June 8, 2021

Invited comments on:

Framework for Risk Assessment of Manufactured Nanomaterials under the *Canadian Environmental Protection Act*, 1999

We are pleased to contribute to pre-consultation on the draft Framework for risk assessment of manufactured nanomaterials (NMs), under *the Canadian Environmental Protection Act*, 1999 (CEPA). The Canadian Environmental Law Association (CELA) provided comments on the need to evaluate nanomaterials as early as 2007 and Prevent Cancer Now (PCN), along with Chemical Sensitivities Manitoba (CSM), provided submissions regarding nanomaterials in 2014[1] and 2016,[2] pertaining to the existing regulatory framework and the need to take a precautionary and preventive approach. We have a long history of engagement with CEPA reform, chemicals management under CEPA, pesticides and the *Pest Control Products Act* (PCPA), and other relevant legislation and regulations, as well as legal reform. Discussion of regulatory challenges and solutions are in section 3 of this submission.

The draft consultation document outlined unique attributes and properties of NMs, noting:

> Different from traditional chemical substances, NMs are designed to exhibit unique attributes (for example, mechanical, catalytic, electrical, optical). NMs have physical-chemical properties that often cannot be predicted based on extrapolation from non-nanoscale substances with the same chemical composition (also referred to as their bulk forms). Engineered characteristics of NMs, or variations of different nanoscale forms of the same chemical substances, can result in different physical-chemical properties, such as size, shape, surface chemistry (for example, identity of surface treated groups) and dissolution rates.[*]

We wish to express concerns that the consultation document does not capture the potential potencies of manufactured NMs, the necessary scientific approaches, nor a substantive commentary and analysis of use of CEPA and the associated, applicable regulatory framework to assess and regulate NMs.

Risk assessment is predicated on hazard assessment plus exposure assessment, which both pose difficult, high-stakes challenges for novel substances not yet deployed or in early days in commerce. New substances data requirements are insufficient to meet the challenges of

[*] Environment and Climate Change Canada and Health Canada. April 2021. Framework for Risk Assessment of Manufactured Nanomaterials under the Canadian Environmental Protection Act, 1999 (DRAFT), p. 7.

substances that, because of their potent attributes, may be used in quantities below notification thresholds.

The present comments cover:

1. Approaches to definitions and unique properties of nanomaterials;
2. Scientific rigour of exposure, hazard and risk assessments; and
3. Features and operationalization of effective regulation (policy) to pre-empt rather than only to react to harms, given the limited data requirements for potent NMs that:
    a. may cause novel effects that may disproportionately affect vulnerable populations and cannot reliably be extrapolated from other substances;
    b. are potentially mobile in organisms and in the environment; and
    c. may be persistent, bioaccumulative, and inherently toxic.

Background

Nanoparticles feature prominently in the continuum of modes of exposure and adverse effects of many substances, such as pollution from combustion (e.g., wildfires, engine exhaust), industrial emissions, chemical drift, particles from clothing with anti-stain or anti-microbial nano-additives, NMs in cosmetics and food packaging.

Airborne nanoparticles travel deep into the lungs, traverse membranes and travel to remote tissues, including the foetus.[3] The particles may cause toxic effects by merit of their surface chemistry, innate chemical effects (as the particle dissolves), or more generally provoke inflammatory responses. These effects can cascade into adverse effects on fetal and child development, and promote chronic diseases and cancers across the life span.

Hazards of NMs do not respect whether the material is "manufactured," and known effects must at a minimum be mirrored in regulatory frameworks, thresholds, information requirements and precautionary approaches. Apart from the chemical toxicities of bulk chemicals, known effects of NMs include the adverse outcomes related to asbestos and dust exposure, and living close to major roadways.[4] The COVID-19 pandemic brought into public focus the reality of even finer airborne aerosol transmission, carrying virions over distances, and deeper into lungs.[5]

1. Definition and Properties of Nanomaterials

The consultation document broadly defines NMs as materials that exist and/or are manipulated at the nano-scale (about 1 to 100 nanometres [nm] in an exterior or interior measure).

The simplest NMs are very small particles of a chemical that is also available in bulk, that is ground up or precipitated from solution. Elaborate molecular chemistry has resulted in NMs with diverse potential, potent biological effects, including those exemplified in the abstracts appended below. **The draft framework makes the very important distinction, to include not only materials with one dimension of 100 nm or smaller, but also**

particles of greater overall size that have fine, nano-scale detail in the structure and/or surface (including surface coatings) that result in unique properties, as well as agglomerated NMs. Consensus has not been reached on this upper size limit; the recommendation by some of 300 nm may capture further important NMs.

Two options are presented to distinguish nanomaterials from regular bulk chemicals, based on either mass, or particle numbers. The mass-based criterion is not included in European Union (EU) or Organization for Economic Cooperation and Development (OECD) NM definitions, and is not supportable given that a vastly greater number of nanoparticles would be needed to counter the mass of a much lower particle fraction of larger pieces, for instance in a coarser screened sample.

NMs should be defined based upon the numerical fraction of particles that are nanoparticles, with the stipulation that the nanoparticle numerical fraction is measured in the final fine powder that may be used for a particular application, such as cosmetics (including sunscreens used on children) or food and supplement additives.

High surface area and nano-scale features of particles may reflect what the consultation document alludes to as "surface chemistry," but the great importance of chemical, electro-chemical and photo-chemical interactions on surfaces as key features for the use of NMs, as well as the root of potential hazards of NMs, could be better communicated. **Surface chemistry as intended, or unintended and incidental to the use of NMs, as well as potential adverse consequences of release of the NM merit further discussion, including how unique features affecting potency must be mirrored in data requirements for assessment**.

Valuable (and potentially hazardous), unique properties include speeding chemical reactions (catalysis) and effects on chemical pathways, as substances interact with NM surfaces (including internal surfaces of particles with nano-scale structures). For example: acceleration of oxidative reactions is cited as a basis of antimicrobial effects on surfaces; oxidative stress is also at the root of diverse harms in non-target species, including humans.

Entry, Fate and Exposure – some questions to be addressed

As numbers and releases of NMs increase, from products in use and from wastes, to land, water and air, how are humans and the environment exposed directly to NMs? How do NMs enter the environment; what is the environmental and biological fate (longevity of intact particles, degradation of particles or novel aspects of particles such as coatings, or total dissolution)? I.e., is there a mechanism by which the nanomaterial will be degraded or dissolved, will it persist, and if so, will it be biologically available? How may persistent NMs continue to circulate, or be remobilized from environmental "sinks"? These questions should not remain unanswered, until the NMs are actually detected in water, air, food and biomonitoring.

Precautionary aspects of environmental fate and effects

Environmental fate of NMs cannot be generalized.

- Some metal-containing materials will dissolve (e.g., zinc oxide) while others will remain in particles (e.g., titanium dioxide);
- Some organic NMs may be degraded by microbes whereas some plastics are considered persistent;
- A variety of environmental interactions are possible in aqueous media, whereas some may persist with catalytic capabilities intact over longer periods;
- Toxic chemicals such as perfluorinated alkyl substances (PFAS) that may be incorporated into materials as nano particles ; and
- Some (e.g., nano plastic particles) may absorb other chemicals from the environment, and enhance bioaccumulation of organic toxicants in the food chain.

As research, tools and supporting data are developed, truly precautionary assumptions should be formulated, looking forward to further models, measures and supporting data (p10, consultation document). **The assumptions underlying choices of groupings, read-across and QSAR methods may to some degree pre-determine conclusions. In the interest of scientific rigour, the methods, choices, data availability and justifications should be open, transparent, and subject to external review and consultation. Otherwise overly narrow, potentially biased assumptions may be "baked into" assessments, without acknowledgement of uncertainties. In particular, the means by which the Precautionary Principle is incorporated into methods, models and analyses should be explicitly stated and may be assessed as case studies.**

Biological effects

Biological effects of nanomaterials and potential interactions with other environmental factors depend upon the route of exposure, tissues exposed, timing and dose, and age and stage of the organism. Potential effects range from local irritation to systemic impacts over longer periods of exposure. For example, inhalational exposures may interact with the olfactory nerve and transient receptor proteins (TRPs) in a manner similar to volatile chemicals, and promote the constellation of neurological and subsequent systemic symptoms seen with multiple chemical sensitivities. NMs in the placenta or foetus interfere with development. NMs in the lung may mimic asbestosis and culminate in chronic lung disease and mesothelioma. That said, while the risk assessment framework discusses threshold toxicants, noticeable by their absence are:

- non-linear effects on endocrine functions and reproduction;
- interactions with other exposures; and
- carcinogenicity, that is mentioned only in a footnote.

NMs can be potent, with multiple applications, and could fall through environmental monitoring, adverse effects and regulatory cracks

Manufactured NMs are being devised to be very potent, in applications from chemistry to medicine; some advances are summarized in the attached abstract collection. Regardless of whether particular NMs are approved eventually under other legislation for pest control or medical indications, precautionary approaches in the absence of specific data should bear in mind the potential capabilities and potency of NMs. As evidenced in the recent research attached, these include dispersion throughout the organism, accumulation of hazardous substances in the environment and subsequent transfer into organisms (e.g. nanoplastics), drug delivery, catalysis of chemical reactions (including with activation by radiofrequency or light irradiation), or even to "seek and destroy" particular cells when activated with radiofrequency radiation. Particles deposited on surfaces or embedded in materials are postulated to result in "self-disinfecting" surfaces, but none of these have been registered by Health Canada as either a medical device for public use, or a pest control product. The Pest Management Regulatory Agency (PMRA) recently announced the intention to assess and regulate air disinfection equipment that utilizes ultraviolet light or ozone, but Health Canada has not to our knowledge addressed disinfecting surface coatings or NMs in materials for efficacy, or health or environmental effects of chemicals/particles shed from the material. **There appears to be gaps in assessment, regulation and monitoring of NM containing "disinfecting" items, for efficacy, as well as eventual biological and environmental fate of the NMs as they are abraded and dissipated.**

A "Nano Lens" for environmental fate and potential biological effects

Manufactured materials may degrade to biologically accessible and potentially toxic nanoparticles

Waste and litter has become a "poster child" for environmental persistence, as it eventually degrades to NMs. One example is manufactured plastic, as large pieces are obviously harmful to wildlife, but then degrade to biologically accessible and harmful smaller particles and eventually to NMs. Many formulations and types of plastic products share this fate, eventually accumulating in biological "sinks" that may include environmental features (e.g., sediment) and biota. The plastic may also accumulate and transfer toxic substances to new environmental receptors.

2. Weight of Evidence and Scientific Rigour

Use of "weight of evidence" (WoE) methods is stated but not referenced in the consultation document. This approach is required for human health and environmental assessments under the *Canadian Environmental Protection Act,* 1999 (CEPA). The Act includes no definition or standard for WoE assessments, but in 2018, Health Canada published *Weight of evidence: general principles and current applications at Health Canada*.[6]

Assessment of risks of potentially toxic exposures hinges on two independent variables: 1) the hazard of the exposure (including dose-response curves for relevant end-points, for humans and other species as information is available, as well as laboratory and computational models – roughly in order of perceived reliability); and 2) the potential

magnitude or dose of exposures via air, water, food, everyday products, workplace exposures. The 2018 WoE guidance mentions the potential use of systematic review methods, but does not mention the necessary rigour and methods to assemble the studies and associated data that may then contribute to lines of evidence for particular outcomes. These steps include:

1. publishing and consulting on review protocols;
2. conducting a thorough systematic review of the peer-reviewed literature;
3. synthesizing issue/topic-specific research and then grading the body of evidence. Best practices are to include *all* studies with potentially relevant data, and then to upgrade or downgrade evidence later in the process;
4. assessing non-monotonic dose responses, as are seen with carcinogens, endocrine disrupting substances (EDCs) and are likely with NMs; and
5. being based on sufficient, up to date, relevant (bio)chemistry, toxicology, and human and environmental exposures data.

Difficulties assessing substances that cause non-linear responses, such as carcinogens, EDCs and NMs are inherent in the hazard/risk methodology and framework, where experimental protocols entail decreasing doses of a given substance from harmful levels, and then to regulate based on the highest dose of a give substance at which the high dose harms do not occur. In this way, environmentally relevant and very different effects seen with lower and environmentally relevant levels of EDCs may not be detected and regulation may not be protective.

As discussed in Section 3, data gaps and insufficient rigour arise under the Chemicals Management Plan (CMP) due to use of available data collected (or not) under CEPA.

Prescriptive WoE methods have been developed in a number of contexts:

1. in health care, detailed methodologies, with descriptions of strengths and discussions of nuances of scientific review steps have been developed by the international Cochrane collaboration,[7,8] and the US Agency for Health Research Quality (AHRQ),[9] using methods that are summarized on the Preferred Reporting Items for Systematic Reviews and meta-Analyses (PRISMA) website; [10,11]
2. in environmental epidemiology, as concepts for randomized controlled trials of drugs have been applied to observational (non-randomized studies and mixed methods) studies in health care, and then for environmental health methods.[12,13] Grading of Recommendations Assessment, Development and Evaluations (GRADE) initiatives for environmental epidemiology are ongoing, with the GRADE group being led by Holger Schunemann at McMaster University.

Examples of systematic review with weighing of evidence in environmental health include studies of bisphenol-A[14] and alternative bisphenols,[15] that are also EDCs. As well, immunotoxicity of per- and poly-fluorinated alky substances was examined by the US

National Toxicology Program, according to a protocol[16] and subsequently published in a monograph.[17]

3. The European Chemicals Agency (ECHA) has carried these methods forward in numerous topics, and provides a brief overview;[18]

4. Work is ongoing as to how to use animal and *in vitro* New Approaches Methodologies (NAMs), particularly for NMs. Current indications in the EU appear to support not implementing a suite of animal experimentation if the NAMs indicate harmful effects, such as genetic damage or endocrine disruption. Taking precautionary actions based on NAMs is expected to meet some resistance among commercial interests.

3. Nanomaterial Assessment and Regulation

The Canadian Environmental Law Association and Prevent Cancer Now provided comments regarding assessment of NMs in 2014[1] and 2016,[2] and the following observations and excerpts remain pertinent:

We do not believe that the existing framework for assessment of substances under the CMP is sufficient to prevent adverse human health and environmental impacts of NMs. Not only may some uses of NMs fall under the authority of other legislation (potentially leaving gaps in oversight), NM specific concerns may circumvent the assessments and actions necessary to prevent adverse effects of potent NMs.

Regulatory Data Requirements

CEPA does not specifically recognize NMs, creating substantial challenges to establishing appropriate criteria to identify NMs, to outline requirements for meaningful assessment, to require data and, where warranted, to manage NMs.

Regulating NMs under the current system will not be adequate for engineered NMs that are potent and hence are potentially lower-volume substances with limited or no reporting requirements:

- data should be required under lower, nano-appropriate reporting thresholds;
- assessment trigger thresholds should be reduced to adequately capture more NMs, including NMs that are present in manufactured articles.

The regulatory system should require nano-specific information, including physical/chemical and toxicological that would differentiate the NM from the micronized or macroform of the substance, when applicable.

Data and methods are necessary to enable assessment of the behaviour and effects of NMs in the context of actual uses, and the impacts of environmentally relevant exposure levels.

The current regulatory framework for NMs would mean that NMs may be permitted into the Canadian marketplace without requirements for ongoing surveillance and monitoring. There is no rigourous reporting or monitoring program on NMs. The NPRI, which is Canada's main pollution release and transfer inventory does not track releases and transfer of NMs. Further consideration in the context of this consultation should be focused on monitoring (including biomonitoring) and surveillance needs associated with NMS in the Canadian market and those NMs notified under CEPA. A substantial delay is entrenched in the regulatory framework associated with the assessment and management of toxic chemicals and nanomaterials.

Assessment Approaches

Lifecycle considerations are important to characterize behaviour of NMs that are used in a product, released with wear, handled at end of life, and are potentially incorporated in recycled materials and items. Furthermore, identification and evaluation of all breakdown products or metabolites and their impacts on the environment and human health are necessary.

Barriers to obtaining/providing information on existing NMs in Canada include the absence of a clear legislative framework in Canada to more clearly address NMs. Significant data gaps are expected for existing NMs, as these substances have been in commerce for many years without industry always acknowledging their use.

The potency, and therefore small quantities of NMs necessary to achieve desired ends may result in substantial gaps in information being provided to the Government of Canada. Although "Nanomaterials" was added to the title of the "New Substances Notification For Chemicals, Biochemicals, Polymers and Biopolymers (including Nanomaterials)" form, the "New Substances Notification Regulations " and "Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers" have not changed since 2005. Reporting requirements are scaled according to quantities manufactured and imported, with no information required for less than 100 kg; information requirements particularly at lower tiers do not address data required to assess health and environmental risks of NMs.

Key limitations with the NSN Regulations for assessing nanomaterials were highlighted and presented in 2014 by CELA and CSM:

> In Canada, the information required at the notification stage for the lowest volume trigger of a new substance are not sufficiently robust to identify accurately the properties of a new nanomaterial in terms of concern and no-concern, and subsequently to use the data for selecting read-across/analogues purposes or even a robust risk assessment. Requesting that industry supplies as much scientific data as possible at the point of notification is not a solution as this is viewed as more of a voluntary measure. A mandatory expanded dataset for manufactured NMs at the notification stage for the NSNR, including parameters from the categories in the

classification scheme are more likely to result in a database with less data gaps and one that would be more useful in determining substances of concern /no-concern and the accurate use of read-across/analogue information. This would require the present Canadian New Substances Regulations to be amended with a significantly lower notification trigger and an expanded schedule requiring substantial safety data to reflect the unique features of nanomaterials. There was no mention of the development of a systematic framework that would help to characterize uncertainty when read-across or analogue data are used to fill in data gaps. Furthermore, the proposed framework does not require the rationale to be provided in situations where there is the possibility of the subsequent use of analogues or read-across data to conduct assessments of other nanomaterials where validation would be required. The development of any such framework should be transparent and include public input.

Recommendations:

- The proposed classification scheme should be expanded for data parameters in each category. Similarly, using accurate scientific data to indicate or validate which parameters are the most appropriate for selection when considering the use of read across/analogues is needed.
- Canada's New Substances Notification Regulations under CEPA 1999 should be amended to address ongoing concerns associated with the risk assessment framework for nanomaterials. The risk assessment approach for nanomaterials should include parameters that are nano-specific at the point of notification (e.g. agglomeration/aggregation, particle size distribution, conductivity, flexibility), starting at the lowest level of notification.
- Further consideration and rationale should be given to review the validity of CBI claims in the proposed framework. In particular, claims of CBI related to human and occupational health should not be protected through CBI.
- Each government should fill in data gaps using its full authority under their respective legislation. Lack of data should trigger measures to prevent or severely restrict the use of the nanomaterial.[†]

The concerns with using the NSNR for nanomaterials remain relevant today as Canada prepares to release the Consultation Document outlining an approach for assessing nanomaterials. The specific purpose as stated:

> ... to establish a framework for the risk assessment of NMs, including both existing NMs on the DSL, and new NMs notified under NSNR(C&P). The framework describes the human health and environmental risk assessment considerations that

[†] CELA and CSM. March 28, 2014. NGO response to Work Element 2 from the Regulatory Cooperation Council's (RCC's) Nanotechnology Results Workshop/Webinar – January 14, 2014. Submission to Environment Canada and Health Canada. Accessed: https://cela.ca/wp-content/uploads/2019/07/CELA-CSM-Nanomaterials-response.pdf

are modified from risk assessment methods traditionally used for chemicals, and would not necessarily be limited to those used under the Chemicals Management Plan (CMP). This framework will provide guidance to regulators on how NMs are to be assessed for their risk to the environment and human health under CEPA. Additionally, the publication of this document serves to inform stakeholders and the general public about the approaches and considerations used by the Government of Canada for assessing NMs under CEPA.[‡]

NSN Regulations must be addressed. The lack of discussion is a significant gap in the Consultation Document. Information provided on CEPA and the risk assessment framework is not extended to the structure of the NSN and how it is applied in notification processes. Concerns that have been raised by NGOs since 2007 related to the use of the New Substances Notification Regulations for NMs outline gaps in Canada's approach. The risk assessment approach presented in the Consultation Document gives a false impression that the risk assessment process is exhaustive, comprehensive and transparent. This is inaccurate. We wish to reiterate that the NSN framework is significantly limited by the absence of public engagement and transparency. Decisions to allow NMs into Canada remain a secretive process. Furthermore, the schedules under NSN Regulations will determine what and how much information (particularly, toxicity data, as well as quantities and fate) is required in the notification forms and the associated timelines (5 days to 75 days) for the government to complete their review of the notification form means that requirements for a fulsome toxicity data set is not necessary for decisions to be made on the NMs.

Needed: a critical analyses or review of the use of the NSN Regulations for assessing NMs. The Consultation Document does not include key information on how the NSN Regulations have been used to assess NMs to support its approach in the NSN Regulations. Some key information that should be provided includes:

- Number of notifications for NM in Canada;
- Number of notifications for NM permitted for use (and restrictions);
- Number of the notifications that led to prohibition in Canada;
- Number of notifications for NM which involve the import of products containing NMs; and
- Number of NMs which have been added to the DSL, according to chemistry, use, and restrictions to limit releases and exposures to humans and to the environment.

[‡]Environment and Climate Change Canada and Health Canada. April 2021. Framework for Risk Assessment of Manufactured Nanomaterials under the Canadian Environmental Protection Act, 1999 (DRAFT).

We urge the government to consider conducting this review as an output of this initial consultation process.

Lack of transparency in the New Substances Notification Regulation framework parallels concerns regarding approaches, prioritization and assessment of existing NMs on Canada's **Domestic Substances List (DSL),** as well as high reporting thresholds for the **National Pollutant Release Inventory (NPRI).**

As acknowledged in the consultation document, a lack of consensus for the nomenclature of nanomaterials adds to the complexity of identifying and obtaining comprehensive, unambiguous information on nanomaterials, further complicating enumerating substances and quantities in commerce and the environment.

Prioritization, and subsequent assessment of existing NMs is reactive; i.e., after the fact. As discussed by Hjorth,[19] this approach to NM regulation is grounded in a risk-based approach, wherein assessments are conducted after substances build up, harm ensues and is eventually proven. We continue to urge the government to establish an approach for nanomaterials through a regulatory framework that is rigorous and precautionary, and one that promotes prevention at the onset.

A preventative approach would emphasize avoiding inherently hazardous properties that could be associated with NMs. Essential aspects include alternatives assessment and assessment of need or "essentiality" (as now promoted in the European Union),[20] rather than an approach that relies heavily on estimating exposure risks.

Given the inherently hazardous properties of many NMs, a preventative approach must require declaration/labelling of NMs, adequately analyzes of imported NMs and manufactured products containing NMs before they are allowed to enter the marketplace. Establishing this knowledge base will result in substantial strides towards the protection of the environment and human health.

A comprehensive Canadian inventory of NMs in imported or manufactured products (consumer and commercial) containing NMs, is particularly necessary when relying upon risk-based assessments. Compiling information on these substances on the DSL is not feasible until the existing nanomaterials have been verified and more information about their uses has been identified. On July 25, 2015, a Notice was issued in the Canada Gazette, Part I: Vol. 149, No. 30 – July 25, 2015 under section 71 of the Canadian Environmental Protection Act, 1999 (CEPA 1999). The Notice applied to the nanoscale forms of 206 substances listed in the Notice. The purpose of the section 71 Notice was to determine the commercial status of these nanomaterials in Canada for the 2014 calendar year, and every person to whom the Notice applied was required to comply by February 23, 2016. What DSL substances of the 206 identified in 2015 have been confirmed to have NMs and have they been notified? The consultation document refers to Section 71 notices, but there is no indication of the scale of the list of NMs (manufactured or otherwise) in commerce in Canada.

A *mandatory* survey should be initiated in order to obtain essential information for a meaningful and accurate prioritization process. The questions should be specific, to attempt to fill the current data gaps. While this may create significant challenges and it is a labour intensive effort, the government has been effective in information gathering through the use of other surveys to reach out to manufacturers and suppliers, and should communicate to the industry stakeholders the importance of this type of information. For imported NMs and NM-containing goods, it is essential that reporting responsibility lies with the importer. Eventually, this information would better inform the government as to the ingredients of imported, manufactured goods entering the country and the end of life management options.

Ethical considerations

Canada cannot detect effects of environmental exposures on human and environmental health without exposure data. This would elevate data on uses and releases of substances under the CMP above strictly regulatory needs to the standards required for exposure data, that can be used to investigate relationships between exposures and health outcomes.

Noticeably absent from the consultation document is the mention of the use of NMs in consumer products, as there is generally inadequate labeling as to their presence. A key question that should be required in the approach on NM is consideration of the value of a NM to address a societal need. This requires an open dialogue with stakeholders incorporated in the assessment approach; consumers should be more aware of the ingredients in products they use.

Vulnerable Populations

In light of potential uses for NMs, the limited knowledge, awareness (and potential avoidance choices) and therefore protections, there should be explicit consideration of vulnerable populations such as workers and their communities, pregnant women, the elderly, those with allergies, sensitivities and chronic diseases, low-socio-economic populations, and First Nations and the Inuit. Children are especially vulnerable to NM-containing products that may be targeted to this particular population, as well as the hazardous residues from wear.

The CELA and CSM 2014 in response to the *Consultation on RCC Nanotechnology Policy Principles for Decision-Making Concerning Regulation and Oversight of Nanotechnology and Nanomaterials* made the following comments and recommendations in recognition of the potential impacts of NMs to Vulnerable populations and vulnerable ecosystems:

> The current regime to evaluate and manage nanomaterials in Canada does not provide any consideration into how it will address unique vulnerabilities by subpopulations such as workers, children, or developing fetuses. In addition, special consideration should be given to the effects and detection of nanomaterials in vulnerable ecosystems in Canada, such as the Great Lakes-St. Lawrence River

Basin or the arctic regions. For these regions, adequate monitoring programs are necessary to track the presence and fate of nanomaterials.

Recommendation:

The government's assessment process should require special consideration for the potential effects of nanomaterials on vulnerable populations such as workers, developing fetuses and children as well as impacts to vulnerable ecosystems such as the Great Lakes-St. Lawrence River Basin or the arctic regions.[§]

The draft Consultation Document, briefly mentions vulnerable populations in the Risk assessment framework sections 3.6.2 and 3.82; however, very few details are presented on what data will be collected and how the data is to be reviewed and weighed in the overall risk assessment framework. The NSN Framework with prescribed Schedules may not adequately address threats, particularly to vulnerable groups.

Risks posed to Vulnerable Populations are proposed to be addressed using a Margin of Exposure (MoE) approach. Inherent in this approach is that a safe level exists. For many NMs, such as those with a high aspect ratio or containing EDCs, there is no safe level of exposure.

Labelling

Labelling is noticeably absent from the consultation document as is the mention of ethical considerations for the use of NMs in consumer products. Labeling the presence of NMs requires an open dialogue with stakeholders; consumers should be more aware of the ingredients in products they use, and lower-risk, least-toxic options.

Conclusion

Numbers, quantities, and diversity of properties, applications and associated risks of manufactured, novel NMs are increasing rapidly. The consultation document is in recognition of the fact that it is essential that the Government of Canada becomes aware of the existence, hazards and exposures to these potentially potent substances as they are imported in manufactured goods, and for Canadian industries; and is able to respond in a nimble fashion to prevent emerging risks.

We support a broad definition of manufactured NMs, recognising catalytic and other particles and agglomerations larger than 100 nm.

Scientific methods and supporting data collection requires more extensive and rigorous efforts, both for regulation and for public and environmental health in Canada.

[§] CELA and CSM. 2013. Re: Response to Consultation on RCC Nanotechnology Policy Principles for Decision-Making Concerning Regulation and Oversight of Nanotechnology and Nanomaterials. Accessed: https://cela.ca/wp-content/uploads/2019/07/957CSMCELAresponseNanomaterialsRCC.pdf

Novel NMs with exaggerated claims might pose risks while under-delivering on benefits. Efficacy has not been a consideration under CEPA, but manufactured NMs bring this concern to the fore. Efficacy considerations are central to alternatives assessment, that is a hallmark of a modernized chemical regulatory regime to address mounting inter-related environmental harms from pollution, ecological decline and the climate crisis.

NMs are used for many purposes, and there is that risk that "anyone's job is done by no-one." This became apparent during the pandemic for manufactured NMs that are purported to have disinfecting properties, as products may be considered pesticides under the purview of the PMRA, or medical devices under the purview of Health Canada. Thus, this consultation should extend beyond CEPA governance.

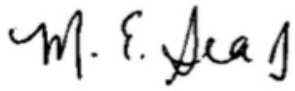
The consultation document outlines important concerns, but lacks the necessary data, and alternatives assessments (including the null alternative), while relying upon regulations dating from 2005. This means that the outlined measures will fall short of what is necessary to restrict as necessary the introduction of NMs, and to track, assess and regulate manufactured NMs in ways that prevent risks and harms.

This consultation is an opportunity to introduce a "nano-lens" to environmental fate considerations; this has come into focus in the context of an escalating global burden of persistent nano-plastics, along with their absorbed burdens of toxic chemicals.

We are pleased to see these steps to address NMs, we thank you for this opportunity, and we would be happy to assist this important endeavour with further information, and discussion.

Sincerely,

Prevent Cancer Now



Meg Sears PhD
Chair
Meg@PreventCancerNow.ca

Canadian Environmental Law Association

Fe de Leon, MPH
Researcher and Paralegal
deleonf@cela.ca

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ATTACHMENT

Behaviours and Effects of Novel Nanomaterials ~ Some Abstracts of Peer-Reviewed Articles

Utembe, Wells, Victor Wepener, Il Je Yu, and Mary Gulumian. "**An Assessment of Applicability of Existing Approaches to Predicting the Bioaccumulation of Conventional Substances in Nanomaterials**." *Environmental Toxicology and Chemistry* 37, no. 12 (2018): 2972–88. https://doi.org/10.1002/etc.4253.

The experimental determination of bioaccumulation is challenging, and a number of approaches have been developed for its prediction. It is important to assess the applicability of these predictive approaches to nanomaterials (NMs), which have been shown to bioaccumulate. The octanol/water partition coefficient (KOW) may not be applicable to some NMs that are not found in either the octanol or water phases but rather are found at the interface. Thus the KOW values obtained for certain NMs are shown not to correlate well with the experimentally determined bioaccumulation. Implementation of quantitative structure–activity relationships (QSARs) for NMs is also challenging because the bioaccumulation of NMs depends on nano-specific properties such as shape, size, and surface area. Thus there is a need to develop new QSAR models based on these new nanodescriptors; current efforts appear to focus on digital processing of NM images as well as the conversion of surface chemistry parameters into adsorption indices. Water solubility can be used as a screening tool for the exclusion of NMs with short half-lives. Adaptation of fugacity/aquivalence models, which include physicochemical properties, may give some insights into the bioaccumulation potential of NMs, especially with the addition of a biota component. The use of kinetic models, including physiologically based pharmacokinetic models, appears to be the most suitable approach for predicting bioaccumulation of NMs. Furthermore, because bioaccumulation of NMs depends on a number of biotic and abiotic factors, it is important to take these factors into account when one is modeling bioaccumulation and interpreting bioaccumulation results. Environ Toxicol Chem 2018;37:2972–2988. © 2018 SETAC

Neuberger, Tobias, Bernhard Schöpf, Heinrich Hofmann, Margarete Hofmann, and Brigitte von Rechenberg. "**Superparamagnetic Nanoparticles for Biomedical Applications: Possibilities and Limitations of a New Drug Delivery System**." *Journal of Magnetism and Magnetic Materials*, Proceedings of the Fifth International Conference on Scientific and Clinical Apllications of Magnetic Carriers, 293, no. 1 (May 1, 2005): 483–96. https://doi.org/10.1016/j.jmmm.2005.01.064.

Nanoparticles can be used in biomedical applications, where they facilitate laboratory diagnostics, or in medical drug targeting. They are used for in vivo applications such as contrast agent for magnetic resonance imaging (MRI), for tumor therapy or cardiovascular disease. Very promising nanoparticles for these applications are superparamagnetic nanoparticles based on a core consisting of iron oxides (SPION) that can be targeted through external magnets. SPION are coated with biocompatible materials and can be functionalized with drugs, proteins or plasmids. In this review, the characteristics and applications of SPION in the biomedical sector are introduced and discussed.

Guo, Ziyi, Joseph J. Richardson, Biao Kong, and Kang Liang. "**Nanobiohybrids: Materials Approaches for Bioaugmentation**." *Science Advances* 6, no. 12 (March 1, 2020): eaaz0330. https://doi.org/10.1126/sciadv.aaz0330.

Nanobiohybrids, synthesized by integrating functional nanomaterials with living systems, have emerged as an exciting branch of research at the interface of materials engineering and biological science. Nanobiohybrids use synthetic nanomaterials to impart organisms with emergent properties outside their scope of evolution. Consequently, they endow new or augmented properties that are either innate or exogenous, such as enhanced tolerance against stress, programmed metabolism and proliferation, artificial photosynthesis, or conductivity. Advances in new materials design and processing technologies made it possible to tailor the physicochemical properties of the nanomaterials coupled with the biological systems. To date, many different types of nanomaterials have been integrated with various biological systems from simple biomolecules to complex multicellular organisms. Here, we provide a critical overview of recent developments of nanobiohybrids that enable new or augmented biological functions that show promise in high-tech applications across many disciplines, including energy harvesting, biocatalysis, biosensing, medicine, and robotics.
We review recent advances and prospects of interfacing functional nanomaterials with biological systems for nanobiohybrids.

El-Shahawy, Ahmed AG, SA Abdel Moaty, A. H. Zaki, Nada A. Mohamed, Yasser GadelHak, R. K. Mahmoud, and A. A. Farghali. "**Prostate Cancer Cellular Uptake of Ternary Titanate Nanotubes/CuFe2O4/Zn-Fe Mixed Metal Oxides Nanocomposite**." *International Journal of Nanomedicine* 15 (January 30, 2020): 619–31. https://doi.org/10.2147/IJN.S228279.

Prostate Cancer Cellular Uptake of Ternary Titanate Nanotubes/CuFe2O4/Zn-Fe Mixed Metal Oxides Nanocomposite Ahmed AG El-Shahawy,1 SA Abdel Moaty,2 AH Zaki,1 Nada A Mohamed,2 Yasser GadelHak,1 RK Mahmoud,2 AA Farghali1 1Materials Science and Nanotechnology Department, Faculty of Postgraduate Studies for Advanced Sciences (PSAS), Beni-Suef University, Beni-Suef, Egypt; 2Chemistry Department, Faculty of Science, Beni-Suef University, Beni-Suef, EgyptCorrespondence: Ahmed AG El-Shahawy Tel +201226798209Email Ahmedelshahawy382@yahoo.comBackground: Certainly, there is a demand for stronger recognition of how nanoparticles can move through the cell membrane. Prostate cancer is one of the forcing sources of cancer-relevant deaths among men. Aim of the Work: The current research studied the power of prostate cancer cells to uptake a ternary nanocomposite TNT/CuFe2O4/Zn-Fe mixed metal oxides (MMO).Methodology: The nanocomposite was synthesized by a chemical method and characterized by a High-resolution transmission electron microscope, Field emission scanning electron microscope, X-ray diffraction, Fourier transmission infra-red, X-ray photoelectron spectroscopy, dynamic light scattering. Besides, it was implemented as an inorganic anticancer agent versus Prostate cancer PC-3 cells.Results: The results revealed cellular uptake validity, cell viability reduction, ultra-structures alterations, morphological changes and membrane damage of PC-3 cells.Conclusion: The prepared ternary nanocomposite was highly uptake by PC-3 cells and possessed cytotoxicity that was dose and time-dependent. To conclude, the study offered the potential

of the investigated ternary nanocomposite as a promising prostate anticancer agent.Keywords: cytotoxicity, inorganic nanomaterials, prostate cancer.

Collection of U.S. Government information on Nanomaterials. Nano.gov NNI Environmental, Health, & Safety-Related Documents https://www.nano.gov/node/1164

Greenemeier, Larry, and Larry Greenemeier. "Study Says Carbon Nanotubes as Dangerous as Asbestos." Scientific American. Accessed March 15, 2018. https://www.scientificamerican.com/article/carbon-nanotube-danger/.

Avramescu, Mary-Luyza, Marc Chénier, S Palaniyandi, and Pat E Rasmussen. "Solubility of Metal Oxice Nanomaterials in Biologically Relevant Fluids Compared to Distilled Water," 1, 2021. https://video.isilive.ca/hcsc/2021-01/english/abstracts/036/.

Nazemof, N, N Assudani, D Breznan, Y Dirieh, E Blais, L Johnston, J Gomes, A Tayabali, and P Kumarathasan. "Examining Relative in Vitro Toxic Potencies of ZnO Nanoforms," 1, 2021. https://video.isilive.ca/hcsc/2021-01/english/abstracts/145/.

Tortella, Gonzalo R., Olga Rubilar, María Cristina Diez, Jorge Padrão, Andrea Zille, Joana C. Pieretti, and Amedea B. Seabra. "**Advanced Material Against Human (Including Covid-19) and Plant Viruses: Nanoparticles As a Feasible Strategy**." *Global Challenges* 5, no. 3 (2021): 2000049. https://doi.org/10.1002/gch2.202000049.

The SARS-CoV-2 virus outbreak revealed that these nano-pathogens have the ability to rapidly change lives. Undoubtedly, SARS-CoV-2 as well as other viruses can cause important global impacts, affecting public health, as well as, socioeconomic development. But viruses are not only a public health concern, they are also a problem in agriculture. The current treatments are often ineffective, are prone to develop resistance, or cause considerable adverse side effects. The use of nanotechnology has played an important role to combat viral diseases. In this review three main aspects are in focus: first, the potential use of nanoparticles as carriers for drug delivery. Second, its use for treatments of some human viral diseases, and third, its application as antivirals in plants. With these three themes, the aim is to give to readers an overview of the progress in this promising area of biotechnology during the 2017–2020 period, and to provide a glance at how tangible is the effectiveness of nanotechnology against viruses. Future prospects are also discussed. It is hoped that this review can be a contribution to general knowledge for both specialized and non-specialized readers, allowing a better knowledge of this interesting topic.

Pardhiya, Sonali, Usha Singh Gaharwar, Rohit Gautam, Eepsita Priyadarshini, Jay Prakash Nirala, and Paulraj Rajamani. "**Cumulative Effects of Manganese Nanoparticle and Radiofrequency Radiation in**

Male Wistar Rats." *Drug and Chemical Toxicology* 0, no. 0 (October 28, 2020): 1–13. https://doi.org/10.1080/01480545.2020.1833905.

Fournier, Sara B., Jeanine N. D'Errico, Derek S. Adler, Stamatina Kollontzi, Michael J. Goedken, Laura Fabris, Edward J. Yurkow, and Phoebe A. Stapleton. "**Nanopolystyrene Translocation and Fetal Deposition after Acute Lung Exposure during Late-Stage Pregnancy**." *Particle and Fibre Toxicology* 17 (October 24, 2020). https://doi.org/10.1186/s12989-020-00385-9.

Background
Plastic is everywhere. It is used in food packaging, storage containers, electronics, furniture, clothing, and common single-use disposable items. Microplastic and nanoplastic particulates are formed from bulk fragmentation and disintegration of plastic pollution. Plastic particulates have recently been detected in indoor air and remote atmospheric fallout. Due to their small size, microplastic and nanoplastic particulate in the atmosphere can be inhaled and may pose a risk for human health, specifically in susceptible populations. When inhaled, nanosized particles have been shown to translocate across pulmonary cell barriers to secondary organs, including the placenta. However, the potential for maternal-to-fetal translocation of nanosized-plastic particles and the impact of nanoplastic deposition or accumulation on fetal health remain unknown. In this study we investigated whether nanopolystyrene particles can cross the placental barrier and deposit in fetal tissues after maternal pulmonary exposure.

Results
Pregnant Sprague Dawley rats were exposed to 20 nm rhodamine-labeled nanopolystyrene beads (2.64 × 1014 particles) via intratracheal instillation on gestational day (GD) 19. Twenty-four hours later on GD 20, maternal and fetal tissues were evaluated using fluorescent optical imaging. Fetal tissues were fixed for particle visualization with hyperspectral microscopy. Using isolated placental perfusion, a known concentration of nanopolystyrene was injected into the uterine artery. Maternal and fetal effluents were collected for 180 min and assessed for polystyrene particle concentration. Twenty-four hours after maternal exposure, fetal and placental weights were significantly lower (7 and 8%, respectively) compared with controls. Nanopolystyrene particles were detected in the maternal lung, heart, and spleen. Polystyrene nanoparticles were also observed in the placenta, fetal liver, lungs, heart, kidney, and brain suggesting maternal lung-to-fetal tissue nanoparticle translocation in late stage pregnancy.

Conclusion
These studies confirm that maternal pulmonary exposure to nanopolystyrene results in the translocation of plastic particles to placental and fetal tissues and renders the fetoplacental unit vulnerable to adverse effects. These data are vital to the understanding of plastic particulate toxicology and the developmental origins of health and disease.

Li, Yan, Yan Liu, Chuanlin Hu, Qing Chang, Qihong Deng, Xu Yang, and Yang Wu. "**Study of the Neurotoxicity of Indoor Airborne Nanoparticles Based on a 3D Human Blood-Brain Barrier Chip**."

Environment International 143 (October 1, 2020): 105598. https://doi.org/10.1016/j.envint.2020.105598.

Background
There is growing public awareness regarding the health effects of indoor nanoscale particulate matter (INPM) since people spend the majority of their time indoors. INPM could have a direct entry route into the brain via the axons of the olfactory nerve and migrating across the blood-brain barrier (BBB). Using animals to explore this possibility is not a reliable method to fully demonstrate human physiological responses. We, therefore, set out to develop a human 3D functional blood-brain barrier model to examine the potential effects of INPM on the cerebral nervous system.

Methods
Human astrocytes were co-cultured and human umbilical vein endothelial cells in 3D within a microfluidic chip to simulate the micro-complex physiological structure of the human BBB. This 3D human organotypic model has then been made to investigate any INPM-induced BBB dysfunction linked to potential cellular responses.

Results
A 3D human functional blood-brain barrier was constructed in this study. We observed the translocation of INPM across the blood-brain barrier. The 3D human organotypic chip initially reflected damage to the nervous system with abnormal astrocyte proliferation and a decline in cell viability. We also looked at the behavior of oxidative stress-related biomarkers (ROS, GSH-Px, and MDA). INPM was implicated in aggravating inflammation via reactive oxygen species (ROS). The Keap1-Nrf2-ARE pathway is a key mechanism in cellular resistance to oxidative stress by mediating and activating a variety of antioxidant and detoxification enzymes. Following ROS accumulation, INPM induced abnormal expression of nuclear transcription factor Nrf2. This behavior disturbed the expression of, γ-glutamate synthase (γ-GCS) and heme oxygenase (HO-1), which further exacerbated the imbalance of the antioxidant system.

Conclusions
This functional 3D human organotypic chip effectively mimics the physiological response of the human BBB. The chip provides a micro-complex structure to simulate the internal environment of the human blood-brain barrier, and partially simulates the physiological responses of the BBB to INPM exposure. Based on this model, INPM was shown to affect the blood-brain barrier biofunction by disrupting the Keap1-Nrf2-ARE pathways.

Wilson, Andrew J., and Prashant K. Jain. "**Light-Induced Voltages in Catalysis by Plasmonic Nanostructures**." *Accounts of Chemical Research* 53, no. 9 (September 15, 2020): 1773–81. https://doi.org/10.1021/acs.accounts.0c00378.

ConspectusPlasmonic nanostructures have garnered widescale scientific interest because of their strong light-matter interactions and the tunability of their absorption across the solar spectrum. At the heart of their superlative interaction with light is the resonant excitation of a collective oscillation of electrons in the nanostructure by the incident electromagnetic field. These resonant oscillations are known as

localized surface plasmon resonances (LSPRs). In recent years, the community has uncovered intriguing photochemical attributes of noble metal nanostructures arising from their LSPRs. Chemical reactions that are otherwise unfavorable or sluggish in the dark are induced on the nanostructure surface upon photoexcitation of LSPRs. This phenomenon has led to the birth of plasmonic catalysis. The rates of a variety of kinetically challenging reactions are enhanced by plasmon-excited nanostructures. While the potential utility for solar energy harvesting and chemical production is clear, there is a natural curiosity about the precise origin(s) of plasmonic catalysis. One explanation is that the reactions are facilitated by the action of the intensely concentrated and confined electric fields generated on the nanostructure upon LSPR excitation. Another mechanism of activation involves hot carriers transiently produced in the metal nanostructure by damping of LSPRs.In this Account, we visit a phenomenon that has received less attention but has a key role to play in plasmonic catalysis and chemistry. Under common chemical scenarios, plasmonic excitation induces a potential or a voltage on a nanoparticle. This photopotential modifies the energetics of a chemical reaction on noble metal nanoparticles. In a range of cases studied by our laboratory and others, light-induced potentials underlie the plasmonic enhancement of reaction kinetics. The photopotential model does not replace other known mechanisms, but it complements them. There are multiple ways in which an electrostatic photopotential is produced by LSPR excitation, such as optical rectification, but one that is most relevant in chemical media is asymmetric charge transfer to solution-phase acceptors. Electrons and holes produced in a nanostructure by damping of LSPRs are not removed at the same rate. As a result, the slower carrier accumulates on the nanostructure, and a steady-state charge is built up on the nanostructure, leading to a photopotential. Potentials of up to a few hundred millivolts have been measured by our laboratory and others. A photocharged nanoparticle is a source of carriers of a higher potential than an uncharged one. As a result, redox chemical reactions on noble metal nanoparticles exhibit lower activation barriers under photoexcitation. In electrochemical reactions on noble metal nanoparticles, the photopotential supplements the applied potential. In a diverse set of reactions, the photopotential model explains the photoenhancement of rates as well as the trends as a function of light intensity and photon energy. With further gains, light-induced potentials may be used as a knob for controlling the activities and selectivities of noble metal nanoparticle catalysts.

Mateos-Cárdenas, Alicia, John O'Halloran, Frank N. A. M. van Pelt, and Marcel A. K. Jansen. "**Rapid Fragmentation of Microplastics by the Freshwater Amphipod Gammarus Duebeni (Lillj.)."** *Scientific Reports* 10, no. 1 (July 30, 2020): 12799. https://doi.org/10.1038/s41598-020-69635-2.

Microplastics have become ubiquitous in all environments. Yet, their environmental fate is still largely unknown. Plastic fragmentation is a key component of plastic degradation, which is mostly caused by abiotic processes over prolonged time scales. Here, it is shown that the freshwater amphipod Gammarus duebeni can rapidly fragment polyethylene microplastics, resulting in the formation of differently shaped and sized plastic fragments, including nanoplastics. Fragments comprised 65.7% of all observed microplastic particles accumulated in digestive tracts. Higher numbers of fragments were found in response to longer exposure times and/or higher microplastic concentrations. Furthermore, the proportion of smaller plastic fragments was highest when food was present during the depuration process. It is concluded that G. duebeni can rapidly fragment polyethylene microplastics and that this is

closely associated with the feeding process. These results highlight the crucial role, currently understudied, that biota may play in determining the fate of microplastics in aquatic ecosystems.

Liew, Zeyan, Jiajun Luo, Ellen A. Nohr, Bodil Hammer Bech, Rossana Bossi, Onyebuchi A. Arah, and Jørn Olsen. "**Maternal Plasma Perfluoroalkyl Substances and Miscarriage: A Nested Case–Control Study in the Danish National Birth Cohort**." *Environmental Health Perspectives* 128, no. 4 (April 22, 2020). https://doi.org/10.1289/EHP6202.

There are many refs to PFAS, as they can break up into nanoparticles – what is the effect of non-nano plastics, PFAS, metals, dusts … when they are ground/degraded/transformed into nano forms?

Background:
Per- and polyfluoroalkyl substances (PFAS) are widespread persistent organic pollutants and endocrine disruptors. High doses of perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) exposure can cause pregnancy loss and infant deaths in animals, but the associations between PFAS exposures and risk of miscarriage in humans are not well studied.

Methods:
Using a case–control study nested within the Danish National Birth Cohort (DNBC, 1996–2002), we compared 220 pregnancies ending in miscarriage during weeks 12–22 of gestation, with 218 pregnancies resulting in live births. Levels of seven types of PFAS [PFOS, PFOA, perfluorohexane sulfonate (PFHxS), perfluoroheptane sulfonate (PFHpS), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluorooctanesulfonic acid (PFOSA)] were measured in maternal plasma collected in early gestation (mean gestational week 8). We estimated the odds ratios (ORs) and 95% confidence intervals (CIs) for miscarriage and each PFAS as a continuous variable or in quartiles, controlling for maternal age, parity, socio-occupational status, smoking and alcohol intake, gestational week of blood sampling, and maternal history of miscarriage. Stratification by parity and PFAS mixture analyses using weighted quantile sum (WQS) regression were also conducted.

Results:
We observed a monotonic increase in odds for miscarriage associated with increasing PFOA and PFHpS levels. The ORs comparing the highest PFOA or PFHpS quartile to the lowest were 2.2 (95% CI: 1.2, 3.9) and 1.8 (95% CI: 1.0, 3.2). The ORs were also elevated for the second or third quartile of PFHxS or PFOS, but no consistent exposure–outcome pattern emerged. An interquartile range (IQR) increment in the WQS index of seven PFAS was associated with 64% higher odds for miscarriage (95% CI: 1.15, 2.34). The associations were stronger in parous women, while findings were inconsistent among nulliparous women.

Conclusion:
Maternal exposures to higher levels of PFOA, PFHpS, and PFAS mixtures were associated with the risk of miscarriage and particularly among parous women. Larger replication studies among nulliparous women are needed to allay concerns about confounding by reproductive history.
https://doi.org/10.1289/EHP6202

Taipale, S. J., E. Peltomaa, J. V. K. Kukkonen, M. J. Kainz, P. Kautonen, and M. Tiirola. "**Tracing the Fate of Microplastic Carbon in the Aquatic Food Web by Compound-Specific Isotope Analysis**." *Scientific Reports* 9, no. 1 (December 27, 2019): 1–15. https://doi.org/10.1038/s41598-019-55990-2.

Increasing abundance of microplastics (MP) in marine and freshwaters is currently one of the greatest environmental concerns. Since plastics are fairly resistant to chemical decomposition, breakdown and reutilization of MP carbon complexes requires microbial activity. Currently, only a few microbial isolates have been shown to degrade MPs, and direct measurements of the fate of the MP carbon are still lacking. We used compound-specific isotope analysis to track the fate of fully labelled 13C-polyethylene (PE) MP carbon across the aquatic microbial-animal interface. Isotopic values of respired CO2 and membrane lipids showed that MP carbon was partly mineralized and partly used for cell growth. Microbial mineralization and assimilation of PE-MP carbon was most active when inoculated microbes were obtained from highly humic waters, which contain recalcitrant substrate sources. Mixotrophic algae (Cryptomonas sp.) and herbivorous zooplankton (Daphnia magna) used microbial mediated PE-MP carbon in their cell membrane fatty acids. Moreover, heteronanoflagellates and mixotrophic algae sequestered MP carbon for synthesizing essential ω-6 and ω-3 polyunsaturated fatty acids. Thus, this study demonstrates that aquatic micro-organisms can produce, biochemically upgrade, and trophically transfer nutritionally important biomolecules from PE-MP.

Hernandez, Laura M., Elvis Genbo Xu, Hans C. E. Larsson, Rui Tahara, Vimal B. Maisuria, and Nathalie Tufenkji. "**Plastic Teabags Release Billions of Microparticles and Nanoparticles into Tea**." *Environmental Science & Technology* 53, no. 21 (November 5, 2019): 12300–310. https://doi.org/10.1021/acs.est.9b02540.

The increasing presence of micro- and nano-sized plastics in the environment and food chain is of growing concern. Although mindful consumers are promoting the reduction of single-use plastics, some manufacturers are creating new plastic packaging to replace traditional paper uses, such as plastic teabags. The objective of this study was to determine whether plastic teabags could release microplastics and/or nanoplastics during a typical steeping process. We show that steeping a single plastic teabag at brewing temperature (95 °C) releases approximately 11.6 billion microplastics and 3.1 billion nanoplastics into a single cup of the beverage. The composition of the released particles is matched to the original teabags (nylon and polyethylene terephthalate) using Fourier-transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS). The levels of nylon and polyethylene terephthalate particles released from the teabag packaging are several orders of magnitude higher than plastic loads previously reported in other foods. An initial acute invertebrate toxicity assessment shows that exposure to only the particles released from the teabags caused dose-dependent behavioral and developmental effects.

Qin, Tao, Ruonan Ma, Yinyan Yin, Xinyu Miao, Sujuan Chen, Kelong Fan, Juqun Xi, et al. "**Catalytic Inactivation of Influenza Virus by Iron Oxide Nanozyme**." *Theranostics* 9, no. 23 (September 21, 2019): 6920–35. https://doi.org/10.7150/thno.35826.

There are many proposals for self-disinfecting surfaces, but these are not approved by the PMRA – where these claims are supposed to lie.

Influenza poses a severe threat to human health in the world. However, developing a universal anti-viral strategy has remained challenging due to the presence of diverse subtypes as well as its high mutation rate, resulting in antigenic shift and drift. Here we developed an antiviral strategy using iron oxide nanozymes (IONzymes) to target the lipid envelope of the influenza virus., Methods: We evaluated the antiviral activities of our IONzymes using a hemagglutination assay, together with a 50% tissue culture infectious doses (TCID50) method. Lipid peroxidation of the viral envelope was analyzed using a maleic dialdehyde (MDA) assay and transmission electron microscopy (TEM). The neighboring viral proteins were detected by western blotting., Results: We show that IONzymes induce envelope lipid peroxidation and destroy the integrity of neighboring proteins, including hemagglutinin, neuraminidase, and matrix protein 1, causing the inactivation of influenza A viruses (IAVs). Furthermore, we show that our IONzymes possess a broad-spectrum antiviral activity on 12 subtypes of IAVs (H1~H12). Lastly, we demonstrate that applying IONzymes to a facemask improves the ability of virus protection against 3 important subtypes that pose a threat to human, including H1N1, H5N1, and H7N9 subtype., Conclusion: Together, our results clearly demonstrate that IONzymes can catalyze lipid peroxidation of the viral lipid envelope to inactivate enveloped viruses and provide protection from viral transmission and infection.

Ding, Yuchen, John R. Bertram, Carrie Eckert, Rajesh Reddy Bommareddy, Rajan Patel, Alex Conradie, Samantha Bryan, and Prashant Nagpal. "**Nanorg Microbial Factories: Light-Driven Renewable Biochemical Synthesis Using Quantum Dot-Bacteria Nanobiohybrids**." *Journal of the American Chemical Society* 141, no. 26 (July 3, 2019): 10272–82. https://doi.org/10.1021/jacs.9b02549.

Living cells do not interface naturally with nanoscale materials, although such artificial organisms can have unprecedented multifunctional properties, like wireless activation of enzyme function using electromagnetic stimuli. Realizing such interfacing in a nanobiohybrid organism (or nanorg) requires (1) chemical coupling via affinity binding and self-assembly, (2) the energetic coupling between optoelectronic states of artificial materials with the cellular process, and (3) the design of appropriate interfaces ensuring biocompatibility. Here we show that seven different core–shell quantum dots (QDs), with excitations ranging from ultraviolet to near-infrared energies, couple with targeted enzyme sites in bacteria. When illuminated by light, these QDs drive the renewable production of different biofuels and chemicals using carbon-dioxide (CO2), water, and nitrogen (from air) as substrates. These QDs use their zinc-rich shell facets for affinity attachment to the proteins. Cysteine zwitterion ligands enable uptake through the cell, facilitating cell survival. Together, these nanorgs catalyze light-induced air–water–CO2 reduction with a high turnover number (TON) of ∼106-108 (mols of product per mol of cells) to biofuels like isopropanol (IPA), 2,3-butanediol (BDO), C11–C15 methyl ketones (MKs), and hydrogen (H2); and chemicals such as formic acid (FA), ammonia (NH3), ethylene (C2H4), and degradable bioplastics polyhydroxybutyrate (PHB). Therefore, these resting cells function as nanomicrobial factories powered by light.

Calderón-Garcidueñas, Lilian, Angélica González-Maciel, Partha S. Mukherjee, Rafael Reynoso-Robles, Beatriz Pérez-Guillé, Carlos Gayosso-Chávez, Ricardo Torres-Jardón, et al. "**Combustion- and Friction-**

Derived Magnetic Air Pollution Nanoparticles in Human Hearts." *Environmental Research*, June 29, 2019, 108567. https://doi.org/10.1016/j.envres.2019.108567.

Air pollution is a risk factor for cardiovascular and Alzheimer's disease (AD). Iron-rich, strongly magnetic, combustion- and friction-derived nanoparticles (CFDNPs) are abundant in particulate air pollution. Metropolitan Mexico City (MMC) young residents have abundant brain CFDNPs associated with AD pathology. We aimed to identify if magnetic CFDNPs are present in urbanites' hearts and associated with cell damage. We used magnetic analysis and transmission electron microscopy (TEM) to identify heart CFDNPs and measured oxidative stress (cellular prion protein, PrPC), and endoplasmic reticulum (ER) stress (glucose regulated protein, GRP78) in 72 subjects age 23.8 ± 9.4y: 63 MMC residents, with Alzheimer Continuum vs 9 controls. Magnetite/maghemite nanoparticles displaying the typical rounded crystal morphologies and fused surface textures of CFDNPs were more abundant in MMC residents' hearts. NPs, ~2–10 × more abundant in exposed vs controls, were present inside mitochondria in ventricular cardiomyocytes, in ER, at mitochondria-ER contact sites (MERCs), intercalated disks, endothelial and mast cells. Erythrocytes were identified transferring 'hitchhiking' NPs to activated endothelium. Magnetic CFDNP concentrations and particle numbers ranged from 0.2 to 1.7 μg/g and ~2 to 22 × 109/g, respectively. Co-occurring with cardiomyocyte NPs were abnormal mitochondria and MERCs, dilated ER, and lipofuscin. MMC residents had strong left ventricular PrPC and bi-ventricular GRP78 up-regulation. The health impact of up to ~22 billion magnetic NPs/g of ventricular tissue are likely reflecting the combination of surface charge, ferrimagnetism, and redox activity, and includes their potential for disruption of the heart's electrical impulse pathways, hyperthermia and alignment and/or rotation in response to magnetic fields. Exposure to solid NPs appears to be directly associated with early and significant cardiac damage. Identification of strongly magnetic CFDNPs in the hearts of children and young adults provides an important novel layer of information for understanding CVD pathogenesis emphasizing the urgent need for prioritization of particulate air pollution control.

Raftis, Jennifer B., and Mark R. Miller. "**Nanoparticle Translocation and Multi-Organ Toxicity: A Particularly Small Problem**." *Nano Today* 26 (June 2019): 8–12. https://doi.org/10.1016/j.nantod.2019.03.010.

Environmental and manufactured nanoparticles share physicochemical properties and could have similar toxicological profiles.
• Particles in air pollution have effects on many organ systems. Is the same true for manufactured nanoparticles?
• Recently inhaled nanoparticles were shown to pass into the circulation in man and amass at sites of vascular inflammation.
• Translocation of nanoparticles into systemic circulation could underlie their toxicity to multiple organs.
• The authors stress the importance of risk assessment for manufactured nanoparticles that considers multiple organ systems.

, Environmental nanoparticles and manufactured nanoparticles (MNMs) can share many of the same physicochemical properties and, therefore, could have similar toxicological profiles. Inhalation of nanoparticles in air pollution has effects throughout the body; however, the potential for inhaled MNMs to affect multiple organs requires further investigation. The biological mechanisms that link

nanoparticles deposition in the lung to their systemic actions remain to be established; however, the passage of nanoparticles into the blood ("translocation") represents a compelling explanation. This article highlights experimental work in animals and man showing that inhaled gold nanoparticles pass into the blood and accumulate at sites of vascular disease. The article discusses the properties of nanoparticles that could influence translocation and highlights some avenues for future research. The processes described have clear relevance, both for MNMs and sources of nanoparticles in air pollution. The authors emphasise the need for risk assessment of potential nanoparticle exposure routes that consider the multiple organ systems.

Shkir, Mohd, I. S. Yahia, V. Ganesh, Y. Bitla, I. M. Ashraf, Ajeet Kaushik, and S. AlFaify. "**A Facile Synthesis of Au-Nanoparticles Decorated PbI 2 Single Crystalline Nanosheets for Optoelectronic Device Applications**." *Scientific Reports* 8, no. 1 (September 14, 2018): 1–10. https://doi.org/10.1038/s41598-018-32038-5.

This research communication presents a rapid and facile microwave-assisted synthesis of single crystalline nanosheets (SCNSs) of hexagonal lead iodide (PbI2) decorated with Au nanoparticles, a potential optoelectronics material. Homogeneous low dimensional AuNP decoration in PbI2 resulted in a new absorption band at ~604 nm and a shift in band gap from 3.23 to 3.00 eV. The significant enhancement of photoluminescent (PL) intensity observed in the AuNP-PbI2 SCNSs is attributed to the coupling of the localized surface plasmon resonanzce of AuNP leading to improved excitation and emission rates of PbI2-SCNSs in the region of the localized electromagnetic field. The Au-PbI2 SCNSs display a compelling increment in photoconductivity, and its fabricated photodetector showed a stable and switchable photo-response. Due to ease of synthesis and enhanced photoconductivity along with appealing PL features, Au-PbI2 SCNS has the potential to be used as a material of choice when fabricating an optoelectronic devices of high performance.

Elena, Poverenov, and Klein Miri. "**Formation of Contact Active Antimicrobial Surfaces by Covalent Grafting of Quaternary Ammonium Compounds**." *Colloids and Surfaces B: Biointerfaces* 169 (September 2018): 195–205. https://doi.org/10.1016/j.colsurfb.2018.04.065.

Different synthetic strategies for the formation of contact active antimicrobial materials utilizing covalent linkage of quaternary ammonium compounds (QACs) were reviewed. There is a demand to find methods that will prevent bacterial fouling without the release of antimicrobial agents, because biocides cause environment pollution and promote the development of bacteria resistance mechanisms. The contact active antimicrobial surfaces may provide a useful tool for this purpose. The covalent surface grafting of QACs seems to be a feasible and promising approach for the formation of safe and effective antimicrobial materials that could be utilized for medical devices, food industry, water treatment systems and other applications. This manuscript reviews covalent attachment of QACs to form contact active antimicrobial materials based on glass, metals, synthetic and natural polymers. The review emphasizes the description of different synthetic methods that are used for the covalent linkage. Direct covalent linkage of QACs to the material surfaces, a linkage via auxiliary nanoparticles (NPs), or spacers, controlled radical polymerization techniques and a linkage to pre-activated surfaces are discussed. The

physico-chemical properties and biological activity of the modified surfaces are also described. This review does not cover non-covalent grafting of QACs and incorporation of QACs into a bulk material.

Yokota, Junko, and Shojiro Kyotani. "**Influence of Nanoparticle Size on the Skin Penetration, Skin Retention and Anti-Inflammatory Activity of Non-Steroidal Anti-Inflammatory Drugs**." *Journal of the Chinese Medical Association* 81, no. 6 (June 1, 2018): 511–19. https://doi.org/10.1016/j.jcma.2018.01.008.

Background
This study aims to evaluate the influence of nanoparticle size on the in vitro percutaneous penetration and retention and in vivo anti-inflammatory efficacy of percutaneously delivered non-steroidal anti-inflammatory drugs.

Methods
Indomethacin, ketoprofen and piroxicam were incorporated into nanoparticles. The nanoparticles, or the bulk-drug equivalents, were suspended in a hydrophilic ointment and compared for their ability to facilitate percutaneous drug penetration and retention in vitro. The formulations were applied cutaneously in a carrageenan-induced footpad inflammation model (acute inflammation) and an adjuvant-induced arthritis model (chronic inflammation) in rats and were assessed for their anti-inflammatory efficacy and potency.

Results
The nanoparticle formulations demonstrated a substantially smaller particle size compared with the bulk-drug formulations. The nanoparticles notably increased drug penetration and retention in vitro. In both the acute and chronic inflammation models, the nanoparticle formulations demonstrated significantly higher anti-inflammatory activity than that of their corresponding bulk-drug formulation at an equivalent dose, and produced better overall healing.

Conclusion
The nanoparticle formulations are highly effective as percutaneous drug carriers, and demonstrate that decreasing particle size leads to increased efficacy and potency. The exploitation of such nanotechnology could drive the development of more effective percutaneous therapeutics.

Hosnedlova, Bozena, Marta Kepinska, Sylvie Skalickova, Carlos Fernandez, Branislav Ruttkay-Nedecky, Qiuming Peng, Mojmir Baron, et al. "**Nano-Selenium and Its Nanomedicine Applications: A Critical Review**." *International Journal of Nanomedicine* 13 (April 10, 2018): 2107–28. https://doi.org/10.2147/IJN.S157541.

Nano-selenium and its nanomedicine applications: a critical review Bozena Hosnedlova,1 Marta Kepinska,2 Sylvie Skalickova,3 Carlos Fernandez,4 Branislav Ruttkay-Nedecky,3 Qiuming Peng,5 Mojmir Baron,1 Magdalena Melcova,6 Radka Opatrilova,3 Jarmila Zidkova,6 Geir Bjørklund,7 Jiri Sochor,1 Rene Kizek2,3 1Department of Viticulture and Enology, Faculty of Horticulture, Mendel University in Brno,

Lednice, Czech Republic; 2Department of Biomedical and Environmental Analyses, Faculty of Pharmacy, Wroclaw Medical University, Wroclaw, Poland; 3Central Laboratory, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic; 4School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen, UK; 5State Key Laboratory of Metastable Materials Science and Technology, Yanshan University, Qinhuangdao, People's Republic of China; 6Department of Biochemistry and Microbiology, University of Chemistry and Technology, Prague, Czech Republic; 7Council for Nutritional and Environmental Medicine, Rana, Norway Abstract: Traditional supplements of selenium generally have a low degree of absorption and increased toxicity. Therefore, it is imperative to develop innovative systems as transporters of selenium compounds, which would raise the bioavailability of this element and allow its controlled release in the organism. Nanoscale selenium has attracted a great interest as a food additive especially in individuals with selenium deficiency, but also as a therapeutic agent without significant side effects in medicine. This review is focused on the incorporation of nanotechnological applications, in particular exploring the possibilities of a more effective way of administration, especially in selenium-deficient organisms. In addition, this review summarizes the survey of knowledge on selenium nanoparticles, their biological effects in the organism, advantages, absorption mechanisms, and nanotechnological applications for peroral administration. Keywords: nanoparticles, biomedicine, drug delivery, oxidative stress, anticancer effect, antimicrobial acitivity, protective effect.

Alimi, Olubukola S., Jeffrey Farner Budarz, Laura M. Hernandez, and Nathalie Tufenkji. "**Microplastics and Nanoplastics in Aquatic Environments: Aggregation, Deposition, and Enhanced Contaminant Transport**." *Environmental Science & Technology* 52, no. 4 (February 20, 2018): 1704–24. https://doi.org/10.1021/acs.est.7b05559.

Plastic litter is widely acknowledged as a global environmental threat, and poor management and disposal lead to increasing levels in the environment. Of recent concern is the degradation of plastics from macro- to micro- and even to nanosized particles smaller than 100 nm in size. At the nanoscale, plastics are difficult to detect and can be transported in air, soil, and water compartments. While the impact of plastic debris on marine and fresh waters and organisms has been studied, the loads, transformations, transport, and fate of plastics in terrestrial and subsurface environments are largely overlooked. In this Critical Review, we first present estimated loads of plastics in different environmental compartments. We also provide a critical review of the current knowledge vis-à-vis nanoplastic (NP) and microplastic (MP) aggregation, deposition, and contaminant cotransport in the environment. Important factors that affect aggregation and deposition in natural subsurface environments are identified and critically analyzed. Factors affecting contaminant sorption onto plastic debris are discussed, and we show how polyethylene generally exhibits a greater sorption capacity than other plastic types. Finally, we highlight key knowledge gaps that need to be addressed to improve our ability to predict the risks associated with these ubiquitous contaminants in the environment by understanding their mobility, aggregation behavior and their potential to enhance the transport of other pollutants.

Rokoff, Lisa B., Sheryl L. Rifas-Shiman, Brent A. Coull, Andres Cardenas, Antonia M. Calafat, Xiaoyun Ye, Alexandros Gryparis, et al. "**Cumulative Exposure to Environmental Pollutants during Early Pregnancy and Reduced Fetal Growth: The Project Viva Cohort**." *Environmental Health* 17 (February 20, 2018). https://doi.org/10.1186/s12940-018-0363-4.

Background
Reduced fetal growth is associated with perinatal and later morbidity. Prenatal exposure to environmental pollutants is linked to reduced fetal growth at birth, but the impact of concomitant exposure to multiple pollutants is unclear. The purpose of this study was to examine interactions between early pregnancy exposure to cigarette smoke, traffic pollution, and select perfluoroalkyl substances (PFASs) on birth weight-for-gestational age (BW/GA).

Methods
Among 1597 Project Viva mother-infant pairs, we assessed maternal cigarette smoking by questionnaire, traffic pollution at residential address by black carbon land use regression model, and plasma concentration of select PFASs in early pregnancy. We calculated sex-specific BW/GA z-scores, an index of fetal growth, from national reference data. We fit covariate-adjusted multi-pollutant linear regression models and examined interactions between exposures, using a likelihood-ratio test to identify a best-fit model.

Results
Two hundred six (13%) mothers smoked during pregnancy. Mean [standard deviation (SD)] for black carbon was 0.8 (0.3) μg/m3, perfluorooctane sulfonate (PFOS) was 29.1 (16.5) ng/mL, and BW/GA z-score was 0.19 (0.96). In the best-fit model, BW/GA z-score was lower in infants of mothers exposed to greater black carbon [− 0.08 (95% CI: -0.15, − 0.01) per interquartile range (IQR)]. BW/GA z-score (95% CI) was also lower in infants of mothers who smoked [− 0.09 (− 0.23, 0.06)] or were exposed to greater PFOS [− 0.03 (− 0.07, 0.02) per IQR], although confidence intervals crossed the null. There were no interactions between exposures. In secondary analyses, instead of PFOS, we examined perfluorononanoate (PFNA) [mean (SD): 0.7 (0.4) ng/mL], a PFAS more closely linked to lower BW/GA in our cohort. The best-fit multi-pollutant model included positive two-way interactions between PFNA and both black carbon and smoking (p-interactions = 0.03).

Conclusions
Concurrent prenatal exposures to maternal smoking, black carbon, and PFOS are additively associated with lower fetal growth, whereas PFNA may attenuate associations of smoking and black carbon with lower fetal growth. It is important to examine interactions between multiple exposures in relation to health outcomes, as effects may not always be additive and may shed light on biological pathways.

Electronic supplementary material
The online version of this article (10.1186/s12940-018-0363-4) contains supplementary material, which is available to authorized users.

Utembe, Wells, Victor Wepener, Il Je Yu, and Mary Gulumian. "**An Assessment of Applicability of Existing Approaches to Predicting the Bioaccumulation of Conventional Substances in Nanomaterials**." *Environmental Toxicology and Chemistry* 37, no. 12 (2018): 2972–88. https://doi.org/10.1002/etc.4253.

The experimental determination of bioaccumulation is challenging, and a number of approaches have been developed for its prediction. It is important to assess the applicability of these predictive approaches to nanomaterials (NMs), which have been shown to bioaccumulate. The octanol/water partition coefficient (KOW) may not be applicable to some NMs that are not found in either the octanol or water phases but rather are found at the interface. Thus the KOW values obtained for certain NMs are shown not to correlate well with the experimentally determined bioaccumulation. Implementation of quantitative structure–activity relationships (QSARs) for NMs is also challenging because the bioaccumulation of NMs depends on nano-specific properties such as shape, size, and surface area. Thus there is a need to develop new QSAR models based on these new nanodescriptors; current efforts appear to focus on digital processing of NM images as well as the conversion of surface chemistry parameters into adsorption indices. Water solubility can be used as a screening tool for the exclusion of NMs with short half-lives. Adaptation of fugacity/aquivalence models, which include physicochemical properties, may give some insights into the bioaccumulation potential of NMs, especially with the addition of a biota component. The use of kinetic models, including physiologically based pharmacokinetic models, appears to be the most suitable approach for predicting bioaccumulation of NMs. Furthermore, because bioaccumulation of NMs depends on a number of biotic and abiotic factors, it is important to take these factors into account when one is modeling bioaccumulation and interpreting bioaccumulation results. Environ Toxicol Chem 2018;37:2972–2988. © 2018 SETAC

Hjorth, Rune. "**The Shortfall of Risk Assessment for Decision-Making**." *Nature Nanotechnology* 12, no. 12 (December 2017): 1109–10. https://doi.org/10.1038/nnano.2017.232.

Worm, Boris, Heike K. Lotze, Isabelle Jubinville, Chris Wilcox, and Jenna Jambeck. "**Plastic as a Persistent Marine Pollutant**." *Annual Review of Environment and Resources* 42, no. 1 (October 17, 2017): 1–26. https://doi.org/10.1146/annurev-environ-102016-060700.

Synthetic organic polymers—or plastics—did not enter widespread use until the 1950s. By 2015, global production had increased to 322 million metric tons (Mt) year−1, which approaches the total weight of the human population produced in plastic every year. Approximately half is used for packaging and other disposables, 40% of plastic waste is not accounted for in managed landfills or recycling facilities, and 4.8–12.7 Mt year−1 enter the ocean as macroscopic litter and microplastic particles. Here, we argue that such mismanaged plastic waste is similar to other persistent pollutants, such as dichlorodiphenyltrichloroethane (DDT) or polychlorinated biphenyls (PCBs), which once threatened a "silent spring" on land. Such a scenario seems now possible in the ocean, where plastic cannot be easily removed, accumulates in organisms and sediments, and persists much longer than on land. New evidence indicates a complex toxicology of plastic micro- and nanoparticles on marine life, and transfer up the food chain, including to people. We detail solutions to the current crisis of accumulating plastic

pollution, suggesting a Global Convention on Plastic Pollution that incentivizes collaboration between governments, producers, scientists, and citizens.

Dudefoi, William, Kristy Moniz, Emma Allen-Vercoe, Marie-Hélène Ropers, and Virginia K. Walker. "**Impact of Food Grade and Nano-TiO2 Particles on a Human Intestinal Community**." *Food and Chemical Toxicology* 106 (August 1, 2017): 242–49. https://doi.org/10.1016/j.fct.2017.05.050.

Titanium dioxide (TiO2) nanoparticles (NPs) are used as an additive (E171 or INS171) in foods such as gum, candy and puddings. To address concerns about the potential hazardous effects of ingested NPs, the toxicity of these food-grade NPs was investigated with a defined model intestinal bacterial community. Each titania preparation (food-grade TiO2 formulations, E171-1 and E171-6a) was tested at concentrations equivalent to those found in the human intestine after sampling 1–2 pieces of gum or candy (100–250 ppm). At the low concentrations used, neither the TiO2 food additives nor control TiO2 NPs had an impact on gas production and only a minor effect on fatty acids profiles (C16:00, C18:00, 15:1 w5c, 18:1 w9c and 18:1 w9c, $p < 0.05$). DNA profiles and phylogenetic distributions confirmed limited effects on the bacterial community, with a modest decrease in the relative abundance of the dominant Bacteroides ovatus in favor of Clostridium cocleatum (−13% and +14% respectively, $p < 0.05$). Such minor shifts in the treated consortia suggest that food grade and nano-TiO2 particles do not have a major effect on human gut microbiota when tested in vitro at relevant low concentrations. However, the cumulative effects of chronic TiO2 NP ingestion remain to be tested.

Guinée, Jeroen B., Reinout Heijungs, Martina G. Vijver, and Willie J. G. M. Peijnenburg. "**Setting the Stage for Debating the Roles of Risk Assessment and Life-Cycle Assessment of Engineered Nanomaterials**." *Nature Nanotechnology* 12, no. 8 (August 2017): 727–33. https://doi.org/10.1038/nnano.2017.135.

Although technological and environmental benefits are important stimuli for nanotechnology development, these technologies have been contested from an environmental point of view. The steady growth of applications of engineered nanomaterials has heated up the debate on quantifying the environmental repercussions. The two main scientific methods to address these environmental repercussions are risk assessment and life-cycle assessment. The strengths and weaknesses of each of these methods, and the relation between them, have been a topic of debate in the world of traditional chemistry for over two decades. Here we review recent developments in this debate in general and for the emerging field of nanomaterials specifically. We discuss the pros and cons of four schools of thought for combining and integrating risk assessment and life-cycle assessment and conclude with a plea for action.

Batool, Nayab, Seokyoung Yoon, Saba Imdad, Minsuk Kong, Hun Kim, Sangryeol Ryu, Jung Heon Lee, Akhilesh Kumar Chaurasia, and Kyeong Kyu Kim. "**An Antibacterial Nanorobotic Approach for the Specific Targeting and Removal of Multiple Drug-Resistant *Staphylococcus Aureus***." *Small* 17, no. 20 (2021): 2100257. https://doi.org/10.1002/smll.202100257.

Methicillin-resistant Staphylococcus aureus (MRSA) causes diseases ranging from skin infections to lethal sepsis and has become a serious threat to human health due to multiple-drug resistance (MDR). Therefore, a resistance-free antibacterial therapy is necessary to overcome MDR MRSA infections. In this study, an antibacterial nanorobot (Ab-nanobot) is developed wherein a cell wall-binding domain (CBD)-endolysin, acting as a sensor, is covalently conjugated with an actuator consisting of an iron oxide/silica core–shell. The CBD-endolysin sensor shows an excellent specificity to detect, bind, and accumulate on the S. aureus USA300 cell surface even in a bacterial consortium, and in host cell infections. Ab-nanobot specifically captures and kills MRSA in response to medically approved radiofrequency (RF) electromagnetic stimulation (EMS) signal. When Ab-nanobot receives the RF-EMS signal on the cell surface, actuator induces cell death in MRSA with 99.999% removal within 20 min by cell-wall damage via generation of localized heat and reactive oxygen species. The in vivo efficacy of Ab-nanobot is proven using a mice subcutaneous skin infection model. Collectively, this study offers a nanomedical resistance-free strategy to overcome MDR MRSA infections by providing a highly specific nanorobot for S. aureus.