# **Bulletin Board**

## Contents

(click on page numbers for links)

### CHEMICAL EFFECTS

#### ENVIRONMENTAL RESEARCH

Occupational and Environmental Exposure Influences the	
Inflammatory (Pro-and Anti-) Status in Benign Prostate Hyperplasia	
and Prostate Carcinoma Patients: A Retrospective Analysis	5
Personal environmental exposure to plasticizers and	
organophosphate flame retardants using silicone wristbands and	
urine: Patterns, comparisons, and correlations	7

### PHARMACEUTICAL/TOXICOLOGY

Phase 1, first-in-human study of TYRP1-TCB (RO7293583), a novel	
active drug monitoring to assess the impact of immune response	
on drug exposure	8
control rice blast disease caused by Magnaporthe oryzae	9

#### OCCUPATIONAL

Squalene Depletion in Skin Following Human Exposure to Ozone under Controlled Chamber Conditions	10
The asbestos-asbestosis exposure-response relationship: a cohort study of the general working population	11
Assessment of occupational musculoskeletal disorders (MSDs) among heavy vehicle drivers	12

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# **Bulletin Board**

## **Technical**

2024

### CHEMICAL EFFECTS

#### Remediation of Metal Oxide Nanotoxicity with a Functional Amyloid

#### 2024-04-06

Understanding the environmental health and safety of nanomaterials (NanoEHS) is essential for the sustained development of nanotechnology. Although extensive research over the past two decades has elucidated the phenomena, mechanisms, and implications of nanomaterials in cellular and organismal models, the active remediation of the adverse biological and environmental effects of nanomaterials remains largely unexplored. Inspired by recent developments in functional amyloids for biomedical and environmental engineering, this work shows their new utility as metallothionein mimics in the strategically important area of NanoEHS. Specifically, metal ions released from CuO and ZnO nanoparticles are sequestered through cysteine coordination and electrostatic interactions with beta-lactoglobulin (bLg) amyloid, as revealed by inductively coupled plasma mass spectrometry and molecular dynamics simulations. The toxicity of the metal oxide nanoparticles is subsequently mitigated by functional amyloids, as validated by cell viability and apoptosis assays in vitro and murine survival and biomarker assays in vivo. As bLg amyloid fibrils can be readily produced from whey in large quantities at a low cost, the study offers a crucial strategy for remediating the biological and environmental footprints of transition metal oxide nanomaterials.

Authors: Yue Wang, Xiufang Liang, Nicholas Andrikopoulos, Huayuan Tang, Fei He, Xiang Yin, Yuhuan Li, Feng Ding, Guotao Peng, Monika Mortimer, Pu Chun Ke

Full Source: Advanced science (Weinheim, Baden-Wurttemberg, Germany) 2024 Apr 6:e2310314. doi: 10.1002/advs.202310314.

#### Interactive impacts of photoaged micro(nano)plastics and co-occurring chemicals in the environment

#### 2024-04-04

In the environment, sunlight or ultraviolet (UV) radiation is considered to be the primary cause of plastic aging, leading to their fragmentation into particles, including micro(nano)plastics (MNPs). Photoaged MNPs possess diverse interactive properties and ecotoxicological implications substantially different from those of pristine plastic particles. This review aims to highlight the mechanisms and implications of UV-induced photoaging of MNPs, with an emphasis on various UV sources and their

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## Technical

CHEMWATCH

interactions with co-occurring organic and inorganic chemicals, as well as the associated ecological and health impacts and factors affecting those interactions. Compared to UV-B, UV-A and UV-C were more widely used in laboratory studies for MNP degradation. Photoaged MNPs act as vectors for the transportation of organic pollutants, organic matter, and inorganic chemicals in the environment. Literature showed that photoaged MNPs exhibit a higher sorption capacity for PPCPs, PAHs, PBDEs, pesticides, humic acid, fulvic acid, heavy metals, and metallic nanoparticles than pristine MNPs, potentially causing significant changes in associated ecological and health impacts. Combined exposure to photoaged MNPs and organic and inorganic pollutants significantly altered mortality rate, decreased growth rate, histological alterations, neurological impairments, reproductive toxicity, induced oxidative stress, thyroid disruption, hepatotoxicity, and genotoxicity in vivo, both in aquatic and terrestrial organisms. Limited studies were reported in vitro and found decreased cellular growth and survival, induced oxidative stress, and compromised the permeability and integrity of the cell membrane. In addition, several environmental factors (temperature, organic matter, ionic strength, time, and pH), MNP properties (polymer types, sizes, surface area, shapes, colour, and concentration), and chemical properties (pollutant type, concentration, and physiochemical properties) can influence the photoaging of MNPs and associated impacts. Lastly, the research gaps and prospects of MNP photoaging and associated implications were also summarized. Future research should focus on the photoaging of MNPs under environmentally relevant conditions, exploiting the polydisperse characteristics of environmental plastics, to make this process more realistic for mitigating plastic pollution.

Authors: Muhammad Junaid, Naima Hamid, Shulin Liu, Zohaib Abbas, Muhammad Imran, Muhammad Rizwan Haider, Bin Wang, Guanglong Chen, Hudda Khaleeq Khan, Qiang Yue, Nan Xu, Jun Wang Full Source: The Science of the total environment 2024 Apr 4:927:172213. doi: 10.1016/j.scitotenv.2024.172213.

### Assessment of the application of selected metal-organic frameworks as advanced sorbents in passive extraction used in the monitoring of contaminants of emerging concern in surface waters

#### 2024-04-03

Water pollution has become a critical global concern requiring effective monitoring techniques and robust protection strategies. Contaminants of emerging concern (CECs) are increasingly detected in various water

## **Bulletin Board**

Water pollution has become a critical global concern requiring effective monitoring techniques and robust protection strategies.

# **Bulletin Board**

## Technical

sources, with their harmful effects on humans and ecosystems continually evolving. Based on literature reports highlighting the promising sorption properties of metal-organic frameworks (MOFs), the aim of this study was to evaluate the suitability of NH2-MIL-125 (Ti) and UiO-66 (Ce) as sorbents in passive sampling devices (MOFs-PSDs) for the collection and extraction of a wide group of CECs. Solvothermal methods were used to synthesize MOFs, and the characterization of the obtained materials was performed using field-emission scanning electron microscopy (FE-SEM), powder X-ray diffractometry (pXRD) and Fourier-transform infrared (FTIR) spectroscopy. The research demonstrated the sorption capabilities of the tested MOFs, the ease and rapidity of their chemical regeneration and the possibility of reuse as sorbents. Using chemometric analysis, the structural properties of CECs determining the sorption efficiency on the surface of NH2-MIL-125 (Ti) were identified. The MOFs-PSDs were lab-calibrated to examine the kinetics of analytes sorption and determine the sampling rates (Rs). MOFs-PSDs and CNTs-PSDs (PSDs containing carbon nanotubes as a sorbent) were then placed in the Elblag River and the Vistula Lagoon to sampling and extraction of the target compounds from the water. CNTs-PSDs were selected, based on our previous research, for the comparison of the effectiveness of the MOFs-PSDs in environmental monitoring. MOFs-PSDs were successfully used in monitoring of CECs in water. The timeweighted average concentrations (CTWA) of 2-hydroxycarbamazepine, carbamazepine-10,11-epoxide, p-nitrophenol, 3,5-dichlorophenol and caffeine were determined in the Elblag River and CTWA of metoprolol, diclofenac, 2-hydroxycarbamazepine, carbamazepine-10,11-epoxide, p-nitrophenol, 3,5-dichlorophenol and caffeine were determine in the Vistula Lagoon using MOFs-PSDs and a high-performance liquid chromatography coupled with triple guadrupole mass spectrometer. Authors: Klaudia Godlewska, Anna Białk-Bielińska, Paweł Mazierski, Szymon Zdybel, Anita Sosnowska, Daniel Górzyński, Tomasz Puzyn, Adriana Zaleska-Medynska, Tomasz Klimczuk, Monika Paszkiewicz Full Source: The Science of the total environment 2024 Apr 3:172215. doi: 10.1016/j.scitotenv.2024.172215.

## CHEMWATCH

Technical

# **Bulletin Board**

### 12. 2024

### **ENVIRONMENTAL RESEARCH**

**Occupational and Environmental Exposure Influences** the Inflammatory (Pro-and Anti-) Status in Benign Prostate Hyperplasia and Prostate Carcinoma Patients: A **Retrospective Analysis** 

#### 2024-04

Multiple diseases and disorders are connected with occupational and environmental exposure risk. It is also well-established that chemicals and chemical mixtures have an influence on the immune cells of humans. This is an important field of research that has been pursued extensively in relation to autoimmune illnesses, allergy/asthma, and lung cancer, but Prostate Carcinoma has received rare reports. Chronic chemical exposure is known to produce inflammation, which is one of the most prominent characteristics of all malignancies. Changes in the ratio of pro-inflammatory to anti-inflammatory molecules are thought to be a key factor in the emergence of inflammation. Prostate gland cells express the pro-inflammatory cytokine interleukin-18 (IL-18), which is a major facilitator of immunological responses. Conversely, interleukin-10 (IL-10) is an anti-inflammatory cytokine that is linked to immune responses and inhibits the development of an inflammatory environment. Our goal is to investigate the inflammatory status of IL-18 (pro-) and IL-10 (anti-) in a variety of occupationally exposed populations in patients with Benign Prostate Hyperplasia (BPH) and patients with Prostate Carcinoma. The present study was conducted with 664 subjects, comprising 285 Prostate Carcinoma patients, 94 BPH patients and 285 controls. The subjects of BPH and Prostate Carcinoma were screened and confirmed on the basis of Prostate Serum Antigen (PSA) and pathological biopsy. All subjects were categorized as per their occupational exposure into various groups. The pro-inflammatory and anti-inflammatory Interleukins (IL-18 and IL-10) and serum PSA levels were analysed by using corresponding quantitative ELISA kits. The results showed that as compared to control participants, the serum PSA levels were higher in the Prostate Carcinoma and BPH groups. When mean levels of IL-18 were compared between various occupational groups, Tanners (tanning industry), Agriculture, and Ordnance workers had significantly higher levels (P < 0.05) of IL-18 than sedentary workers. The pro-inflammatory cytokine (IL-18) levels were also found to be aggravated in Prostate Carcinoma compared to BPH and controls. According to the findings of the current study, the levels of inflammatory cytokines (IL-18 and IL-10) in various occupational groups of BPH, Prostate Carcinoma,

Multiple diseases and disorders are connected with occupational and environmental exposure risk.

## Bulletin Board

## Technical

and controls were altered. Long-term occupational exposure may have a negative influence on inflammation levels and the immune system; therefore, preventative measures should be explored for improved health. Authors: Shailendra Dwivedi, Praveen Sharma, Apul Goel, Sanjay Khattri, Sanjeev Misra, Kamlesh Kumar Pant Full Source: Indian journal of clinical biochemistry : IJCB 2024 Apr;39(2):241-247. doi: 10.1007/s12291-023-01112-9.

Personal environmental exposure to plasticizers and organophosphate flame retardants using silicone wristbands and urine: Patterns, comparisons, and correlations

#### 2024-04-04

Plasticizers (PLs) and organophosphate flame retardants (OPFRs) are ubiguitous in the environment due to their widespread use and potential for leaching from consumer products. Environmental exposure is a critical aspect of the human exposome, revealing complex interactions between environmental contaminants and potential health effects. Silicone wristbands (SWBs) have emerged as a novel and non-invasive sampling device for assessing personal external exposure. In this study, SWBs were used as a proxy to estimate personal dermal adsorption (EDdermal) to PLs and OPFRs in Belgian participants for one week; four morning urine samples were also collected and analyzed for estimated daily intake (EDI). The results of the SWBs samples showed that all the participants were exposed to these chemicals, and the exposure was found to be highest for the legacy and alternative plasticizers (LP and AP), followed by the legacy and emerging OPFRs (LOPFR and EOPFR). In urine samples, the highest levels were observed for metabolites of diethyl phthalate (DEP), di-isobutyl phthalate (DiBP) and di-n-butyl phthalate (DnBP) among LPs and di(2-ethylhexyl) terephthalate (DEHT) for APs. Outliers among the participants indicated that there were other sources of exposure that were not identified. Results showed a significant correlation between EDdermal and EDI for DiBP, tris (2-butoxyethyl) phosphate (TBOEP) and triphenyl phosphate (TPhP). These correlations indicated their suitability for predicting exposure via SWB monitoring for total chemical exposure. The results of this pilot study advance our understanding of SWB sampling and its relevance for predicting aggregate environmental chemical exposures, while highlighting the potential of SWBs as low-cost, non-invasive personal samplers for future research. This innovative approach has the

Plasticizers (PLs) and organophosphate flame retardants (OPFRs) are ubiquitous in the environment due to their widespread use and potential for leaching from consumer products.

202

## CHEMWATCH

## **Bulletin Board**

## Technical

#### potential to advance the assessment of environmental exposures and their impact on public health.

Authors: Shanshan Yin, Fatima den Ouden, Paulien Cleys, Anna Klimowska, Jasper Bombeke, Giulia Poma, Adrian Covaci Full Source: The Science of the total environment 2024 Apr 4:172187. doi: 10.1016/j.scitotenv.2024.172187.

### PHARMACEUTICAL/TOXICOLOGY

Phase 1, first-in-human study of TYRP1-TCB (RO7293583), a novel TYRP1-targeting CD3 T-cell engager, in metastatic melanoma: active drug monitoring to assess the impact of immune response on drug exposure

#### 2024-03-21

Introduction: Although checkpoint inhibitors (CPIs) have improved outcomes for patients with metastatic melanoma, those progressing on CPIs have limited therapeutic options. To address this unmet need and overcome CPI resistance mechanisms, novel immunotherapies, such as T-cell engaging agents, are being developed. The use of these agents has sometimes been limited by the immune response mounted against them in the form of anti-drug antibodies (ADAs), which is challenging to predict preclinically and can lead to neutralization of the drug and loss of efficacy. Methods: TYRP1-TCB (RO7293583; RG6232) is a T-cell engaging bispecific (TCB) antibody that targets tyrosinase-related protein 1 (TYRP1), which is expressed in many melanomas, thereby directing T cells to kill TYRP1expressing tumor cells. Preclinical studies show TYRP1-TCB to have potent anti-tumor activity. This first-in-human (FIH) phase 1 dose-escalation study characterized the safety, tolerability, maximum tolerated dose/optimal biological dose, and pharmacokinetics (PK) of TYRP1-TCB in patients with metastatic melanoma (NCT04551352).

Results: Twenty participants with cutaneous, uveal, or mucosal TYRP1positive melanoma received TYRP1-TCB in escalating doses (0.045 to 0.4 mg). All participants experienced  $\geq 1$  treatment-related adverse event (TRAE); two participants experienced grade 3 TRAEs. The most common toxicities were grade 1-2 cytokine release syndrome (CRS) and rash. Fractionated dosing mitigated CRS and was associated with lower levels of interleukin-6 and tumor necrosis factor-alpha. Measurement of active drug (dual TYPR1- and CD3-binding) PK rapidly identified loss of active drug exposure in all participants treated with 0.4 mg in a flat dosing schedule for  $\geq$ 3 cycles. Loss of exposure was associated with development



Introduction: Although checkpoint inhibitors (CPIs) have improved outcomes for patients with metastatic melanoma, those progressing on CPIs have limited therapeutic options.

## **Bulletin Board**

## Technical

of ADAs towards both the TYRP1 and CD3 domains. A total drug PK assay, measuring free and ADA-bound forms, demonstrated that TYRP1-TCB-ADA immune complexes were present in participant samples, but showed no drug activity in vitro.

Discussion: This study provides important insights into how the use of active drug PK assays, coupled with mechanistic follow-up, can inform and enable ongoing benefit/risk assessment for individuals participating in FIH dose-escalation trials. Translational studies that lead to a better understanding of the underlying biology of cognate T- and B-cell interactions, ultimately resulting in ADA development to novel biotherapeutics, are needed.

Authors: Anna Spreafico, Eva Muñoz Couselo, Anja Irmisch, Juliana Bessa, George Au-Yeung, Oliver Bechter, Inge Marie Svane, Miguel F Sanmamed, Valentina Gambardella, Meredith McKean, Margaret Callahan, Reinhard Dummer, Christian Klein, Pablo Umaña, Nicole Justies, Florian Heil, Linda Fahrni, Eugenia Opolka-Hoffmann, Inja Waldhauer, Conrad Bleul, Roland F Staack, Vaios Karanikas, Stephen Fowler

Full Source: Frontiers in oncology 2024 Mar 21:14:1346502. doi: 10.3389/ fonc.2024.1346502.

#### Antifungal plant flavonoids identified in silico with potential to control rice blast disease caused by Magnaporthe oryzae

#### 2024-04-05

Rice blast disease, caused by the fungus Magnaporthe oryzae, poses a severe threat to rice production, particularly in Asia where rice is a staple food. Concerns over fungicide resistance and environmental impact have sparked interest in exploring natural fungicides as potential alternatives. This study aimed to identify highly potent natural fungicides against M. oryzae to combat rice blast disease, using advanced molecular dynamics techniques. Four key proteins (CATALASE PEROXIDASES 2, HYBRID PKS-NRPS SYNTHETASE TAS1, MANGANESE LIPOXYGENASE, and PRE-MRNA-SPLICING FACTOR CEF1) involved in M. oryzae's infection process were identified. A list of 30 plant metabolites with documented antifungal properties was compiled for evaluation as potential fungicides. Molecular docking studies revealed that 2-Coumaroylquinic acid, Myricetin, Rosmarinic Acid, and Quercetin exhibited superior binding affinities compared to reference fungicides (Azoxystrobin and Tricyclazole). High throughput molecular dynamics simulations were performed, analyzing parameters like RMSD, RMSF, Rg, SASA, hydrogen bonds, contact analysis, Gibbs free energy, and cluster analysis. The results revealed stable

Rice blast disease, caused by the fungus Magnaporthe oryzae, poses a severe threat to rice production, particularly in Asia where rice is a staple food.

2024

## Technical

CHEMWATCH

interactions between the selected metabolites and the target proteins, involving important hydrogen bonds and contacts. The SwissADME server analysis indicated that the metabolites possess fungicide properties, making them effective and safe fungicides with low toxicity to the environment and living beings. Additionally, bioactivity assays confirmed their biological activity as nuclear receptor ligands and enzyme inhibitors. Overall, this study offers valuable insights into potential natural fungicides for combating rice blast disease, with 2-Coumaroylquinic acid, Myricetin, Rosmarinic Acid, and Quercetin standing out as promising and environmentally friendly alternatives to conventional fungicides. These findings have significant implications for developing crop protection strategies and enhancing global food security, particularly in ricedependent regions.

Authors: Abu Tayab Moin, Tanjin Barketullah Robin, Rajesh B Patil, Nurul Amin Rani, Anindita Ash Prome, Tahsin Islam Sakif, Mohabbat Hossain, Dil Umme Salma Chowdhury, Shah Samiur Rashid, A K M Moniruzzaman Mollah, Saiful Islam, Mohammad Helal Uddin, Mohammad Khaleguzzaman, Tofazzal Islam, Nazneen Naher Islam Full Source: PloS one 2024 Apr 5;19(4):e0301519. doi: 10.1371/journal. pone.0301519.

### **OCCUPATIONAL**

### Squalene Depletion in Skin Following Human Exposure to **Ozone under Controlled Chamber Conditions** 2024-04-05

A major component of human skin oil is squalene, a highly unsaturated hydrocarbon that protects the skin from atmospheric oxidants. Skin oil, and thus squalene, is continuously replenished on the skin surface. Squalene is also quickly consumed through reactions with ozone and other oxidants. This study examined the extent of squalene depletion in the skin oils of the forearm of human volunteers after exposure to ozone in a climate chamber. Temperature, relative humidity (RH), skin coverage by clothing, and participants' age were varied in a controlled manner. Concentrations of squalene were determined in skin wipe samples collected before and after ozone exposure. Exposures to ozone resulted in statistically significant decreases in post-exposure squalene concentrations compared to pre-exposure squalene concentrations in the skin wipes when squalene concentrations were normalized by concentrations of co-occurring cholesterol but not by co-occurring pyroglutamic acid (PGA). The rate of squalene loss due to ozonolysis

## **Bulletin Board**

A major component of human skin oil is squalene, a highly unsaturated hydrocarbon that protects the skin from atmospheric oxidants.

## **Bulletin Board**

## Technical

was lower than its replenishment on the skin surface. Within the ranges examined, temperature and RH did not significantly affect the difference between normalized squalene levels in post-samples versus pre-samples. Although not statistically significant, skin coverage and age of the volunteers (three young adults, three seniors, and three teenagers) did appear to impact squalene depletion on the skin surfaces.

Authors: Sarka Langer, Charles J Weschler, Gabriel Bekö, Glenn Morrison, Ann Sjöblom, Georgios Giovanoulis, Pawel Wargocki, Nijing Wang, Nora Zannoni, Shen Yang, Jonathan Williams

Full Source: Environmental science & technology 2024 Apr 5. doi: 10.1021/ acs.est.3c09394.

### The asbestos-asbestosis exposure-response relationship: a cohort study of the general working population

#### 2024-04-05

Objectives: The association between asbestos exposure and asbestosis in high-exposed industrial cohorts is well-known, but there is a lack of knowledge about the exposure-response relationship for asbestosis in a general working population setting. We examined the exposure-response relationship between occupational asbestos exposure and asbestosis in asbestos-exposed workers of the Danish general working population. Methods: We followed all asbestos-exposed workers from 1979 to 2015 and identified incident cases of asbestosis using the Danish National Patient Register. Individual asbestos exposure was estimated with a quantitative job exposure matrix (SYN-JEM) from 1976 onwards and backextrapolated to age 16 for those exposed in 1976. Exposure-response relations for cumulative exposure and other exposure metrics were analyzed using a discrete time hazard model and adjusted for potential confounders.

Results: The range of cumulative exposure in the population was 0.001 to 18 fibers per milliliter-year (f/ml-year). We found increasing incidence rate ratios (IRR) of asbestosis with increasing cumulative asbestos exposure with a fully adjusted IRR per 1 f/ml-years of 1.18 [95% confidence interval (CI) 1.15--1.22]. The IRR was 1.94 (95% CI 1.53-2.47) in the highest compared to the lowest exposure tertile. We similarly observed increasing risk with increasing cumulative exposure in the inception population. Conclusions: This study found exposure-response relations between cumulative asbestos exposure and incident asbestosis in the Danish

**Objectives:** The association between asbestos exposure and asbestosis in high-exposed industrial cohorts is well-known, but there is a lack of knowledge about the exposure-response relationship for asbestosis in a general working population setting.

## CHEMWATCH

## **Bulletin Board**

## Technical

general working population with mainly low-level exposed occupations, but there is some uncertainty regarding the exposure levels. Authors: Inge Brosbøl Iversen, Jesper Medom Vestergaard, Johan

Ohlander, Susan Peters, Elisabeth Bendstrup, Jens Peter E Bonde, Vivi Schlünssen, Jakob H Bønløkke, Finn Rasmussen, Zara A Stokholm, Michael B Andersen, Hans Kromhout, Henrik A Kolstad Full Source: Scandinavian journal of work, environment & health 2024 Apr 5:4153. doi: 10.5271/sjweh.4153.

### Assessment of occupational musculoskeletal disorders (MSDs) among heavy vehicle drivers

#### 2024-04-02

Background: Professional driving requires long hours of work, uncomfortable seats, negotiating rough terrain and highways, and possibly minor repairs and other auxiliary transportation duties. Heavy vehicle drivers driving vehicles such as trucks, bulldozers, etc. due to such working structures are more prone to various musculoskeletal disorders (MSDs) and pain, which is of great concern.

Objectives: In the present study, it is planned to investigate possible ergonomic risk factors such as age, weight, driving exposure, seat suspension systems, lifting heavy weights causing MSDs in drivers of various heavy vehicles. The results of the study are expected to help drivers reduce the risk of MSDs.

Methods: For the present study, the Nordic questionnaire on musculoskeletal disorders was modified and standardized and was administered to the 48 heavy vehicle drivers randomly selected to collect the data.

Results: The analysis divulged that over the past 12 months, lower back pain (LBP) emerged as the most dominant pain experienced by 56% of drivers, followed by knee pain (KP) (43%) and neck pain (NP) (39%) respectively. The prevalence of shoulder pain (SP) was observed to be much lower than in previous literature. The logistic regression model further revealed that increasing age, poor suspension system and poor body posture were significantly associated with lower back pain. Additionally, a poor suspension system and lifting heavy weights had significant effect on the drivers' knee pain.

Conclusion: The results demonstrated the evident necessity for ergonomic consideration in vehicle designing and ergonomic training for heavy vehicle drivers.

Authors: Mohammad Raza, Rajesh Kumar Bhushan, Abid Ali Khan Full Source: Work (Reading, Mass.) 2024 Apr 2. doi: 10.3233/WOR-230655.



**Background: Profes**sional driving requires long hours of work, uncomfortable seats, negotiating rough terrain and highways, and possibly minor repairs and other auxiliary transportation duties.