ASELL

Turning Science Into Solutions

Biodosimetry Capabilities Summary

September 2021

Prepared in support of IARPA TEI-REX Proposers Day

Our Mission: **Technology development to strengthen security and emergency preparedness**

Our Focus: **Development of biodosimetry and dosimetry technologies**

Highlights:

- Active biodosimetry and dosimetry programs funded by BARDA, NIAID, DoD
- Extensive capabilities in technology development, verification, validation, and deployment
- Extensive network of biodosimetry development partners
- Demonstrated success in technology development to meet government objectives
- Small business with established program management, contracts, and subcontracts management systems

ASELL is a Maryland-based small business that develops and applies emerging technologies to meet the federal government's national security and emergency response challenges. Led by an executive team with more than 100 years of combined experience, ASELL delivers successful development, validation, deployment and support of complex technical solutions for US Government customers. ASELL has mature and robust systems and processes that are more typical of larger companies, coupled with the agility of a small company. As described further below, ASELL was founded to advance the development of a high-throughput quantitative biodosimetry system. ASELL built our team with expertise across the various disciplines needed to evaluate and advance biodosimetry technologies. Our team includes multiple PhD level scientists with deep domain expertise and proven experience developing cell-based, protein biomarker and molecular detection assays and technologies; preclinical expertise including small and large animal biodosimetry model experience; clinical research capabilities, including design and execution of studies with radiotherapy patients to validate biodosimetry biomarkers; algorithm development, quality assurance and regulatory expertise; and program managers with decades of experience managing complex technology development programs. We complement internal core competencies through collaborative relationships with organizations that have experience and capabilities relevant to the development of radiation exposure tools, including specialists in emerging technologies, statistics, radiation biology, dosimetry, manufacturing, and radiation physics, among others. As summarized in the table below, ASELL and our existing collaborators have much of the requisite expertise needed to meet the needs of the TEI-REX program.

	ASELL	Partners
3D full-thickness skin models		X
Analytical Biochemistry	X	X
Biodosimetry	X	X
Biomarker discovery		X
Dosimetry	X	X
Exposure Modeling	X	X
Glycomics		
In vitro models	X	X
Ionizing Radiation	X	X
Large animal models	X	X
Lipidomics		
Low-dose Radiation Physics		X

	ASELL	Partners
Machine Learning	X	
Mass spectrometry		
Metabolomics		
Multiomics		
Non traditional models		
Other post-translational modifications		
Proteomics	X	X
Radiation Physics		X
RAMAN		
Small animal models	X	X
Testing and Evaluation	X	X
Program Management	X	

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ASELL's experience in biodosimetry and other national security programs

The ASELL team has proven success executing early-stage exploratory research programs through advanced development and deployment including meeting structured quality management system requirements. This team also has deep experience in the very rapid delivery of biotechnology programs to meet national security demands. By example, many of the team contributed to the national response to the anthrax attacks following 9-11. These activities have parallels to the goals of the TEI-REX program including meeting technical program objectives through the exploration and application of emerging cutting-edge technologies combined with the structured, advanced development and validation needed to ultimately support an operational program with high confidence.

Our team has been developing biodosimetry technologies for US government applications for more than a decade, initiated with a program to develop a high-throughput, laboratory-based system to enable the federal government to measure absorbed dose in the civilian population following a large-scale radiological / nuclear incident. The technical challenges of this program were substantial. Amongst many others, there is an objective to analyze 400,000 or more samples in just 7 days with enough sensitivity and specificity to ensure that limited emergency response and medical resources can be most effectively delivered. There was no existing technology sufficiently mature to meet these objectives. In addition to the technical requirements, there is a requirement that the technology be developed in a manner that enables eventual regulatory authorization as an in-vitro diagnostic, a requirement that has driven technology selection and the test and evaluation approach. The ASELL team approached the challenge without *a priori* restrictions on specific instrumentation or platforms. In collaboration with our partners, we surveyed the state-of-the art in biodosimetry and settled upon a cytogenetic approach which has been significantly advanced to meet specific program objectives. As the technology has matured, the ASELL team has inserted new instrumentation and developed novel chemistries, cell culture formulations, image analysis algorithms and data processing techniques to produce what is now labelled as CytoRADx, a high throughput, quantitative biodosimetry platform that is pending final validation studies to meet FDA regulatory requirements. The technical and programmatic success of this program has been demonstrated through sustained support from the Biomedical Advanced Research and Development Authority (BARDA). Through this experience, ASELL team has developed deep core competencies in the development, test, and evaluation of biodosimetry technologies. We have built a deeply engaged network of academic, medical center, preclinical and clinical sites, national labs, manufacturing partners, and other collaborators to complement internal competencies and ensure success in our biodosimetry initiatives.

Building upon the success of the BARDA program, ASELL has subsequently expanded our portfolio of biodosimetry research and development programs. ASELL is currently an awardee under the National Institute of Allergy and Infectious Diseases (NIAID) Radiation Biodosimetry Assays and Devices U01 Cooperative Agreement program. Under this effort, ASELL is evaluating soluble, cell surface, and intracellular proteins along with hematologic biomarkers for potential future applications in a field portable point-of-care biodosimetry device. This instrumentation relies on the integration of a unique imaging technology and neural network-based image processing for detection. The integration of this instrument platform, biomarkers of exposure and a unique algorithm will enable fieldable screening for radiological exposure.

Still further, ASELL has been collaborating with a partner to support the early-stage development of a new approach to apply electron spin resonance (ESR) technology for physical dosimetry applications. There is a long history and deep scientific basis for using ESR technology to detect radiation exposure. However, application of ESR for broad use in emergency response scenarios has been plagued by confounding factors of background signatures, the inability to distinguish between different types of radiation, and instrumentation that is incapable of rapidly measuring low levels of radiation exposure, amongst others. Under this program, new instrumentation and supporting technology is being developed that promises to overcome these confounding issues.

Many of the ASELL team's research and development activities have been business sensitive or had national security restrictions. Some of our activities have been suitable for public dissemination and below we have summarized select public presentations in which our biodosimetry research and development has been shared.

Demographic Study Using the Cytokinesis-Block MicroNucleus (CBMN) Assay to Assess the Need for Separate Calibration Curves Among Different Demographic Groups in Determining Past Acute Radiation Exposure Richard Kowalski, Ryan Mahnke, Johnny Ho, Matthew Snyder, Xiang Ma, Monta Whitney, Nariman Panahian, David J. Brenner, Guy Garty, Adayabalam Balajee, Helen Turner, Jay Perrier, Courtney Ashton, Evan Hempel, and Douglas Henderson, presented at the 2014 Radiation Research Society Annual Meeting

Development of a unified culture media (UCM) for the cytokinesis-block micronucleus (CBMN) assay for radiation dose assessment in both non-human primate (NHP) and human lymphocytes Chris Capaccio, Kenneth Damer, Ryan Mahnke, David J. Brenner, Mohammad Haseeb Durrani, Jay Perrier, Maria Taveras, Helen Turner, Adayabalam Balajee, Stanley Lue, and Richard Kowalski presented at the 2016 Radiation Research Society Annual Meeting

A High-throughput, Standardized Biodosimetry Diagnostic System Based on the CBMN Assay Chris Capaccio, Jay R. Perrier, Lídia Cunha, Ryan C. Mahnke, Thomas Lörch, Michael Porter, Chris L. Smith, Ken Damer, J. Daniel Bourland, Bart Frizzell, Jennifer Torelli, Marie Vasquez, Jeremy B. Brower, Melanie Doyle-Eisele, Maria Taveras, Helen Turner, David J. Brenner, and Richard Kowalski presented at the 2020 Radiation Research Society Annual Meeting

CytoRADx: A High-throughput, Automated CBMN-Based Biodosimetry System Richard Kowalski, Invited talk at the 2021 Conference on Radiation Topics.

POC Biodosimetry System and Triage Assessment: Radiation-induced Hematological and Protein Biomarkers, Chris L. Smith presented at a virtual presentation of the 2021 Military Health Systems Research Symposium.

CytoRADx: A High-Throughput, Standardized Biodosimetry Diagnostic System Based on the Cytokinesis-Block Micronucleus Assay Chris Capaccio, Jay R. Perrier, Ryan C. Mahnke, Michael Porter, Chris L. Smith, Ken Damer, and Richard Kowalski, in press. Radiation Research Journal

Beyond, biodosimetry the ASELL team has deep experience in developing CBRNE technologies in support of government national security and intelligence programs. These have included programs developing technologies and analytical approaches for the detection of chemical and biological weapon signatures, transferring laboratory-based technologies to far forward field applications including mobile laboratories, environmental detection systems, mail screening systems, and deployment of these technologies into austere environments.

In addition to ASELL-led research and development, ASELL also provides supporting services to other technology and product development organizations. This includes scientific support, such as reviewing and designing experimental approaches and product development plans, advising teams on program management planning and systems, and providing quality assurance and regulatory services needed to support commercial product launch.

Our Team

Our collective experience has proven that a multidisciplinary team is essential to meet the most challenging national security technical development programs. We bring forth a team in which deep technical expertise is complemented with proven program management skills and a mindset towards eventual operational deployment. Our team has decades of experience understanding and meeting the unique requirement of sensitive national security programs including classified programs. To that end, ASELL has assembled a program leadership team with the proven experience to deliver all these key program elements

Richard Kowalski, PhD, Chief Scientist Dr. Kowalski has over 30 years of experience developing and supporting devices for the detection of biomarkers including confirmatory assays for radiation exposure and infectious disease pathogens and using mesenchymal stem cells for bone repair, cancer treatment, and gene therapy and platelet-rich plasma support for wound care. For the past 8 years, Dr. Kowalski has focused research efforts on the development of biodosimetry technologies including serving

as the Principal Investigator for our program funded by the Biomedical Advanced Research and Development Authority to develop and validate the CytoRADx high throughput biodosimetry system. In addition, he is leading early-stage NIH funded programs examining the utility of protein biomarkers to enable point-of-care biodosimetry. Immediately prior to joining ASELL, Dr. Kowalski was the Principal Investigator at Northrop Grumman where he led assay development, clinical and non-clinical studies of the CytoRADx System. Prior to Northrop Grumman, Dr. Kowalski led Medical and Clinical Affairs teams and early Product Development at Cylex Inc. As lead of Product Development at Cylex, Dr. Kowalski brought the Cylex Immune Cell Function Assay (ImmuKnow®) from bench to bedside by leading the clinical and analytical validation studies to support clearance of ImmuKnow for marketing in the US. Dr. Kowalski drives ASELL's scientific leadership to execute early-stage proof-of concept studies through down select, optimization, verification and validation. As ASELL's Chief Scientist, Dr. Kowalski provides subject matter expertise and advises on technical issues including experimental design, optimization, and validation. He received his doctorate in Molecular Biology at Vanderbilt University and held post-doctoral fellowships in biochemistry and molecular biology and molecular pharmacology at the University of Florida and the National Cancer Institute.

Matthew Snyder, Vice President of Operations Mr. Snyder has more than 20 years of experience in engineering and program management and has been the Vice President of Operations and Senior Program Manager at ASELL since 2017. Prior to moving to ASELL he was a Program Manager at Northrop Grumman where he led a variety of national security programs for the development, operations and maintenance of CBRNE and diagnostic technology programs including the CytoRADx™ high-throughput biodosimetry in vitro diagnostic device, which involved complex technology integration and required a deep understanding of customer needs. Mr. Snyder began his career in engineering and has worked in product development, large-scale production, deployment, and sustainment involving biotechnology. Most recently he has been leading the program management activities in support of the CytoRADx Biodosimetry IVD device development. Mr. Snyder drives ASELL's structured program management, ensuring that program activities from early-stage exploration through operational deployment meet programmatic objectives. Mr. Snyder graduated from the University of Rochester with a Bachelor's degree in Biology and a Master's degree in Mechanical Engineering, has completed a certificate in Program Management from the University of California Irvine, and has held an active Project Management Professional (PMP) certificate since 2008.

Kenneth Damer, Vice President of Engineering and Technology Development Mr. Damer has more than 20 years of experience in various technical, engineering and program management leadership roles serving a broad range of customers. Since 2001, Mr. Damer has focused on leading challenging CBRNE technology development programs. He has led the development of a variety of CBRNE technologies and platforms, including radiological biodosimetry, biological threat agent detection/identification (PCR, immunoassay, UV-LIF, etc.), aerosol particle collection and concentration, and microfluidics. He is currently the Product Development Manager on the CytoRADx High Throughput Biodosimetry IVD device program for BARDA, directing all technical activities. Mr. Damer was previously a Program and Engineering Manager at Northrop Grumman, where he managed complex technical efforts in biotechnology spanning the entire program lifecycle, from early concept development and technology assessments through post-production operations and maintenance. Mr. Damer has decades of experience in structured test and evaluation programs and has deep experience distilling operational program objectives to drive technology development. He holds degrees in engineering and technical management from Worcester Polytechnic Institute and Johns Hopkins University.

Michael Zdanis, Director of Clinical Research and Operations Mr. Zdanis has over 25 years of experience in pre-clinical through Phase I-III clinical trials, post-marketing surveillance studies, and health economics and outcomes studies. He has led the development of protocols, legal and ethical submissions, development of statistical analysis plans and submission of regulatory filings. He has been responsible for the conduct of both prospective and retrospective clinical studies involving both academic medical centers and community providers that have ranged in scale from fewer than 100 patients to

hundreds of sites and thousands of patients. He holds a B.A. degree in Economics from Haverford College and a Master's degree in Economics from Johns Hopkins University.

Our Approach to TEI-REX

Our approach to meeting the demanding TEI-REX objectives will follow the partner-based model that ASELL has successfully followed in previous technology development efforts. We have reviewed the recently shared performance goals, and our subject matter experts are currently assessing the gaps between existing technologies (including biomarkers and measurement techniques) and the program objectives. As part of this assessment, we have engaged our academic, national lab and private sector collaborators as we consider a broad range of emerging biodosimetry approaches. We are unhindered by commitments to any specific technology or biomarkers at this time and are currently seeking to identify collaborators that complement our internal competencies to meet the unique challenges of the TEI-REX program. Our approach to technology development is partnering with best-in-class collaborators to meet the specific demands at each phase of development. At earlier stages, this includes academic partners with biomarker discovery research pipelines. At this stage, ASELL provides an independent testbed to quickly assess technology suitability and ensures technologies are developed to support later tech transfer. Importantly, we also apply our deep operational perspective to even earlier stage proof of concepts studies, helping ensure that all research and development efforts are aligned with the ultimate goal of enabling operational systems. As the biomarkers are verified and detection techniques matured, ASELL engages partners with additional capabilities including additional in-vitro and animal models. Through interim reviews we assess progress towards near term technical goals as well as the future vision, mitigating against the research creep from deployment that can plague some early-stage programs. Early research and development can be slowed when burdensome quality management efforts are applied uniformly, and later stage operational goals can be delayed when quality management is not adequately addressed. ASELL applies our scalable, structured quality management system to ensure appropriate quality measures are incorporated throughout. This model ensures that the most appropriate biomarkers and measurement systems will be selected and developed to meet TEI-REX program goals.

We are excited to further explore how ASELL can apply our extensive biodosimetry capabilities and technical development expertise to meet IARPA's TEI-REX program goals. If you wish to discuss how we might collaborate, please contact Michael Ehret at mehret@asell.com.

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