

United States Government
 Interagency Agreement (IAA) – Agreement Between Federal Agencies
 General Terms and Conditions (GT&C) Section

IAA Number CPSC-1-16-0017 - 0000 -
 GT&C # _____ Order # Amendment/Mod # _____

DEPARTMENT AND/OR AGENCY		
1.	Requesting Agency of Products/Services	Servicing Agency Providing Products/Services
	Name Consumer Product Safety Commission (CPSC/OHIR)	Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health
	Address 4330 East West Highway Bethesda MD 20814	1095 Willowdale Road, MS L-4020 Morgantown WV 26505
2. Servicing Agency Agreement Tracking Number (Optional) <u>CDC IAA #16-NS16-01</u>		
3. Assisted Acquisition Agreement Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>		
4. GT&C Action (Check action being taken)		
<input checked="" type="checkbox"/> New		
<input type="checkbox"/> Amendment – Complete only the GT&C blocks being changed and explain the changes being made.		
<input type="checkbox"/> Cancellation – Provide a brief explanation for the IAA cancellation and complete the effective End Date.		
5. Agreement Period Start Date <u>05-15-2016</u> End Date <u>12-31-2018</u> of IAA or effective cancellation date <small>MM-DD-YYYY MM-DD-YYYY</small>		
6. Recurring Agreement (Check One) A Recurring Agreement will continue, unless a notice to discontinue is received.		
Yes <input type="checkbox"/> If Yes, is this an: Annual Renewal <input type="checkbox"/>		
Other Renewal <input type="checkbox"/> State the other renewal period: _____		
No <input checked="" type="checkbox"/>		
7. Agreement Type (Check One) <input checked="" type="checkbox"/> Single Order IAA <input type="checkbox"/> Multiple Order IAA		
8. Are Advance Payments Allowed for this IAA (Check One) <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		
If Yes is checked, enter Requesting Agency's Statutory Authority Title and Citation		
Note: Specific advance amounts will be captured on each related Order.		

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9. Estimated Agreement Amount (The Servicing Agency completes all information for the estimated agreement amount.) (Optional for Assisted Acquisitions)							
<table style="width:100%; border-collapse: collapse;"> <tr> <td style="width:60%;">Direct Cost</td> <td style="text-align: right;">\$275,229.00</td> </tr> <tr> <td>Overhead Fees & Charges</td> <td style="text-align: right;">\$24,771.00</td> </tr> <tr> <td>Total Estimated Amount</td> <td style="text-align: right;">\$300,000.00</td> </tr> </table>	Direct Cost	\$275,229.00	Overhead Fees & Charges	\$24,771.00	Total Estimated Amount	\$300,000.00	Provide a general explanation of the Overhead Fees & Charges CDC Estimated Overhead at 9%
Direct Cost	\$275,229.00						
Overhead Fees & Charges	\$24,771.00						
Total Estimated Amount	\$300,000.00						
10. STATUTORY AUTHORITY							
a. Requesting Agency's Authority (Check One) Franchise Fund <input type="checkbox"/> Revolving Fund <input type="checkbox"/> Working Capital Fund <input type="checkbox"/> Economy Act (31 U.S.C. 1535/FAR 17.5) <input type="checkbox"/> Other Authority <input checked="" type="checkbox"/>							
Fill in Statutory Authority Title and Citation for Franchise Fund, Revolving Fund, Working Capital Fund, or Other Authority For CPSC: Section 27(g) of the Consumer Product Safety Act (15 U.S.C. 2076(g))							
b. Servicing Agency's Authority (Check One) Franchise Fund <input type="checkbox"/> Revolving Fund <input type="checkbox"/> Working Capital Fund <input type="checkbox"/> Economy Act (31 U.S.C. 1535/FAR 17.5) <input type="checkbox"/> Other Authority <input checked="" type="checkbox"/>							
Fill in Statutory Authority Title and Citation for Franchise Fund, Revolving Fund, Working Capital Fund, or Other Authority For CDC/NIOSH: Section 301(b)(1) of the Public Health Service Act of 1944 (42 U.S.C. 241(b)(1)), and 29 U.S.C. 669							
11. Requesting Agency's Scope (State and/or list attachments that support Requesting Agency's Scope.) Research to support project entitled "Environmental Health and Safety Implications from Engineered Nanomaterials (ENMs) Released from Nano-Enabled Products (NEPs) During Consumer Use: Case Study of Printer Emitted Engineered Nanoparticles (PEPs)." 							
12. Roles & Responsibilities for the Requesting Agency and Servicing Agency (State and/or list attachments for the roles and responsibilities for the Requesting Agency and the Servicing Agency.) See attached Statement of Work							

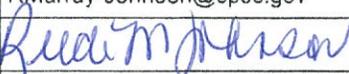
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<p>13. Restrictions (Optional) (State and/or attach unique requirements and/or mission specific restrictions specific to this IAA).</p>
<p>14. Assisted Acquisition Small Business Credit Clause (The Servicing Agency will allocate the socio-economic credit to the Requesting Agency for any contract actions it has executed on behalf of the Requesting Agency.)</p>
<p>15. Disputes: Disputes related to this IAA shall be resolved in accordance with instructions provided in the Treasury Financial Manual (TFM) Volume 1, Part 2, Chapter 4700, Appendix 10; Intragovernmental Business Rules.</p>
<p>16. Termination (Insert the number of days that this IAA may be terminated by written notice by either the Requesting or Servicing Agency.)</p> <p style="padding-left: 40px;">30</p> <p>If this agreement is canceled, any implementing contract/order may also be canceled. If the IAA is terminated, the agencies shall agree to the terms of the termination, including costs attributable to each party and the disposition of awarded and pending actions.</p> <p>If the Servicing Agency incurs costs due to the Requesting Agency's failure to give the requisite notice of its intent to terminate the IAA, the Requesting Agency shall pay any actual costs incurred by the Servicing Agency as a result of the delay in notification, provided such costs are directly attributable to the failure to give notice.</p>
<p>17. Assisted Acquisition Agreements – Requesting Agency's Organizations Authorized To Request Acquisition Assistance for this IAA. (State or attach a list of Requesting Agency's organizations authorized to request acquisition assistance for this IAA.)</p> <p>N/A</p>
<p>18. Assisted Acquisition Agreements – Servicing Agency's Organizations authorized to Provide Acquisition Assistance for this IAA. (State or attach a list of Servicing Agency's organizations authorized to provide acquisition for this IAA.)</p> <p>N/A</p>
<p>19. Requesting Agency Clause(s) (Optional) (State and/or attach any additional Requesting Agency clauses.)</p>

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<p>20. Servicing Agency Clause(s) (Optional) (State and/or attach any additional Servicing Agency clauses.) EQUIPMENT - Unless otherwise requested by the requesting agency, CDC/NIOSH will retain title to any equipment procured in order to provide service.</p>		
<p>21. Additional Requesting Agency and/or Servicing Agency Attachments (Optional) (State and/or attach any additional Requesting Agency and/or Servicing Agency attachments.) Confidentiality Requirements: To the extent permitted by law, all information reported to or otherwise obtained by CPSC or its agents under the Consumer Product Safety Act (CPSA) and provided to or shared with NIOSH, which contains or relates to a trade secret or other matter referred to in section 1905 of title 18, United States Code, or subject to section 552(b)(4) of the title 5, United States Code, shall be held in confidence by NIOSH personnel.</p>		
<p>22. Annual Review of IAA By signing this agreement, the parties agree to annually review the IAA if the agreement period exceeds one year. Appropriate changes will be made by amendment to the GT&C and/or modification to any affected Order(s).</p>		
<p align="center">AGENCY OFFICIAL</p> <p>The Agency Official is the highest level accepting authority or official as designated by the Requesting Agency and Servicing Agency to sign this agreement. Each Agency Official must ensure that the general terms and conditions are properly defined, including the stated statutory authorities, and, that the scope of work can be fulfilled per the agreement.</p> <p>The Agreement Period Start Date (Block 5) must be the same as or later than the signature dates.</p> <p>Actual work for this IAA may NOT begin until an Order has been signed by the appropriate individuals, as stated in the Instructions for Blocks 37 and 38.</p>		
23.	Requesting Agency	Servicing Agency
Name	Rudi M. Johnson	Teresa Miles
Title	Contracting Officer, CPSC	Acting Management Official, NIOSH
Telephone Number(s)	(301) 504-7028	(404) 498-2599
Fax Number	(301) 504-0628	(404) 638-5597
Email Address	RMurray-Johnson@cpsc.gov	TMILES@CDC.GOV
SIGNATURE		Teresa Miles - S <small>Digitally signed by Teresa Miles, DN: cn=Teresa Miles, o=U.S. Government, ou=NIOSH, ou=NIOSH, email=tmiles@cdc.gov, c=US, Date: 2016.05.11 13:25:51 -0400</small>
Approval Date	5.12.2016	

IAA Order

IAA Number CPSC-I-16-0017 - 0001 - _____ Servicing Agency's Agreement
 GT&C # Order # Amendment/Mod # Tracking Number (Optional) 16-NS16-01

28. Order Line/Funding Information													Line Number _____					
Requesting Agency Funding Information													Servicing Agency Funding Information					
ALC																		
Component	SP	ATA	AID	BPOA	EPOA	A	MAIN	SUB	SP	ATA	AID	BPOA	EPOA	A	MAIN	SUB		
TAS Required by 10/1/2014			61	2016	2016						75	2016	2016		0943	000		
OR Current TAS format			61-16-0100						75-16-0943									
BETC			2370400000						COLL									
Object Class Code (Optional)			255A0						2538									
BPN			069287522 (DUNS)						972645465 (DUNS)									
BPN + 4 (Optional)			DISB						COLL									
Additional Accounting Classification/Information (Optional)			0100A16DSE 2016 2370400000 EXHR004000 255A0 EIN: 520978750						Fund Code: 0921602016RAD BA 5611 RF 1101 EIN: 586051157									
Requesting Agency Funding Expiration Date 09-30-2016 MM-DD-YYYY									Requesting Agency Funding Cancellation Date 09-30-2021 MM-DD-YYYY									
Project Number & Title																		
Description of Products and/or Services, including the Bona Fide Need for this Order (State or attach a description of products/services, including the bona fide need for this Order.) CPSC will provide \$300,000 in FY 2016 to support collaborative research on a project entitled "Environmental Health and Safety Implications from Engineered Nanomaterials (ENMs) Released From Nano-Enabled Products (NEPs) During Consumer Use: Case Study of Printer Emitted Engineered Nanoparticles (PEPs)," as described in the attached Statement of Work.																		
North American Industry Classification System (NAICS) Number (Optional) _____																		
Breakdown of Reimbursable Line Costs									OR Breakdown of Assisted Acquisition Line Cost:									
Unit of Measure									Contract Cost		\$							
Quantity		Unit Price		Total				Servicing Fees		\$								
1		\$275,229.00		\$ 275,229.00				Total Obligated Cost		\$ 0.00								
Overhead Fees & Charges				\$ 24,771.00				Advance for Line (-)		\$								
Total Line Amount Obligated				\$ 300,000.00				Net Total Cost		\$ 0.00								
Advance Line Amount (-)				\$				Assisted Acquisition Servicing Fees Explanation										
Net Line Amount Due				\$ 300,000.00														
Type of Service Requirements																		
<input type="checkbox"/> Severable Service <input checked="" type="checkbox"/> Non-severable Service <input type="checkbox"/> Not Applicable																		

IAA Order

IAA Number CPSC-I-16-0017 - 0001 - _____ Servicing Agency's Agreement
 GT&C # Order # Amendment/Mod # Tracking Number (Optional) 16-NS16-01

29. Advance Information (Complete Block 29 if the Advance Payment for Products/Services was checked "Yes" on the GT&C.)

Total Advance Amount for the Order \$ _____ [All Order Line advance amounts (Block 28) must sum to this total.]

Revenue Recognition Methodology (according to SFFAS 7) (Identify the Revenue Recognition Methodology that will be used to account for the Requesting Agency's expense and the Servicing Agency's revenue)

- Straight-line – Provide amount to be accrued \$ _____ and Number of Months _____
- Accrual Per Work Completed – Identify the accounting posting period:
 - Monthly per work completed & invoiced
 - Other – Explain other regular period (bimonthly, quarterly, etc.) for posting accruals and how the accrual amounts will be communicated if other than billed. _____

30. Total Net Order Amount: \$ 300,000.00
 [All Order Line Net Amounts Due for reimbursable agreements and Net Total Costs for Assisted Acquisition Agreements (Block 28) must sum to this total.]

31. Attachments (State or list attachments.)

- Key project and/or acquisition milestones (Optional except for Assisted Acquisition Agreements)

- Other Attachments (Optional)

1. Statement of Work - CDC

BILLING & PAYMENT INFORMATION

32. Payment Method (Check One) [Intra-governmental Payment and Collection (IPAC) is the Preferred Method.]
 If IPAC is used, the payment method must agree with the IPAC Trading Partner Agreement (TPA).

- Requesting Agency Initiated IPAC Servicing Agency Initiated IPAC
- Credit Card Other – Explain other payment method and reasoning _____

33. Billing Frequency (Check One)

[An Invoice must be submitted by the Servicing Agency and accepted by the Requesting Agency BEFORE funds are reimbursed (i.e., via IPAC transaction)]

- Monthly Quarterly Other Billing Frequency (include explanation) _____

34. Payment Terms (Check One)

CDC will not IPAC customer nor will customer IPAC CDC during the last 3 business days of the fiscal year.

- 7 days Other Payment Terms (include explanation): _____

IAA Order

IAA Number CPSC-I-16-0017 - 0001 - Servicing Agency's Agreement
 GT&C # Order # Amendment/Mod # Tracking Number (Optional) 16-NS16-01

35. Funding Clauses/Instructions (Optional) (State and/or list funding clauses/instructions.)

36. Delivery/Shipping Information for Products (Optional)

Agency Name	U.S. Consumer Product Safety Commission
Point of Contact (POC) Name & Title	Treye Thomas
POC Email Address	tthomas@cpsc.gov
Delivery Address /Room Number	5 Research Place, Rockville, MD 20850
POC Telephone Number	(301) 987-2560
Special Shipping Information	

APPROVALS AND CONTACT INFORMATION

37. PROGRAM OFFICIALS
 The Program Officials, as identified by the Requesting Agency and Servicing Agency, must ensure that the scope of work is properly defined and can be fulfilled for this Order. The Program Official may or may not be the Contracting Officer depending on each agency's IAA business process.

	Requesting Agency	Servicing Agency
Name	Treye Thomas	Don Beezhold
Title	Contracting Officer Representative (COR)	Director, HELD
Telephone Number	(301) 987-2560	(304) 285-5963
Fax Number		(304) 285-6126
Email Address	TTHOMAS@CPSC.GOV	ZEC1@CDC.GOV
SIGNATURE	Treye Thomas	<i>[Signature]</i>
Date Signed		5/6/16

38. FUNDING OFFICIALS - The Funds Approving Officials, as identified by the Requesting Agency and Servicing Agency, certify that the funds are accurately cited and can be properly accounted for per the purposes set forth in the Order. The Requesting Agency Funding Official signs to obligate funds. The Servicing Agency Funding Official signs to start the work, and to bill, collect, and properly account for funds from the Requesting Agency, in accordance with the agreement.

	Requesting Agency	Servicing Agency
Name	James Baker	Teresa Miles
Title	Budget Officer, CPSC	Acting Management Official, NIOSH
Telephone Number	(301) 504-7575	(404) 498-2599
Fax Number		(404) 638-5597
Email Address	JBAKER@CPSC.GOV	TMILES@CDC.GOV
SIGNATURE	JBaker	Teresa Miles -S
Date Signed		

**Statement of Work
For
Interagency Agreement
CPSC# - CPSC-1-16-0017
CDC IAA # 16-NS16-01**

Between

**U.S. Consumer Product Safety Commission
And the
Centers for Disease Control and Prevention,
National Institute for Occupational Safety and Health**

1. **Title:** Environmental Health and Safety Implications from engineered nanomaterials (“ENMs”) released from nano-enabled products (“NEPs”) during consumer use: Case study of printer emitted engineered nanoparticles (“PEPs”)

2. Background/Introduction

This Interagency Agreement establishes the terms under which the National Institute for Occupational Safety and Health (“NIOSH”), the servicing agency, will conduct an assessment to investigate environmental health and safety implications from engineered nanomaterials (“ENMs”) released from nano-enabled products (“NEPs”) during consumer use for the Consumer Product Safety Commission (“CPSC”), the requesting agency.

3. Project Summary and Statement of Work

The unique physicochemical properties of ENMs are being exploited for use in a growing variety of commercial NEPs, including electronics, cosmetics, and structural materials, as well as a wide variety of products for medical applications. Numerous *in vitro* and *in vivo* studies have investigated the possible adverse effects of inhalation exposure to pristine ENMs during synthesis and handling by workers and consumers. However, human exposure is not limited to pristine ENMs, but also includes a wide variety of particles released from NEPs across their life cycle, including consumer use and disposal. Therefore, these results cannot be correlated to exposures at consumer level since the test particles used are not representative of the “real world” exposure of consumers to PEPs. Indeed, the potential for exposure from such life cycle particulate matter (“LCPM”) may exceed that of pristine engineered nanoparticles (“ENPs”). Moreover, the physico-chemical properties and toxicological profiles of LCPM may differ greatly from those of pristine ENPs. Despite the potential for LCPM exposure, most nanotoxicological studies have focused on pristine ENPs, and toxicological evaluation of LCPM has been limited. NIOSH and the EPA have therefore recommended life cycle analyses in their nanotechnology research programs. Most importantly, the servicing agency must to develop a methodology that can link real world LCPM exposures to toxicology and cardiopulmonary risk. This study will specifically address this important research gap.

Numerous epidemiologic studies have shown strong associations between inhalation of ambient particulate matter (“PM”) and cardiovascular mortality and morbidity, with mortality from cardiovascular causes exceeding that from respiratory causes. Animal studies also indicate that the cardiovascular system may be more sensitive to pulmonary exposure to PM than the lung. To date,

however, most nanotoxicology studies have focused primarily on the pulmonary effects of ENP exposure. This study will address this research gap using a multi-tier approach, including *in vitro*, *in vivo*, and genomic approaches, to evaluate pulmonary and cardiovascular effects of LCPM exposure.

The printer is one of the most common pieces of office equipment. Recently, it was reported that toner formulations for printing equipment constitute nano-enabled products and contain ENMs that become airborne during printing. To date, insufficient research has been performed to understand the potential toxicological properties of printer-emitted particles (“PEPs”) with several studies using bulk toner particles as test particles. These studies demonstrated the ability of toner particles to cause chronic inflammation and fibrosis in animal models. However, the toxicological implications of inhalation exposures to ENMs emitted from laser printing equipment remain largely unknown.

Researchers at Harvard Public Health’s Center for Nanotechnology and Nanotoxicology developed an exposure generation system, Printer Exposure Generation System (“PEGS”), to monitor and assess nanoparticle emissions during use of printer. NIOSH and Harvard have been working together for the last three years to study the presence of ENMs in toner formulations currently in use in laser printers and assess safety implications during consumer use. Researchers at West Virginia University have utilized computational toxicology approaches to identify signaling pathways related to multi-walled carbon nanotubes (“MWCNT”)-induced lung fibrosis from gene expression profiles of MWCNT-treated mouse lungs. The main objective of the research supported by this agreement is to study emitted ENMs-induced pulmonary and cardiovascular effects resulting from the use of laser printers. It is anticipated that research will be completed in two phases.

In FY2016, this study will consist of the following research conducted by the servicing agency: particle generation, characterization and fractionation, *in vitro* dosimetric determination, *in vitro* toxicity investigation in multiple cell lines, *in vivo* evaluation of PEPs-induced cardiovascular effects via inhalation.

a. Objective

This study has the objective to characterize biological outcomes on pulmonary and cardiovascular organ systems from rodents exposed to printer-emitted particles (PEPs) *via* whole-body inhalation and intratracheal instillation. Moreover, the biokinetic studies will be performed to investigate the clearance and translocation of PEPs in rats.

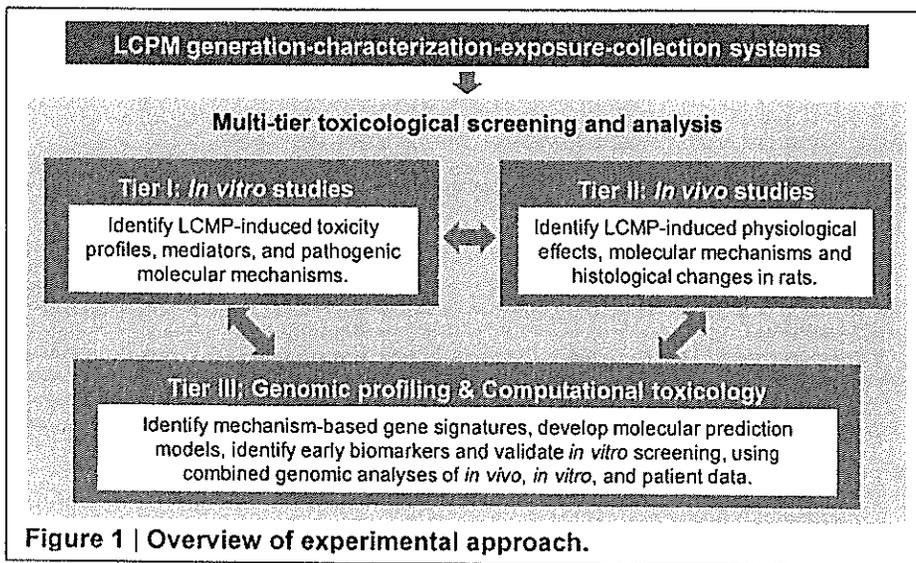
b. Hypothesis

Exposure to particles released by a high-emitting laser printer may lead to pulmonary inflammation, fibrosis and damage and adverse cardiovascular responses in rats.

c. Experimental Design

The servicing agency will employ novel exposure-generation systems to produce real-world PEPs exposure atmospheres and develop an integrated multi-tier experimental screening approach to assess toxicological outcomes with emphasis on cardiopulmonary responses (Fig. 1). State-of-the-art *in vitro* (Tier-I) and *in vivo* (Tier-II) bioassays will be performed to assess mechanisms of potential PEPs-induced cardiopulmonary disease. The integrated approach will identify mechanistic pathways

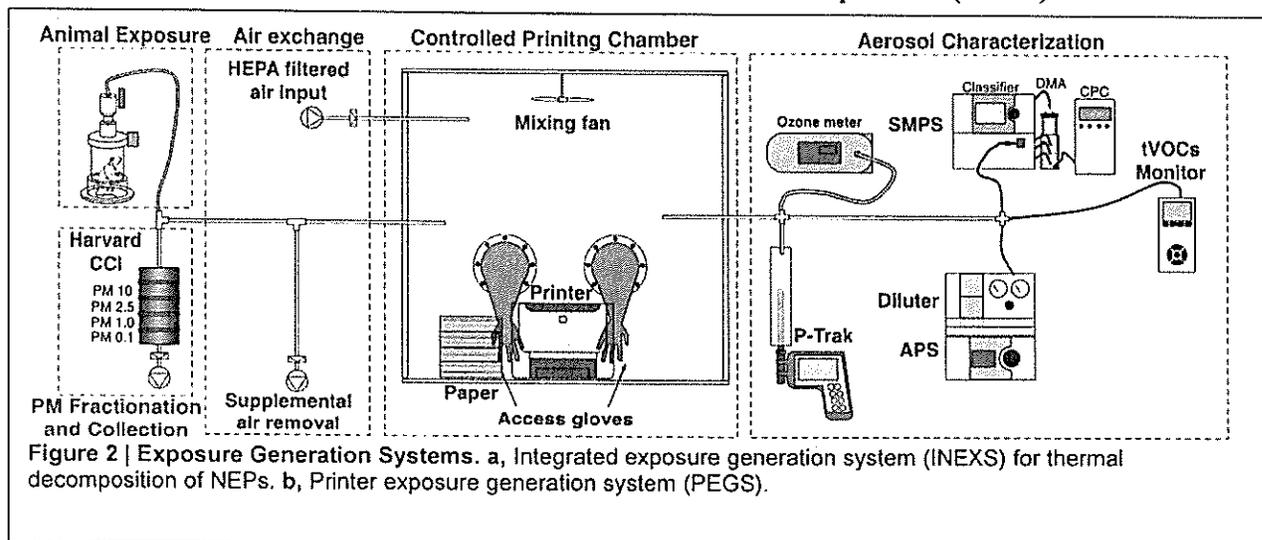
predictive of LCMP-induced cardiopulmonary diseases in animal models. In Aim 1, the servicing agency will use recently-developed particle generation and exposure methods to create and characterize real-world PEPs exposures for the assessment of cardiopulmonary effects. In Aim 2, the servicing agency will assess bioactivity of PEPs in epithelial cell and macrophage mono-culture and alveolar-capillary co-culture, and use results



to determine relevant doses for use in subsequent animal studies. In Aim 3, the servicing agency will perform *in vivo* inhalation experiments to validate and extend the *in vitro* findings. The servicing agency believes that this multi-disciplinary screening approach, linking *in vitro* and *in vivo* LCMP exposures to *in vitro* and *in vivo* toxicological evaluation, will provide a robust and useful framework for risk assessment of engineered nanomaterials across their life cycle.

d. Methods

Aim 1: Generate and characterize particles released from Nano-Enabled Printers during use: PEPs will be generated as outlined in Figure 2. Size fractionated samples will be collected for physicochemical and morphological characterization (size, shape and composition) using state-of-the-art analytical methods. Size fractionated PEPs samples will also be collected for *in vitro* studies. The servicing agency will focus on the PM_{0.1} size fraction of PEPs particles (Aim 2).



Aim 2: Evaluate the bioactivity of PEPs using in vitro assays (Tier-I):

In vitro studies will be performed using two mono-cell culture systems (primary human monocyte-derived alveolar-like macrophages (“hMDAMs”), and the human small airway epithelial cell line (“SAEC”)), as well as a co-culture system consisting of SAEC and human microvascular endothelial cells (“HMVEC”). The in vitro assays to be performed in Aim 2 are summarized in Table 1.

Cell types investigated	Endpoint/category	Measured parameter(s)	Assay/method
mono-culture hMDAMs and SAEC + co-culture SAEC and HMVEC	Particle Entry/Uptake	electron dense puncta	TEM
	Cytotoxicity	LDH leakage	LDH colorimetry
		live/dead imaging	BOBO-3 I/Calcein AM
		apoptosis	Caspase-3/7 activity (CellEvent)
		Proliferation	Total DNA (CyQUANT)
	Genotoxicity	DS DNA breaks	Nano-CometChip assay
	Inflammatory mediators	cytokine/chemokine production	Multiplex bead assay (MILLIPLEX)
	Reactive oxygen species (ROS)	general ROS	CellROX, CM-H2DCFDA
		Superoxide	DHE
	Oxidative injury	lipid peroxidation	TBARS
protein oxidation (carbonyl products)		Carbonyl Immunoblot Kit	
Signaling pathways	key signaling protein phosphorylation	Signaling Nodes Multi-Target Phos. ELISA	
co-culture SAEC and HMVEC	Specific pathogenicity factors	fibrogenesis (TGF-β and PDGF)	TGF-β ELISA
		adhesion factors (fibronectin)	fibronectin ELISA
		inflammation (c-reactive protein)	c-reactive protein ELISA
		growth factors (VEGF)	VEGF ELISA
	Alv.-capillary barrier damage	altered permeability	ECIS, image analysis, dye elution
	EMT, EndoMT	E-cadherin, fibronectin expression	E-Cadherin, fibronectin immunostain
cell morphology		confocal microscopy analysis	
co-culture HMVEC	Gap formation	gap VE-cadherin	VE-Cadherin immunostain
	Angiogenesis	tube formation	Microscopic analysis

Table 1. Summary of in vitro studies

Aim 3: Evaluate the bioactivity of PEPs particles using rat exposure studies (Tier-II):

Sprague-Dawley rats will be exposed to 1 million/cc PEPs particle aerosols from the LCPM generation platforms for totals of 40 hours (8 consecutive days at 5 hours exposure/d). Particle concentration (mass/m³), total particle count/m³, size distribution, and gases within the exposure chamber will be monitored throughout the study as described in Aim 1. Chamber temperature, humidity and particle concentration will be maintained. Respiratory and cardiovascular function data will be collected continuously during exposures, and for four hour intervals at 1, 7 days post exposure.

Respiratory data collection: The servicing agency has published a number of studies using breathing pattern analyses with particle exposures. Briefly, rats will be exposed to PEPs or filtered air in individual plethysmography chambers, and continuous respiratory measures will be collected using an automated acquisition system (Buxco/Ponemah, DSI, St. Paul, MN). Data will be reduced to 10 min. averages of the following parameters: frequency (f), tidal volume (TV), inspiratory time (Ti), expiratory time (Te), enhanced pause (Penh), accumulated volume (AV), minute volume (MV), peak inspiratory flow (PIF), peak expiratory flow (PEF), relaxation time (RT), end inspiratory pause (EIP), end expiratory pause (EEP), expiratory flow at 50 % (EF50), and pause (PAU). Other derived parameters will be calculated, including inspiratory duty cycle (IDC) and minute ventilation (Vi). BAL fluid will be analyzed 1 day post-exposure to assess cytotoxic lung injury (acellular LDH), air-

blood barrier damage (albumin), and markers of inflammation and fibrogenesis (total and differential cell counts, cytokine and chemokine concentrations). At 7 day post-exposure, lung tissue will be examined histologically for inflammation and fibrosis, and collagen expression in lung tissue will be measured to further assess fibrogenesis. Lung and heart will be evaluated *in vivo* for microvascular ROS generation by *in situ* chemiluminescence immediately after exposure.

In addition, serum samples will be taken at each time point to evaluate its potential to activate naïve endothelial cells in culture. Specifically, the servicing agency will measure 1) relative mRNA changes for *Vcam1*, *Icam1*, *Cxcl2*, *Ccl2* and *IL6*; 2) cell migration; and 3) proliferation.

Inhalation exposure: Animals will spontaneously breathe emitted PM generated in the chamber as described in specific Aim 1. Size fractionated PM will be directed from the chamber to “Rochester” type inhalation chambers in which rats will be placed in individual restraining cages. Temperature, relative humidity, and aerosol flow through the chamber will be controlled and monitored. Additionally CO, CO₂ and NO_x concentration levels in the inhalation chamber will also be monitored. Aerosol level and duration of exposure will be chosen to achieve lung burdens similar to those for the intratracheal instillation studies. At 1 and 7 days post-exposure, inflammation (BAL cell differentials) and lung damage (BAL levels of albumin and LDH) will be determined as described above. Breathing rate and airway resistance will also be monitored. Lastly, cardiovascular response will be determined by measuring the responsiveness of the excised tail artery to vasodilator or vasoconstrictor agents.

4. Projected Schedule

FY 2016:

- Generate and characterize particles released from Nano-Enabled Printers during use: 6 months.
- Evaluate the bioactivity of PEPs using in vitro assays (Tier-I): 12 months.
- Evaluate the bioactivity of PEPs particles using rat exposure studies (Tier-II): 12 months.

5. Reporting Requirements/Deliverables

Within 60 calendar days of completion of all the testing, NIOSH will issue a draft final report for CPSC staff review. Following CPSC staff review, NIOSH will have an additional 30 calendar days to deliver the final report summarizing the test data, including all photographs taken during the studies. NIOSH shall include in the final report any comments, edits or suggested changes requested by CPSC.

A. All recorded test data and findings	2 copies	December 31, 2018
B. Representative photographs	2 copies	December 31, 2018
C. Final NOAEL report	2 copies	December 31, 2018

6. Resources

Under the Interagency Agreement, CPSC will provide funding of \$300,000 during Fiscal Year 2016 to CDC/NIOSH.

FY16: \$300,000

Materials and Supplies	Cost (estimated budget FY 2016)
Obj Code 25 - Services	
Contract (Particle generation, characterization and fractionation, in vitro dosimetric determination, in vitro genotoxicity, in vivo evaluation of the bioactivity of PEPs via inhalation)	\$213,000
Obj Code 26 - Supplies, Chemicals, Reagents, Assay Kits, labware	
Evaluate the bioactivity of PEPs using in vitro assays (NIOSH/Qian Lab)	\$42,229
Investigate the activation of naïve endothelial cells in culture with rat serum (NIOSH/Erdely Lab)	\$10,000
Genomic profiling pilot assays (NIOSH/Qian Lab)	\$10,000
TOTAL Direct	
CDC Indirect Overhead charge (9%-projected)	\$24,771
TOTAL	\$300,000

7. Confidentiality Requirements and Data Sharing

- a. To the extent permitted by law, all information reported to or otherwise obtained by CPSC or its agents under the Consumer Product Safety Act (CPSA) and provided to or shared with NIOSH, which contains or relates to a trade secret or other matter referred to in section 1905 of title 18, United States Code, or subject to section 552(b)(4) of the title 5, United States Code, shall be held in confidence by NIOSH and any NIOSH contractor personnel.
- b. To the extent permitted by law, including the Freedom of Information Act, NIOSH and any NIOSH contractor shall agree not to release the identity of any manufacturer of any product being tested or reviewed in conjunction with this agreement. These provisions are consistent with and do not supersede, conflict with, or otherwise alter the employee obligations, rights, or liabilities created by existing statute or Executive Order relating to (1) classified information, (2) communications to Congress, (3) the reporting to an Inspector General of a violation of any law, rule, or regulation, or mismanagement, a gross waste of funds, an abuse of authority, or a substantial and specific danger to public health or safety, or (4) any other whistleblower protection. The definitions, requirements, obligations, rights, sanctions, and liabilities created by controlling Executive Orders and statutory provisions are incorporated into this agreement and are controlling.

- c. All documents and other materials developed pursuant to this agreement shall have appropriate statements to indicate that the work was performed pursuant to the agreement by CPSC; that the documents and other materials produced are the views of the staff or members (present or past) of the servicing agency; and that although the documents and other materials may have been developed in conjunction with CPSC staff, the documents and other materials do not necessarily represent the views of the Consumer Product Safety Commission.
- d. Any publications of or publicity pertaining to the work performed under this agreement shall include the following:

“This project was funded by CPSC. The content of this publication does not necessarily reflect the views of the Commission, nor does mention of trade names, commercial products, or organizations imply endorsement by the Commission.”
- e. NIOSH agrees that any report, manuscript or other document intended for publication or disclosure to the public and containing the results of work performed under this agreement (the “Report”) shall not identify a manufacturer, private labeler, or particular consumer product. To ensure that the Report does not identify a manufacturer, private labeler, or particular consumer product, NIOSH shall submit the Report to CPSC for review in accordance with section 6(b) of the Consumer Product Safety Act (15 U.S.C. § 2055(b), CPSC regulations at 16 C.F.R. part 1101, and CPSC Directives (Order No. 1450.2). In connection with this review, CPSC will redact from the Report the names of manufacturers and private labelers and the identities of consumer products. If the report contains information that reflects on the safety of a class of consumer products, CPSC will follow its procedures for review of that information.
- f. The servicing agency shall insure that the rights to all information, uses, processes, patents, and other developments resulting from the grant activity will be made available to the public without charge on a nonexclusive basis.

8. Scientific Integrity

CPSC has adopted the following principles in the spirit of the 2009 presidential memorandum on scientific integrity, which CPSC and NIOSH agree to adhere to while performing work pursuant to this agreement:

- Open communication among scientists and technical staff within and outside the Commission is encouraged.
- Professional growth and development of CPSC’s scientific and technical staff are supported.
- The credibility of staff’s scientific and technical work is encouraged, supported, and recognized.
- Accountability and transparency are expected and supported in communicating to the public the results of scientific and technical work.
- Scientific and technical staff are expected to adhere to a professional code of ethics.
- Protections exist and are expected to be followed to shield staff from undue influence or suppression.

9. Duration of Agreement and Amendments

This agreement will become effective on the last date of signature by the parties. The agreement will terminate 32 months after the last date of signature of the agreement by both parties, but may be amended at any time by mutual written consent of the parties.

10. Disagreements

In the event that CPSC and NIOSH have a disagreement arising under this agreement, the parties shall cooperatively seek to resolve the disagreement by themselves. If the disagreement cannot be resolved between them, the parties agree to seek the assistance of a third party in resolving the disagreement.

11. NIOSH will provide personnel, laboratory support, and equipment to perform tasks described under this agreement.

APPROVED AND ACCEPTED FOR THE NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH/CENTERS FOR DISEASE CONTROL AND PREVENTION:

BY: Don Beezhold 5/10/16
Don Beezhold Date
Director, Health Effects Laboratory Division, NIOSH

APPROVED AND ACCEPTED FOR CONSUMER PRODUCT SAFETY COMMISSION

BY: Rudolph Johnson 5.12.2016
CPSC Contracting Officer Date