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CONTRACTOR PERFORMANCE ASSESSMENT REPORT (CPAR)

Nonsystems

Name/Address of Contractor:

Company Name: STEMINA BIOMARKER DISCOVERY, INC

Division Name:

Street Address: 504 S ROSA RD # 150

City: MADISON

State/Province: WI Zip Code: 537191256

Country: USA

CAGE Code:

DUNS Number: 794516695

PSC: AJ33 NAICS Code: 541711

Evaluation Type: Interim

Contract Percent Complete:

Period of Performance Being Assessed: 01/08/2014 - 01/07/2016

Contract Number: EPD13055 **Business Sector & Sub-Sector:** Nonsystems - Science and Technology

Contracting Office: DCO00 **Contracting Officer:** NICOLE HAIRSTON **Phone Number:** 919-541-4826

Location of Work:

Award Date: 01/08/2013 **Effective Date:**

Completion Date: 01/07/2019 **Estimated/Actual Completion Date:**

Total Dollar Value: $10,637,000 **Current Contract Dollar Value:** $100,000

Complexity: High **Termination Type:** None

Competition Type: Full and Open Competition after Exclusion of Sources **Contract Type:** Firm Fixed Price

Key Subcontractors and Effort Performed:

DUNS:

Effort:

DUNS:

Effort:

DUNS:

Effort:

Project Number:

Project Title:

Support for EPA's ToxCast and Virtual Tissue Model programs

Contract Effort Description:

federally-funded research) exposed to test compounds to predict the developmental toxicity potential of the compound and identify human metabolites and metabolic pathways that may be subject to chemically induced alterations and to identify trends which may equate to their potential developmental toxicity in a human system, as defined in the individual task orders issued by the Contracting Officer. The contractor shall receive compounds in 96-well plates in DMSO and test these in profiling panels of devTOX quickPredict and cell-titre assays. Measure ornithine and cystine levels in culture medium on day-3 to determine the ornithine/cystine ratio by HILC-HRMS, in relation to viable cell number. Ornithine is derived from arginine breakdown during the citric acid cycle (mitochondrial matrix); Cystine is formed by oxidation of two cysteine molecules that covalently link via a disulfide bond. HILC-HRMS (hydrophilic interaction liquid chromatography coupled to high-resolution mass spectrometry) measures these metabolites based on what cells utilize and produce (secretome). Although it is not currently known how or why the assay works to predict teratogenicity, it may be dependent on biology such as transporter status, mitochondrial function, and redox states in progenitor (pluripotent) cells. Each compound is tested in triplicate with neutral control (0.1% DMSO – interferes at 0.25%) and positive reference (methotrexate – human teratogen). Undifferentiated H9 cells (WA09, WiCell Research Institute, Madison, WI) are exposed for 72 hr; conditioned media from the last 24-hr treatment period is collected and added to acetonitrile to quench metabolism. Positive and

negative reference controls are included on each plate to test that teratogenicity predictions are within specifications. The negative control is methotrexate (MTX) at 5 nM and the positive control is MTX at 1 µM. Stemina's standard exposure ranges from 0.1 µM to 300 µM at half-log dilutions; however, the target exposure range has been set based on ToxCast's cytotox burst, compound availability, and/or compound insolubility in DMSO. Stocks diluted 1:1000 in mTeSR1 media and then mTeSR1 containing 0.1% DMSO such that the final concentration of DMSO will be 0.1% in all treatments. Cell viability is assessed using the CellTiter-Fluor Cell Viability Assay in parallel as per the manufacturer instructions (Promega, Madison, WI). The relative fluorescence unit (RFU) of each sample is background corrected by subtracting the treatment specific media sample RFU from the cell sample RFU. Values are then normalized to the mean RFU of the reference treatment (0.1% DMSO). Report outputs are endogenous ornithine and cystine levels and ratio in cell-conditioned media normalized to C13-labeled spike-in standard.

Small Business Utilization:

Does this contract include a subcontracting plan? No

Date of last Individual Subcontracting Report (ISR) / Summary Subcontracting Report (SSR): N/A

Evaluation Areas	Past Rating	Rating
Quality:	Exceptional	Exceptional
Schedule:	Exceptional	Exceptional
Cost Control:	N/A	N/A
Management:	Exceptional	Exceptional
Utilization of Small Business:	N/A	N/A
Regulatory Compliance:	N/A	N/A
Other Areas:		
(1) :		N/A
(2) :		N/A
(3) :		N/A

Variance (Contract to Date):

Current Cost Variance (%): Variance at Completion (%):

Current Schedule Variance (%):

Assessing Official Comments:

QUALITY: The quality of product/services from the Contractor (Stemina) is rated as exceptional. Contractor provides a key platform in support of EPA's ToxCast and Virtual Tissue Model programs, including an assay on human embryonic stem cell metabolism that is highly unique to this contractor as they specialize in metabolomics profiling. The Contractor has provided a high level of quality control measures with regard to their data generation as can be effectively validated by the consistency in data between reference compounds and replicate compounds in a blinded study. In each of these areas, the Contractor consistently exceeded performance expectations and successfully delivered timely, high quality, responsive services and products. This performance period was the second year of a 5 year contract. The new contract instituted a number of new services and CLINS to address biological and technological gaps across the ToxCast research program, particularly to broaden EPA's coverage of prenatal developmental toxicity to predict the teratogenic potential of the compound and identify human metabolites and metabolic pathways that may be subject to chemically induced alterations and to identify trends which may equate to their potential developmental toxicity in a human system. Stemina has a strong ability to provide metabolomic readouts and targeted metabolite features extracted from LC-MS based analysis on a federally-approved human embryonic stem (hES) cell line exposed to large numbers of test compounds.
During the period of performance evaluated here (1/7/15 to 1/6/16) the Contractor worked closely with the COR to ensure the technical plans that were set in place for Task Order (TO) 2 and TO3 were detailed and achievable based on determined timelines. The Contractor worked closely with the TOCOR to address a small number of data insufficiencies or inconsistencies, and ultimately improve data quality issues pertaining to documenting of chemical sample details. In particular, in consultation with the TOCOR, new procedures are being developed and put in place to address the sensitivity and specificity of the data analysis methods for predictive modeling of prenatal developmental toxicity. The Contractor expanded the duties of the Project Coordinator / Head of Operations to oversee all aspects of the EPA contract to ensure consistency and adherence to strict quality control procedures. In particular, after determining that a technical issue arose with some sample volumes or LC/MS detector settings, the Contractor reconciled the problem and performed additional sensitivity analysis to confirm there was no impact to the quality of the results. The Contractor corrected the detector

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assignment to avoid this problem in the future. In each of these cases, the Contractor worked closely with the TOCOR to understand the nature of the problem and to recommend solutions and improvements to procedures to improve the quality assurance of EPA's data management, well beyond the minimum required by the Contract specifications. In addition, the Contractor has worked closely with the TOCOR to improve efficiencies in ordering of subsequent task orders of the same inventory compounds so as to minimize freeze-thaw cycles which compromise the integrity of the samples.

A quality review site-visit of the Stemina facility was conducted by the TOCOR and EPA's QA Manager on July 27, 2015, meeting with Stemina's CEO, CSO, Project Manager, QA Manager, and staff scientists. The audit covered two objectives: (1) to conduct a Quality System Audit (QSA) based on the EPA-approved, contractually-required, Quality Management Plan (QMP), focusing on the development and implementation of the organizational elements described in the QMP; and (2) to conduct a Technical System Audit (TSA) to evaluate Stemina's facilities, equipment, personnel, training, procedures, recordkeeping, data validation, data management, and reporting, focusing on technical activities typically described in standard operating procedures (SOPs). The final audit report was signed on 8/31/15. There were no findings from the audit, but some practices were observed that could either affect future chemical throughput or represented good practices to be noted: (a) chemical processing, dosing and extraction is manual, not automated (no reflection on current performance is noted); (b) monthly quality council reviews and weekly chats or data reviews with the TOCOR and multiple internal reviews by the QA Manager (good practice); and (c) both the stem cell biology and the instrumental chemistry analysis are in the same facility and adjacent rooms, which facilitates more rapid turnaround between dosing and analysis which reduces the chance of chemical degradation (good practice). No follow-up was necessary.

SCHEDULE: Stemina is rated Exceptional in the timeliness of performance in every area in which they directly provide services, particularly in the core areas of chemical registration, data validation, solubilizations, platings and data delivery. The Contractor consistently performed well beyond expectations with respect to turn-around time for the assays, which were consistently completed well within the time allowed for the service, and ahead of or on schedule. Stemina consistently demonstrates excellent, trustworthy professional judgment and takes a proactive stance in proposing solutions to problems as they arise to keep orders on schedule. When orders are submitted by the COR, these are quickly reviewed and processed by the Contractor, who communicates with the TOCOR to clarify any questionable elements of orders as they move forward to ensure accurate processing. Once an order is entered into the queue, an estimated data delivery date is provided plus contingency plans in the event of unforeseen problems. The Contractor has an excellent track record of meeting these estimated target dates, which greatly facilitates EPA's planning and communication with vendors and collaborators. For example, TO2 data on 140 samples for CLIN 2/3, a complex assay, were delivered 90-days after the order; and TO3 data on 4 samples for CLIN 2/3 were delivered 21-days after the order. The Contractor regularly communicated the status of the order with the TOCOR through weekly updates, which helps both parties to manage time constraints and plan for the completion and publication of the work.

COST CONTROL: A rating for cost is not required for firm fixed price contracts.

MANAGEMENT: Stemina assigns exceptionally competent professional staff to support the EPA Contract. The Program Coordinator, Laura Egnash has taken on oversight of all aspects of the EPA contract services as Head of Operations and oversees all aspects of the EPA Contract TO processing, including placing orders in the queue, monitoring progress, assuring data pass their internal quality control standards and timely submission of the data sets as they are validated. The exceptional competence and responsiveness of the Program Coordinator, the experience in this position, and the authority given to this position within Stemina has been central to the highly effective functioning of the Contract. The Program Coordinator is always highly organized, receptive to EPA TOCOR suggestions, and effectively conveys any issues pertaining to processing of issued TOs and CLINs. The Program Coordinator has also been instrumental in suggesting and instituting improvements to processes to give the government the best value and planning of subsequent task orders. All representatives of Stemina have been exceptionally responsive, courteous, and professional in all TOCOR interactions, and take a proactive approach to anticipating EPA future needs. The evidence for this is in the collaborative presentation of a poster presentation of the results of the work performed during the initial year of this contract at the 2015 Society of Toxicology and Teratology Society meetings, and an abstract on work performed during the 2-years of this contract accepted for poster presentation at the 2016 Society of Toxicology meeting. The TOCOR is in regular email contact with the Program Coordinator, and weekly calls to review all in-process orders, TO summaries, future planned orders, and any issues that need addressing. In addition, Stemina's COO, Bob Burrier, and CEO, Beth Donley periodically meet with the COR at different scientific conferences to obtain feedback on Contractor performance and assess any areas for improvement.

RECOMMENDATION:

Given what I know today about the contractor's ability to perform in accordance with this contract or order's most significant requirements, I would recommend them for similar requirements in the future.

Name and Title of Assessing Official:

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Name: Nicole A. Hairston

Title: Contracting Officer

Organization: EPA/OARM/OAM/RTPPOD

Phone Number: 919-541-4826 Email Address: hairston.nicole@epa.gov

Date: 01/15/2016

Contractor Comments:

ADDITIONAL/OTHER: The evaluation was delivered/received by the contractor on 01/15/2016. The contractor neither signed nor offered comment in response to this evaluation.

Name and Title of Contractor Representative:

Name:

Title:

Phone Number: Email Address:

Date: 05/31/2016

Review by Reviewing Official:

Review by Reviewing Official not required.

Name and Title of Reviewing Official:

Name:

Title:

Organization:

Phone Number: Email Address:

Date:

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