

# Bulletin Board

## Contents

MAR. 03, 2023

(click on page numbers for links)

### CHEMICAL EFFECTS

Adverse Human Health Effects of Chromium by Exposure Route: A Comprehensive Review Based on Toxicogenomic Approach.....	3
Impact of Pollutant Ozone on the Biophysical Properties of Tear Film Lipid Layer Model Membranes .....	3
Toxicity overview of endocrine disrupting chemicals interacting in vitro with the oestrogen receptor .....	4

### ENVIRONMENTAL RESEARCH

The role of systemic inflammation and oxidative stress in the association of particulate air pollution metal content and early cardiovascular damage: A panel study in healthy college students .....	5
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### PHARMACEUTICAL/TOXICOLOGY

Implementation of effect biomarkers in human biomonitoring studies: A systematic approach synergizing toxicological and epidemiological knowledge .....	6
Perfluoroalkyl substance exposure is associated with asthma and innate immune cell count in US adolescents stratified by sex .....	7
Prenatal exposure to persistent and non-persistent chemical mixtures and associations with adverse birth outcomes in the Atlanta African American Maternal-Child Cohort .....	8

### OCCUPATIONAL

Assessment of the Genotoxic and Cytotoxic Effects of Turpentine in Painters .....	9
Occupational Risk Factors by Sectors: An Observational Study of 20,000 Workers .....	10
Use of the Benchmark-dose (BMD) approach to derive Occupational Exposure Limits (OELs) for genotoxic carcinogens: N-nitrosamines .....	11

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## Bulletin Board

## Technical

MAR. 03, 2023

## CHEMICAL EFFECTS

**Adverse Human Health Effects of Chromium by Exposure Route: A Comprehensive Review Based on Toxicogenomic Approach**

2023-02-08

Heavy metals are defined as metals with relatively high density and atomic weight, and their various applications have raised serious concerns about the environmental impacts and potential human health effects. Chromium is an important heavy metal that is involved in biological metabolism, but Cr exposure can induce a severe impact on occupational workers or public health. In this study, we explore the toxic effects of Cr exposure through three exposure routes: dermal contact, inhalation, and ingestion. We propose the underlying toxicity mechanisms of Cr exposure based on transcriptomic data and various bioinformatic tools. Our study provides a comprehensive understanding of the toxicity mechanisms of different Cr exposure routes by diverse bioinformatics analyses.

Authors: Dong Yeop Shin, Sang Min Lee, Yujin Jang, Jun Lee, Cheol Min Lee, Eun-Min Cho, Young Rok Seo

Full Source: International journal of molecular sciences 2023 Feb 8;24(4):3410. doi: 10.3390/ijms24043410.

**Impact of Pollutant Ozone on the Biophysical Properties of Tear Film Lipid Layer Model Membranes**

2023-01-28

Ozone exposure from environmental smog has been implicated as a risk factor for developing dry eye disease (DED). The tear film lipid layer (TFLL), which is the outermost layer of the tear film and responsible for surface tension reduction while blinking, is in direct contact with the environment and serves as the first line of defense against external aggressors such as environmental pollution. The impact of exposure to ozone on the biophysical properties of three TFLL model membranes was investigated. These model membranes include a binary mixture of cholesteryl oleate (CO) and L- $\alpha$ -phosphatidylcholine (egg PC), a ternary mixture of CO, glyceryl trioleate (GT) and PC, as well as a quaternary mixture of CO, GT, a mixture of free fatty acids palmitic acid and stearic acid (FFAs) and PC. Biophysical impacts were evaluated as changes to the surface activity, respreadability, morphology and viscoelastic properties of the films. Expansion to higher molecular areas was observed in all the TFLL model membrane films which is attributable to the accommodation

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## Bulletin Board

## Technical

MAR. 03, 2023

of the cleaved chains in the film. Significant morphological changes were observed, namely fluidization and the disruption of the phase transition behaviour of GT, and multilayer formation of CO. This fluidization reduces the hysteresis loops for the model membranes. On the other hand, the viscoelastic properties of the films exhibited differential impacts from ozone exposure as a function of composition. These findings are correlated to chemical changes to the lipids determined using ESI-MS.

Authors: Mahshid Keramatnejad, Christine DeWolf

Full Source: Membranes 2023 Jan 28;13(2):165. doi: 10.3390/membranes13020165.

**Toxicity overview of endocrine disrupting chemicals interacting in vitro with the oestrogen receptor**

2023-02-23

The oestrogen receptor (ER) from the nuclear receptor family is involved in different physiological processes, which can be affected by multiple xenobiotics. Some of these compounds, such as bisphenols, pesticides, and phthalates, are widespread as consequence of human activities and are commonly present also in human organism. Xenobiotics able to interact with ER and trigger a hormone-like response, are known as endocrine disruptors. In this review, we aim to summarize the available knowledge on products derived from human industrial activity and other xenobiotics reported to interact with ER. ER-disrupting chemicals behave differently towards oestrogen-dependent cell lines than endogenous oestradiol. In low concentrations, they stimulate proliferation, whereas at higher concentrations, are toxic to cells. In addition, most of the knowledge on the topic is based on individual compound testing, and only a few studies assess xenobiotic combinations, which better resemble real circumstances. Confirmation from in vivo models is lacking also.

Authors: Raul Alva-Gallegos, Alejandro Carazo, Přemysl Mladěnka

Full Source: Environmental toxicology and pharmacology 2023 Feb 23;104089. doi: 10.1016/j.etap.2023.104089.

The oestrogen receptor (ER) from the nuclear receptor family is involved in different physiological processes, which can be affected by multiple xenobiotics.

## Bulletin Board

## Technical

MAR. 03, 2023

## ENVIRONMENTAL RESEARCH

The role of systemic inflammation and oxidative stress in the association of particulate air pollution metal content and early cardiovascular damage: A panel study in healthy college students

2023-02-23

Exposure to fine particulate matter (PM<sub>2.5</sub>) has been associated with adverse cardiovascular outcomes. However, the effects of toxic metals in PM<sub>2.5</sub> on cardiovascular health remain unknown. To investigate the early cardiovascular effects of specific PM<sub>2.5</sub> metal constituents at the personal level, we conducted a panel study on 45 healthy college students in Caofeidian, China. Personal exposure concentrations and cardiovascular effect markers were monitored simultaneously within one year in four study periods. Four linear mixed-effects models were used to analyze the relationship between personal exposure to PM<sub>2.5</sub> and 15 metal fractions (Al, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Mo, Cd, Sb, and Pb) with soluble CD36 (sCD36), C-reactive protein (CRP), and oxidized low-density lipoprotein (OX-LDL) levels, heart rate, and blood pressure. The concentrations of most individual metals (Mn, Cu, Zn, As, Se, Mo, Cd, Sb and Pb) were the highest in winter. Meanwhile, there were significant differences in inflammatory (sCD36 and CRP) and oxidative stress (OX-LDL) markers in the serum of participants over the four seasons. In particular, the estimated effects of personal metal exposure (such as V, As, Se, Cd, and Pb) on sCD36 and pulse pressure (PP) levels were consistently significant across the four LME models. A significant mediating role of sCD36 was also found in the relationship between personal exposure to Zn and Cr and changes in PP levels. Our findings provide clues and potential mechanisms regarding the cardiovascular effects of specific toxic constituents of PM<sub>2.5</sub> in healthy young adults.

Authors: Lei Zhang, Bo Fang, Haotian Wang, Hao Zeng, Nan Wang, ManMan Wang, Xuesheng Wang, Yulan Hao, Qian Wang, Wenqi Yang  
Full Source: Environmental pollution (Barking, Essex : 1987) 2023 Feb 23;323:121345. doi: 10.1016/j.envpol.2023.121345.

Exposure to fine particulate matter (PM<sub>2.5</sub>) has been associated with adverse cardiovascular outcomes.

## Bulletin Board

## Technical

MAR. 03, 2023

## PHARMACEUTICAL/TOXICOLOGY

Implementation of effect biomarkers in human biomonitoring studies: A systematic approach synergizing toxicological and epidemiological knowledge

2023-02-24

Human biomonitoring (HBM) studies have highlighted widespread daily exposure to environmental chemicals. Some of these are suspected to contribute to adverse health outcomes such as reproductive, neurological, and metabolic disorders, among other developmental and chronic impairments. One of the objectives of the H2020 European Human Biomonitoring Initiative (HBM4EU) was the development of informative effect biomarkers for application in a more systematic and harmonized way in large-scale European HBM studies. The inclusion of effect biomarkers would complement exposure data with mechanistically-based information on early and late adverse effects. For this purpose, a stepwise strategy was developed to identify and implement a panel of validated effect biomarkers in European HBM studies. This work offers an overview of the complete procedure followed, from comprehensive literature search strategies, selection of criteria for effect biomarkers and their classification and prioritization, based on toxicological data and adverse outcomes, to pilot studies for their analytical, physiological, and epidemiological validation. We present the example of one study that demonstrated the mediating role of the effect biomarker status of brain-derived neurotrophic factor BDNF in the longitudinal association between infant bisphenol A (BPA) exposure and behavioral function in adolescence. A panel of effect biomarkers has been implemented in the HBM4EU Aligned Studies as main outcomes, including traditional oxidative stress, reproductive, and thyroid hormone biomarkers. Novel biomarkers of effect, such as DNA methylation status of BDNF and kisspeptin (KISS) genes were also evaluated as molecular markers of neurological and reproductive health, respectively. A panel of effect biomarkers has also been applied in HBM4EU occupational studies, such as micronucleus analysis in lymphocytes and reticulocytes, whole blood comet assay, and malondialdehyde, 8-oxo-2'-deoxyguanosine and untargeted metabolomic profile in urine, to investigate, for example, biological changes in response to hexavalent chromium Cr(VI) exposure. The use of effect biomarkers in HBM4EU has demonstrated their ability to detect early biological effects of chemical exposure and to identify subgroups that are at higher risk. The roadmap developed in HBM4EU confirms the utility of effect biomarkers,

Human biomonitoring (HBM) studies have highlighted widespread daily exposure to environmental chemicals.

## Bulletin Board

## Technical

MAR. 03, 2023

and support one of the main objectives of HBM research, which is to link exposure biomarkers to mechanistically validated effect and susceptibility biomarkers in order to better understand the public health implications of human exposure to environmental chemicals.

Authors: Andrea Rodríguez-Carrillo, Vicente Mustieles, Elena Salamanca-Fernández, Alicia Olivas-Martínez, Beatriz Suárez, Lola Bajard, Kirsten Baken, Ludek Blaha, Eva Cecilie Bonefeld-Jørgensen, Stephan Couderq, Shereen Cynthia D'Cruz, Jean-Baptiste Fini, Eva Govarts, Claudia Gundacker, Antonio F Hernández, Marina Lacasaña, Federica Laguzzi, Birgitte Linderman, Manhai Long, Henriqueta Louro, Christiana Neophytou, Axel Oberemn, Sylvie Remy, Anna Kjerstine Rosenmai, Anne Thoustrup Saber, Greet Schoeters, Maria Joao Silva, Fatima Smagulova, Maria Uhl, Anne Marie Vinggaard, Ulla Vogel, Maria Wielsøe, Nicolás Olea, Mariana F Fernández

Full Source: International journal of hygiene and environmental health 2023 Feb 24;249:114140. doi: 10.1016/j.ijheh.2023.114140.

### Perfluoroalkyl substance exposure is associated with asthma and innate immune cell count in US adolescents stratified by sex

2023-02-25

Exposure to perfluoroalkyl substances (PFAS) may be harmful to humans; however, previous studies have been inconsistent regarding the potential for PFAS-induced immunosuppression. This study explored the relationship between PFAS exposure and risks of asthma, wheezing, and immunosuppression in 12-19 year-olds using the National Health and Nutrition Examination Survey (NHANES) data. Logistic regression models were used to reveal associations between serum PFAS levels and risks of asthma, wheezing, asthma attack, and emergency department visits. Pearson's correlation was used to determine the relationship between serum PFAS levels and leukocyte count. Data were also stratified by sex. We found that medium-low levels of serum perfluorooctane sulfonate (PFOS) (6.90-12.40 ng/mL) and serum perfluorooctanoic acid (PFOA) (2.43-3.60 ng/mL) were negatively related, respectively, to current asthma and wheezing in boys, and to wheezing in girls. Meanwhile, boys with medium-high levels (1.50-3.00 ng/mL) of serum perfluorohexanesulfonate (PFHxS) had a high risk of wheezing. Among asthmatic participants, both medium-high levels (3.75-5.07 ng/mL) of serum PFOA and high levels (> 3.92 ng/mL) of PFHxS correlated with asthma attacks in boys; likewise, medium-low levels (0.70-0.99 ng/mL) of serum PFNA correlated with asthma attacks in girls. Also, PFOA and PFNA levels were weakly positively

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## Bulletin Board

## Technical

MAR. 03, 2023

correlated with basophil count, whereas PFOS levels were weakly negatively correlated with eosinophils in asthmatic boys, indicating that basophils may be important in the immune response to PFAS exposure among asthmatics.

Authors: Zhenzhen Pan, Yun Guo, Qin Zhou, Qian Wang, Shanshan Pan, Shiyao Xu, Ling Li

Full Source: Environmental science and pollution research international 2023 Feb 25. doi: 10.1007/s11356-023-26065-7.

### Prenatal exposure to persistent and non-persistent chemical mixtures and associations with adverse birth outcomes in the Atlanta African American Maternal-Child Cohort

2023-02-25

Background: African Americans (AAs) experience higher rates of preterm birth and fetal growth restriction relative to other pregnant populations. Differential in utero exposure to environmental chemicals may partially explain these health disparities, as AAs are disproportionately exposed to environmental hazards.

Objective: We examined the individual and mixture effects of non-persistent chemicals and persistent organic pollutants (POPs) on gestational age at birth and birthweight for gestational age z-scores within a prospective cohort of pregnant AAs.

Methods: First-trimester serum and urine samples obtained from participants within the Atlanta African American Maternal-Child cohort were analyzed for 43 environmental chemicals, including per- and polyfluoroalkyl substances (PFAS), polybrominated diphenyl ethers (PBDEs), organochlorine pesticides, pyrethroid insecticides, phthalates, bisphenol A, nicotine, and the primary metabolite of delta-9-tetrahydrocannabinol. Linear regression was used to estimate individual associations between chemicals and gestational age and birthweight z-scores (N ranging from 107 to 523). Mixture associations were estimated using quantile g-computation, principal component (PC) analyses, and hierarchical Bayesian kernel machine regression among complete cases (N = 86).

Results: Using quantile g-computation, increasing all chemical exposures by one quantile was modestly associated with a reduction in gestational age (mean change per quartile increase = -0.47, 95% CI = -1.56, 0.61) and birthweight z-scores (mean change per quartile increase = -0.49, 95% CI = -1.14, 0.15). All PCs were associated with a reduction in birthweight z-scores; associations were greatest in magnitude for the two PCs

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## Bulletin Board

## Technical

MAR. 03, 2023

reflecting exposure to combined tobacco, insecticides, PBDEs, and phthalates. In single pollutant models, we observed inconsistent and largely non-significant associations.

**Significance:** We conducted multiple targeted exposure assessment methods to quantify levels of environmental chemicals and leveraged mixture methods to quantify their joint effects on gestational age and birthweight z-scores. Our findings suggest that prenatal exposure to multiple classes of persistent and non-persistent chemicals is associated with reduced gestational age and birthweight z-scores in AAs.

**Impact:** African Americans (AAs) experience higher rates of preterm birth and fetal growth restriction relative to other pregnant populations. Differential in utero exposure to environmental chemicals may partially explain these health disparities, as AAs are disproportionately exposed to environmental hazards. In the present study, we analyzed serum and urine samples for levels of 43 environmental chemicals. We used quantile g-computation, principal component analysis, and BKMR to assess associations between chemical exposure mixtures and adverse birth outcomes. Our findings suggest that prenatal exposure to multiple classes of chemicals is associated with reduced birthweight z-scores, a proxy for fetal growth, in AAs.

**Authors:** Stephanie M Eick, Youran Tan, Kaitlin R Taibl, P Barry Ryan, Dana Boyd Barr, Anke Hüls, Jasmin A Eatman, Parinya Panuwet, Priya E D'Souza, Volha Yakimavets, Grace E Lee, Patricia A Brennan, Elizabeth J Corwin, Anne L Dunlop, Donghai Liang

**Full Source:** Journal of exposure science & environmental epidemiology 2023 Feb 25. doi: 10.1038/s41370-023-00530-4.

## OCCUPATIONAL

## Assessment of the Genotoxic and Cytotoxic Effects of Turpentine in Painters

2023-02-15

Turpentine is a fluid used mainly as a solvent for thinning oil-based paints, obtained by distilling the resin of coniferous trees. Fine art painters use turpentine on a daily basis. The aim of this study was to investigate the genotoxic effect of turpentine and to determine the lymphocyte proliferation index in the peripheral blood of individuals occupationally exposed to turpentine. For this purpose, the cytokinesis-block micronucleus assay (CBMN) was used to determine the total number of micronuclei (MNI), nucleoplasmic bridges (NPB), and nuclear buds (NBUD), as well as the cell proliferation index (CBPI) in the peripheral

Turpentine is a fluid used mainly as a solvent for thinning oil-based paints, obtained by distilling the resin of coniferous trees.

## Bulletin Board

## Technical

MAR. 03, 2023

blood lymphocytes of the subjects. Twenty-two subjects exposed to turpentine daily through their work participated in the study and were compared to twenty subjects in the control group. The results showed a significant increase in the number of micronuclei and other genotoxicity parameters, as well as significant cytotoxicity based on CBPI values. In addition, the genotoxic and cytotoxic effects of turpentine were found to be time-dependent, i.e., the deleterious effects of turpentine on genetic material increase with prolonged exposure. These results strongly suggest that exposure to turpentine vapors may affect genome stability and that occupational safety measures should be taken when using turpentine.

**Authors:** Sara Kević Dešić, Barbara Viljević, Jasenka Wagner

**Full Source:** Life (Basel, Switzerland) 2023 Feb 15;13(2):530. doi: 10.3390/life13020530.

## Occupational Risk Factors by Sectors: An Observational Study of 20,000 Workers

2023-02-18

**Objective:** We aimed to assess the prevalence of exposure by sector and the sectors of activity most exposed to each exposure, using routine occupational health data, and to quantify the risk of being exposed.

**Method:** Occupational risk factors were assessed by workers followed by the Occupational Health Service of Cher, using self-reported questionnaires. The sectors of activity were grouped into seven sectors, and the risks were grouped into six occupational exposure groups. Comparisons were made using the Chi-squared test and Cramer's V, and the odds ratios were calculated by using logistic regression.

**Results:** We included 19,891 workers. The construction sector had the highest prevalence ( $p < 0.05$  vs. all other sectors) of exposure to physical (76%) and biomechanical factors (82%), as well as chemical risks (75%). Human health and social work was the sector with the highest prevalence of exposure to biological factors (69%), psychosocial factors (90%), and atypical working hours (61%). With workers from administrative and support sectors as the reference, construction workers had more chance of declaring exposure to physical factors (OR = 3.28, 95%CI = 2.89 to 3.72), biomechanical factors (1.82, 1.58 to 2.09), and chemical agents (3.83, 3.38 to 4.33). Workers from the human health and social sectors had more chance of being exposed to biological agents (13.4, 11.9 to 15.2), atypical working hours (1.93, 1.75 to 2.14), and psychosocial factors (2.74, 2.38 to 3.16).

**Conclusion:** Psychosocial risk factors were commonly reported in all sectors. Workers in the construction, human health, and social sectors

**Objective:** We aimed to assess the prevalence of exposure by sector and the sectors of activity most exposed to each exposure, using routine occupational health data, and to quantify the risk of being exposed.

# Bulletin Board

## Technical

MAR. 03, 2023

seem to report more exposures than those in other sectors. The analysis of occupational exposures is a necessary basis to build an efficient preventive strategy for occupational health.

Authors: Luther Dogbla, Cédric Gouvenelle, Florence Thorin, François-Xavier Lesage, Marek Zak, Ukadike Chris Ugbole, Barbara Charbotel, Julien S Baker, Bruno Pereira, Frédéric Dutheil

Full Source: International journal of environmental research and public health 2023 Feb 18;20(4):3632. doi: 10.3390/ijerph20043632.

### Use of the Benchmark-dose (BMD) approach to derive Occupational Exposure Limits (OELs) for genotoxic carcinogens: N-nitrosamines

2023-02-25

N-Nitrosamines are potent carcinogens and considered non-threshold carcinogens in various regulatory domains. However, recent data indicate the existence of a threshold for genotoxicity, which can be adequately demonstrated. This aspect has a critical impact on selecting the methodology that is applied to derive Occupational Exposure Limits (OELs). OELs are used to protect workers potentially exposed to various chemicals by supporting selection of appropriate control measures and ultimately reducing risk of occupational cancer. Occupational exposures to nitrosamines occur during manufacturing processes, mainly in the rubber and chemical industry. The present study derives OELs for inhaled N-nitrosamines, employing the benchmark dose (BMD) approach if data are adequate and read-across for nitrosamines without adequate data. Additionally, BMDL (Benchmark Dose Lower Confidence Limit) is preferred and more suitable Point-of-Departure (PoD) to calculate human health guidance values, including OEL. The lowest OEL (0.2 µg/m<sup>3</sup>) was derived for nitrosodiethylamine (NDEA), and nitrosopiperidine (NPIP) (OEL=0.2 µg/m<sup>3</sup>), followed by nitrosopyrrolidine (NPYR) (0.4 µg/m<sup>3</sup>), nitrosodimethylamine (NDMA), nitrosodimethylamine (NMEA), and nitrosodipropylamine (NDPA) (0.5 µg/m<sup>3</sup>), nitrosomorpholine (NMOR) (OEL=1 µg/m<sup>3</sup>), and nitrosodibutylamine (NDBA) (OEL = 2.5 µg/m<sup>3</sup>). Limits based on “non-threshold” TD50 slope calculation were within a 10-fold range. These proposed OELs do not consider skin absorption of nitrosamines, which is also a possible route of entry into the body nor oral or other environmental sources. Furthermore, we recommend setting a

N-Nitrosamines are potent carcinogens and considered non-threshold carcinogens in various regulatory domains.

# Bulletin Board

## Technical

MAR. 03, 2023

limit for total nitrosamines based on the occupational exposure scenario and potency of components.

Authors: Kamila Blum, Rex FitzGerald, Martin Wilks, Ester Lovsin Barle, Nancy B Hopf

Full Source: Journal of applied toxicology : JAT 2023 Feb 25. doi: 10.1002/jat.4455.