Survey requesting the nomination of substances for research under HBM4EU

Introduction

Aim of this survey

Practical details

What can you nominate?

What information are we asking for?

How will we use your input?

Thank you very much!

Applicant identification

Step 1: Your contact details

Applicant Name

Natacha Cingotti

Which institution do you represent?

Health and Environment Alliance

Please enter your email address

natacha@env-health.org

Please indicate whether you are a:

- Member of the Stakeholder Forum

If you are a National Hub, please identify your country

Chemical Substance identification

Step 2: Nomination of a chemical substance or group of substances

Please select your preference from the list below

a group of substances

Group of substances

Please provide a name for the group of substances

Organophosphorus flame retardants (including chlorinated organophosphorus flame retardants)

Please identify the rationale for the grouping.

- The substances have similar uses, with the possibility of substitution within the group.

If you have another rationale for grouping the substances, please briefly describe it below.

Organophosphate flame retardants (OPFRs) are increasingly used as replacements for the phased-out polybrominated diphenyl ether (PBDE) mixtures due to the health and environmental concerns related to the latter. Nowadays, OPFRs are routinely detected in indoor environments. However, little is known about human exposure to these chemicals because they cannot be easily measured in blood or serum. Many of them are endocrine disrupting chemicals; some are anticipated to be human carcinogens, suspected carcinogens or carcinogenic in animals, and some are toxic [see appendix 1 in Flame retardant briefing from Breast Cancer UK attached]

If possible, please identify a "lead substance" in this group that captures the principle characteristics of the group. This will allow us to broadly judge the risks associated with the substance group.

Lead substances could include: For chlorinated organophosphorus flame retardants • TDCPP tris(1,3-dichloro-2-propyl) phosphate • TCEP tris(2-chloroethyl) phosphate and For organophosphorus flame retardants • TPP triphenyl phosphate

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- Background-Briefing-Flame-retardants-15.8.17.pdf

New knowledge

Step 3: What new knowledge do you need?

Please enter your text in the box below.

Better research about exposure of populations – in particular vulnerable groups – to OPFRs is needed, considering that their use is increasing worldwide as a replacement for old (so-called 'legacy' flame retardants).

This should include sampling groups of people who spend a lot of time indoors.

Please tick all the boxes that describe the research activities that would answer your questions

- New data on a specific population groups or subgroups
- Development of new research activities
- New approaches to the analysis of existing data

Please propose any other relevant research activities below.

Hazardous properties

Step 4: Hazardous properties

Current knowledge gaps regarding hazardous properties

In the text box below, please describe any specific knowledge gaps regarding the hazard profile of the substance, or group of substances.

●Toxicity data for OPFRs is insufficient. Short-term and long-term toxicological data are needed, including additive or synergistic effects of FR mixtures
● Carcinogenicity data is incomplete, especially for hormonal cancers such as prostate
● Long-term and chronic exposure effects to health are not known
● Effects of exposures in utero, on mammary glands and on reproduction health should be further investigated
● More information on all endocrine disrupting effects (including sex hormones, thyroid and on other nuclear receptors) is needed
● Determination of which OPFRs are POPs is needed

Hazard classifications

If the substances is a carcinogen, please identify the IARC classification.

If the substance is a carcinogen, please enter the CLP classification.

If the substance is a mutagen, please enter the CLP classification.

If the substance is toxic to reproduction, please enter the CLP classification.

Is the substance classified for Specific Target Organ Toxicity on the basis of single exposure (STOT-SE)?

Is the substances classified for Specific Target Organ Toxicity on the basis of repeated exposure (STOT-RE)?

Is the substance neurotoxic?

Is the substance immunotoxic?

Is the substance a respiratory sensitizer?

Is the substance an endocrine disruptor?

Other classifications

Is the substance a Substance of Very High Concern?

Please enter information on any other relevant classifications.

In your opinion, is the substance an emerging substance?

YES – see response to Step 3. Question 1

Persistence and bioaccumulation potential

Is the substance Persistent, Bioaccumulative and Toxic (PBT)?

Is the substance very Persistent and very Bioaccumulative?

Is the substance very Persistent?

Additional information and references

Please add any other information that you consider relevant.

Please list relevant references and provide hyperlinks, where available. Alternatively you can upload files below.

Hou et al. (2016). Review of OPFRs in animals and humans. Absorption, Bioaccumulation; Metabolism and Internal Exposure. Chemosphere 153 78-90

Wei et al. (2015). Organophosphorus flame retardants and plasticizers: sources, occurrence, toxicity and human exposure. Environmental Pollution 196: 29-46.

Upload files

Exposure

Step 5: Exposure characteristics

Current knowledge gaps regarding exposure

Please describe knowledge gaps in understanding exposure to the substance and explain how human biomonitoring might address those gaps.

● Long-term studies on exposure to OPFRs in humans and animals are needed
● Exposure assessments of the biological effects of OPFRs in wild-life are needed. There is little data on how OPFRs are taken up by animals under different environmental conditions.
● Assessment of bioaccumulation and biomagnification is needed to clarify species-specific risk and define environmental stress.
● Information on sediment and biota to enable full understanding of the environmental fate of OPFRs.
● Discharge of OPFRs from wastewater treatment plants as a potential source should be investigated.
● More human biomonitoring is needed to help determine which absorption pathways are most relevant (inhalation/dust/diet/dermal exposure/).
● Total exposure to humans through all routes is unknown (most studies focus on inhalation). A comprehensive risk assessment to evaluate the relative importance of different exposure routes of populations in different countries is needed.
● More information on OPFR metabolism is needed; (using in silico models and in vitro methods).
● Epidemiological studies that include OPFRs enable an assessment of links between exposure and potential human health outcomes.

Is human biomonitoring data on the substance or group of substances available?

If yes, please provide references to publications or datasets. Please include hyperlinks, where available.

Exposure media

Please identify the media through which human exposure takes place.

- Multisource exposure

If exposure occurs through consumer products, please specify product types in the box below.

Exposure through consumer products includes but is not limited to: furnitures, plasticisers, building materials, cars, or electronics.

Please identify any other media through which exposure may take place.

Exposure sources, production volumes and environmental releases

Please identify sources of exposure in the box below.

If available, please provide the production volume according to the ECHA database.

0-10 tonnes per annum

Has the substances been recognised as an environmental contaminant? If yes, please provide references to any relevant sources of monitoring data.

Is data about environmental release of the substance available, for example in the European Pollutant Release and Transfer Register (E-PRTR)? If yes, please provide details in the box below.

Human exposure

Please tick all relevant human exposure routes

- Dermal
- Inhalation
- Oral
- Trans placental

Please estimate the prevalence of population exposure.

- There is widespread exposure of the general population

Other comments on the prevalence of exposure.

Several studies have highlighted people's exposure in the indoor environment through inhalation of dust. Therefore future samples of monitored population should include groups who spend a lot of time indoors.

Please tick all groups that may be highly exposed to the substance or groups of substances

- Infants and children
- Adults
- Pregnant women
- Workers (professional and/or industrial)

Please identify any other highly exposure groups.

Vulnerable groups

Please identify any vulnerable groups.

- Pregnant women
- Infants and children
- Workers (professional and/or industrial)

Please identify any other vulnerable population groups.

Additional information and references

Please add any other information on exposure that you consider relevant.

Please list relevant references and provide hyperlinks, where available. Alternatively you can upload files below.

Bergh, C., Magnus Åberg, K., Svartengren, M., Emenius, G., & Östman, C. (2011). Organophosphate and phthalate esters in indoor air: a comparison between multi-storey buildings with high and low prevalence of sick building symptoms. Journal of environmental monitoring : JEM, 13(7), 2001–9. doi:10.1039/c1em10152h

Brommer, S., Harrad, S., Van den Eede, N., & Covaci, A. (2012). Concentrations of organophosphate esters and brominated flame retardants in German indoor dust samples. Journal of environmental monitoring : JEM, 14(9), 2482–7. doi:10.1039/c2em30303e

Jonsson, O. B., Dyremark, E., & Nilsson, U. L. (2001). Development of a microporous membrane liquid-liquid extractor for organophosphate esters in human blood plasma: identification of triphenyl phosphate and octyl diphenyl phosphate in donor plasma. Journal of chromatography. B, Biomedical sciences and applications, 755(1-2), 157–64. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11393700

Meeker, J. D., Cooper, E. M., Stapleton, H. M., & Hauser, R. (2013). Urinary metabolites of organophosphate flame retardants: temporal variability and correlations with house dust concentrations. Environmental health perspectives, 121(5), 580–5. doi:10.1289/ehp.1205907

Meeker, J. D., & Stapleton, H. M. (2010). House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters. Environmental health perspectives, 118(3), 318–23. doi:10.1289/ehp.0901332

Vykoukalová M, Venier M, Vojta Š, Melymuk L, Bečanová J, Romanak K, Prokeš R, Okeme JO, Saini A, Diamond ML, Klánová J. Organophosphate esters flame retardants in the indoor environment. https://www.ncbi.nlm.nih.gov/pubmed/28624751

Hoffman K, Garantziotis S, Birnbaum LS, Stapleton HM. Monitoring indoor exposure to organophosphate flame retardants: hand wipes and house dust. https://www.ncbi.nlm.nih.gov/pubmed/25343780

Brommer S, Harrad S. Sources and human exposure implications of concentrations of organophosphate flame retardants in dust from UK cars, classrooms, living rooms, and offices. https://www.ncbi.nlm.nih.gov/pubmed/26232632

Stapleton, H. M., Klosterhaus, S., Eagle, S., Fuh, J., Meeker, J. D., Blum, A., & Webster, T. F. (2009). Detection of organophosphate flame retardants in furniture foam and U.S. house dust. Environmental science & technology, 43(19), 7490–5. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2782704&tool=pmcentrez&rendertype=abstract

Sundkvist, A. M., Olofsson, U., & Haglund, P. (2010). Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. Journal of environmental monitoring : JEM, 12(4), 943–51. doi:10.1039/b921910b

Van den Eede, N., Dirtu, A. C., Neels, H., & Covaci, A. (2011). Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. Environment international, 37(2), 454–61. doi:10.1016/j.envint.2010.11.010

Chen, D., Letcher, R. J., & Chu, S. (2012). Determination of non-halogenated, chlorinated and brominated

organophosphate flame retardants in herring gull eggs based on liquid chromatography-tandem quadrupole mass spectrometry. Journal of chromatography. A, 1220, 169–74. doi:10.1016/j.chroma.2011.11.046

Cristale, J., Katsoyiannis, A., Sweetman, A. J., Jones, K. C., & Lacorte, S. (2013). Occurrence and risk assessment of organophosphorus and brominated flame retardants in the River Aire (UK). Environmental pollution (Barking, Essex : 1987), 179C(null), 194–200. doi:10.1016/j.envpol.2013.04.001

Eggen, T., Heimstad, E. S., Stuanes, A. O., & Norli, H. R. (2012). Uptake and translocation of organophosphates and other emerging contaminants in food and forage crops. Environmental science and pollution research international. doi:10.1007/s11356-012-1363-5

Farhat, A., Crump, D., Chiu, S., Williams, K. L., Letcher, R. J., Gauthier, L. T., & Kennedy, S. W. (2013). In Ovo Effects of Two Organophosphate Flame Retardants–TCPP and TDCPP–on Pipping Success, Development, mRNA Expression, and Thyroid Hormone Levels in Chicken Embryos. Toxicological sciences : an official journal of the Society of Toxicology. doi:10.1093/toxsci/kft100

Fries, E., & Mihajlović, I. (2011). Pollution of soils with organophosphorus flame retardants and plasticizers. Journal of environmental monitoring : JEM, 13(10), 2692–4. doi:10.1039/c1em10538h

Lehner, A. F., Samsing, F., & Rumbeiha, W. K. (2010). Organophosphate ester flame retardant-induced acute intoxications in dogs. Journal of medical toxicology : official journal of the American College of Medical Toxicology, 6(4), 448–58. doi:10.1007/s13181-010-0105-7

Liu, X., Ji, K., & Choi, K. (2012). Endocrine disruption potentials of organophosphate flame retardants and related mechanisms in H295R and MVLN cell lines and in zebrafish. Aquatic toxicology (Amsterdam, Netherlands), 114-115, 173–81. doi:10.1016/j.aquatox.2012.02.019

Möller, A., Sturm, R., Xie, Z., Cai, M., He, J., & Ebinghaus, R. (2012). Organophosphorus flame retardants and plasticizers in airborne particles over the Northern Pacific and Indian Ocean toward the Polar Regions: evidence for global occurrence. Environmental science & technology, 46(6), 3127–34. doi:10.1021/es204272v

Möller, A., Xie, Z., Caba, A., Sturm, R., & Ebinghaus, R. (2011). Organophosphorus flame retardants and plasticizers in the atmosphere of the North Sea. Environmental pollution (Barking, Essex : 1987), 159(12), 3660–5. doi:10.1016/j.envpol.2011.07.022

REEMTSMA, T., QUINTANA, J., RODIL, R., GARCIALOPEZ, M., & RODRIGUEZ, I. (2008). Organophosphorus flame retardants and plasticizers in water and air I. Occurrence and fate. Trends in Analytical Chemistry, 27(9), 727–737. doi:10.1016/j.trac.2008.07.002

Regnery, J, Püttmann, W., Merz, C., & Berthold, G. (2011). Occurrence and distribution of organophosphorus flame retardants and plasticizers in anthropogenically affected groundwater. Journal of environmental monitoring : JEM, 13(2), 347–54. doi:10.1039/c0em00419g

Regnery, Julia, & Püttmann, W. (2010a). Seasonal fluctuations of organophosphate concentrations in precipitation and storm water runoff. Chemosphere, 78(8), 958–64. doi:10.1016/j.chemosphere.2009.12.027

Regnery, Julia, & Püttmann, W. (2010b). Occurrence and fate of organophosphorus flame retardants and plasticizers in urban and remote surface waters in Germany. Water research, 44(14), 4097–104. doi:10.1016/j.watres.2010.05.024

Sundkvist, A. M., Olofsson, U., & Haglund, P. (2010). Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. Journal of environmental monitoring : JEM, 12(4), 943–51. doi:10.1039/b921910b

Hou et al. (2016). Review of OPFRs in animals and humans. Absorption, Bioaccumulation; Metabolism and Internal Exposure. Chemosphere 153 78-90

Wei et al. (2015). Organophosphorus flame retardants and plasticizers: sources, occurrence, toxicity and human exposure. Environmental Pollution 196: 29-46.

File

Regulation and policy

Step 6: Regulatory status

Is the substance covered by Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

Please identify all other EU policies that apply to the substance or substance group in the box below. This can include policies in the domain of occupational health and safety, food safety, environment and consumer safety.

Please identify any regulations that you know of that apply to the substance or substance group at national level, either in Europe or beyond.</p>

Current policy questions

Please outline current policy questions on the substance or substance group in the box below. Please indicate how human biomonitoring might answer these questions.

Data gathered through human biomonitoring is critical to:
- understand how much people across Europe are exposed to organophosphorus flame retardants, which are increasingly used and particularly affect people through dust inhalation;
- in so doing, gather precise data about the exposure of vulnerable groups of the population – young children and pregnant women in particular – to OPFRs;
- advance knowledge about the toxicity of OPFRs, as individual substances and as mixtures of substances occurring in the indoor environment or ingestion;
- understand whether the measured exposure to OPFRs poses a risk for human health – with emphasis on vulnerable groups;
- compare how the measured exposure of OPFRs to that of regulated FRs (such as PBDE)

This should feed in reflections to inform political action at the EU level in the future, including:
● Future changes to all EU member states' furniture fire safety regulations that will remove the need for use of organic flame retardants and create genuine impetus for designing out both flammability and toxicity.
● Introduction of requirement for a visible display label, to provide consumers with point-of-purchase information on the presence and type of flame retardants contained in the product, similar to the EU energy label. This is also important for recycling and safe disposal of products.
● Eventual phase out of hazardous organophosphorus flame retardants in all consumer and industrial products and

their replacement with safer alternatives.

Regulatory guidance values

Please provide details of any toxicity reference values that are available for the substance in the box below. Please provide reference to relevant materials.

Please provide details of any biomonitoring guidance values that are available for the substance in the box below. Please provide reference to relevant materials.

Additional information and references

Please provide references for any risk assessments on the substance that are publicly available in the box below.

We also welcome references for materials that address the potential to reduce human exposure to the substance.

You may either provide references and hyperlinks in the text box below, or alternatively you may upload files.

File Upload

Upload file

Public concern

Step 7: Public concern

Please identify any materials that provide evidence of the social concern regarding the substance or substance group. This may include the results of surveys conducted by Eurobarometer, campaigns conducted by specific interest groups, media coverage or other relevant materials. You are welcome to include materials from both the European and national level.

• This group of substances is hardly on the radar yet, or is not as well known as other FRs yet, however use of organosphosphorus flame retardants has skyrocketed over the last 15 years. OPFRs represented 16% of the FR market in 2013, while Western Europe and North America were the second biggest consumers of flame retardants after China (https://www.flameretardants-online.com/flame-retardants/market - consulted 27 September 2017).

• (Kate Hoffman, Craig M. Butt, Thomas F. Webster, Emma V. Preston, Stephanie C. Hammel, Colleen Makey, Amelia

M. Lorenzo, Ellen M. Cooper, Courtney Carignan, John D. Meeker, Russ Hauser, Adelheid Soubry, Susan K. Murphy, Thomas M. Price,Cathrine Hoyo,Emma Mendelsohn, Johanna Congleton,

● Julie L. Daniels, and Heather M. Stapleton, “Temporal Trends in Exposure to Organophosphate Flame Retardants in the United States”, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5352975/) as a more and more commonly used replacement for PBDE mixtures

• We need to be careful about harmful substitution

• In Europe, concerns have been raised in Europe following the detection of organophosphate FRs in the urine of women (EFIC, 2016: http://www.efic.eu/News.aspx?id=41), with European manufacturers committing to flame retardant-free furnitures

• In the meantime, in the US awareness raising campaigns about the risks that flame retardants pose to human health increasingly include OPFRs. Examples include: ; http://greensciencepolicy.org/topics/flame-retardants/ http://www.sierraclub.org/toxics/toxic-fire-retardants-continue-threaten-human-health

Is the substance included on the SIN List managed by ChemSec?

File

Technical feasibility

Step 8: Technical feasibility

Please indicate whether biomarkers are available for the substances in the drop down box below.

Please indicate whether analytical methods are available for the substances in the drop down box below.

Please describe any work that would be required to develop new methods to allow for human biomonitoring activities on this substance or substance group.

Additional information

Please provide any additional information on the feasibility of conducting human biomonitoring research on the substance or substance group. Please provide references, where available, or upload files in the file drop below.

File

Submission Date