CHEMWATCH

Bulletin Board

Contents

JUL. 02, 2021

(click on page numbers for links)

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CHEMICAL EFFECTS

Safety and efficacy of a feed additive consisting of ferric (III) ammonium hexacyanoferrate (II) for ruminants (domestic and wild), calves prior the start of rumination, lambs prior the start of rumination, kids prior the start of rumination and pigs (domestic and wild) (Honeywell Specialty Chemicals Seelze GmbH)

2021-06-11

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of ferric (III) ammonium hexacyanoferrate (II) as technological feed additive for ruminants (domestic and wild), calves prior the start of rumination, lambs prior the start of rumination, kids prior the start of rumination and pigs (domestic and wild). The additive is already authorised for use in ruminants (domestic and wild), calves prior the start of rumination, lambs prior the start of rumination, kids prior the start of rumination and pigs (domestic and wild). The additive is effective at the minimum recommended concentration of 50 mg/kg complete feedingstuffs (corresponding to about 10 mg/10 kg bw) in reducing the contamination of food derived from ruminants (domestic and wild), calves, lambs and kids prior to the start of rumination, and pigs (domestic and wild) by caesium. Considering the scarce information available, the Panel is not in the position to conclude on the safety of the additive for the target species. The use of ferric (III) ammonium hexacyanoferrate (II) in feed for ruminants, calves, lambs, kids and pigs at the maximum recommended concentration of 500 mg/kg feed (corresponding to about 150 mg ferric (III) ammonium hexacyanoferrate (II)/10 kg bw) is safe for the consumer. In the absence of data, the Panel is not in the position to conclude on the safety of the additive for the user. The use of ferric (III) ammonium hexacyanoferrate (II) as a feed additive is considered safe for the environment.

Authors: EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Matteo Lorenzo Innocenti, Fabiola Pizzo, Jaume Galobat, Orsolya

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of ferric (III) ammonium hexacyanoferrate (II) as technological feed additive for ruminants (domestic and wild), calves prior the start of rumination, lambs prior the start of rumination, kids prior the start of rumination and pigs (domestic and wild).

CHEMWATCH
Bulletin Board
Technical
JUL. 02, 2021

Holczknecht, Georges Bories, Jürgen Gropp, Carlo Nebbia, Gabriele Aquilina
Full Source: EFSA journal. European Food Safety Authority 2021 Jun 11;19(6):e06628. doi: 10.2903/j.efsa.2021.6628.

Exposure and Toxicity Characterization of Chemical Emissions and Chemicals in Products: Global Recommendations and Implementation in USEtox

2021-05

Purpose: Reducing chemical pressure on human and environmental health is an integral part of the global sustainability agenda. Guidelines for deriving globally applicable, life cycle based indicators are required to consistently quantify toxicity impacts from chemical emissions as well as from chemicals in consumer products. In response, we elaborate the methodological framework and present recommendations for advancing near-field/far-field exposure and toxicity characterization, and for implementing these recommendations in the scientific consensus model USEtox.

Methods: An expert taskforce was convened by the Life Cycle Initiative hosted by UN Environment to expand existing guidance for evaluating human toxicity impacts from exposure to chemical substances. This taskforce evaluated advances since the original release of USEtox. Based on these advances, the taskforce identified two major aspects that required refinement, namely integrating near-field and far-field exposure and improving human dose-response modeling. Dedicated efforts have led to a set of recommendations to address these aspects in an update of USEtox, while ensuring consistency with the boundary conditions for characterizing life cycle toxicity impacts and being aligned with recommendations from agencies that regulate chemical exposure. The proposed framework was finally tested in an illustrative rice production and consumption case study.

Results and discussion: On the exposure side, a matrix system is proposed and recommended to integrate far-field exposure from environmental emissions with near-field exposure from chemicals in various consumer product types. Consumer exposure is addressed via submodels for each product type to account for product characteristics and exposure settings. Case study results illustrate that product-use related exposure dominates overall life cycle exposure. On the effect side, a probabilistic dose-response approach combined with a decision tree for identifying reliable points of departure is proposed for non-cancer effects, following recent guidance from the World Health Organization. This approach allows for explicitly

Purpose: Reducing chemical pressure on human and environmental health is an integral part of the global sustainability agenda.

considering both uncertainty and human variability in effect factors. Factors reflecting disease severity are proposed to distinguish cancer from non-cancer effects, and within the latter discriminate reproductive/developmental and other non-cancer effects. All proposed aspects have been consistently implemented into the original USEtox framework. Conclusions: The recommended methodological advancements address several key limitations in earlier approaches. Next steps are to test the new characterization framework in additional case studies and to close remaining research gaps. Our framework is applicable for evaluating chemical emissions and product-related exposure in life cycle assessment, chemical alternatives assessment and chemical substitution, consumer exposure and risk screening, and high-throughput chemical prioritization.
Authors: Peter Fantke, Weihsueh A Chiu, Lesa Aylward, Richard Judson, Lei Huang, Suji Jang, Todd Gouin, Lorenz Rhomberg, Nicolò Aurisano, Thomas McKone, Olivier Jolliet
Full Source: The international journal of life cycle assessment 2021 May;26(5):899-915. doi: 10.1007/s11367-021-01889-y.

Endocrine-disrupting chemicals in a typical urbanized bay of Yellow Sea, China: Distribution, risk assessment, and identification of priority pollutants

2021-06-16

Endocrine-disrupting chemicals (EDCs) in water are receiving particular attention as they pose adverse effects on aquatic systems, even at trace concentrations. A comprehensive study was conducted on 14 EDCs (five estrogens and nine household and personal care products (HPCPs)) in the water of the urbanized Jiaozhou Bay in the Yellow Sea during summer and winter. Results showed that the total concentration of 14 EDCs ranged from 100 to 658 ng L-1 and 56.7-212 ng L-1 in the estuarine and bay water, respectively. The average total concentration of five estrogens in summer was significantly ($p < 0.05$) lower than that in winter due to the higher precipitation dilution and degradations during summer, whereas the average total concentration of nine HPCPs was significantly ($p < 0.05$) higher during the summer than that during the winter because of the higher usage and emissions during the summer. Estrogens and HPCPs were dominated by 17α-ethinylestradiol and p-hydroxybenzoic acid (PHBA), respectively. High PHBA concentrations may be related to the hydrolysis of parabens. The total concentrations of EDCs were higher in the eastern coastal seawater of the bay due to the strong influence of domestic and industrial wastewater discharge. Estrogens may interfere with the endocrine system of aquatic organisms in the bay

Endocrine-disrupting chemicals (EDCs) in water are receiving particular attention as they pose adverse effects on aquatic systems, even at trace concentrations.

CHEMWATCH
Bulletin Board
Technical
JUL. 02, 2021

because the total estradiol equivalent concentration exceeded 1 ng L-1. 17α-ethinylestradiol was the main contributor to the estrogenic activity. The EDC mixtures posed high risks (RQ > 1) to mollusks, crustaceans, and fish, and low to moderate risks (RQ < 1) to algae. Fish was the most sensitive aquatic taxon to the EDC mixtures. Given the concentration and frequency of EDCs, the optimized risk quotient method revealed that 17α-ethinylestradiol, estrone, triclocarban, triclosan, and 17β-estradiol should be prioritized in ecological management because of their high risks (prioritization index of >1).
Authors: Shuang Lu, Chunye Lin, Kai Lei, Ming Xin, Baodong Wang, Wei Ouyang, Xitao Liu, Mengchang He
Full Source: Environmental pollution (Barking, Essex : 1987) 2021 Jun 16;287:117588. doi: 10.1016/j.envpol.2021.117588.

ENVIRONMENTAL RESEARCH

Exploring the impacts of microplastics and associated chemicals in the terrestrial environment - Exposure of soil invertebrates to tire particles

2021-06-13

Abrasion of tire wear is one of the largest sources of microplastics to the environment. Although most tire particles settle into soils, studies on their ecotoxicological impacts on the terrestrial environment are scarce. Here, the effects of tire particles (<180 µm) on three ecologically relevant soil invertebrate species, the enchytraeid worm Enchytraeus crypticus, the springtail Folsomia candida and the woodlouse Porcellio scaber, were studied. These species were exposed to tire particles spiked in soil or in food at concentrations of 0.02%, 0.06%, 0.17%, 0.5% and 1.5% (w/w). Tire particles contained a variety of potentially harmful substances. Zinc (21 900 mg kg-1) was the dominant trace element, whilst the highest concentrations of the measured organic compounds were detected for benzothiazole (89.2 mg kg-1), pyrene (4.85 mg kg-1), chlorpyrifos (0.351 mg kg-1), HCB (0.134 mg kg-1), methoxychlor (0.116 mg kg-1) and BDE 28 (0.100 mg kg-1). At the highest test concentration in soil (1.5%), the tire particles decreased F. candida reproduction by 38% and survival by 24%, and acetylcholinesterase (AChE) activity of P. scaber by 65%, whilst the slight decrease in the reproduction of E. crypticus was not dose-dependent. In food, the highest test concentration of tire particles reduced F. candida survival by 38%. These results suggest that micro-sized tire particles can affect soil invertebrates at concentrations found at

Abrasion of tire wear is one of the largest sources of microplastics to the environment.

roadsides, whilst short-term impacts at concentrations found further from the roadsides are unlikely.
Authors: Salla Selonen, Andraž Dolar, Anita Jemec Kokalj, Lyndon N A Sackey, Tina Skalar, Virgínia Cruz Fernandes, Diana Rede, Cristina Delerue-Matos, Rachel Hurley, Luca Nizzetto, Cornelis A M van Gestel
Full Source: Environmental research 2021 Jun 13;201:111495. doi: 10.1016/j.envres.2021.111495.

A comprehensive review on the analytical method, occurrence, transformation and toxicity of a reactive pollutant: BADGE

2021-06-17
Bisphenol A diglycidyl ether (BADGE)-based epoxy resin is one of the most widely used epoxy resins with an annual production amount of several million tons. Compared with all other legacy or emerging organic compounds, BADGE is special due to its toxicity and high reactivity in the environment. More and more studies are available on its analytical methods, occurrence, transformation and toxicity. Here, we provided a comprehensive review of the current BADGE-related studies, with focus on its production, application, available analytical methods, occurrences in the environment and human specimen, abiotic and biotic transformation, as well as the in vitro and in vivo toxicities. The available data show that BADGE and its derivatives are ubiquitous environmental chemicals and often well detected in human specimens. For their analysis, a water-free sample pretreatment should be considered to avoid hydrolysis. Additionally, their complex reactions with endogenous metabolites are areas of great interest. To date, the monitoring and further understanding of their transport and fate in the environment are still quite lacking, comparing with its analogues bisphenol A (BPA) and bisphenol S (BPS). In terms of toxicity, the summary of its current studies and Environmental Protection Agency (EPA) ToxCast toxicity database suggests BADGE might be an endocrine disruptor, though more detailed evidence is still needed to confirm this hypothesis in in vivo animal models. Future study of BADGE should focus on its metabolic transformation, reaction with protein and validation of its role as an endocrine disruptor. We believe that the elucidation of BADGEs can greatly enhance our understandings of those reactive compounds in the environment and human.
Authors: Dongqi Wang, Haoduo Zhao, Xunchang Fei, Shane Allen Synder, Mingliang Fang, Min Liu
Full Source: Environment international 2021 Jun 17;155:106701. doi: 10.1016/j.envint.2021.106701.

Bisphenol A diglycidyl ether (BADGE)-based epoxy resin is one of the most widely used epoxy resins with an annual production amount of several million tons.

CHEMWATCH
Bulletin Board
Technical
JUL. 02, 2021

Perturbation of amino acid metabolism mediates air pollution associated vascular dysfunction in healthy adults

2021-06-21
The molecular mechanisms of air pollution-associated adverse cardiovascular effects remain largely unknown. In the present study, we investigated the impacts of ambient air pollution on vascular function and the potential mediation effects of amino acids in a longitudinal follow-up of 73 healthy adults living in Beijing, China, between 2014 and 2016. We estimated associations between air pollutants and serum soluble intercellular adhesion molecule 1 (sICAM-1) and plasma levels of amino acids using linear mixed-effects models, and elucidated the biological pathways involved using mediation analyses. Higher air pollutant levels were significantly associated with increases in sICAM-1 levels. Metabolomics analysis showed that altered metabolites following short-term air pollution exposure were mainly involved in amino acid metabolism. Significant reductions in levels of plasma alanine, threonine and glutamic acid of 2.1 μM [95% confidence interval (CI): -3.8, -0.3] to 62.0 μM (95% CI: -76.1, -47.9) were associated with interquartile range increases in moving averages of PM2.5, BC, CO and SO2 in 1-7 days prior to clinical visits. Mediation analysis also showed that amino acids can mediate up to 48% of the changes in sICAM-1 associated with increased air pollution exposure. Our results indicated that air pollution may prompt vascular dysfunction through perturbing amino acid metabolism.
Authors: Baihuan Feng, Changjie Liu, Tieci Yi, Xiaoming Song, Yang Wang, Shengcong Liu, Jie Chen, Qian Zhao, Yi Zhang, Tong Wang, Hongbing Xu, Sanjay Rajagopalan, Robert Brook, Jianping Li, Lemin Zheng, Wei Huang
Full Source: Environmental research 2021 Jun 21;111512. doi: 10.1016/j.envres.2021.111512.

The molecular mechanisms of air pollution-associated adverse cardiovascular effects remain largely unknown.

Ecotoxicological effects of new generation pollutants (nanoparticles, amoxicillin and white musk) on freshwater and marine phytoplankton species

2021-09
Phytoplankton occupies a key trophic level in aquatic ecosystems. Chemical impacts on these primary producers can disrupt the integrity of an entire ecosystem. Two freshwater (Pseudokirchneriella subcapitata-Ps and Scenedesmus obliquus-S) and three marine (Phaeodactylum tricornutum-P, Isochrysis galbana-I, Tetraselmis suecica-T) microalgae species were exposed to dilutions of four chemicals: nanoparticles (n-TiO2, n-ZnO), amoxicillin (antibiotic), and white musk (personal care fragrance)

to determine the half maximal effective concentration (EC50) after 72 h of exposure under standardized and controlled environmental conditions. Cell cultures were exposed to EC50 to determine sublethal effects (72 h) based on biochemical (chlorophylls a, b, c), molecular (changes in outer cell wall structure), and morphological alterations. We report for the first time EC50 values for nanoparticles in not standardized species (S, I and T) and for amoxicillin and white musk in all tested species. Standardized species (Ps and P) were less sensitive than non-standardized in some cases. Fourier-transformed infrared spectroscopy showed a marked spectral alteration (from 10.44% to 90.93%) of treated cultures compared to negative controls; however, principal component analysis disclosed no differences in molecular alteration between the five microalgae species or the two aquatic habitats considered. There was a significant decrease in chlorophylls content in all species exposed to EC50 compared to controls (Kruskal Wallis test; $p < 0.05$). There was a significant increase in cell-size (Mann-Whitney U test; $p < 0.05$) in I, P and T exposed to white musk and S exposed to amoxicillin. Findings highlight ecotoxicological risks from new generation pollutants for primary producers in aquatic ecosystems.

Authors: Andrea Broccoli, Serena Anselmi, Andrea Cavallo, Vittoria Ferrari, Daniela Prevedelli, Paolo Pastorino, Monia Renzi

Full Source: Chemosphere 2021 Sep;279:130623. doi: 10.1016/j.chemosphere.2021.130623.

OCCUPATIONAL

Implementation of a triage monitoring program for internal exposure to short-lived radionuclides in Israel - Challenges and recommendations

2021-06-23

Monitoring internal exposure to short-lived radionuclides is challenging, due to the frequent measurements required. ISO Standard 16637 and the Swiss Personal Dosimetry Ordinance describe a screening measurement (triage monitoring) conducted in the workplace to identify workers suspected of internal exposure. Based on a previous study that examined the feasibility of using several commonly found radiation monitors in Israel in a triage monitoring program, we conducted a pilot study towards the implementation of triage monitoring in nuclear medicine facilities in Israel. The pilot study was conducted while considering the current Israeli regulations and local safety culture. We implemented the triage monitoring program in three nuclear medicine facilities in Israel, with a total of 55 monitored workers. The pilot study consisted of two stages: a short-term stage conducted in the largest manufacture of radiopharmaceuticals in Israel and a long-term stage in two nuclear medicine departments in Israel. During the first stage of the study, participants were asked to conduct a daily measurement at the end of the workday and send a urine sample to the national internal dosimetry laboratory. The second stage lasted 5 months in a major hospital and 18 months in a regional hospital. The workers were asked to perform the measurement at the end of the shift and send a urine sample if a defined threshold had been crossed. The mean participation rate in the long-term stage(>70%) indicates that implementation of the triage monitoring program could be successful in Israel. Based on the findings of the study, practical recommendations are listed: suitable monitoring devices, allocating a monitoring location, time of measurement, training of the workers, record keeping and coordination with a certified dosimetry laboratory. The pilot study recommendations were submitted to the Israel Institute for Occupational Safety and Hygiene at the Ministry of Labor, Social Affairs and Social Services.

Monitoring internal exposure to short-lived radionuclides is challenging, due to the frequent measurements required.

Authors: Rachel Hen Shukrun, Lior Epstein, Jean Koch, David Benmaman, Lotem Buchbinder, Shani Cohen, Maya Veinguer, Hanan Datz

Full Source: Journal of radiological protection : official journal of the Society for Radiological Protection 2021 Jun 23. doi: 10.1088/1361-6498/ac0df1.

The interaction effects of FEN1 rs174538 polymorphism and polycyclic aromatic hydrocarbon exposure on damage in exon 19 and 21 of EGFR gene in coke oven workers

2021-06-23

Polycyclic aromatic hydrocarbon (PAH) exposure and genetic susceptibility were conductive to genotoxic effects including gene damage, which can increase mutational probability. We aimed to explore the dose-effect associations of PAH exposure with damage of exons of epidermal growth factor receptor (EGFR) and breast cancer susceptibility gene 1 (BRCA1), as well as their associations whether modified by Flap endonuclease 1 (FEN1) genotype. Two hundred eighty-eight coke oven male workers were recruited, and we detected the concentration of 1-hydroxypyrene (1-OH-pyr) as PAH exposure biomarker in urine and examined base modification in exons of EGFR and BRCA1 respectively, and genotyped FEN1 rs174538 polymorphism in plasma. We found that the damage indexes of exon 19 and 21 of EGFR (EGFR-19 and EGFR-21) were both significantly associated with increased urinary 1-OH-pyr (both Ptrend < 0.001). The levels of

Polycyclic aromatic hydrocarbon (PAH) exposure and genetic susceptibility were conductive to genotoxic effects including gene damage, which can increase mutational probability.

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urinary 1-OH-pyr were both significantly associated with increased EGFR-19 and EGFR-21 in both smokers and nonsmokers (both P < 0.001). Additionally, we observed that the urinary 1-OH-pyr concentrations were linearly associated with both EGFR-19 and EGFR-21 only in rs174538 GA+AA genotype carriers (both P < 0.001). Moreover, FEN1rs rs174538 showed modifying effects on the associations of urinary 1-OH-pyr with EGFR-19 and EGFR-21 (both Pinteraction < 0.05). Our findings revealed the linear dose-effect association between exon damage of EGFR and PAH exposure and highlight differences in genetic contributions to exon damage and have the potential to identify at-risk subpopulations who are susceptible to adverse health effects induced by PAH exposure.

Authors: Siqin Chen, Yuefeng He, Maosheng Yan, Yun Zhou, Qinghua He, Jingwen Tan, Binyao Yang

Full Source: Environmental science and pollution research international 2021 Jun 23. doi: 10.1007/s11356-021-15013-y.

PHARAMACEUTICAL/TOXICOLOGY

Evaluation of external contamination on the vial surfaces of some hazardous drugs that commonly used in Chinese hospitals and comparison between environmental contamination generated during robotic compounding by IV: Dispensing robot vs. manual compounding in biological safety cabinet

2021-06-24

Objectives: The aims of the study were to evaluate the external contamination of hazardous drug vials used in Chinese hospitals and to compare environmental contamination generated by a robotic intelligent dispensing system (WEINAS) and a manual compounding procedure using a biological safety cabinet (BSC).

Methods: Cyclophosphamide, fluorouracil, and gemcitabine were selected as the representative hazardous drugs to monitor surface contamination of vials. In the comparative analysis of environmental contamination from manual and robotic compounding, wipe samples were taken from infusion bags, gloves, and the different locations of the BSC and the WEINAS robotic system. In this study, high-performance liquid chromatography coupled with double mass spectrometer (HPLC-MS/MS) was employed for sample analysis.

Results: (1) External contamination was measured on vials of all three hazardous drugs. The contamination detected on fluorouracil vials was

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CHEMWATCH
Bulletin Board
Technical
JUL. 02, 2021

the highest with an average amount up to 904.33 ng/vial, followed by cyclophosphamide (43.51 ng/vial), and gemcitabine (unprotected vials of 5.92 ng/vial, protected vials of 0.66 ng/vial); (2) overall, the environmental contamination induced by WEINAS robotic compounding was significantly reduced compared to that by manual compounding inside the BSC. Particularly, compared with manual compounding, the surface contamination on the infusion bags during robotic compounding was nearly nine times lower for cyclophosphamide (10.62 ng/cm2 vs 90.43 ng/cm2), two times lower for fluorouracil (3.47 vs 7.52 ng/cm2), and more than 23 times lower for gemcitabine (2.61 ng/cm2 vs 62.28 ng/cm2). Conclusions: The external contamination occurred extensively on some hazardous drug vials that commonly used in Chinese hospitals. Comparison analysis for both compounding procedures revealed that robotic compounding can remarkably reduce environmental contamination.

Authors: Hao Ml, Wang T, Zhu Jq, Song Yj, Gong Tj, Zou Lk, Liu J, Yan Jf

Full Source: Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners 2021 Jun 24;10781552211023571. doi: 10.1177/10781552211023571.