White House Office of Science and Technology Policy (OSTP)
National Science and Technology Council
National Nanoscale Science Engineering and Technology (NSET) Subcommittee

Request For Information (RFI): 2023 National Nanotechnology Initiative (NNI) Environment Health and Safety (ERS) Research Strategy[1]

June 16, 2023

Transmitted Electronically

The Institute for Agriculture and Trade Policy (IATP)[2] appreciates this opportunity to contribute to the RFI and is grateful for the comment deadline extension that allows us to do so. IATP last wrote to OSTP about NNI EHS research strategy in November 2020, in the context of our response to a RFI about NNI's Strategic Plan.[3] We advocated for the inclusion of research on ethical, legal and societal implications (ELSI) of nanotechnology in the EHS strategy. IATP is pleased to see that this RFI includes a question concerning the integration of ELSI research into EHS strategy. Since 2020, IATP has analyzed research towards the commercialization of nanotechnology enabled pesticide products ("nanopesticides") and protection of workers manufacturing and applying those products.[4] This letter will reference some of that research and ELSI related issues to protecting workers, particularly from underserved populations, from inhalation and dermal exposure to nanopesticides.

This letter responds to three of the RFI questions:

2. *What research gaps remain in addressing the six NNI EHS core research areas listed in question 1?* We address the core research areas of 2) Human Exposure Assessment; (5) Risk Assessment and Risk Management Methods.

Human Exposure Assessment: Two scientists involved in the development of engineered nanomaterial coated RNA interferon (i.e., double stranded RNA) pesticide products wrote in 2020 that "At present, there seems to be an absence of published data concerning the potential biological impact of inhalation of RNA molecules."[5] Nevertheless, they conclude, "the plausibility of systemic dsRNA exposure from

[1] https://www.regulations.gov/document/OSTP-POLICY-2023-0005-0001
[2] IATP is a U.S. nonprofit, 501(c)(3) nongovernmental organization, headquartered in Minneapolis, Minnesota (U.S.), with offices in Washington, D.C. and Berlin, Germany. We have participated in National Nanotechnology Coordinating Office activities and National Nanotechnology Initiative agency comment opportunities since 2011, mostly concerning food and agricultural applications of nanotechnology and nanomaterials.
[3] https://www.iatp.org/documents/request-information-2021-national-nanotechnology-initiative-nni-strategic-plan
[4] Steve Suppan, "The next big (pesticide) thing and protecting farmworker health," Institute for Agriculture and Trade Policy, May 25, 2022. https://www.iatp.org/blog/202205/next-big-pesticide-thing-and-protecting-farmworker-health
[5] Rodrigues TB and Petrick JS (2020) Safety Considerations for Humans and Other Vertebrates Regarding Agricultural Uses of Externally Applied RNA Molecules. Front. Plant Sci. 11:407. doi: 10.3389/fpls.2020.00407

agricultural applications at levels capable of initiating RNAi machinery saturation is highly questionable."[6] They also advise the use of "appropriate personal protective equipment (PPE)," but to our knowledge, there is no such PPE for nano-enabled pesticide products. Because most of the scientists' safety assessment concerns oral exposure to dsRNA, IATP believes on there is an urgent need for studies on inhalation exposure to dsRNA, particularly the chronic exposure of farmworkers spraying these nano-encapsulated dsRNA pesticide products.

The commercial use of this new generation of pesticide products could be imminent, hence our characterization of the research needs as "urgent." On March 7, one product developer, GreenLight Bioscience, Inc., announced that it was "actively preparing for commercial launch prior to end of 2023 of our leading dsRNA solution, Calantha™, subject to regulatory approval."[7] Although the Environmental Protection Agency (EPA) has yet to issue an experiment use permit for field trials of this and other dsRNA-based products, EPA scientists have participated in a large literature and patent review of dsRNA pesticide products.[8] The review of more than 500 research articles and 36,000 patents "identified 569 Type 1 [anti-microbial nano-metals and metal oxides] and 1,094 Type 2 [nano-encapsulation of current Active Ingredients] nanopesticides."

EPA publicized this review and heralded the potential of dsRNA as a tool for sustainable agriculture.[9] The nanomaterial coating serves both to protect the dsRNA from destruction by ultra-violet light and to dosing the dsRNA in response to an environmental signal. If the nano-coated pesticide particle bioaccumulates in the lower part of the lungs, it would be important to understand whether that exposure would result in immunosuppressive effects. A related research question would be if the composition of a nanomaterial coating would increase possible immunosuppressive impacts. We return in our response to the ESLI question to the problem of PPE for farmworkers and others with chronic inhalation exposure risk.

Risk Assessment and Risk Management Methods

According to our notes from one of the panelists at the May 31-June 1 "Refreshing the NNI's Environment Health and Safety Research Strategy" meeting,[10] most risk assessment studies of Manufactured Nanomaterials (MNs) still do not use well-characterized MNs from a standardized "library," such as that of the Organization for Economic Cooperation and Development (OECD). Therefore, the results of such risk assessments, however well conducted, cannot be compared for regulatory use in making risk management decisions. A NNI EHS research strategy should prioritize surveying the reasons that researchers are not using well-characterized MNs in their risk assessments. The results of the survey could be used to propose some research funding rules that would commit applicants to using and reporting the use of well-characterized MNs or scientifically relevant comparators in their risk assessments.

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[6] Ibid.

[7] https://www.greenlightbiosciences.com/greenlight-biosciences-outlines-development-strategy-and-highlights-portfolio-updates-at-plant-health-rd-day/

[8] Wang, D., Saleh, N.B., Byro, A. *et al.* Nano-enabled pesticides for sustainable agriculture and global food security. *Nat. Nanotechnol.* **17,** 347–360 (2022), at 348. https://doi.org/10.1038/s41565-022-01082-8

[9] https://www.epa.gov/sciencematters/advancing-epas-understanding-next-generation-pesticides

[10] https://www.nano.gov/ehsstrategymeeting

A great deal of work has been done to categorize MNs for regulatory purposes, e.g., to ensure that toxicological studies are valid and scientifically accepted.[11] Given the proliferation of new MNs, including nano-bio compounds, it must not be easy for researchers who are designing an experiment to risk assess a new MN by finding in a library of well-characterized MNs a relevant MN comparable to the one/s subject to the risk assessment, even with the aid of nano-informatic data bases. However, the alternative to experimental design without reference to well characterized MNs and their relevant comparators (if they exist), is a proliferation of risk assessments that are much less relevant to the scientific information needs of regulators.

3. The ethical, legal, and societal implications (ELSI) of nanotechnology are considered across the core research areas of the 2011 strategy. What additional ways could ELSI be more fully integrated throughout a refreshed NNI EHS research strategy?

Much of ELSI research focuses on legal issues in the regulation of nanotechnology, and social science surveys and public engagement about building public trust in nanotechnology and its products.[12] IATP recommends that a NNI EHS Research Strategy incorporate ELSI research in two projects.

Almost fifteen years ago, Ronald Sandler wrote, "responsible development of nanotechnology is incomplete if it does not address the issue of environmental justice."[13] How and how well has NNI EHS research strategy addressed environmental justice and injustice in nanotechnology? Sandler described an ethical quandary of nanotechnology without identifying it as such:

> a substantial new manufacturing infrastructure—one that includes everything from production of basic nanomaterials through finished products, as well as process and end-of-life waste disposal—must be established. Because of social, economic and institutional factors currently in place, the majority of the new facilities are sited in or near low-income and high-minority communities, ensuring that members of those communities are disproportionately exposed to the environmental (and attendant health) hazards associated with nanoscale particle releases into the environment.[14]

The imperative of siting, permitting, financing, building, insuring and operating nanotechnology infrastructure becomes an ethical issue if and when negative environmental and health impacts of those facilities are discovered and publicized, raising the questions of what could have been done and will be done to remedy past harms and prevent future impacts. Sandler's description of the factors in siting nanotechnology infrastructure facilities is qualitative, based on survey results of the location of hazardous material production sites.

The future of environmentally just nanotechnology development has many research needs, but a fundamental one is to map the locations of current nanotechnology infrastructure facilities to

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[11] Günter Oberdörster and Thomas A.J. Kuhlbusch, "*In vivo* effects: Methodologies and biokinetics of inhaled nanoparticles," *NanoImpact*, 10 (2018), 38-60. https://www.sciencedirect.com/science/article/pii/S2452074817300629

[12] Agnieszka Baran, "Legal and Ethical Issues in Nanotechnology," *Economics and Management*, Vol. 8:1 (2016), pp. 47-53. https://sciendo.com/pdf/10.1515/emj-2016-0005

[13] Ronald Sandler, "Nanotechnology: The Social and Ethical Issues," Woodrow Wilson Center Project on Emerging Nanotechnologies, January 2009, p. 26. https://www.pewtrusts.org/-/media/legacy/uploadedfiles/phg/content_level_pages/reports/nanofinalpdf.pdf

[14] Ibid., p. 25.

understand whether their operations present any risks to the surrounding community for which the facility does not have plans to mitigate and of which the community is unaware. IATP participated in a U.S.-EU Communities of Research roleplaying risk management exercise about a nanomaterial transportation accident and found the exercise to be challenging.[15] We believe that NNI should expand this EHS exercise to include municipal officials, medical personnel, facilities operators and community leaders from selected sites where nanomaterial infrastructure facilities are already operating. One set of ELSI researchers could be involved in designing and organizing the exercise, while another would be involved in its reporting and evaluation.

A second project might appear to only concern occupational safety with no ELSI research needs. However, the National Institute for Occupational Health and Science (NIOSH) has decided to orient its PPE extramural research program towards the needs of populations that often do not benefit from EHS research. In June 2021, NIOSH put out a RFI concerning "Needs and Challenges in Personal Protective Equipment (PPE) Use for Underserved User Populations."[16] In November 2022, NIOSH held a virtual workshop on "Equitable Personal Protective Equipment," in which IATP participated. The NIOSH researchers had not considered that farm workers might be among the "underserved user populations" that might benefit from more comfortable, lightweight and form-fitting PPE. As impressive as the workshop research was, most of it was a few years from prototyping, much less from field testing and commercialization.

An ELSI issue for NNI EHS research strategy about PPE is whether nanotechnology products whose manufacture and/or use entails risks of chronic exposure to hazardous MNs or nano-biomaterial compounds, such as nanopesticides, should be approved for commercialization prior to the development of technologically adequate PPE that employers effectively deploy. In the case of nanopesticides, NIOSH could be working already with EPA's Pesticide Worker Safety Program to develop affordable, effective and field condition appropriate PPE for farmworkers under NIOSH's program to protect the nanotechnology workforce. However, the Pesticide Worker Safety Program is implemented by state agencies. ELSI research on how those state programs operate would help facilitate effective implementation of the employer deployment of PPE for nano-enabled RNA interferon and other nanopesticide products.

4. What broad themes should the revised strategy adopt to integrate and connect the six research areas?

The broad theme that we encourage the EHS strategy to incorporate is resilience to and mitigation of climate change impacts. During the May 31-June 1 NNI EHS workshop, Professor Mark Wiesner said that climate change was not only the greatest public policy challenge of our times, but also that it presented a great challenge to nanotechnology.

The dire state of the climate is generally known: CO_2 equivalent emissions peaked in May; within six years the planet may exceed the Paris Agreement target of warming no more than 1.5^{0}C beyond the pre-

[15] Steve Suppan, "Nano Inc.: There's been an accident on Highway 15?" Institute for Agriculture and Trade Policy, July 28, 2015. https://www.iatp.org/blog/201607/%E2%80%9Cnano-inc-there%E2%80%99s-been-an-accident-on-highway-15%E2%80%9D

[16] https://www.federalregister.gov/documents/2021/06/24/2021-13263/needs-and-challenges-in-personal-protective-equipment-ppe-use-for-underserved-user-populations

industrial age level.[17] The response of many nanotechnology researchers is to develop products that mitigate one aspect or another of climate change, e.g., nano-coated fertilizers that reduce nitrous oxide emissions.[18] However, nano-fertilizers and other agricultural "climate smart" products enable the continuation of current agricultural systems, e.g., nitrogen hungry field corn.

Professor Wiesner has said that to develop a nanotechnology product or analytic tool, you first must understand the system into which it is inserted. In the case of climate change, an effective NNI EHS strategy begins with understanding the Earth System. The Intergovernmental Panel on Climate Change (IPCC) reports are key to this understanding.

In 2021, the IPCC concluded with "medium confidence" that fossil fuel emissions cannot be offset on a one-to-one ratio by land-based (biogenic) emissions sequestration.[19] (Chapter 5.6.2.1) A short summary of that asymmetry is described in a 2021 *Nature Climate Change* article based on climate modeling findings: "Results indicate that a CO_2 emission into the atmosphere is more effective at raising atmospheric CO_2 than an equivalent CO_2 removal is at lowering it, with the **asymmetry increasing with the magnitude of the emission/removal**."[20] (IATP emphasis). The asymmetry ensures that it is scientifically impossible to offset equivalent amount of fossil fuel emissions with an equivalent amount biogenic removal. Nevertheless, "climate smart" products, even those requiring fossil fuel inputs, are developed with the claim of offsetting emissions.

Because IPCC reports take five to six years to produce, the scientific literature that updates reports is crucial for developing an ongoing NNI EHS strategy on climate change. Understanding the current state of climate science is a task that can be distributed among NNI agencies. Developing an EHS research strategy from that understanding is a Office of Science and Technology Policy "Grand Challenge" for NNI even though climate change is too broad a challenge to be the focus of a NNI "Signature Initiative."

Thank you for considering the above information and IATP's opinions in revising NNI's EHS research strategy.

Steve Suppan, Ph.D.
Senior Policy Analyst

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[17] Camilla Hodgson, Steve Bernard and Chris Campbell, "Climate graphic of the week: the fast-shrinking carbon budget," *Financial Times*, June 7, 2023. https://www.ft.com/content/5ef31328-2855-4637-9045-318267cc999c

[18] Steve Suppan, "Apply Nanotechnology to Fertilizers: Rationales, research, risks and regulatory challenges," Institute for Agriculture and Trade Policy, October 11, 2017. https://www.iatp.org/documents/applying-nanotechnology-fertilizer-rationales-research-risks-and-regulatory-challenges

[19] IPCC, 2021: Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change [Masson-Delmotte, V., P. Zhai, A. Pirani, S.L. Connors, C. Péan, S. Berger, N. Caud, Y. Chen, L. Goldfarb, M.I. Gomis, M. Huang, K. Leitzell, E. Lonnoy, J.B.R. Matthews, T.K. Maycock, T. Waterfield, O. Yelekçi, R. Yu, and B. Zhou (eds.)]. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA, 2391 pp. doi:10.1017/9781009157896.

[20] Zickfeld, K., Azevedo, D., Mathesius, S. *et al.* Asymmetry in the climate–carbon cycle response to positive and negative CO_2 emissions. *Nat. Clim. Chang.* **11**, 613–617 (2021). https://doi.org/10.1038/s41558-021-01061-2