Final CRADA Report
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT

(hereinafter “CRADA”) No. ORNL02-0662

By and Between

UT-Battelle, LLC
Under its U. S. Department of Energy (DOE) Contract No. DE-AC05-00OR22725
(hereinafter “Contractor”)

And

MDS Sciex
(hereinafter “MDS”)

And

ESA, Inc.
(hereinafter (ESA))”

The CRADA Final Report may describe the research done under the CRADA and/or incorporate technical data as needed to support conclusions.

As an outline for the Final CRADA Report, the PI may include the following:

1. Abstract

The purpose of this Cooperative Research and Development Agreement (CRADA) between UT-Battelle (Contractor) and MDS Sciex (Participant) and ESA, Inc. (Participant) is to research, develop and apply new types of ionization sources and sampling/inlet systems for analytical mass spectrometry making use of the Participants’ state-of-the-art atmospheric sampling mass spectrometry electrochemical cell technology instrumentation and ancillary equipment.

The Contractor at Oak Ridge National Laboratory has been at the forefront in exploring the fundamentals and developing new applications of a variety of ion sources and inlet systems for inorganic, organic and biological mass spectrometry under the sponsorship of the Department of Energy, Office of Basic Energy Sciences. Limited resources for new state-of-the-art instrumentation has always been a challenge to faster, more significant progress in the Contractor’s research. MDS Sciex, generally recognized as the industrial leader in analytical mass spectrometry, will supply the contractor with state-of-the-art mass spectrometry instrumentation to facilitate the Contractor’s ongoing work. As a recognized leader in the manufacture of electrochemical instrumentation, ESA, Inc. will work closely with the other

Participants and Contractor to develop electrochemical technologies as they bear on both ion source development and mass spectrometry in general. The fundamental knowledge acquired, new ion sources and inlet systems developed, and new applications demonstrated by the Contractor, facilitated by the use of MDS Sciex and ESA, Inc. instrumentation and prototype refinements, will help MDS Sciex and ESA, Inc. maintain a leadership role in the analytical mass spectrometry and electrochemistry instrumentation marketplaces, respectively.

2. Statement of Objectives

The two overriding goals of this research project are: to understand the relationship among the various instrumental components and operational parameters of the various ion sources and inlet systems under study, the chemical nature of the gases, solvents, and analytes in use, and the nature and abundances of the ions ultimately observed in the mass spectrometer; and to develop new and better analytical and fundamental applications of these ion sources and inlet systems or alternative sources and inlets coupled with mass spectrometry on the basis of the fundamental understanding obtained in Goal 1.

The end results of this work are expected to be: (!) an expanded utility for the ion sources and inlet systems under study (such as the analysis of new types of analytes) and the control or alteration of the ionic species observed in the gas-phase; (2) enhanced instrument performance as judged by operational figures-of-merit such as dynamic range, detection limits, susceptibility to matrix signal suppression and sensitivity; and (3) novel applications (such as surface sampling with electrospray) in both applied and fundamental studies.

The research projects outlined herein build upon work initiated under the previous CRADA between the Contractor and MDS Sciex on ion sources and inlet systems for mass spectrometry. Specific ion source and inlet systems for exploration of the fundamental properties and practical implementation of these principles are:

3. Benefits to the Funding DOE Office's Mission

The Contractor at ORNL has been in the forefront in exploring the fundamentals and developing new applications of a variety of ion sources and inlet systems for inorganic, organic, and biological mass spectrometry under the sponsorship of the DOE, Office of Basic Energy Sciences. Participant will prove State of the art instrumentation and prototypes that will allow DOE to remain in the forefront of continued research.

4. Technical Discussion of Work Performed by All Parties. All significant advances resulting from this CRADA work have been published in the peer-reviewed scientific literature. The

list below includes all papers that included at least partial credit to this CRADA in the acknowledgement section of the respective paper.

- Kertesz, V.; Van Berkel, G. J. "Improved DESI-MS Performance using Edge Sampling and a Rotational Sample Stage," *Rapid Commun. Mass Spectrom.*, in press.
- Kertesz, V.; Van Berkel, G. J. "Improved Imaging Resolution in Desorption Electrospray Ionization Mass Spectrometry," *Anal. Chem.*, **2008**, 22, 2639-2644.
- Kertesz, V.; Van Berkel, G. J.; Vavrek, M.; Koeplinger, K. A.; Schneider, B.B.; Covey, T. R. "Comparison of Drug Distribution Images from Whole-Body Thin Tissue Sections Obtained Using Desorption Electrospray Ionization Tandem Mass Spectrometry and Autoradiography," *Anal. Chem.*, **2008**, 80, 5168-5177.
- Pasilis, S. P.; Kertesz, V.; Van Berkel, G. J.; Schulz, M.; Schorcht, S. "HPTLC/DESI-MS Imaging of Tryptic Protein Digests Separated in Two Dimensions," *J. Mass Spectrom.* **2008**, in press.
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- Pasilis, S. P.; Kertesz, V.; Van Berkel, G. J. "Unexpected Analyte Oxidation during Desorption Electrospray Ionization - Mass Spectrometry," *Anal. Chem.* **2008**, 80, 1208-1214.
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- Van Berkel, G. J.; Tomkins, B. A.; Kertesz, V. "Thin-Layer Chromatography/Desorption Electrospray Ionization Mass Spectrometry: Investigation of Goldenseal Alkaloids," *Anal. Chem.* **2007**, 79, 2778-2789.
- Van Berkel, G. J.; Kertesz, V. "Automated Sampling and Imaging of Analytes Separated on Thin-Layer Chromatography Plates Using Desorption Electrospray Ionization Mass Spectrometry," *Anal. Chem.* **2006**, 78, 4938-4944.

- Eckenrode, B. A.; Ramsey, S. A.; Stockham, R. A.; Van Berkel, G. J.; Asano, K. G.; Wolf, D. A. "Performance Evaluation of the Scent Transfer UnitTM (STU-100) for Organic Compound Collection and Release." *J. Forensic Sci.* **2006**, *51*, 780-789.
- Van Berkel, G. J.; Kertesz, V. "Novel Use of a Battery-Powered Two-Electrode Emitter Cell for Electrospray Mass Spectrometry," *J. Am. Soc. Mass Spectrom.* **2006**, *17*, 953-961.
- Van Berkel, G. J.; Kertesz, V. "Expanded Electrochemical Capabilities of the Electrospray Ion Source using Porous Flow-Through Electrodes as the Upstream Ground and Emitter High Voltage Contact," *Anal. Chem.* **2005**, *77*, 8041-8049.
- Kertesz, V.; Ford, M. J.; Van Berkel, G. J. "Automation of a Surface Sampling Probe/Electrospray Mass Spectrometry System," *Anal. Chem.* **2005**, *77*, 7183-7189.
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Van Berkel, G. J.; Llave, J. J.; Apadoca, M. F.; Ford, M. J. “Rotation Planar Chromatography Coupled On-Line with Atmospheric Pressure Chemical Ionization Mass Spectrometry,” *Anal. Chem.* **2004**, 76, 479-482.

5. Subject Inventions (As defined in the CRADA)

ID2096	Concept and Implementation of Automated Formation and Withdrawal of a Sampling Probe-to-Surface Liquid Microjunction for Surface Sampling Purposes
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6. Commercialization Possibilities. Partner SCIEX has so far declined to license or commercial any of the relevant IP. However, ESA has licensed IP arising during the prior CRADA with SCIEX and is evaluating the commercialization of a controlled potential electrospray ionization source.

7. Plans for Future Collaboration

A new CRADA agreement is under negotiation with MDS Analytical Technologies (Formally MDS Sciex)

8. Conclusions

The basic research objectives were met and, as often happens in science, many new areas of inquiry were opened up along with a new set of questions. Along with this are opportunities for commercialization of new analytical tools that might result by the increased understanding of the phenomena understudy in this work.