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LLNL-TR-740348

Development of HANAA to Achieve Commercialization Final Report CRADA No. TC-2025-01

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Disclaimer

This work performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344.

DEVELOPMENT OF HANAA TO ACHIEVE COMMERCIALIZATION

Final Report
CRADA No. TC-2025-01
Date Technical Work Ended: June 30, 2002

Date: December 10, 2002 Revision: 1

A. Parties

This project was a relationship between Lawrence Livermore National Laboratory (LLNL) and Environmental Technologies Group, Inc. (ETG), a wholly owned subsidiary of Smiths Group.

The Regents of the University of California
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B. Project Scope

The objective of this project was to provide DOD and the intelligence agencies with highly portable, advanced, bio-detection instruments and to further the DOE objective of putting advanced instrumentation for the detection of biological terrorism agents into the hands of first responders.

All sponsors of the HANAA development work at LLNL believed that the technology must be commercialized to fully contribute to their missions. Intelligence organizations, military teams, and first responders must be able to purchase the instruments for a

reasonable price and obtain maintenance services and support equipment from a reliable supplier in order for the instrument to be useful to them.

The goal was to efficiently transfer HANAA technology from LLNL to ETG, a company that would manufacture the instrument and make it commercially available to the constituencies important to our sponsors. This was to include a current beta test instrument and all knowledge of problems with the instrument and recommendations for solving those problems in a commercial version.

The following tasks were to be completed under this CRADA.

1. General Tasks

1.1 ETG will redesign the instrument case and packaging, redesign the electronics and rewrite the software. LLNL will provide advice during this process.

1.2 LLNL will immediately involve ETG in the beta test activity.

1.3 The objective of the LLNL work is to determine causes of problems in the HANAA and to recommend solutions.

2. Beta Test Support Tasks

2.1 LLNL personnel will continue to coordinate the beta test of the HANAA currently underway.

2.2 Upon execution of this CRADA, LLNL will schedule a briefing with ETG to discuss the following: design of the beta test, current beta test participants, and results of beta test to date.

2.3 LLNL will forward copies of all monthly beta test participant reports to ETG within ten (10) business days after receipt of the reports at LLNL.

2.4 LLNL will meet with ETG personnel at the end of the beta test to review the results of the test.

2.5 LLNL will inform all beta test participants that ETG is LLNL's commercialization partner for the HANAA, and is authorized to:

- discuss the beta test results, and
- possibly witness a small fraction of beta tests when it is convenient to all parties

3. Technology Transfer Tasks

3.1 LLNL will ship one HANAA instrument, along with operating manual, sufficient reagents, and other supplies to perform twenty five (25) tests, to ETG within three (3) weeks after execution of the CRADA;

3.2 LLNL will ship the following to ETG within six (6) weeks of the execution of this CRADA: all drawings related to the manufacture of HANAA, all production processes related to the manufacture of HANAA, other written material describing the manufacture of the HANAA or its components, and test protocols and results;

3.3 LLNL will meet with ETG technical personnel at LLNL for approximately one (1) week during month two (2) of the CRADA to:
- answer any ETG questions on the material described in Task 3.1 above
- demonstrate the fabrication of the instrument and its critical components
- demonstrate the testing of the HANAA
- advise ETG on the best way to obtain large quantities of reagents for the domestic preparedness application

3.4 Within three (3) months after the CRADA is executed, LLNL will provide sufficient reagent and analyte to ETG to perform approximately 250 tests of the HANAA system at ETG.

3.5 LLNL will meet with ETG at LLNL for 1 to 2 days to review the progress on this program and make recommendations on future plans at the following points after the CRADA execution: month 4, month 7, month 12, month 15.

4. Development Tasks, Part 1 – Thermal Cycling Tasks

LLNL will perform the following development tasks, and will submit a report to ETG at the end of each month (from one month of execution through month 6) summarizing progress on each item.

4.1 Document and interpret the control software and provide conceptual redesign of the cooling fans to eliminate an intermittent sticking at the hold temperature during thermal cycling.

4.2 Provide recommendations to improve the thermal stability of the thermocycler, which may involve:
- determining the mechanism limiting the thermal stability
- depositing SiN under the platinum heater
- characterizing changes in TAG as a function of several parameters

4.3 Characterize the variation as a function of depth within the insert. Redesign and test (if necessary).

4.4 Assess the possibilities of increasing the cooling rate by modifying the air ducting. The modified ducting could incorporate an air filter.

5. Development Tasks, Part 2 – Detection Tasks

5.1 Reduce the signal level variation and threshold cycle variation from chamber to chamber, which may involve characterizing and modifying:
- LED alignment and throughput
- filters
- photodiode circuit
- normalization algorithm

5.2 Improve the duplex mode performance, which may include:
- characterizing the performance
- writing compensation algorithm
- separating the threshold values for different channels

5.3 Investigate options to minimize integration times and maximize signals, which may include:
- driving LEDs harder
- using a broader bandpass filter
- testing a larger internal optical aperture
- collimating LEDs

5.4 Characterize and recommend ways to reduce ambient light leakage.

This CRADA was executed on April 2, 2001, with an expected duration of eight months. A no-cost time extension was executed on November 26, 2001, extending the CRADA to June 15, 2002 to allow more time to complete the existing tasks under the Statement of Work (SOW). On June 13, 2002 an amendment to the CRADA was initiated to increase the funds-in from ETG, which were required to complete the final tasks under the SOW, and to extended the expiration date of the CRADA to July 15, 2002. Amendment One to the CRADA was executed on July 12, 2002.

C. Technical Accomplishments

The goals of the project have been accomplished. HANAA technology has been transferred to ETG and flaws in the original design eliminated. ETG has commercialized the technology and is beginning to market the redesigned instrument (called Bio-Seeq).

1. General Tasks

Tasks successfully completed
- 1.1 – Completed by LLNL and ETG
- 1.2 – Completed by LLNL
- 1.3 – Completed by LLNL

2. Beta Test Support Tasks

Tasks successfully completed
- 2.1 – Completed by LLNL
- 2.2 – Completed by LLNL
- 2.3 – Completed by LLNL
- 2.4 – Completed by LLNL
- 2.5 – Completed by LLNL

3. Technology Transfer Tasks

Tasks successfully completed
- 3.1 – Completed by LLNL
- 3.2 – Completed by LLNL
- 3.3 – Completed by LLNL
- 3.4 – Completed by LLNL
- 3.5 – Completed by LLNL
- 3.6 – It was mutually agreed by both parties to add this task – LLNL will provide 30 thermal cyclers to ETG.

4. Development Tasks, Part 1 – Thermal Cycling Tasks

Tasks successfully completed
- 4.3 – Completed by ETG
- 4.4 – Completed by ETG with consultation from LLNL

The following tasks were not completed:
- 4.1 – It was mutually agreed by the parties that this task was no longer needed.
- 4.2 – It was mutually agreed by the parties that this task was no longer needed.

5. Development Tasks, Part 2 – Detection Tasks

Tasks successfully completed
- 5.1 – Completed by LLNL
- 5.2 – Completed by LLNL
- 5.3 – Completed by LLNL

The following tasks were not completed:
- 5.4 – It was mutually agreed by the parties that this task was no longer needed.

LLNL has achieved all of the deliverables as listed in the CRADA.

D. Expected Economic Impact

This CRADA will result in the commercial availability of the HANAA for purchase and use by intelligence organizations, military, and first responders to incidents of bio-terrorism. First responders must be able to purchase the instruments for a reasonable price and obtain maintenance services and support equipment from a reliable supplier in order for the instrument to be useful to them.

E. Partner Contribution

ETG provided sufficient funds for the LLNL HANAA team to work with the ETG design team to correct known flaws in the design and to avoid problems already experienced by the LLNL team. That interaction has been successful and a commercial HANAA (called Bio-Seeq) was redesigned during the ETG-LLNL collaboration of this CRADA. The Bio-Seeq is currently in production by ETG. No new inventions were created during the course of this CRADA and the solution of HANAA design problems.

F. Documents/Reference List

Reports

CRADA reports were written on May 7, 2001, July 17, 2001, September 5, 2001, and February 14, 2002. All work was completed by June 30, 2002.

Copyright Activity

All new software, drawings and data were developed by ETG during this CRADA.

Subject Inventions

No new inventions were disclosed by either ETG or LLNL during this CRADA.

Background Intellectual Property

LLNL declared the following Background Intellectual Property (BIP) for this project:

1. U.S Patent No. 5,589,136 (LLNL Docket IL-9707A) - *Silicon-Based Sleeve Devices for Chemical Reactions*; issued 12/31/96; Inventors: M. Allen Northrup, Raymond P. Mariella, Anthony V. Carrano, Joseph W. Balch

2. U.S Patent No. 6,524,532 (LLNL Docket IL-9707B) - *Microfabricated Sleeve Devices for Chemical Reactors*; issued 2/25/03; Inventor: Milton A. Northrup

3. IL-10517: Patent Pending

4. U.S. Patent No. 6,503,750 (LLNL Docket IL-10301) - *PCR Thermocycler*; issued 1/07/03; Inventors: William J. Benett, James B. Richards

G. Acknowledgement

Participant's signature of the final report indicates the following:

1) The Participant has reviewed the final report and concurs with the statements made therein.
2) The Participant agrees that any modifications or changes from the initial proposal were discussed and agreed to during the term of the project.
3) The Participant certifies that all reports either completed or in process are listed and all subject inventions and the associated intellectual property protection measures generated by his/her respective company and attributable to the project have been disclosed and included in Section E or are included on a list attached to this report.
4) The Participant certifies that if tangible personal property was exchanged during the agreement, all has either been returned to the initial custodian or transferred permanently.
5) The Participant certifies that proprietary information has been returned or destroyed by LLNL.

3/4/03

John C. Schmidt, Ph.D., Chief Technology Officer — Date
Smiths Detection - Edgewood
(formerly Environmental Technologies Group, Inc.)

3/11/03

Ronald P. Koopman , LLNL Principal Investigator — Date
Lawrence Livermore National Laboratory

3/24/03

Karena D. McKinley, IPAC Director — Date
Lawrence Livermore National ~~Laboratory~~

Attachment I – Final Abstract

DEVELOPMENT OF HANAA TO ACHIEVE COMMERCIALIZATION

Final Abstract (Attachment I)
CRADA No. TC-2025-01
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B. Purpose and Description

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The following deliverables were successfully completed under the CRADA.

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LLNL forwarded copies of all monthly beta test participant reports to ETG within ten (10) business days after receipt of the reports at LLNL.

2. **Technology Transfer**

2.1 LLNL shipped one HANAA instrument, along with operating manual, sufficient reagents, and other supplies to perform twenty (25) tests, to ETG within three (3) weeks after execution of the CRADA.

2.2 LLNL shipped the following to ETG within six (6) weeks of the execution of this CRADA: all drawings related to the manufacture of HANAA, all production processes related to the manufacture of HANAA, other written material describing the manufacture of the HANAA or its components, and test protocols and results.

2.3 Within three (3) months after the CRADA was executed, LLNL provided sufficient reagent and analyte to ETG to perform approximately 250 tests of the HANAA system at ETG.

3. **Development Tasks**

LLNL performed development tasks, and submitted a report to ETG at the end of each month (one month of execution through month 6) summarizing progress on each item.

This CRADA was executed on April 2, 2001, with an expiration date of December 2, 2001. A no-cost time extension was executed on November 26, 2001 extending the project to June 15, 2002 to allow more time to complete the existing tasks under the CRADA Statement of Work. On June 13, 2002 an amendment to the CRADA was initiated to increase the funds-in from ETG, which were required to complete the final tasks under the SOW, and to extended the expiration date of the CRADA to July 15, 2002. Amendment One to the CRADA was executed on July 12, 2002.

C. Benefit to Industry

The goals of the project have been accomplished. As a result of the ETG-LLNL collaboration, the instrument (now called Bio-Seeq) has been redesigned. As soon as the license has been executed, Smiths Detection-Edgewood will begin to market the redesigned instrument.

D. Benefit To DOE/LLNL

This project will directly benefit DOE's Chem/Bio National Security Program (part of NN-20). Creation of HANAA has resulted in a highly portable, advanced, bio-detection instrument that can further the DOE objective of putting advanced instrumentation for the detection of biological terrorist agents into the hands of first responders. The DOE sponsor of the HANAA development work at LLNL believes that the technology must be commercialized to fully contribute to their mission. First responders must be able to purchase the instruments for a reasonable price and obtain maintenance services and support equipment from a reliable supplier in order for the instrument to be useful to them.

E. Project Dates

April 2, 2001 through June 30, 2002.