Case Studies of ARS Technology Transfer Using Patents

This chapter provides descriptions of the technology transfer process for four specific patented technologies, summarized in table 5. It allows the observation of idiosyncratic aspects of patented technologies and special circumstances of licensee firms, as well as other details of technology transfer that might not appear at a more abstract, statistical level of analysis. Observation of these case studies is primarily based on interviews with technology transfer practitioners, including research scientists, licensing professionals, and technology partners at licensed firms. The cases provide detailed observations of research and licensing behavior as it is practiced in reality.

The selection of cases is an important element of case study analysis. For instance, the choice of cases involving the transfer of patented technology limits the scope of the study to technologies for which ARS primarily pursued patent protection rather than other channels of technology transfer. In general, selecting too narrow a range of cases can lead researchers to overlook issues that do not happen to be prominent in the cases at hand. Likewise, issues that happen to be important for the selected cases might be otherwise uncommon.

We limited the case studies to ARS technologies protected by patents because of the significance of this method of technology transfer. As discussed in previous chapters, the use of patents and licensing is a relatively new and increasingly important means of technology transfer not just for ARS but also for other Federal research agencies. Furthermore, the case studies described in this chapter also show that other technology transfer methods such as CRADAs and open publication often accompany patent-assisted technology transfer. To avoid other pitfalls from case selection, this report drew its case studies from research in very different fields of science. Also, the case study technologies resulted in a variety of licensing outcomes that range from a successfully commercialized product that is still generating licensing royalty revenue for ARS, to licenses that are still at various phases of development, to still other licenses that have been abandoned.

With these precautions in place, the case studies in this chapter are representative of major licensing practices at ARS. They serve as a basis for observing a wide range of patenting and licensing policies as they are currently implemented, and do so at a level of detail that complements the statistical analyses presented in the "Technology Transfer by Federal Agencies" and "Technology Transfer at the Agricultural Research Service" chapters.

Case 1: Enhancement of Nitrogen Fixation with *Bradyrhizobium japonicum* Mutants

In the late 1970s, ARS researchers began working with bacteria from the genus *Bradyrhizobium* that were eventually the subject of a U.S. patent. Researchers isolated a particular strain of *Bradyrhizobia* that was effective in inducing nodulation in leguminous plants. Nodulation is a symbiotic process in which a leguminous seedling (such as soy) secretes the amino

Table 5
Patents used in case studies

Patent number and issue date	Inventor	Title	Abstract
5,021,076 June 4, 1991	Kuykendall et al.	Enhancement of nitrogen fixation with *Bradyrhizobium japonicum* mutants	"A prototrophic revertant of a *Bradyrhizobium japonicum* tryptophan auxotroph was isolated and found to fix more nitrogen symbiotically than wild-type bacteria. The increase in nitrogen fixation is due to an increase in nodule mass because of an increase in nodule number. The physiological basis for this improved symbiosis appears to be an alteration of the tryptophan biosynthetic pathway."
5,591,434 January 7, 1997	Jenkins et al.	DNA sequence encoding surface protein of *Cryptosporidium parvum*	"Recombinant proteins have been developed for the immunization of animals against cryptosporidiosis. The proteins are effective for the immunization of a variety of animals against *Cryptosporidium parvum*, particularly for the production of hyperimmune colostrum that may be used to confer passive immunity against the parasite. Isolated DNA sequences which encode these proteins have also been developed. The DNA sequences may be inserted into recombinant DNA molecules such as cloning vectors or expression vectors for the transformation of cells and the production of the proteins." Also see United States Patent 6,277,973 B1, Cloning and expression of a DNA sequence encoding a 41 kDa *Cryptosporidium parvum* oocyst wall protein.
5,689,054 November 18, 1997	Raboy	Low-phytic-acid mutants and selection thereof	"Single-gene, nonlethal mutations responsible for low-phytic-acid-containing seeds are selectable by means of a method for assaying seeds which are otherwise phenotypically, or nearly phenotypically, normal. Maize mutants having from 20 percent to 95 percent reductions in kernel phytic acid phosphorus compared to the wild-type, without any noticeable reduction in total phosphorus, were isolated by this method. Mutants obtained in accordance with the invention are useful for developing commercial, low phytic acid seed, plant lines." Also see United States Patent 6,111,168, Low-phytic-acid mutants and selection thereof.
5,705,030 January 6, 1998	Gassner, III et al.	Fiber and fiber products produced from feathers	"A wide variety of end products may be manufactured from fibers or fiber pulp derived from feathers. Examples of such end products are paper and paper-like products, non-woven and woven fibers, insulation,filters, extrusions, and composite sheets and plates." Also see United States Patent 6,027,608, Conversion of avian feather-waste stream to useful products. (Not assigned to the U.S. Department of Agriculture.)

Source: U.S. Patent and Trademark Office.

acid tryptophan, which encourages the growth of *Bradyrhizobia*. These *Bradyrhizobia* infect the seedling, after which they secrete an enzyme that increases seedling nitrogen fixation. Nitrogen fixation helps plants make more efficient use of fertilizer, which can improve yields or reduce fertilizer input requirements.

The patent application for the *Bradyrhizobium* strain was filed in 1989, and the patent was granted in 1991. At the time the patent was issued, ARS did not have a technology partner to market the discovery, but research at ARS indicated that coating soy seeds with the bacteria through a process called inoculation generated higher yields in some tests. ARS negotiated material transfer agreements with both major suppliers in the relatively small U.S. inoculant market so that they could perform further testing and development. Although one inoculant supplier declined to license the technology, the other firm agreed to a licensing agreement with ARS in 1994. Sales of an inoculant product using the *Bradyrhizobium* strain began shortly thereafter, generating licensing royalty payments to ARS. This license has been recognized with several awards for successful implementation of technology transfer commercialization.

Case 2: DNA Sequence Encoding Surface Protein of *Cryptosporidium parvum*

Cryptosporidiosis is a diarrheal disease caused by a microscopic parasite, *Cryptosporidium parvum*. This parasite can live in the intestine of humans and animals and is passed in the stool of an infected person or animal. It had been a particularly difficult disease to prevent or treat because infected animals were unresponsive to vaccines and no medications were available to treat infections. Kansas State University researchers discovered a protein antibody that could be used in the diagnosis of cryptosporidiosis, and ARS researchers joined the research effort to clone the gene associated with this antibody and produce recombinant proteins suitable for vaccinations. Kansas State was relatively new to the patenting process, and as a result assigned patent rights to ARS. ARS filed a patent application in 1994 and was awarded a patent in 1997.

Initial private sector interest in the technology came from the human pharmaceutical market. In particular, acquired immunodeficiency syndrome (AIDS) patients with compromised immune systems were at higher risk for cryptosporidiosis. A CRADA with a pharmaceutical company led to an exclusive license for the antibody. As new human immunodeficiency virus (HIV) drugs became available, one of their beneficial side effects was to reduce the risk of cryptosporidiosis in these patients. With the accompanying decrease in the potential market for the antibody, the pharmaceutical company terminated its technology license.

Licensing interest shifted to development of a veterinary vaccine, particularly for cryptosporidiosis in bovines. Correspondence with two companies with substantial animal health product lines began by 1999, and they negotiated terms for co-exclusive licenses. As required by the Federal Technology Transfer Act of 1996, ARS published a notice in the *Federal Register* of its intent to issue the licenses. Before the licenses could issue, another company with an animal health product line objected. To accommodate this third company, ARS agreed to issue another co-exclusive license. ARS agreed to limit the number of co-exclusive licenses to these three firms. To date, at least one of these firms is continuing efforts to develop and commercialize a vaccine using the licensed technology.

Case 3: Low-Phytic-Acid Mutants and Selection Thereof

Research into the metabolic pathways of phytic acid was first motivated by nutritional needs of both humans and animals, but environmental considerations also became a consideration for this research. High-phytic-acid concentrations in animal feed prevent monogastric animals like swine and poultry from absorbing phosphorus, an important nutrient. Dietary supplements such of phytase enzymes can increase phosphorus availability to the animals, but at an additional expense. Another effect of unabsorbed phosphorus is that it can pass into animal waste, eventually leading to phosphorous contamination of land surfaces and surface and ground water.

Low-phytic-acid mutants in maize—a major source of animal feed in the U.S.—were isolated by an ARS researcher in the early 1990s. A potential application of this discovery was for animal feed that did not require supplements, improving animal health and reducing phosphorus runoff in the environment. ARS contacted 12 companies to gauge interest in technology licenses. Of those companies, six expressed interest, and eventually a CRADA was signed with a large seed/genetic research company in 1993, before the first patent application was filed in 1994. The patent was granted in 1997. A license was negotiated with the original CRADA partner, but two other seed/genetic research companies requested and successfully negotiated co-exclusive licenses. Two of the three seed companies were large companies that have since been acquired by multinational chemical/life sciences firms. The other genetic research company was a small company spun off from a large seed multinational in 1994 but bought by a large multinational chemical/life sciences firm in 2000.

Three aspects of the low-phytic-acid breeding technology have posed problems for commercial development:

(1) Cultivated varieties with the low phytic acid trait also appear to carry a yield penalty. Neither the potential cost savings from a reduction in phytase dietary supplements nor the increase in animal health from greater phosphorus uptake are sufficient to make up for the higher cost of producing the low phytic acid maize varieties.

(2) Changes in ownership among the licensees may have brought corresponding changes in the R&D strategies of the licensee firms.

(3) Views on the importance of mitigating environmental release of phosphorus may have changed since the initial research project.

This remains an active license, although no commercial products are immediately forthcoming.

Case 4: Fiber and Fiber Products Produced from Feathers

In the course of research into chemical and physical properties of materials, ARS scientists discovered that keratin from chicken feathers can be made into fibers that behave similarly to plant fibers made from cellulose. Chicken feathers make up a large waste stream for modern poultry production facilities, so an alternative use for this material could possibly have environmental as well as economic benefits. In addition, the market for fiber products from cellulose-base sources is very large: examples include diapers, industrial and automotive filters, fabrics, insulation, and structural components. This large market improves the chances of finding a market segment for which feather fibers offer a cost or performance advantage.

There are currently three possible means of disposing of poultry feathers:

(1) Burning, which poses environmental concerns and is difficult and costly because the feathers emerge wet from chicken-processing facilities

(2) Burying, which is uneconomical because of their low density

(3) Grinding into feather meal, a low-cost, low-quality animal feed

A patent application for a technique of cleaning and drying feathers and mechanically separating keratin fibers was filed in 1995 and a patent issued in 1998. Initially a large poultry producer collaborated with ARS in a 3-year CRADA, and had the option to license the technology exclusively. After a few extensions from ARS, this producer declined to exercise its licensing rights.

ARS followed this unsuccessful attempt at technology transfer by licensing the technology co-exclusively to three firms: a different large poultry producer, which also needed to manage its feather waste stream; a rendering plant, which had the same need; and a firm that was already using the quill component of feathers as a production input for a line of nutritional and cosmetic products. Although one firm has abandoned its license, at least one other firm is actively pursuing new commercial applications of the technology.