4-7): 1005-10.
6779	Neuberger, M.,Kundi, M.,Jager, R. (1998). Chloracne and morbidity after dioxin exposure (preliminary results). Toxicol Lett 96-97: 347-50.
6780	Neuberger, M.,Rappe, C.,Bergek, S.,Cai, H.,Hansson, M.,Jager, R.,Kundi, M.,Lim, C. K.,Wingfors, H.,Smith, A. G. (1999). Persistent health effects of dioxin contamination in herbicide production. Environ Res 81(3): 206-14.
6801	Nishijo, M.,Pham, T. T.,Nguyen, A. T.,Tran, N. N.,Nakagawa, H.,Hoang, L. V.,Tran, A. H.,Morikawa, Y.,Ho, M. D.,Kido, T.,Nguyen, M. N.,Nguyen, H. M.,Nishijo, H. (2014). 2,3,7,8-Tetrachlorodibenzo-p-dioxin in breast milk increases autistic traits of 3-year-old children in Vietnam. Mol Psychiatry 19(11): 1220-6.
6803	Nishijo, M.,Tai, P. T.,Nakagawa, H.,Maruzeni, S.,Anh, N. T.,Luong, H. V.,Anh, T. H.,Honda, R.,Morikawa, Y.,Kido, T.,Nishijo, H. (2012). Impact of perinatal dioxin exposure on infant growth: a cross-sectional and longitudinal studies in dioxin-contaminated areas in Vietnam. PLoS One 7(7): 1-10.
6829	Oh, E.,Lee, E.,Im, H.,Kang, H. S.,Jung, W. W.,Won, N. H.,Kim, E. M.,Sul, D. (2005). Evaluation of immuno- and reproductive toxicities and association between immunotoxicological and genotoxicological parameters in waste incineration workers. Toxicology 210(1): 65-80.
6943	Pavuk, M.,Michalek, J. E.,Ketchum, N. S. (2006). Prostate cancer in US Air Force veterans of the Vietnam war. J Expo Sci Environ Epidemiol 16(2): 184-90.
6949	Pavuk, M.,Schecter, A. J.,Akhtar, F. Z.,Michalek, J. E. (2003). Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) levels and thyroid function in Air Force veterans of the Vietnam War. Ann Epidemiol 13(5): 335-43.
6955	Pelclova, D.,Fenclova, Z.,Dlaskova, Z.,Urban, P.,Lukas, E.,Prochazka, B.,Rappe, C.,Preiss, J.,Kocan, A.,Vejlupkova, J. (2001). Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. Arch Environ Health 56(6): 493-500.
6956	Pelclova, D.,Fenclova, Z.,Preiss, J.,Prochazka, B.,Spacil, J.,Dubska, Z.,Okrouhlik, B.,Lukas, E.,Urban, P. (2002). Lipid metabolism and neuropsychological follow-up study of workers exposed to 2,3,7,8-tetrachlordibenzo- p-dioxin. Int Arch Occup Environ Health 75 (Suppl): S60-6.
6979	Pesatori, A. C.,Baccarelli, A.,Consonni, D.,Lania, A.,Beck-Peccoz, P.,Bertazzi, P. A.,Spada, A. (2008).

	Aryl hydrocarbon receptor-interacting protein and pituitary adenomas: a population-based study on subjects exposed to dioxin after the Seveso, Italy, accident. Eur J Endocrinol 159(6): 699-703.
7197	Roh, E.,Kwak, S. H.,Jung, H. S.,Cho, Y. M.,Pak, Y. K.,Park, K. S.,Kim, S. Y.,Lee, H. K. (2015). Serum aryl hydrocarbon receptor ligand activity is associated with insulin resistance and resulting type 2 diabetes. Acta Diabetol 52(3): 489-95.
7263	Saberi Hosnijeh, F.,Boers, D.,Portengen, L.,Bueno-de-Mesquita, H. B.,Heederik, D.,Vermeulen, R. (2011). Long-term effects on humoral immunity among workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Occup Environ Med 68(6): 419-24.
7264	Saberi Hosnijeh, F.,Lenters, V.,Boers, D.,Portengen, L.,Baeten, E.,Bueno-de-Mesquita, H. B.,Heederik, D. J.,Bloem, A. C.,Vermeulen, R. (2012). Changes in lymphocyte subsets in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Occup Environ Med 69(11): 781-6.
7266	Saberi Hosnijeh, F.,Portengen, L.,Bueno-de-Mesquita, H. B.,Heederik, D.,Vermeulen, R. (2013). Circulating soluble CD27 and CD30 in workers exposed to 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD). Cancer Epidemiol Biomarkers Prev 22(12): 2420-4.
7414	Serdar, B.,LeBlanc, W. G.,Norris, J. M.,Dickinson, L. M. (2014). Potential effects of polychlorinated biphenyls (PCBs) and selected organochlorine pesticides (OCPs) on immune cells and blood biochemistry measures: a cross-sectional assessment of the NHANES 2003-2004 data. Environ Health 13(114): 1-12.
7451	Shimizu, K.,Ogawa, F.,Thiele, J. J.,Lee, J. B.,Bae, S.,Sato, S. (2008). Increased levels of urinary nitrite and nitrotyrosine in Yusho victims 40 years after accidental poisoning with polychlorinated biphenyls in Nagasaki, Japan. J Appl Toxicol 28(8): 1040-4.
7475	Sjoberg Lind, Y.,Lind, L.,Salihovic, S.,van Bavel, B.,Lind, P. M. (2013). Persistent organic pollutants and abnormal geometry of the left ventricle in the elderly. J Hypertens 31(8): 1547-53.
7476	Sjoberg Lind, Y.,Lind, P. M.,Salihovic, S.,van Bavel, B.,Lind, L. (2013). Circulating levels of persistent organic pollutants (POPs) are associated with left ventricular systolic and diastolic dysfunction in the elderly. Environ Res 123: 39-45.
7492	Smith, S.,Schecter, A.,Papke, O.,Do, T.,Coulibaly, D.,Brandt-Rauf, P. (1998). Quantitation of the extracellular domain of epidermal growth factor receptor in the plasma of dioxin-exposed individuals. Am J Ind Med 34(1): 1-5.
7542	Steenland, K.,Calvert, G.,Ketchum, N.,Michalek, J. (2001). Dioxin and diabetes mellitus: an analysis of the combined NIOSH and Ranch Hand data. Occup Environ Med 58(10): 641-8.
7547	Steenland, K.,Piacitelli, L.,Deddens, J.,Fingerhut, M.,Chang, L. I. (1999). Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Natl Cancer Inst 91(9): 779-86.
7621	Tai, P. T.,Nishijo, M.,Anh, N. T.,Maruzeni, S.,Nakagawa, H.,Van Luong, H.,Anh, T. H.,Honda, R.,Kido, T.,Nishijo, H. (2013). Dioxin exposure in breast milk and infant neurodevelopment in Vietnam. Occup Environ Med 70(9): 656-62.
7733	Triebig, G.,Werle, E.,Papke, O.,Heim, G.,Broding, C.,Ludwig, H. (1998). Effects of dioxins and furans on liver enzymes, lipid parameters, and thyroid hormones in former thermal metal recycling workers. Environ Health Perspect 106 (Suppl 2): 697-700.
7767	Tuomisto, J. T.,Pekkanen, J.,Kiviranta, H.,Tukiainen, E.,Vartiainen, T.,Tuomisto, J. (2004). Soft-tissue sarcoma and dioxin: A case-control study. Int J Cancer 108(6): 893-900.
7780	Turunen, A. W.,Verkasalo, P. K.,Kiviranta, H.,Pukkala, E.,Jula, A.,Mannisto, S.,Rasanen, R.,Marniemi, J.,Vartiainen, T. (2008). Mortality in a cohort with high fish consumption. Int J Epidemiol 37(5): 1008-17.
7792	Uemura, H.,Arisawa, K.,Hiyoshi, M.,Kitayama, A.,Takami, H.,Sawachika, F.,Dakeshita, S.,Nii, K.,Satoh, H.,Sumiyoshi, Y.,Morinaga, K.,Kodama, K.,Suzuki, T.,Nagai, M.,Suzuki, T. (2009). Prevalence of

	metabolic syndrome associated with body burden levels of dioxin and related compounds among Japan's general population. Environ Health Perspect 117(4): 568-73.
7793	Uemura, H.,Arisawa, K.,Hiyoshi, M.,Satoh, H.,Sumiyoshi, Y.,Morinaga, K.,Kodama, K.,Suzuki, T.,Nagai, M.,Suzuki, T. (2008). Associations of environmental exposure to dioxins with prevalent diabetes among general inhabitants in Japan. Environ Res 108(1): 63-8.
7898	Viel, J. F.,Floret, N.,Deconinck, E.,Focant, J. F.,De Pauw, E.,Cahn, J. Y. (2011). Increased risk of non-Hodgkin lymphoma and serum organochlorine concentrations among neighbors of a municipal solid waste incinerator. Environ Int 37(2): 449-53.
7921	Vreugdenhil, H. J.,Lanting, C. I.,Mulder, P. G.,Boersma, E. R.,Weisglas-Kuperus, N. (2002). Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. J Pediatr 140(1): 48-56.
7922	Vreugdenhil, H. J.,Mulder, P. G.,Emmen, H. H.,Weisglas-Kuperus, N. (2004). Effects of perinatal exposure to PCBs on neuropsychological functions in the Rotterdam cohort at 9 years of age. Neuropsychology 18(1): 185-93.
8131	Yi, S. W.,Hong, J. S.,Ohrr, H.,Yi, J. J. (2014). Agent Orange exposure and disease prevalence in Korean Vietnam veterans: the Korean veterans health study. Environ Res 133: 56-65.
8132	Yi, S. W.,Ohrr, H. (2014). Agent Orange exposure and cancer incidence in Korean Vietnam veterans: a prospective cohort study. Cancer 120(23): 3699-706.
8133	Yi, S. W.,Ohrr, H.,Won, J. U.,Song, J. S.,Hong, J. S. (2013). Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels and their association with age, body mass index, smoking, military record-based variables, and estimated exposure to Agent Orange in Korean Vietnam veterans. J Prev Med Public Health 46(5): 226-36.
8142	Yoshida, J.,Kumagai, S.,Tabuchi, T.,Kosaka, H.,Akasaka, S.,Oda, H. (2005). Effects of dioxin on metabolism of estrogens in waste incinerator workers. Arch Environ Occup Health 60(4): 215-22.
8146	Yoshida, R.,Ogawa, Y.,Mori, I.,Nakata, A.,Wang, R.,Ueno, S.,Shioji, I.,Hisanaga, N. (2003). Associations between oxidative stress levels and total duration of engagement in jobs with exposure to fly ash among workers at municipal solid waste incinerators. Mutagenesis 18(6): 533-7.

Appendix D – Data extraction pilot test

1. Overview

Following completion of the screening of studies for relevance, data were extracted from relevant studies using the agreed data extraction form with EFSA. As part of the data extraction pilot study data were extracted from ten studies. Each team extracted data from five studies. For the studies, data extraction forms were first 'part filled' by a member of a project team with the senior member of the project team providing the expert evaluation part of the process. The pilot test was not performed in DistillerSR® at this stage with the extraction process involving filling out forms before completing the form on DistillerSR®. The form is the same as that of the data extraction form in DistillerSR® which allows the answers to be copied over. This process allowed the project team to clarify any points and amend the data extraction form on DistillerSR® before the full data extraction process.

1.1. Outcome of the data extraction pilot test

From the pilot test, data were fully extracted from studies. As part of the pilot test process, a number of general comments and questions arose and these were discussed with EFSA. The questions that the project team had were about clarifying the specific information that EFSA were seeking for each of the data extraction points. During discussions with EFSA the project team's questions were answered and each pilot study was discussed.

Following the discussions minor amendments were made to some of the answer selection options as part of the data extraction form in DistillerSR®.