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Report to the Vice Chairman, Joint Economic Committee, U.S. Congress

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TECHNOLOGY TRANSFERS

Benefits of Cooperative R&D Agreements

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Resources, Community, and
Economic Development Division

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The Honorable Paul S. Sarbanes
Vice Chairman, Joint
Economic Committee
Congress of the United States

Dear Mr. Vice Chairman:

Technology transfer between federal laboratories and industry is increasingly viewed as a significant factor in the economic growth and well-being of the United States. Cooperative Research and Development Agreements (CRADAs) are one of several mechanisms whereby federal laboratories and private industry collaborate on research and development (R&D). CRADAs define the terms and conditions of the collaboration.

You asked us to review the role of CRADAs in successfully transferring technology to the private sector. Subsequently, we agreed with your office to develop a series of case studies that highlight the benefits of engaging in such collaborations at the Departments of Agriculture, Army, Commerce, and Health and Human Services. We did not attempt to assess the costs of these collaborations.

Results in Brief

While all CRADAs may not achieve the same level of benefits, both the federal agencies and private companies we reviewed benefited from the collaborations. Specifically, we identified the following:

- The CRADAs offered opportunities for federal laboratories and industry to collaborate on research while meeting their missions.
- Technology from federal laboratories was transferred to the private sector, resulting in commercial products.
- R&D programs were advanced.
- The sharing of resources aided federal laboratories and private companies in accomplishing the CRADA's objectives.

In addition, some of the CRADAs demonstrated a potential for long-term improvements to our nation's economy, health, and environment.

Background

Beginning in 1980, the Congress enacted a series of laws to renew, expand, and strengthen cooperation between federal laboratories and private

industry. The Stevenson-Wydler Technology Innovation Act of 1980 (P.L. 96-480) made the transfer of federal technology a national priority. This act was amended by the Federal Technology Transfer Act of 1986 (P.L. 99-502), which authorized government-operated laboratories to enter into CRADAs with nonfederal parties to conduct specific R&D. The 1986 act authorized the use of the laboratories' resources such as staff and equipment for CRADA projects but specifically prohibited the transfer of federal funds to a collaborator. In addition, the technology transfer legislation placed few limits on CRADA collaborations but did require that R&D efforts be consistent with the laboratories' missions.

CRADAs Have Met Agencies' and Companies' Missions

For the 10 CRADAs that we reviewed, both the missions of federal laboratories and the interests of private companies were being met through cooperation on research of mutual interest.

In 1988, the Agricultural Research Service (ARS) and W.R. Grace and Company, for example, entered into a CRADA that offered an opportunity for government and industry to collaborate on research to develop disease control measures in plants by using natural products as alternatives to chemicals. The mission of one of ARS' laboratories is to perform basic and applied research to discover and improve methods for biologically controlling plant diseases. The laboratory seeks alternatives or supplements to applying chemical fungicides to soil to control these diseases because chemical fungicides can cause environmental pollution. W.R. Grace, which markets goods for producing bedding plants in greenhouses, had an interest in obtaining the biological control technology developed by ARS and adapting and converting the technology to a commercial product. The CRADA resulted in a granular formulation that when added to soil or soilless mixes, will protect plants from diseases causing seedling rot. The laboratory and W.R. Grace have renewed the CRADA to develop additional supplements to chemical fungicides.

In another example, the Walter Reed Army Institute of Research (WRAIR) entered into a CRADA with OraVax, Incorporated, to collaborate on R&D of encapsulated oral vaccines against certain infectious diseases. WRAIR has extensive experience in encapsulation technologies[1] and attempts to find ways of protecting soldiers. OraVax develops and manufactures oral vaccines and has experience in a specialized field of immunity that detects disease-causing microorganisms. As a result of the CRADA, WRAIR and

[1]Encapsulation is a process whereby vaccine proteins are wrapped in a biodegradable material. The vaccine is ingested. After a period of time, the coating dissolves and the proteins are released, initiating the immunity to the disease.

OraVax developed an encapsulated vaccine against a bacterium that causes diarrhea, one of the most debilitating diseases confronting soldiers. Soon, WRAIR and OraVax will sign an amendment to the CRADA to expand the collaboration to develop vaccines against other diseases.

CRADAs Have Resulted in Commercial Products

Some proponents of technology transfer argue that many technologies generated in the federal laboratory system could have commercial value if further developed by private industry. Among the CRADAs we reviewed, we found examples in which private companies were manufacturing and selling products that directly resulted from federal research.

In the early 1980s, for example, the Forest Service's Forest Products Laboratory developed and patented a structural product called "spaceboard," a strong yet lightweight molded-fiber panel made from waste wood that had potential use in commercial and residential construction and packaging applications. After learning about the technology, Gridcore Systems International entered into a CRADA with the laboratory to design processes, materials, components, and systems for the best use of recycled and other fiber products in the construction and furniture industries. Today, Gridcore markets panels, curves, and columns by using the spaceboard technology. According to the company, potential uses of the product include furniture, stage sets, doors, ceiling tiles, and partitions.

R&D Programs Have Been Advanced

Collaborating on research by federal agencies and private companies can advance R&D programs. An effort between the National Institutes of Health (NIH) and Genetic Therapy, Incorporated, illustrates that advances in research are being made because of CRADAs.

In 1987, NIH scientists believed that an aspect of recombinant genetic engineering[2] that they had been studying was almost ready for clinical trials on human beings. However, NIH did not have the laboratory facilities or staff to produce the amount and quality of cells necessary to conduct human clinical trials. Recognizing the potential of NIH's gene therapy research, Genetic Therapy entered into a CRADA with NIH to develop genetically engineered products based on the research. Both collaborators told us that the CRADA has advanced the R&D program to the point where

[2]Recombinant genetic engineering is a range of techniques that rebuild or manipulate genetic material from organisms.

the technology has been successfully demonstrated in human clinical trials.

Sharing of Resources Aided Federal Laboratories and Companies in Accomplishing CRADA's Objectives

The following examples demonstrate a variety of ways that the laboratories and companies we reviewed exchanged their resources to accomplish the CRADA's research objectives:

- Expertise: Often, one collaborator contributed specific knowledge and experience that the other collaborator did not have for the success of the CRADA. For example, ARS scientists developed a plant cell culture system for producing small, or research-scale, amounts of an anticancer drug. Scientists from Phyton, Incorporated, had the expertise—engineering and business training and skills—to develop a system capable of producing commercial quantities of the drug.
- Personnel: Government and industry personnel were often exchanged between facilities to perform research functions. Such personnel included scientists, technicians, and support staff. For example, OraVax assigned several of its staff to work full-time at the WRAIR to perform research on the CRADA involving oral vaccines as well as other laboratory projects.
- Facilities and materials: For some of the CRADAs we reviewed, federal and private researchers shared an assortment of facilities and materials to meet the objectives of the research. Such items included laboratories, production facilities, test equipment, and research samples. For example, NIH provided its clinical center to Genetic Therapy for conducting clinical trials involving gene therapy.

Conclusions

Our observations of the 10 CRADAs that we reviewed suggest that collaborative R&D agreements can be a valuable asset in the government's portfolio of technology transfer programs. As we stated earlier, these CRADAs have provided opportunities for laboratories and companies to share expertise and resources, advance R&D programs, and transfer technology resulting in commercial products. While we did not attempt to measure the overall benefits to the economy, we believe that government-industry collaboration can have a positive impact on certain economic, health, and environmental needs of the United States.

Agency Comments

We discussed the factual information in this report with technology transfer and laboratory officials from the Army, ARS, Forest Service, NIH, and the National Institute of Standards and Technology and with the

industry collaborators involved in the CRADAs we reviewed. They agreed with the accuracy of the facts. However, as agreed with your office, we did not obtain written agency comments on a draft of this report.

Scope and Methodology

We developed a series of case studies that highlight CRADAs' benefits. We asked agency officials to select several CRADAs that have led to a commercially useful technology, an improvement to a process, or an advancement in an R&D program. From this group, we selected 10 CRADAs that represent a range of technologies and laboratories. The CRADAs, federal laboratories, and private companies that we reviewed are identified in appendix I of this report. During our review, we visited the federal laboratories and private companies involved in these CRADAs, reviewed documents and materials related to the CRADAs, and interviewed federal laboratory personnel, industry officials, and financial analysts specializing in technology-based industries to determine what benefits were produced as a result of these collaborations. Because these CRADAs were judgmentally selected, they are not necessarily representative of all CRADAs. The 10 case studies are presented in appendix II. We conducted our review from March through October 1994 in accordance with generally accepted government auditing standards.

We are sending copies of this letter to the Secretaries of Agriculture, Commerce, Defense, and Health and Human Services and to the Director, Office of Management and Budget. We will also make copies available to others on request.

Please contact me at (202) 512-3841 if you or your staff have any questions. Major contributors to this report are listed in appendix III.

Sincerely yours,

Victor S. Rezendes
Director, Energy and Science Issues

Contents

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ARS	Agricultural Research Service
CRADA	Cooperative Research and Development Agreement
GAO	General Accounting Office
GRASS	Geographic Resources Analysis Support System
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
R&D	research and development
WRAIR	Walter Reed Army Institute of Research

CRADAs That GAO Reviewed

CRADA	Federal laboratory	Collaborator
Retroviral mediated gene therapy	National Cancer Institute, Rockville, Md.[a]	Genetic Therapy, Inc., Gaithersburg, Md.
Manufacturing information	Manufacturing Engineering Laboratory, Gaithersburg, Md.[b]	PDES, Inc., North Charleston, S.C.
Microheating element manufacture	Semiconductor Electronics Division Laboratory, Gaithersburg, Md.[b]	Optical ETC, Huntsville, Ala.
Anticancer drug	National Cancer Institute, Rockville, Md.[a]	Bristol-Myers Squibb Co., Princeton, N.J.
Plant cell culture technology	Plant, Soil, and Nutrition Research Laboratory, Ithaca, N.Y.[c]	Phyton, Inc., Ithaca, N.Y.
Chemical fungicide	Biocontrol of Plant Diseases Laboratory, Beltsville, Md.[c]	W.R. Grace and Co., Columbia, Md.
Oral vaccine	Walter Reed Army Institute of Research, Silver Spring, Md.[d]	OraVax, Inc., Cambridge, Mass.
Geographic information system	Construction Engineering Research Laboratories, Champaign, Ill.[d]	Open GIS Foundation, Cambridge, Mass.
Wood fire retardant/ preservative	Forest Products Laboratory, Madison, Wis.[e]	Northwest Independent Forest Manufacturers, Beaver, Wash.
Recycled materials	Forest Products Laboratory, Madison, Wis.[e]	Gridcore Systems International, Carlsbad, Calif.

Legend

CRADA = Cooperative Research and Development Agreement.

[a]National Institutes of Health.

[b]National Institute of Standards and Technology.

[c]Agricultural Research Service.

[d]U.S. Army.

[e]Forest Service.

Case Studies of 10 CRADAs That GAO Reviewed

This appendix summarizes the following for each Cooperative Research and Development Agreement (CRADA) that we reviewed: (1) the technical objectives, (2) the collaborators' roles and contributions of resources, and (3) the emanating results, including the direct benefits and broader impacts.

Retroviral Mediated Gene Therapy, National Institutes of Health/Genetic Therapy, Inc.

Shortly after birth, doctors found that Ashanthi and Cynthia suffered from a rare and usually fatal genetic birth defect that affects the immune system. At about the same time, several National Institutes of Health (NIH) scientists were ready to begin human clinical trials with retroviral mediated gene therapy. This therapy uses reconstructed genetic material from an animal virus to replace missing or defective genes responsible for illnesses in humans. Although NIH was well equipped to produce small quantities of this new material for research, NIH's laboratory facilities and personnel were not equipped or prepared to produce quality cells in the volume needed for the clinical trials. Recognizing the potential of this new technology to help those afflicted with genetic and acquired diseases, a private-sector scientist opened the doors of Genetic Therapy, Incorporated, on July 1, 1987. Shortly thereafter, NIH and this company began a CRADA collaboration to conduct trials using retroviral mediated gene therapy.

NIH's mission is to improve the health of the American people. To do this, the agency conducts and supports biomedical research into the causes, prevention, and cure of diseases; develops research resources; and uses modern methods to communicate biomedical information. For the CRADA collaboration, NIH supported about six laboratory researchers so that they could perform preclinical animal and human studies, developed the original idea of using recombinant viruses as genetic therapeutic agents, and provided the resources of its clinical center, including the efforts of its attending physicians. Genetic Therapy obtained venture capital and manufacturing facilities and materials; supported about 30 researchers in the company's own laboratory and 4 researchers at NIH; completed 2 years worth of laboratory testing; and secured the required approval from the Food and Drug Administration. NIH and Genetic Therapy worked together to obtain the approvals from an NIH committee overseeing recombinant genetic research.[1].

[1]The NIH Recombinant DNA Advisory Committee was created to monitor genetic research including the review and approval of human-gene therapy.

The president of Genetic Therapy said that this CRADA put his company in business. The CRADA affirmed the use of gene therapy, and the company was able to raise money in equity markets and to reduce the liability associated with conducting clinical trials on human patients. The company also benefited because NIH bore the cost of treating the patients at the Institutes' clinical center. For NIH, this collaboration provided the resources for needed laboratory improvements and expansion. For the children, the treatment that they received as a result of this CRADA brought a greatly improved quality of life. Other treatments for this deficiency, involving the use of an animal product, are typically not long lasting and are extremely expensive. In contrast, because gene therapy corrects the body's own cells to produce what is missing, it is anticipated that mediated gene therapy should provide full restoration of function for the patient's lifetime.

This company, which employees about 150 highly skilled scientific specialists, and about 30 other new firms that were founded on this CRADA-developed technology are researching many new applications, such as treating brain tumors, Acquired Immune Deficiency Syndrome (AIDS), cystic fibrosis, melanoma (a deadly form of skin cancer), kidney disease, and ovarian, breast, and colon cancer. Several financial analysts that we contacted said that today, these 30 companies spend or add between $20 million and $30 million a month to the economy. These analysts estimated that if gene therapy fulfills its promise and gene transplants replace pills and surgery, the impact on the economy will be substantial. If this fundamental technology supporting gene therapy proves that it can cure a few of the above diseases, including cancer, the contribution will be even greater.

Figure II.1: Ashanthi and Cynthia

Source: March of Dimes Birth Defects Foundation.

The Standardization of Manufacturing Information, National Institute of Standards and Technology/ PDES, Inc.

The success of U.S.-manufactured products in competitive international markets depends, in large measure, on the time and cost of getting a product to market. Unfortunately, many companies and departments that work together continue to use different standards and technical languages to design and describe identical products or processes. As a result, when engineers, product managers, and service personnel need to exchange manufacturing information, additional time and money are required to translate one language to another. In any one product's life, multiple translations are not unusual and are frequently accompanied by some

inadvertent loss of data. This inability to demonstrate a product's capabilities by providing clear, uniform, and error-free information is cause for concern, especially with the continuing emphasis on making improvements in U.S. manufacturing. In 1988, the National Institute of Standards and Technology (NIST) used a CRADA to join PDES, Inc., a group of six companies that has since grown to become an international consortia of 25 corporations and 3 government agencies. The CRADA requires the cooperation of manufacturing companies, who are major competitors in some cases, to develop and implement a set of international standards for the exchange of product data. The standards will provide a complete, unambiguous, computer interpretable definition of the physical and functional characteristics of a product throughout the different stages of the product's life.[2]

NIST was established to assist industry in the development of technology needed to improve products' quality and reliability, modernize manufacturing, and facilitate commercialization. NIST and two other government consortia members contribute the use of laboratory facilities and two full time-engineers including associated expenses for training and travel. NIST's contribution is valued at between $800,000 and $900,000 a year. The private sector consortia members each contribute $50,000 or $100,000 and one or two engineers each year. Without leaving their own corporate locations, this CRADA organizes its technical expertise together with an on-line network system and frequent conference calls and meetings in what has been described as a "virtual" company. The CRADA is managed by an official of the South Carolina Research Authority (Charleston, South Carolina), who estimated that the members' contributions to the consortia are valued at about $10 million a year, about $7 million of which is contributed from industry and almost $3 million from the federal government.

The CRADA has enabled several collaborators who are software manufacturers to market new products on the basis of common data-exchange standards developed under the CRADA. In addition, the CRADA is currently conducting several pilot programs. Under one pilot program, a major airplane manufacturer is requiring that three of its engine suppliers use the CRADA-developed standards to assemble its new plane. This pilot program will mark the first time that one of the engine manufacturers develops the engine without relying on traditional physical models. A consortia company official said that within 1 year, this CRADA

[2]In manufacturing, a product's life is defined by different stages—concept, design, fabrication, assembly, test/delivery, and support.

would be responsible for reducing the cost and time to manufacture the company's product. When this standardization is fully integrated in normal manufacturing operations and eliminates the need for design language translations, the official's company could save tens of millions of dollars. The CRADA manager for PDES, Inc., estimated that as the manufacturing industry moved from physical models used during the 1800s to engineering drawings and blueprints and to individual computer-aided design programs, the productivity in the manufacturing industry increased about sixfold. In addition, with full implementation of standards for the exchange of product data, the CRADA manager estimated that the productivity of U.S. industries' would increase another three to six times. He said that because U.S. products would be of high quality and would reach international markets sooner, U.S. companies would be able to sell more than their international competition.

Microheating Element Manufacture, National Institute of Standards and Technology/Optical ETC

"Smart bombs" are only as smart as the reliability of the computer chips that guide them to their targets. However, the generation of guidance hardware currently in use does not test the operation of the missile's imaging system before the missile is launched. In 1992, a NIST engineer and a former professor of electrical engineering formalized their professional discussions by establishing a CRADA to develop and test their ideas for a new technique to manufacture microheating elements on standard silicon chips. The microheating elements, which resemble thousands of miniaturized hot plates, display, in real time, heat patterns (temperature variations) emitted from moving objects, like people. These patterns are used to test and calibrate a missile's guidance system.

The Semiconductor Electronics Division Laboratory at NIST develops state-of-the-art measurement procedures and materials for the microelectronics manufacturing industry. Five NIST researchers worked on projects related to this CRADA and used about $250,000 worth of laboratory equipment. Optical ETC contributed between 2 and 3 years worth of technical effort, $10,000 to $15,000, and use of the company's equipment to conduct the company's part of the CRADA work.

Optical ETC officials credit the CRADA for the company's growth from three to nine employees and enhancing the company's worth by about $1 million. Researchers at NIST said the CRADA collaboration provided their research program with the optical component of the sensor technology, which further expanded the technology's potential field of applications

and provided NIST with a mechanism for making and selling this technology in commercial markets.

The Department of Defense is interested in this technology because it represents a cheaper and less risky means of testing military equipment and less training time for the soldiers who will operate the equipment. Commercially, work from this CRADA-developed technology is being applied to sense the presence of air pollutants and to trigger air-bags during the rapid deceleration preceding a car crash.

Anticancer Drug Commercialization, National Institutes of Health/Bristol-Myers Squibb Co.

Research in the 1960s demonstrated that paclitaxel,[3] a natural product found in extremely small quantities in the bark of the Pacific Yew tree, is a highly effective treatment for cancerous tumors. However, 25 years later, little progress had been made in developing a useful drug. The development of such an anticancer drug was complicated by two problems—obtaining enough paclitaxel for all the patients who might eventually need treatment and finding a company to commercialize the drug. To address these problems, NIH solicited a number of CRADA proposals from different companies. After a series of reviews, NIH selected the Bristol-Myers Squibb Company, a large pharmaceutical company with experience in anticancer drug development and natural products research.

The Division of Cancer Treatment in the National Cancer Institute at NIH is devoted to identifying new anticancer agents, evaluating their antitumor activity, and supporting any clinical trials necessary to make a promising compound available to the American public. For the collaboration, NIH provided the data from preclinical animal studies, the clinical data from its national clinical trial's network, research expertise in the development of different anticancer agents, and enough isolated paclitaxel and yew tree bark to continue the clinical trials until Bristol-Myers Squibb was able to supply the agent. To complete the large number of remaining clinical trials and provide adequate drug supplies, a Bristol-Myers Squibb official said her company (1) improved procedures to increase the amount of paclitaxel that could be extracted from existing bark supplies and developed additional sources; (2) supported research for commercially feasible and naturally renewable sources of paclitaxel such as a partially synthetic process that begins with material extracted from the yew tree needle trimmings and a new technology called plant cell culture, which was developed under a separate CRADA between ARS and Phyton, Inc.;[4]

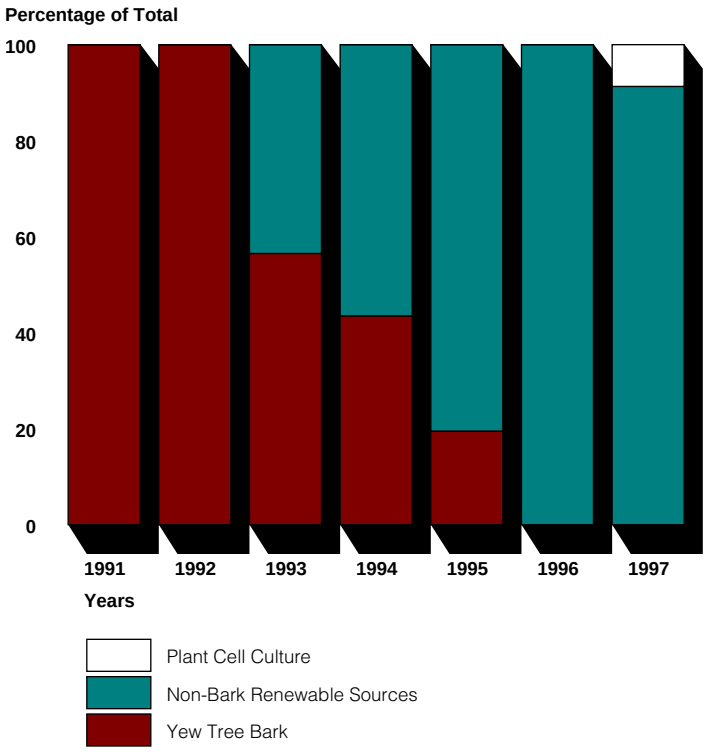
[3]Paclitaxel is the active drug substance in Bristol-Myers Squibb's anticancer drug Taxol®.

[4]See the next case summary on p. 16 for the CRADA involving ARS/Phyton, Inc.

(3) obtained the Food and Drug Administration's approval by conducting, in addition to NIH's trials, the company's own clinical trials to provide necessary additional data; (4) conducted research to enhance the method of administering the drug to cancer patients; and (5) made Taxol[R] available for other NIH programs. A company official estimated that through June 1994, the company's actual expenditures had exceeded $300 million. She also estimated that personnel efforts had gone beyond the 125-person-years specified in the CRADA agreement.

An NIH official said that the results of this CRADA provided NIH scientists with the basis for pursuing three other promising antitumor compounds that had no pharmaceutical sponsor. A Bristol-Myers Squibb official said that the CRADA was responsible for adding an important new product to the company's existing line of anticancer drugs. Both NIH and company officials said that this CRADA demonstrates how cooperation in research and development (R&D) can overcome major supply limitations for a promising anticancer drug without depleting our natural resources. Figure II.2 shows the plans that Bristol-Myers Squibb has for developing nonyew tree bark alternatives for making Taxol[R].

Figure II.2: Plans for Alternative Sources of Taxol



Source: Adapted from information obtained from Bristol-Myers Squibb Company.

Plant Cell Culture Technology, Agricultural Research Service/Phyton, Inc.

Sometimes, the amount of natural product found in plants is so small, as is the case with paclitaxel, that there is little doubt that alternatives to the traditional ways of making new medicines must be found. On the basis of nature's ability for plant cells to reproduce themselves indefinitely, Agricultural Research Service (ARS) scientists developed a plant cell culture system for making paclitaxel. The process removes cells from the original plant and, under scientifically controlled conditions, manipulates the cell's reproduction and metabolism. Recognizing a commercial opportunity to apply plant cell culture technology to drug supply problems and commercialize other valuable plant-derived compounds, three graduate students started Phyton, Inc. In 1990, ARS signed a CRADA and gave Phyton an exclusive license to adapt laboratory-scale procedures into a plant cell culture process that was able to produce commercial quantities of Taxol®.

ARS supports research in animal and plant protection. One aspect of this work is the development of different microbiological plant technologies that convert low-value agricultural products into high-value technology-based products. The anticipated results of this kind of work allow U.S. industry to rely on renewable resources for the supply of raw materials and to move away from the use of limited and, therefore, presumably expensive and possibly environmentally damaging sources of supply. During the CRADA collaboration, ARS provided research personnel, some equipment and materials, and different cell culture samples and developed and catalogued various factors for the maximum drug yield. During the 3-year span of the CRADA, Phyton's activities were almost completely focused on the drug's development. A company official said he would estimate that Phyton contributed the efforts of seven people and between 10 and 30 percent of the company's resources to work out the CRADA-identified problems associated with increasing the production of Taxol[R].

Collaborating on the CRADA enhanced ARS' basic research efforts by allowing ARS' laboratory to research a new technology and has encouraged other ARS researchers to undertake more high-risk, long-term endeavors. The CRADA enabled Phyton to broaden the scope of its R&D program to include other active plant cell culture products, enhanced the company's technical credibility, and resulted in greater leverage for the company's financing, such as the subsequent contract that Phyton won to make Taxol[R] for Bristol-Myers Squibb. Phyton, which began with 3 people, now employs 61. Both ARS and Phyton officials said this CRADA proved that the potential exists for plant cell culture technology to create drugs cheaply, quickly, and in commercial-sized quantities with no negative impact on the environment. An official of a major pharmaceutical company said that from the results to date, she anticipated that plant cell culture technology will generate drug-processing improvements and cost savings similar to those that drug companies experienced when they adopted tissue fermentation to manufacture antibiotics.

Chemical Fungicide Reduction, Agricultural Research Service/W.R. Grace and Company

Diseases causing seedling rot are commonly found in commercial greenhouses and have caused extensive losses in the bedding plant industry. Applying chemical fungicides to soil has been an accepted method of controlling the pathogenic fungi that cause such diseases. However, chemical fungicides are not the most desirable means of disease control because, among other things, they can cause environmental pollution. In 1988, ARS entered into a CRADA with W.R. Grace and Company

to develop disease control measures using natural products as alternatives or adjuncts to chemicals.

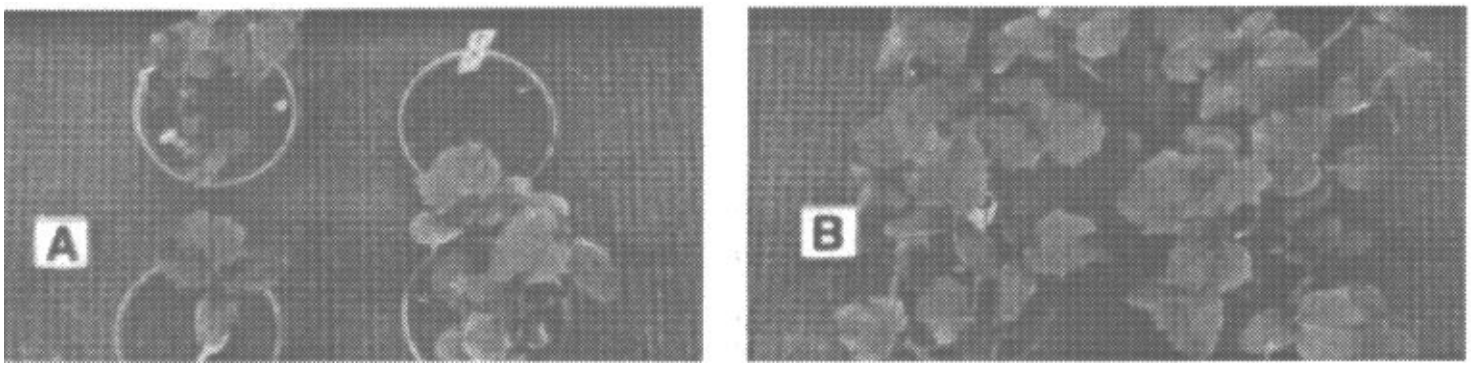
The CRADA offered an opportunity for government and industry research personnel to interact to develop a product useful to agricultural production. Both ARS and W.R. Grace benefited from the CRADA because they had a mutual interest in developing biological control technologies for bedding plants.

ARS' interest is to perform basic and applied research to discover and improve methods for biologically controlling plant diseases. ARS has extensive experience in performing biological control research and has expertise in bedding plant production. For example, ARS identified fungi that control diseases causing seedling rot. For the CRADA, ARS supplied strains of the fungi for small-scale studies and provided personnel, laboratories, and related equipment and supplies.

W.R. Grace is a specialty chemicals and health care company that markets goods for production in bedding plants in greenhouses. The company's interest was to obtain the biological control technology provided by ARS and then adapt and convert it to a commercial product. For the CRADA, W.R. Grace provided facilities and expertise to produce large quantities of biological control formulations developed by ARS for laboratory and field tests. W.R. Grace also provided funds to ARS to support laboratory staff, field testing, and operating expenses.

The CRADA resulted in a granular formulation that when added into soil or soilless mixes, will protect noninfected plants from seedling rot. Today, W.R. Grace produces limited amounts of GlioGard^{R} and sells the product to a commercial fertilizer company. W.R. Grace and ARS renewed the CRADA in 1993 to continue to develop biological control additives and supplements to soil and soilless mixes to replace, in total or in part, chemical fungicides currently used in commercial greenhouse nurseries.

Figure II.3: Effects of Formulation Developed by ARS on Cucumber Plants



Legend

A = Untreated soil.

B = Treated soil.

Source: W.R. Grace and Company.

Oral Vaccine Development, Army/OraVax, Inc.

One of the most debilitating diseases confronting soldiers is the diarrhea caused by a number of different microorganisms including enterotoxigenic Escherichia coli (E. coli). This bacterium results in an estimated 650,000,000 cases of diarrheal disease annually in developing countries and leads to 500,000 deaths worldwide, mostly in children. In 1992, the Walter Reed Army Institute of Research (WRAIR) signed a CRADA with OraVax, Incorporated, to collaborate in the research and development of encapsulated oral vaccines against infectious diseases, including disease caused by E. coli. Encapsulation offers the potential of eliminating the need for multiple injections of a vaccine, protecting vaccines against high temperatures, and stimulating better immunity against disease.

The Army and OraVax have a joint interest in developing oral vaccines. WRAIR, which has extensive experience in encapsulation technologies, attempts to find ways of protecting soldiers against infectious diseases. On the other hand, OraVax seeks to develop and manufacture oral vaccines. OraVax has experience in regulatory approval and commercialization procedures for vaccines as well as expertise in a specialized field of immunity that detects disease-causing microorganisms.

For the CRADA, the Army provided its bioprocessing facility and staff at Silver Spring, Maryland, where it conducts R&D and produces and tests vaccines. The facility was designed to manufacture vaccines that meet federal requirements for products that are intended for human use. OraVax contributed expertise, support personnel, and funds to conduct preclinical trials. For example, OraVax paid about $100,000 to validate the Army's laboratory equipment. Validation is a process to ensure that equipment is operating according to specifications and will perform its function over time.

The CRADA resulted in an encapsulated oral vaccine for E. coli that is intended for future human clinical trials. Also, an amendment to the original CRADA will expand the collaboration to develop vaccines against diseases such as gastritis, ulcers, dysentery, and colitis.

Geographic Information System, Army/Open GIS Foundation

Developing new applications for existing computer software offers the potential to greatly reduce the time, cost, and effort needed to develop and maintain high-quality software. In the early 1980s, the Army Construction Engineering Research Laboratories created a computer-based geographic information software system, called the Geographic Resources Analysis Support System (GRASS), to help manage its training areas. GRASS allowed training range managers to develop digital map overlays displaying land characteristics, such as the location of water, soil types, and archeological sites. Subsequently, an interagency working group was formed to promote and coordinate other uses for GRASS such as law enforcement and public safety applications after federal agencies, academic institutions, and the private sector developed additional uses for the system.

The Construction Engineering Research Laboratories have been largely responsible for the support and development of the GRASS user community. However, the Army decided to divest itself from all GRASS-related activities that were not mission-related. Therefore, the laboratories entered into a CRADA with the Open GIS Foundation. The Open GIS Foundation is a not-for-profit corporation, which was organized in 1992 to complement the functions of the interagency working group. The ongoing CRADA provides the framework for sharing resources and technical expertise between the Army and the private sector. For example, the Army is responsible for transferring technical information such as software specifications, architecture, and coding techniques to the foundation on a continuing basis so that it can implement and maintain a technical support program for commercial, university, and government distributors of GRASS. In turn,

the Open GIS Foundation assumed the laboratory's GRASS business affairs, including managing a newsletter; conducting an annual user's conference; publishing and selling GRASS manuals; and selling and distributing a GRASS mailing list.

According to the Construction Engineering Research Laboratories' staff, the CRADA is the vehicle that allowed GRASS to get out to the public, and the CRADA has allowed the laboratory to continue its tradition of interacting with the private sector. On the other hand, the Open GIS Foundation's Executive Director told us that the CRADA gave the foundation the ability to begin operations and provided the linkage that gave the foundation credibility among its users.

Fire Retardant/ Preservative for Wood, Forest Service/Northwest Independent Forest Manufacturers

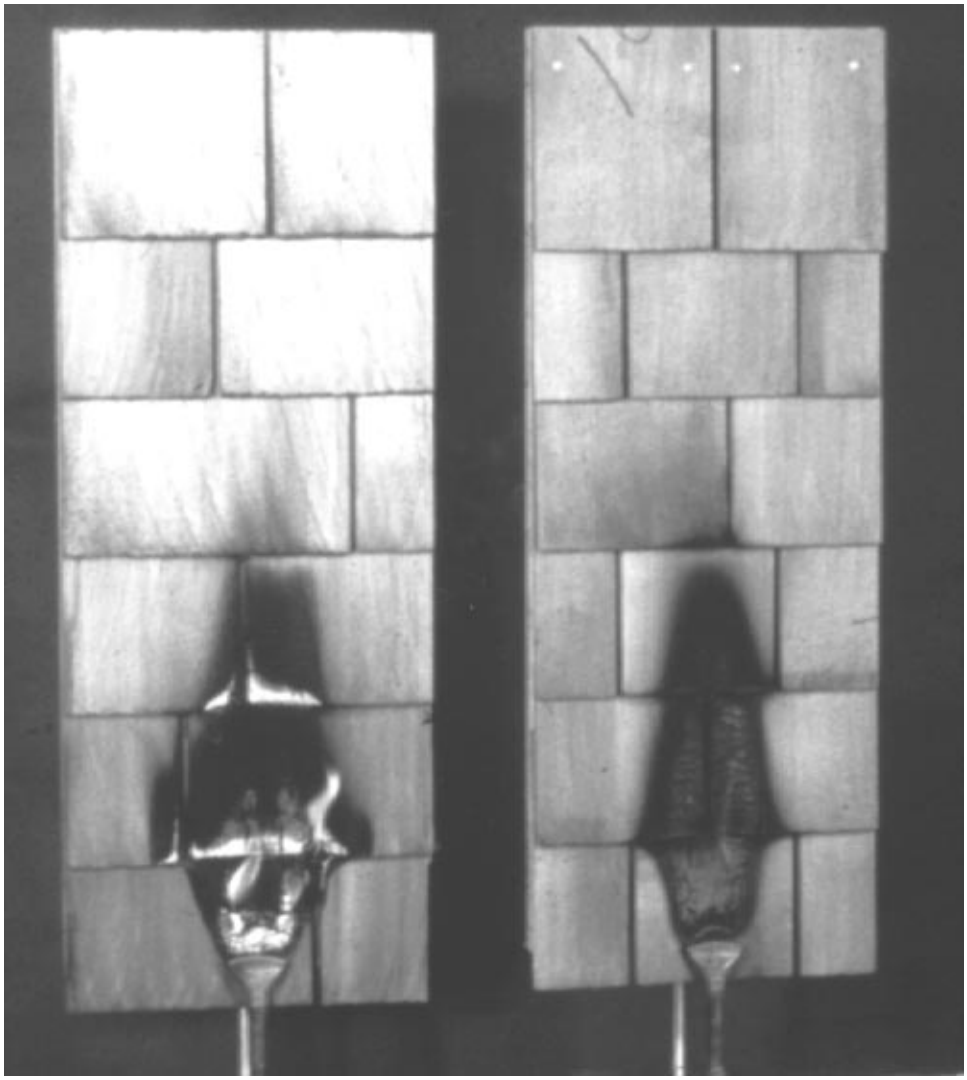
Every year, homes in the western United States are subjected to fires that result in extensive damage to property and the environment as well as injury and death to local residents and fire fighters. At the same time, many homeowners in these same areas consider wood shakes and shingles an attractive and high-value option for roofing material. Red cedar, the wood generally used for roofing material on these homes, is naturally resistant to decay but requires the application of a retardant to resist damage from fires. The increasing foreign demand for and environmental concern about the overharvesting of mature red cedar trees in the United States led the Forest Service and the Northwest Independent Forest Manufacturers to sign a CRADA in December 1988. The CRADA's objective was to develop a fire retardant and preservation treatment for wood products that would be a low-cost alternative to western red cedar shakes and shingles.

The Forest Service, an agency within the Department of Agriculture, was established, in part, to develop and make available the technology that would advance the management, use, and protection of the nation's forest resources. For the CRADA, the Department's Forest Products Laboratory studied different approaches to imparting both fire retardant properties and decay resistance to products from other soft wood species, such as alder, grand and white fir, hemlock, and ponderosa pine trees. The Laboratory's development and testing of a one-step process for pressure impregnation of both the fire retardant and preservative was valued at about $75,000 a year and covered materials, chemicals, supplies of additional power, and the time of some research personnel. Northwest Independent Forest Manufacturers, an association of shake and shingle mills, contributed about $300,000 in cash for the almost 5 years worth of

R&D efforts, contributed milled wood products for testing, and provided reports on the progress of the technology's development.

Officials at the laboratory said that engaging in the CRADA broadened their technical expertise to other applications beyond treatments for wood shakes and shingles. Because of the success of the CRADA's R&D, the association was able to acquire further funding from the state of Washington to continue commercial development.

Figure II.4: Fire Retardant Testing



Left: Untreated wood shingles that were fire tested. Notice flame and wide area of damage. Right: Fire-retardant-treated wood shingles that were fire tested.

Source: The Forest Products Laboratory.

Recycled Materials, Forest Products Laboratory/Gridcore Systems International

A significant environmental challenge facing the United States is finding disposal and recycling methods for an enormous and ever-increasing accumulation of waste products. Nearly one-half of the municipal solid waste stream is made up of wood waste and wastepaper. In 1992, the Department of Agriculture's Forest Products Laboratory signed a CRADA with Gridcore Systems International to design processes, materials, components, and systems for using recycled paper and other wood fiber in products in the construction and furniture industries. The joint research was based on the creation of a structural product developed and patented by Forest Product Laboratory researchers. The product is called "spaceboard," a strong yet lightweight molded-fiber panel made from waste wood.

The Forest Products Laboratory and Gridcore both benefited from the cooperative agreement. In this case, a federal laboratory, whose research goal is to enhance the competitive position of U.S. forest products in the global economy, developed a technology that has potential for use in commercial and residential construction and packaging applications. Through a CRADA, the laboratory made its personnel and facilities in Madison, Wisconsin, available to Gridcore to develop molding techniques for new applications of the spaceboard technology. Gridcore, in turn, paid some of the expenses of the Forest Service researchers and support personnel who work in the cooperative relationship.

Today, Gridcore uses the molded fiber technology developed by the Forest Products Laboratory to produce and market panels, curves, and columns under the name GRIDCORE™. The company manufactures the product from a variety of recycled materials such as corrugated containers, mixed office waste, and agricultural fibers. Potential uses of the product include furniture, stage sets, and interior building products such as doors, ceiling tiles, and partitions. According to the company, using GRIDCORE™ products in place of solid wood products will contribute toward slowing deforestation, provide a range of nontoxic building products, and establish markets for recycled materials.

Figure II.5: Child's Table Made From Gridcore

Source: Gridcore Systems International.

Major Contributors to This Report

Resource, Community, and Economic Development Division, Washington, D.C.

Jim Wells, Associate Director
Robin M. Nazzaro, Assistant Director
John E. Bagnulo, Senior Evaluator
Amy L. Manheim, Evaluator

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