GRADIENT

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In This Issue

NEWS AND RECENT GOVERNMENT BRIEFS

US EPA TechDirect Notifies on Availability of NanoRem Toolbox

On April 1 and May 1, 2017, the United States Environmental Protection Agency's (US EPA) TechDirect site provided information on the NanoRem Project, a research project conducted from 2013 to 2017 and funded through the European Commission's Seventh Framework Programme for Research and Technical Development. In response to the relatively slow adoption of nanoremediation, NanoRem was focused on the intensive development and optimization of different nanoparticles, as well as analytical and testing methods, to support the use of nanotechnology in restoring land and water resources. The project focused on facilitating practical, safe, economic, and available nanotechnology for *in situ* remediation, the results of which are summarized in 12 bulletins. Additional materials are available in the NanoRem Toolbox, which serves as the primary repository for detailed results and other information on the project.

The bulletins can be downloaded here:
http://www.nanorem.eu/Displaynews.aspx?ID=938

The NanoRem Toolbox is located here:
http://nanorem.eu/toolbox/index.aspx

Additional information can be found here:
http://www.jdsupra.com/legalnews/epa-techdirect-reports-availability-of-95668/

Article Reviewing and Analyzing TSCA Reform Provisions Related to Nanoscale Materials

On January 26, 2017, Bergeson *et al.*, of Bergeson & Campbell PC, published an article, "Practitioner Insights: A Review and Analysis of the Toxic Substances Control Act (TSCA) Reform Provisions Pertinent to Manufacturers and Processors of Nanoscale Materials," in BNA's *Daily Environment Report*. The article "reviews and analyzes TSCA as amended and focuses narrowly on how new TSCA specifically impacts nanoscale materials." Unlike earlier versions of the TSCA reform bill, which had explicitly addressed nanoscale materials and pertinent nano-related definitions (*e.g.,* "substance characteristics"), the new TSCA rule omitted words and phrases related to nanomaterials (*e.g.,* nano, nanoscale), meaning that "there are no specific or additional requirements that apply explicitly to such materials." In their article, Bergeson *et al.* highlight key sections of the new TSCA that may affect manufacturers and processors of nanomaterials, and recommend that stakeholders carefully review the new TSCA rule and engage with US EPA during the TSCA implementation process.

Bergeson *et al.* (2017) can be downloaded here:
http://nanotech.lawbc.com/wp-content/uploads/sites/539/2017/01/00201189.pdf

Additional information can be found here:
http://www.jdsupra.com/legalnews/new-article-discusses-tsca-reform-56503/

Challenges of Deriving Occupational Exposure Limits

On February 1, 2017, the US National Institute for Occupational Safety and Health (NIOSH) published a blog post by colleagues from Finland regarding occupational exposure limits (OELs) for nanomaterials. Jos Verbeek, of the Finnish Institute for Occupational Health, and Raluca Mihalache, a public health expert at the University of Eastern Finland, systematically searched for proposed OELs for new nanomaterials as part of the development of a new World Health Organization

(WHO) guideline for working safely with nanomaterials. Traditional methods of deriving OELs using animal and human studies have proved challenging in the case of nanomaterials due to the large numbers of nanomaterials and because the length of time required for testing means that companies are unable to quickly commercialize new nanomaterials. In response, scientists have proposed other methods for deriving OELs, including read-across (*i.e.*, comparing a nanomaterial to a similar substance with an existing OEL, such as some nanofibers and asbestos), application of additional safety factors to OELs for traditional-sized substances, grouping nanomaterials with similar toxicities, and quantitative structure-activity relationship modeling. In addition, there is uncertainty in how to express a nanomaterial OEL; in contrast to most OELs that are expressed as a mass concentration (*e.g.,* mg/m^3), nanomaterial OELs may need to account for what aspect of the nanomaterial is associated with its toxicity (*e.g.,* mass concentration, number concentration, surface concentration), which may vary from one group of nanomaterials to another. Available OELs for the same nanomaterial varied substantially among information sources, making it difficult for workplaces to implement OELs. Thus, consensus is needed on how to derive nanomaterial OELs and how they should be made available (*e.g.,* online, in government reports) so that workplaces can put them into effect.

The NIOSH blog post can be found here:
https://blogs.cdc.gov/niosh-science-blog/2017/02/01/nano-oels/

Additional information can be found here:
http://www.jdsupra.com/legalnews/niosh-publishes-blog-item-on-art-and-82395/

Re-evaluation of Titanium Dioxide Nanoparticles in a Food Additive

In September 2016, the European Food Safety Authority (EFSA) published its opinion, after a re-evaluation of the literature, that a food additive of titanium dioxide (TiO_2) nanoparticles (E171) did not constitute a health risk. However, a recent study by Bettini *et al.* (2017) demonstrated that titanium dioxide (TiO_2) nanoparticles in a white food coloring (E171) crossed the intestinal barrier into the bloodstream and into other parts of the body, including animals' livers, increasing the risk of chronic intestinal inflammation and carcinogenesis. This study prompted the French ministers for health and agriculture to request the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) to conduct a safety reassessment of TiO_2 as a food additive. On April 12, 2017, ANSES responded to the request, concluding that, "although the results presented in this publication [Bettini *et al.,* 2017], do not currently call into question EFSA's assessment, the study does demonstrate effects that had not been identified so far, specifically potential promoting effects for carcinogenesis." ANSES recommended that additional studies be conducted to fully characterize the potential health effects associated with ingestion of the food additive.

Bettini *et al.* (2017) can be downloaded here:
https://www.nature.com/articles/srep40373

Additional information can be found here:
https://www.anses.fr/en/content/titanium-dioxide-nanoparticles-food-additive-e171-biological-effects-need-be-confirmed

Additional information can be found here:
http://www.foodqualitynews.com/Regulation-and-safety/Fresh-concerns-over-titanium-dioxide-safety-as-study-prompts-French-re-evaluation?utm_source=newsletter_daily&utm_medium=email&utm_campaign=24-Jan-2017&c=mFNuu%2BUCwy3DgnHyvHTnWw%3D%3D&p2=

Nanomaterials Under the New TSCA Rule and Under REACH

The effective date of US EPA's TSCA Section 8(a) reporting rule for nanoscale materials in commerce has been extended from May 12, 2017, until August 14, 2017. The rule, which was published on January 12, 2017, requires manufacturers and companies that import or process nanomaterials to report certain information to US EPA, including specific chemical identity, production volume, methods of manufacture and processing, exposure and release information, and information on environmental and human health effects. In Europe, nanomaterials are regulated under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), and, recently, the European Chemicals Agency (ECHA) advanced several REACH guidance documents on nanomaterials to the next step in the consultation process. For example, in May 2017, ECHA published a new "Practical Guide," entitled "How to Prepare Registration Dossiers that Cover Nanoforms : Best Practices," which provides the steps that potential registrants need to follow before submission to ECHA in technical dossiers. According to the "Practical Guide," a "nanoform" is "a form of a substance that meets the requirements of the Commission Recommendation for the definition of nanomaterial," which is in turn determined by "the size of the constituent particles of a material," and includes natural, incidental, and manufactured materials. Its goal "is to give clear **recommendations for criteria** for re-

porting nanoforms that can be applied consistently by different actors, while at the same time being sufficiently flexible to be implementable for the diversity of registered substances that may cover nanoforms" [emphasis in original]. Potential registrants need to consider nano-related characteristics (*i.e.,* particle size, particle shape, and surface chemistry) that may influence the hazard profile. ECHA also recommends that registrants report nanoforms and non-nanoforms as separate composition records so that registrants can demonstrate that they have adequately addressed their obligation to collect and generate a base set of relevant data and that the hazard profile for each form is accurate.

Both the TSCA and REACH regulations will have far-reaching implications for companies that conduct business in both Europe and the US, although much is still uncertain about how each framework will be implemented.

Additional information can be found here:
https://www.environmentalleader.com/2017/02/nanomaterials-guidance-reach-review/

The TSCA *Federal Register* notices is available here:
https://www.federalregister.gov/d/2017-00052

The ECHA Practical Guide can be downloaded here:
https://echa.europa.eu/documents/10162/13655/how_to_register_nano_en.pdf/f8c046ec-f60b-4349-492b-e915fd9e3ca0

The Commission Recommendation on the Definition of Nanomaterial can be downloaded here:
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:en:PDF

UK IOM Analysis of OECD Nanomaterial Dossiers

In December 2016, the UK Institute of Occupational Medicine (IOM) released a report that was commissioned by the Center for International Environmental Law (CIEL), the European Environmental Citizens' Organisation for Standardisation (ECOS), and the Oeko-Institute. The IOM report confirmed many of the criticisms and limitations highlighted by Hansen *et al.* (2017), who concluded "that the information in the dossiers present [*sic*] an incomplete portfolio of nanomaterial ecotoxicological evaluations that are difficult to draw substantive conclusions from and that most of the studies were not designed to investigate the validity of the OECD test guidelines." Both Hansen *et al.* (2017) and IOM evaluated the Organisation for Economic Co-operation and Development's (OECD's) Sponsorship Testing Programme for Nanomaterials, which ran from 2007 to 2017, and produced dossiers on the safety of 11 key nanomaterials. IOM screened the raw data in each dossier, and then analyzed all characterization and toxicity data for three selected nanomaterials (fullerenes, single-walled carbon nanotubes, and zinc oxide). The authors highlighted numerous data gaps, concluding that "the dossiers contain insufficient data informing about exposure to workers, humans and ecosystems, which allows the conclusion that the dossiers alone are insufficient to assess the RISK of nanomaterials in the sense of risk being a function of exposure and hazard." The IOM report made recommendations on future steps on the governance of nanomaterials, particularly regarding policy-making in the European Union.

The IOM report can be downloaded here:
http://www.ciel.org/wp-content/uploads/2017/02/IOM-Analysis-of-OECD-dossiers_Full.pdf

Additional information can be found here:
http://www.ciel.org/news/11500-page-oecd-dossiers-11-nanomaterials-little-no-value-assessing-risks/
https://chemicalwatch.com/54512/can-test-guidelines-for-regular-substances-work-for-nanomaterials
https://chemicalwatch.com/54514/the-role-of-the-oecds-nanosafety-testing-programme

Hansen *et al.* (2017) is available for purchase here:
http://pubs.rsc.org/en/content/articlelanding/2016/en/c6en00465b#!divAbstract

OECD Publishes New Report on Safety of Manufactured Nanomaterials

On January 30, 2017, the Organisation for Economic Co-operation and Development (OECD) published a new report as part of its Series on the Safety of Manufactured Nanomaterials: *Alternative Testing Strategies in Risk Assessment of Manufactured Nanomaterials: Current State of Knowledge and Research Needs to Advance Their Use* (No. 80). According to the report, "[a]lternative testing strategies, or strategies that reduce or replace the use of animal testing, have the potential to expedite the evaluation of new and existing substances by reducing the time and resources required to generate data compared

to that of conventional tests. They promise to provide rapid screening and detailed mechanistic and cellular level toxicity information. Ultimately, data from methodologies for alternative testing strategies are expected to improve regulatory decision-making." Over a period of several years, experts from academia, industry, public interest groups, and government researched and discussed how alternative testing strategies could be used in risk analysis to inform human health, ecosystem health, and exposure data needs. The objectives of the project (which were met) included creating a database of methods and alternative testing strategies that were in use, performing a meta-analysis of physical and chemical properties and endpoints, and identifying steps needed for these methods to be widely adopted. One conclusion of the project was that alternative testing strategies are being used for screening and that, in the near future, alternative testing strategies could be developed for read-across or categorization decision making.

The report can be downloaded here:
http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2016)63&doclanguage=en

Additional information can be found here:
http://www.natlawreview.com/article/oecd-publishes-report-alternative-testing-strategies-risk-assessment-manufactured

IARC Publishes New Monograph

The International Agency for Research on Cancer (IARC) recently published a new monograph entitled, "Some Nanomaterials and Some Fibers, Volume 111," that focused on carbon nanotubes (CNTs). The Working Group (WG), which is responsible for gathering, reviewing, summarizing, and evaluating the relevant data, limited the scope of its CNT evaluation to engineered/manufactured CNTs (excluding carbon nanofibers or CNTs designed for medical purposes). The WG acknowledged that CNT preparations vary substantially in terms of diameter, length, atomic structure, surface chemistry, and defects, as well as in physical properties (including mechanical, electrical, optical, thermal characteristics, and specific surface area), aggregation state, and bulk density. In addition to describing their production and use, and the occurrence of CNTs in the environment, the Monograph discusses exposure to CNTs, both to workers and the general population. Regarding regulations and guidelines, "[n]o legal occupational exposure limit has been set for CNT[s]," although various organizations and agencies have made recommendations for occupational exposures. Although animal toxicological data were reviewed, no data were available to the WG to evaluate the potential carcinogenicity of CNTs in humans. The WG concluded that certain multi-walled CNTs (MWCNT-7) are *possibly carcinogenic to humans* (Group 2B) and multi-walled CNTs other than MWCNT-7 and single-walled CNTs are *not classifiable* as to their carcinogenicity in humans.

The Monograph can be downloaded here:
http://monographs.iarc.fr/ENG/Monographs/vol111/mono111.pdf

Toxicity

Buckley, A; Warren, J. Hodgson, A, *et al.* 2017. "Slow lung clearance and limited translocation of four sizes of inhaled iridium nanoparticles." *Part. Fibre Toxicol.* 14(1):5. doi: 10.1186/s12989-017-0185-5.

Disposition of inhaled nanoparticles is of potential concern, in particular for particles with low solubility, which may be more biopersistent than soluble particles. With the primary objective of evaluating long-term clearance and translocation of inhaled, poorly soluble nanoparticles, Buckley and colleagues exposed female rats *via* nose-only exposure to radioactive iridium-192 (I-192) spark-generated nanoparticles (NPs), as a model for poorly soluble NPs, rather than as a toxicologically significant NP. Rats were exposed to I-192 particle sizes of 10, 15, 35 and 75 nm, for 2, 1.25, 3 and 1 hours, respectively. At mass concentrations of 17, 140, 430 and 690 $\mu g/m^3$, respectively, the mass of particles deposited in the lungs would be comparable to that potentially associated with daily use of a consumer spray product for several months. I-192 content in various organs, tissues, and excreta was measured at various times following exposure, for approximately 80 days post-exposure. Whole body clearance during the first few days post-exposure was fast, due to removal from the pelt, the head, and *via* the mucociliary elevator. This initial rapid clearance was followed by a much slower clearance, with size-independent pulmonary retention half-times of several hundred days. This half-time is considerably longer than that estimated for other NPs. However, other studies used aerosols of micron-sized NP agglomerates; evaluated clearance for only 7 days post-exposure, when clearance would be dominated by the initially rapid mucociliary process; or delivered aerosols *via* intratracheal instillation, for which distribution in the lungs would differ from that following inhalation exposure. Less than 0.4%

of I-192 particles deposited in the lung translocated to either the kidney or liver, with I-192 kidney concentrations increasing only up to approximately 30 days post-exposure, and I-192 liver concentrations increasing through the end of the study. For both the kidney and liver, the extent of translocation decreased with increasing particle size. I-192 NPs were excreted mainly *via* the feces. Evaluation of bronchoalveolar lavage fluid (BALF) at 3 and 7 days post-exposure showed a small increase in neutrophils at 3, but not 7 days. Cytotoxicity, as indicated by lactate dehydrogenase in BALF, was increased only immediately following exposure (on day 0). Although the transient increase in neutrophils and cytotoxicity raises some concerns for health effects associated with exposure to poorly soluble NPs, it is not clear that such effects would be observed under expected exposure scenarios involving much lower concentrations than those used in this study.

Exposure

Asbach, C; Alexander, C; Clavaguera, S; Dahmann, D; Dozol, H; Faure, B; Fierz, M; Fontana, L; Iavicoli, I; Kaminski, H; MacCalman, L; Meyer-Plath, A; Simonow, B; van Tongeren, M; Todea, AM. 2017. "Review of measurement techniques and methods for assessing personal exposure to airborne nanomaterials in workplaces." *Sci. Total Environ.* doi: 10.1016/j.scitotenv.2017.03.049.

This paper provides a comprehensive review of commercially available measurement devices for characterizing personal exposures to engineered nanomaterials in the workplace. It distinguishes between two types of available measurement devices, namely personal monitors that are defined as direct-reading instruments capable of providing real-time data on metrics of personal exposure to airborne nanomaterials (*e.g.,* particle number concentration, surface area concentration, average particle diameter), and personal samplers that are used to collect airborne nanomaterials for off-line chemical and physical analyses. The paper draws upon both literature data and unpublished data from the European nanoINDEx project to characterize the accuracy, comparability, and field applicability of the limited, but growing, number of these measurement devices.

Presently available personal monitors include several diffusion charger-based instruments that provide estimates of alveolar lung-deposited surface area (LDSA) concentrations (and in some cases, also estimates of particle number concentrations and average particle diameters), an aethalometer for measurement of black carbon concentrations, and a single personal condensation particle counter (CPC) for measurement of particle number concentrations. Personal samplers are available that preferentially collect nanosized particles onto filters for chemical analysis or microscopic analysis, *e.g.,* the NANOBADGE and personal nanoparticle respiratory deposition (NRD) sampler; that collect nanosized particles onto transmission electron microscope (TEM) grids, *e.g.,* the commercial handheld electrostatic precipitator ESPnano model 100, the partector TEM, and the Thermal Precipitator Sampler (TSP); and that size fractionate nanoparticles and/or their agglomerates, *e.g.,* the miniMOUDI and the Sioutas Cascade Impactor. With the exception of the personal CPC (the PUFP C100) that has been shown to agree with stationary CPCs (*i.e.,* non-personal or full-sized CPCs) within ±10% or better, Asbach *et al.* reported that personal monitors generally have somewhat reduced accuracy and comparability compared to their stationary, full-sized counterparts . For example, the typical accuracy of the LDSA concentration measurements from personal monitors has been shown to be ±30 % *versus* stationary, full-sized instruments. Noting the absence of any studies to assess the comparability of personal nanoparticle samplers with each other, Asbach *et al.* discussed some evidence of minor deviations in particle collection efficiencies for some of the personal samplers, as well as the detection limit challenges posed by the low flow rates of most of the samplers. Overall, Asbach *et al.* concluded that commercially available personal monitors and samplers are "robust and ready for field use with sufficient accuracy and comparability."

Finally, this paper also briefly touches on key components of a measurement strategy for nanoparticles in workplaces, concluding that a combination of personal monitors and personal samplers may be a sound approach for many situations. As emphasized by the study authors, the current generation of personal monitors and samplers may have somewhat reduced accuracy compared to more sophisticated stationary instruments; however, this is more than compensated for by their ability to better measure concentrations representative of the personal breathing zone.

International Conference & Exhibition on Advanced & Nano Materials (ICANM 2017)

August 7-9, 2017
Toronto, Canada

http://icanm2017.iaemm.com/
The ICANM organizing committee invites you to attend the International Conference & Exhibition on Advanced & Nano Materials in Toronto, Canada. The main objective of this conference is to explore the innovations and latest accomplishments in the areas of advanced materials and nanomaterials, focusing on their processing, and the latest developments in the field. Presentation and poster sessions will cover a wide range of topics, such as nanomaterials and nanotechnology, the applications of nanomaterials, bio-nanomaterials, and novel nanomanufacturing methods.

12th International Conference on the Environmental Effects of Nanoparticles and Nanomaterials (ICEENN 2017)

September 3-6, 2017
University of Birmingham, Birmingham, United Kingdom
http://www.birmingham.ac.uk/schools/gees/research/conferences/nano2017/index.aspx
The University of Birmingham invites researchers, regulators, and industry leaders to the 12th International Conference on the Environmental Effects of Nanoparticles and Nanomaterials (ICEENN). There will be presentations and poster sessions focusing on topics such as advancements in nanomaterial analysis methods, surface chemistry of nanomaterials in complex matrices, *in vivo* and *in vitro* toxicology of nanomaterials, and applications of nanomaterials in health and the environment. A preconference workshop will be offered in which attendees can experience hands-on analysis of nanomaterials datasets and learn how to apply risk assessment for regulatory decision making.

6th Sustainable Nanotechnology Organization Conference (SNO 2017)

November 5-7, 2017
Los Angeles, CA
http://www.susnano.org/
The 2017 Sustainable Nanotechnology Organization (SNO) Conference will host a series of sessions organized around selected "systems" within which nanotechnology currently plays or has the potential to play a significant role (*e.g.,* air-water systems, energy systems, food agricultural systems, *etc.*). Scientists and researchers from across the globe will present on the applications and implications of nanotechnology across the respective life cycles of each system. Posters and presentations will aim to identify ways that nanotechnology can improve the sustainability of each system, highlight recent advancements in analytical methods and instrumentation, and integrate knowledge regarding the applications and environmental health and safety implications of nanotechnology.

Good to the Last Drop – Nanocoated Shampoo Bottles Could Help You Squeeze More Shampoo Out of the Bottle

Frustrated by that last bit of shampoo that you have to toss away with the not-quite-empty bottle of shampoo? A new coating developed by Ohio State University scientist Bharat Bhushan could help you avoid wasting those pesky last drops of shampoo and reduce the amount of shampoo sent to landfills. Unlike water-based liquids with high surface tension, such as juice and ketchups, that stick to each other rather than the surface of the bottle, liquids such as shampoo have low surface tension, and tend to stick to the bottle. To decrease the affinity of liquids such as shampoo, Bhushan devised a coating comprised of silica nanoparticles in xylene. The silica particles, which are applied to hot plastic, become embedded in the plastic surface as it cools, forming hooked structures above the surface of the plastic. This surface is then treated with UV light and coated with the neutral molecule fluorosilane. While the shampoo savings per bottle or even per person over the course of a year may not be remarkable, the savings worldwide, both in terms of shampoo and in potential environmental impacts, is significant.

Additional information can be found here:
https://www.newscientist.com/article/2095066-shampoo-bottles-get-nano-makeover-to-squeeze-out-every-drop/

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