A. COVER PAGE

Project Title: Multiplex Sensor Platform for Biological Monitoring	
Grant Number: 5R01OH011023-04	**Project/Grant Period:** 09/01/2016 - 08/31/2020
Reporting Period: 09/01/2019 - 08/31/2020	**Requested Budget Period:** 09/01/2019 - 08/31/2020
Report Term Frequency: Annual	**Date Submitted:** 12/01/2021
Program Director/Principal Investigator Information: JORDAN NED SMITH , BS BS PHD **Phone Number:** (509) 371-6801 **Email:** jordan.smith@pnnl.gov	**Recipient Organization:** BATTELLE PACIFIC NORTHWEST LABORATORIES BATTELLE PACIFIC NORTHWEST NATIONAL LABORATORY BOX 999, 902 BATTELLE BLVD RICHLAND, WA 993520999 **DUNS:** 032987476 **EIN:** 1314379427A3 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: ABRAHAM C MENDOZA 902 Battelle Blvd PO BOX 999 Richland, WA 99352 **Phone number:** 5093754357 **Email:** Abraham.Mendoza@pnnl.gov	**Signing Official:** ABRAHAM C MENDOZA 902 Battelle Blvd PO BOX 999 Richland, WA 99352 **Phone number:** 5093754357 **Email:** Abraham.Mendoza@pnnl.gov
Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

This research project is focused on developing a multiplex sensor array for pesticides and their metabolites that are known to be readily excreted from blood to saliva. This novel platform will enable a more accurate prediction of occupational exposures, and once validated, can readily be employed to assess dosimetry of pesticide mixture exposures in support of biomonitoring and epidemiology studies.

Three Specific Aims have been proposed:
Aim 1. Develop a multiplex quantum-dot biosensor capable of detecting mixtures of pesticides, metabolites and cholinesterase activity at occupational concentrations. A rapid, sensitive, selective, and multiplex biosensor for detecting/screening of mixed pesticide exposures in readily obtainable biological fluids will be developed. The analytical performance (figure-of-merits) of this biosensor will be established, and the capability of the biosensor to simultaneously detect multiple biomarkers (e.g. parent pesticides, metabolites, ChE) will be validated in human samples (Aim 3).
Aim 2. Estimate saliva and blood concentrations for occupational pesticide exposures utilizing a blood:saliva compartmental computational model. The goal is to utilize simple compartmental pharmacokinetic models for individual pesticides and metabolites to enable accurate prediction of saliva and blood analyte concentrations at relevant occupational exposure levels. This will directly support Aim 1 by establishing the target limits of detection (LOD) and quantification (LOQ).
Aim 3. In vitro validation of biosensor for quantifying mixed pesticide exposures in human bio-matrices. Data will be used to validate the response of the multiplex biosensor (Aim 1) to quantify saliva, blood and urine pesticide concentrations following in vitro exposure to a mixture of pesticides over a range of relevant concentrations.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File Uploaded : Training_Professional_Development.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Research from this project was presented at:

Smith JN. Pesticide Toxicology and Human Health Risk Assessment. 11/29/17. Oregon Agricultural Chemicals and Fertilizers Association (OACFA), Safety Seminar for pesticide applicators. Pendleton, OR.

Smith JN. Better Understanding Exposures to PAHs and Pesticides. ATSDR investigator initiated research translation activity.

4/20/17. Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, GA.

Smith JN. Understanding the Dose that Makes the Poison Using an Experimental and Computational Approach. Seminar. 2/1/17. Oregon State University, Corvallis, OR.

Timchalk C, Carver ZA, Weber TJ, and Smith JN. Implications of Protein Binding for Predicting Pesticide Salivary Transport Using a Combination Experimental and Computational Approach. Poster. Annual Society of Toxicology Meeting. 3/2017 Baltimore, MD.

Smith JN, Han AA, Carver ZA, Weber TJ, Ouyang H, Du D, Lin Y. Salivary biomonitoring for rapid assessment of chemical exposures. Poster at Military Health System Research Symposium (MHSRS), Orlando FL, 8/2018.

Han AA, Carver ZA, Weber TJ, Timchalk C, Smith JN. 8/2018. Coupling in vitro and computational methods to investigate the transport of herbicide/insecticide mixtures into saliva. Poster session presented at PNNL Post Graduate Research Symposium, Richland, WA.

Han AA, Carver ZA, Weber TJ, Timchalk C, Smith JN. In vitro to in vivo translation of salivary concentrations for non-invasive biomonitoring of 2,4-dichlorophenoxyacetic acid (2,4-D). Poster at Society of Toxicology Annual Meeting 3/2019, Baltimore, MD. Biological Modeling Section of the Society of Toxicology (SOT) awarded post-doctoral trainee Dr. Alice Han Honorable Mention, Best Trainee Abstract Award at the recent SOT annual meeting for this work.

Smith JN. Quality Assurance Review of Physiologically Based Pharmacokinetic Models for Regulatory Use. 3/10/19. Society of Toxicology continuing education course: Applications and Review of Physiologically Based Pharmacokinetic Modeling for Regulatory Risk Assessment, Baltimore, MD.

Cheng N, Zhao Z, Zhu W, Du D, Lin Y. "Nanomaterials Amplified Detection with Smartphone Readout" Graduate and Professional Students Association. Academic Showcase Research Exposition at WSU, 3/28/2019.

Han AA, Wang Y, Du D, Lin Y, Smith JN. Occupational biomonitoring and interpretation of 2,4-dichlorphenoxyacetic acid (2,4-D) using field deployable sensors and PBPK modeling. SOT Poster at Society of Toxicology Annual Meeting 4/2020. Virtual.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

Accomplishments

This project developed a number of new sensors for commonly used pesticides and computational models for intrepreting and translating sensor measurements to expsoures and internal.

Wang et al. (2017) developed a novel sensor for rapid detection of 2,4-dichlorophenoxyacetic acid (2,4-D) in environmental and biological specimens. This portable smartphone platform is capable of screening eight samples in a single-stripe microplate. The device combined the advantages of small size (50 × 100 × 160 mm3) and low cost ($10). The platform was calibrated by using two different dye solutions, i.e. methyl blue (MB) and rhodamine B, for the red and green channels. Results showed good correlation with results attained from a traditional laboratory reader. We demonstrated the application of this platform for detection of the herbicide 2,4-dichlorophenoxyacetic acid in the range of 1 to 80 ppb. Spiked samples of tap water, rat serum, plasma, and human serum were tested by our device. Recoveries obtained varied from 95.6% to 105.2% for all of the spiked samples using the microplate reader and from 93.7% to 106.9% for all of the samples using the smartphone device.

Carver et al. (2018) completed an assessment of 2,4-D transport into saliva using a serous-acinar chemical transport assay and an in vivo assessment of 2,4-D exposure in rats. Analysis revealed a non-linear protein binding response in plasma, indicating saturated protein binding and increased levels of unbound 2,4-D at higher doses. A strong correlation between concentrations in saliva and unbound 2,4-D in plasma was observed (Pearson correlation coefficient = 0.95). Saliva:plasma 2,4-D ratios measured in vivo (0.0079) were comparable over dose but significantly different than ratios measured in vitro (physiological conditions) (0.034), possibly due to 2,4-D concentrations in saliva not being at equilibrium with 2,4-D concentrations in blood, as well as physiological features absent in in vitro settings (e.g. blood flow). We demonstrated that 2,4-D is consistently transported into saliva using both in vitro and in vivo models, making 2,4-D a potential candidate for human non-invasive salivary biomonitoring.

Using 2,4-D transport data, Han et al. (2019) modified an existing physiologically based pharmacokinetic (PBPK) model to translate observations from the cell culture model to those in animal models and further evaluate 2,4-D kinetics in humans. While apparent differences in experimental *in vitro* and *in vivo* saliva/plasma ratios (0.034 and 0.0079, respectively) were observed, simulations with the PBPK model demonstrated dynamic saliva/plasma ratios over time and captured time points agreeing with both ratios. The model suggested that 2,4-D exhibited diffusion limited transport to saliva *in vivo* and required a longer time to reach equilibrium between saliva/plasma concentrations. Sampling time after exposures is then a critical component for interpreting salivary 2,4-D biomonitoring data. This work utilized PBPK modeling in linking observations made with *in vitro* and *in vivo* approaches and additionally explored the benefits and obstacles of salivary analysis for occupational biomonitoring. The Biological Modeling Section of the Society of Toxicology (SOT) awarded post-doctoral trainee Dr. Alice Han Honorable Mention, Best Trainee Abstract Award at the recent SOT annual meeting for this work.

Ouyang et al. (2018) synthesized manganese dioxide nanoflowers (MnO2 NFs) used as a dual readout probe to develop a novel immunochromatographic test strip (ITS) for detecting chlorpyrifos residues. MnO2 NFs-labeled antibody for chlorpyrifos was employed as the signal tracer for conducting the ITS. After 10 min competitive immunoreaction, the tracer antibody was captured by the immobilized immunogen in the test strip, resulting in the captured MnO2 NFs on test line. The captured MnO2 NFs led to the appearance of brown color on the test line, which could be easily observed by the naked eye as a qualitative readout. Due to the very slight colorimetric difference of chlorpyrifos at trace concentrations, the semiquantitative readout by naked eyes could not meet the demand of quantitative analysis. MnO2 NFs showed a significant effect on the luminol-H2O2 chemiluminescent (CL) system, and the CL signal driven by MnO2 NFs were used to quantify the trace concentrations of chlorpyrifos. 1,3-Diphenylisobenzofuran quenching studies and TMB-H2O2 coloration assays were conducted for studying the enhancing mechanism of MnO2 NFs, which was based on the oxidant activity to decompose H2O2 for forming reactive oxygen species. Under optimal conditions, the linear range of chlorpyrifos was 0.1-50 ng/mL with a low detection limit of 0.033 ng/mL (S/N = 3).

Smith et al. (2017) used a combination experimental and computational approach to predict chemical transport of 3,5,6-trichloro-2-pyridinol (TCPy), a metabolite of the pesticide chlorpyrifos, into saliva. A serous-acinar chemical transport assay measured TCPy transport with non-physiological (standard cell culture medium) and physiological (using surrogate plasma and saliva medium) conditions. High levels of TCPy protein binding were observed in cell culture medium and rat plasma resulting in different TCPy transport behaviors in the two experimental conditions. In the non-physiological transport experiment, TCPy reached equilibrium at equivalent concentrations in apical and basolateral chambers. At higher TCPy doses, increased unbound TCPy was observed, and TCPy concentrations in apical and basolateral chambers reached equilibrium faster than lower doses, suggesting only unbound TCPy is able to cross the cellular monolayer. In the physiological experiment, TCPy transport was slower than non-physiological conditions, and equilibrium was achieved at different concentrations in apical and basolateral chambers at a comparable ratio (0.034) to what was previously measured in rats dosed with TCPy (saliva:blood ratio: 0.049). A cellular transport computational model was developed based on TCPy protein binding kinetics and simulated all transport experiments reasonably well using different permeability coefficients for the two experimental conditions (1.14 vs 0.4 cm/hr for non-physiological and physiological experiments, respectively). The computational model was integrated into a PBPK model and accurately predicted TCPy concentrations in saliva of rats dosed with TCPy. Overall, this study demonstrates an approach to predict chemical transport in saliva, potentially increasing the utility of salivary biomonitoring in the future. Smith et al. (2017) was named a Top 9 Outstanding Modeling Paper in the Field of Toxicology in 2017 by the Society of Toxicology (SOT) Biological Modeling Specialty Section.

Zhao et al. (2021) developed a smartphone-based dual-channel immunochromatographic test strip (ICTS) for rapid biomonitoring of exposure to cypermethrin by simultaneous detection of cypermethrin and its metabolite, 3-phenoxybenzoic acid (3-PBA). Polymer carbon dots (PCDs) with ultrahigh fluorescent brightness were synthesized and used as a signal amplifier in ICTS assay. Cypermethrin (a representative pyrethroid pesticide) and its major metabolite 3-PBA were simultaneously detected to provide more comprehensive analysis of cypermethrin exposure. After competitive immunoreactions between the target sample and the coating antigens preloaded on the test line, the tracer antibody (PCD-conjugated antibody) was quantitatively captured on the test lines. The captured PCDs were inversely proportional to the amount of the target compound in the sample. The red fluorescence on the test line was then recorded using a smartphone-based device capable of conducting image analysis and recording. Under optimal conditions, the sensor showed excellent linear responses for detecting cypermethrin and 3-PBA ranging from 1 to 100 ng/mL and from 0.1 to 100 ng/mL, respectively, and the limits of detection were calculated to be ~0.35 ng/mL for cypermethrin and ~0.04 ng/mL for 3-PBA. The results demonstrate that the ICTS device is promising for accurate biomonitoring of pesticide exposure at point of care.

Ruan et al. (*in preparation*) developed a smartphone sensor for quantification of diaminochlorotriazine (DACT), the major metabolite and biomarker of atrazine exposure, using an Au@PtPd nanozyme (NZ) amplified lateral flow immunoassay (LFIA) integrated with a portable, low-cost 3D printed smartphone-based dual-functional optical platform (DFOP) for rapid quantification of urinary DACT. In the presence of DACT, the Au@PtPdNZs labeled antibody conjugated with DACT and was captured by the haptens immobilized on the test line. Due to the high catalytic performance of Au@PtPdNZs, an increased sensitivity for DACT detection was achieved. Both the direct chromogenic signal on LFIA and the catalytic absorbance signal were recorded by our 3D printed DFOP. The DFOP integrates the dual quantification functions of test strip chromogenic result and 8-wells absorbance output, which relies on smartphone camera and image analysis software to achieve intelligent optical inspection. With Au@PtPdNZs catalytic amplified readout, a detectable range was achieved from 10 pg/mL to 100 ng/mL, with the detection limit of 11 pg/mL. The enhanced sensitivity was attributed to the outstanding peroxidase-like activity of the hyperbranched mesoporous core-shell structure of Au@PtPdNZs. The 3D-printed DFOP integrated with LFIA shows comparable results as commercial instruments, with miniaturized size and enhanced portability for onsite applications.

Opportunities for training and professional development

This project supported a number of trainees. At WSU, this grant supported Wenlei Zhu (Post Doc), Shichao Ding (PhD student), Zhaoyuan Lyu (PhD Student), Yijia Wang (PhD student), Hui Ouyang (PhD Student), Nan Cheng (PhD Student), Chengzhou Zhu (Post Doc), and Xiaofan Ruan (PhD student). At PNNL, this grant supported Zana Carver (PhD Student) and Alice Han (Post Doc).

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Ouyang H, Lu Q, Wang W, Song Y, Tu X, Zhu C, Smith JN, Du D, Fu Z, Lin Y. Dual-Readout Immunochromatographic Assay by Utilizing MnO2 Nanoflowers as the Unique Colorimetric/Chemiluminescent Probe. Analytical Chemistry. 2018 March 28;90(8):5147-5152.
N/A: Not NIH Funded	Weber TJ, Qian WJ, Smith JN, Gritsenko MA, Hu D, Chrisler WB, Timchalk C. Stable Acinar Progenitor Cell Model Identifies Treacle-Dependent Radioresistance. Radiation research. 2019 August;192(2):135-144. PubMed PMID: 31141469; DOI: 10.1667/RR15342.1.
N/A: Not NIH Funded	Niu X, Shi Q, Zhu W, Liu D, Tian H, Fu S, Cheng N, Li S, Smith JN, Du D, Lin Y. Unprecedented peroxidase-mimicking activity of single-atom nanozyme with atomically dispersed Fe-N_x moieties hosted by MOF derived porous carbon. Biosensors & bioelectronics. 2019 October 1;142:111495. PubMed PMID: 31310943; DOI: 10.1016/j.bios.2019.111495.
N/A: Not NIH Funded	Han AA, Timchalk C, Carver ZA, Weber TJ, Tyrrell KJ, Sontag RL, Gibbins T, Chrisler WB, Weitz KK, Du D, Lin Y, Smith JN. Physiologically Based Pharmacokinetic Modeling of Salivary Concentrations for Noninvasive Biomonitoring of 2,4-Dichlorophenoxyacetic Acid (2,4-D). Toxicological sciences : an official journal of the Society of Toxicology. 2019 December 1;172(2):330-343. PubMed PMID: 31550007; DOI: 10.1093/toxsci/kfz206.
N/A: Not NIH Funded	Smith JN, Skinner AW. Translating nanoparticle dosimetry from conventional in vitro systems to occupational inhalation exposures. Journal of aerosol science. 2021 February 17;155.
N/A: Not NIH Funded	Zhao Y, Ruan X, Song Y, Smith JN, Vasylieva N, Hammock BD, Lin Y, Du D. Smartphone-Based Dual-Channel Immunochromatographic Test Strip with Polymer Quantum Dot Labels for Simultaneous Detection of Cypermethrin and 3-Phenoxybenzoic Acid. Analytical chemistry. 2021 October 12;93(40):13658-13666. PubMed PMID: 34591463; DOI: 10.1021/acs.analchem.1c03085.

Non-compliant Publications Previously Reported for this Project

Public Access Compliance	Citation
N/A: Not NIH Funded	Wang Y, Zeinhom MMA, Yang M, Sun R, Wang S, Smith JN, Timchalk C, Li L, Lin Y, Du D. A 3D-Printed, Portable, Optical-Sensing Platform for Smartphones Capable of Detecting the Herbicide 2,4-Dichlorophenoxyacetic Acid. Analytical chemistry. 2017 September 5;89(17):9339-9346. PubMed PMID: 28727917; DOI: 10.1021/acs.analchem.7b02139.
N/A: Not NIH Funded	Ouyang H, Tu X, Fu Z, Wang W, Fu S, Zhu C, Du D, Lin Y. Colorimetric and chemiluminescent dual-readout immunochromatographic assay for detection of pesticide residues utilizing g-C_3N_4/$BiFeO_3$ nanocomposites. Biosensors & bioelectronics. 2018 May 30;106:43-49. PubMed PMID: 29414087; DOI: 10.1016/j.bios.2018.01.033.
N/A: Not NIH Funded	Wang Y, Zeinhom MMA, Yang M, Sun R, Wang S, Smith JN, Timchalk C, Li L, Lin Y, Du D. A

	3D-Printed, Portable, Optical-Sensing Platform for Smartphones Capable of Detecting the Herbicide 2,4-Dichlorophenoxyacetic Acid. Analytical chemistry. 2017 September 5;89(17):9339-9346. PubMed PMID: 28727917; DOI: 10.1021/acs.analchem.7b02139.
N/A: Not NIH Funded	Ouyang H, Tu X, Fu Z, Wang W, Fu S, Zhu C, Du D, Lin Y. Colorimetric and chemiluminescent dual-readout immunochromatographic assay for detection of pesticide residues utilizing g-C_3N_4/$BiFeO_3$ nanocomposites. Biosensors & bioelectronics. 2018 May 30;106:43-49. PubMed PMID: 29414087; DOI: 10.1016/j.bios.2018.01.033.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Other	A number of new sensors, sensoring technologies, and computational model for interpreting biomarkers were developed. See accomplishments.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
JORDANSMITH	Y	Smith, Jordan Ned	BS,BS,PHD	PD/PI	4.1	0.0	0.0			NA
YUEHELIN	Y	Lin, Yuehe	BS,MS,PHD,PHD	PD/PI	0.0	0.0	1.0			NA
DANDUPNNL	Y	Du, Dan	PHD	PD/PI	10.0	0.0	0.0			NA
HANALICE	N	Han, Alice	PHD,AB	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.2	0.0	0.0			NA
	Y	Li, Suiqiong		Co-Investigator	4.0	0.0	0.0			NA
WENLEIZHU	Y	Zhu, Wenlei		Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	5.0	0.0	0.0			NA
KAGAITHER	N	Gaither, Kari Ann	BS,PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.4	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

G. SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

NOTHING TO REPORT

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT
No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE
Not Applicable
G.11 PROGRAM INCOME
Not Applicable
G.12 F&A COSTS
Not Applicable

I. OUTCOMES

I.1 What were the outcomes of the award?

Human exposure is rarely to single chemical agents but rather to complex chemical mixtures. This is particularly true in the Agricultural Industry Sector (a NIOSH priority) where multiple pesticides are utilized in combination and/or sequential application to crops. Due to the complexity of occupational exposures and biological systems, measurement of a single biomarker is not an adequate quantitative assessment of exposure. Hence, this project developed, validated, and refined a novel multiplex sensor platform capable of quantifying multiple biomarkers associated with pesticide exposures (dose), utilizing saliva, blood, and urine as relevant biological fluids (a NIOSH Cross Sector- Exposure Assessment priority) and pharmacokinetic models to interpret sensor measurements, including:

• Developed a novel sensor for rapid detection of 2,4-dichlorophenoxyacetic acid (2,4-D) in environmental and biological specimens.
• Assessed 2,4-D transport into saliva using a serous-acinar chemical transport assay and an in vivo assessment of 2,4-D exposure in rats.
• Modified an existing physiologically based pharmacokinetic (PBPK) model to translate observations from the cell culture model to those in animal models and further evaluate 2,4-D pharmacokinetics in humans.
• Synthesized manganese dioxide nanoflowers (MnO_2 NFs) used as a dual readout probe to develop a novel immunochromatographic test strip (ITS) for detecting chlorpyrifos residues.
• Developed a cellular and computational model for predicting chemical transport of 3,5,6-trichloro-2-pyridinol (TCPy), a metabolite of the pesticide chlorpyrifos, into saliva.
• Developed a smartphone-based dual-channel immunochromatographic test strip (ICTS) for rapid biomonitoring of exposure to cypermethrin by simultaneous detection of cypermethrin and its metabolite, 3-phenoxybenzoic acid (3-PBA).
• Developed a smartphone sensor for quantification of diaminochlorotriazine (DACT), the major metabolite and biomarker of atrazine exposure, using an Au@PtPd nanozyme (NZ) amplified lateral flow immunoassay (LFIA) integrated with a portable, low-cost 3D printed smartphone-based dual-functional optical platform (DFOP) for rapid quantification of urinary DACT.