Patent Protection and Project Management in the Development of New Crop Varieties: Case Study of the High Pectin Tomato

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Introduction

Intellectual property protection is essential for investments in biotechnology innovation. It allows developers of new technology, such as genetically modified (GM) crops, to prevent imitation of their research results and to recoup costs and earn returns on investments in research and development. Intellectual property rights (IPR) are therefore an important public policy mechanism for promoting technological growth. However, protecting intellectual property is only one element of a successful R&D project. The process leading from scientific discovery in a high-technology area, such as agricultural biotechnology, to marketing of a retail product incorporates a complex series of events and relationships.

To assess the importance of IPR within this context, we examine a case study to track the creation of a GM crop variety from R&D to the marketing of the resulting crop. The case study approach allows us to weigh all the factors that influence product value, enabling us to better evaluate the specific contribution of IPR in promoting research and development (R&D). Other contributing factors important in the development of a new crop variety include supporting and enabling technologies, human capital, available R&D funding, prior accumulation of scientific knowledge, collaborative efforts, and efficient management of the R&D process. We can examine the effects of processing, marketing and retail requirements, as well as the influence of consumer demand and GM food regulation on product value. We explore the various instruments available for protecting intellectual property (IP) related to new plant varieties, such as utility patents and Plant Variety Protection Certificates (PVPCs) and determine the extent to which these IPR are substitutes or complements. Recognizing that complex innovations in high technology may require the use of several patented technologies, such as research tools, we study the role of patents and licensing in R&D. One finding that emerged during the case study was the importance of factors besides patent protection for developing a new technology and products, such as effective partnering and supply chain management.

The GM crop that we chose as the focus of our case study is a high-pectin (HP) tomato jointly developed by Zeneca Plant Science (now AstraZeneca, but formerly related to Imperial Chemical Industries, ICI) with the University of Nottingham and Petoseed (now a subsidiary of Seminis owned by Savia). The collaborative research and commercialization efforts to develop and market the tomato required the transatlantic coordination of these organizations, each providing specialized inputs into the development and marketing chain.

The paper proceeds as follows. First, we discuss the processing and consumer benefits of the high pectin tomato, and we present information about the R&D process and funding. In the next section, we explore the use of intellectual property protection and licensing of enabling technology. In the third section, we examine the strategy employed by Zeneca to manage the supply chain, regulatory process and marketing of the final product. We close with a section describing the fate of the tomato, followed by concluding comments.

Advantages of the high-pectin tomato

Most applications of biotechnology have focused on introducing traits in plants to reduce farm production costs. The most prominent examples are plants genetically modified to resist herbicides and pests. These cost-reducing technologies potentially increase profits for growers who adopt the modified seed. While traits that reduce input use or lower production costs can provide benefits to producers and technology developers, the only possible benefit to consumers is lower commodity prices. Some economic research suggests that consumer benefits may be negligible for some of the GM crops currently on the market, such as Bt cotton and herbicide-tolerant soybeans (Falck-Zepeda and Traxler, 2000a and 2000b). However, other estimates of the welfare effects of GM crops, specifically herbicide-tolerant soybeans, found that consumers may benefit substantially more than innovators and producers (Moschini et al., 2000). The results of these studies are sensitive to several factors, including assumptions about the shape of consumer demand and supplier market power. Given initial consumer resistance to GM foods, acceptance of agricultural biotechnology could be curtailed if consumers do not recognize benefits from adoption of GM crops. The next generation of genetically modified traits – of which the HP tomato is a precursor – most likely will focus on quality-enhanced crops, such as crops with enhanced flavor or nutrient content (Fernandez-Cornejo et al., 1999). The benefits of these traits ultimately may be more tangible and apparent to consumers, perhaps leading to greater consumer acceptance. For next-generation applications of biotechnology to succeed, the value-enhanced crop must have desirable properties for which growers can receive a premium and from which crop developers can recoup the high cost of R&D.

The main benefits of the HP tomato involve its composition and structure. Fruit pectin is a polysaccharide compound that constitutes cell walls and thus shapes fruit structure and consistency. Because it is typically water insoluble, pectin is indigestible. However, as part of the natural senescence (ripening) process, enzymes are released that change pectin to a soluble form, causing fruits to soften as they grow ripe. By discovering and then altering the chemical pathways over which pectin is broken down, the creators of the HP tomato were able to affect the content of tomato solids and the timing of ripening.
U.S. Patent #5,387,757 succinctly summarizes the potential benefits of tomatoes with reduced expression of polygalacturonase, an enzyme that leads to pectin change and fruit softening:

> *"Preliminary results indicate that tomatoes of the invention having a reduced level of expression of polygalacturonase retain their firmness for a longer period after harvesting than similar tomatoes having normal levels of expression of fruit softening enzymes. They are consequently expected to soften more slowly on the plant, be harder at the time of harvesting and have a longer shelf life, with potentially increased resistance to infection. It is useful to be able to harvest fruit later when flavour, aroma and colour may have developed more fully. Fruit according to our invention may also show increased solids content and altered pectin and cell wall components, with consequent processing advantages. These advantages include energy savings during tomato puree production, increased insoluble solids, and improved gelling qualities and colour of puree."*

The HP tomato can be categorized as a crop that combines cost-reducing and value-enhanced traits. Reduced growing, transport and processing costs can be attributed to the increased pectin (insoluble solids) content associated with the tomato. The higher pectin content assists tomato cultivation because there is higher yield than the traditional counterpart. This also translates into less water input to produce the same amount of tomato solids. Additionally, because the HP tomato contains less water than a conventional tomato of the same size, it facilitates processing by reducing energy costs. While the primary benefits are associated with increased tomato solid yields and lower shipping and processing costs, the claimed benefits of the value-enhanced HP tomato include richer flavor and color.[1]

R&D History

Early tomato research at the University of Nottingham began around 1974 in Dr. Donald Grierson's lab (see timeline in Table 1). Their main research objectives were to address some fundamental scientific questions related to plant physiology, biochemistry and genetics. This original research identified several fruit enzymes with important roles in the natural ripening process: polygalacturonase (PG) and pectinesterase in texture change, phytoene synthase in color expression, and ACC oxidase in ethylene control.[2]

The research effort that directly facilitated the development of the HP tomato began with collaborative work in 1982/83 between the University of Nottingham (Dr. Grierson) and Dr. Wolfgang Schuch from the biotechnology group at Zeneca. The biotechnology group at Zeneca was interested in exploring research areas

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[1] House of Lords, accessed 5/17/00, http:\\www.parliament.the-station…9/ldselect/ldeucom/ 11/8061706.htm.

[2] Ethylene is a naturally occurring chemical compound in tomatoes that acts as an agent in fruit senesence. In commercial harvesting, tomatoes are often picked in a firm, incompletely ripe state to reduce spoilage and shipping damage, and then exposed to ethylene gas to induce the color, flavor and texture changes associated with ripening.

with future commercial potential, and they were familiar with Dr. Grierson's tomato research program. The research question approached in the joint work between the labs was whether they could identify, isolate and control the genes responsible for expression of PG in order to control texture. From the outset, neither party had a clear sense of the commercial potential of the research. Regardless of commercial potential, the research collaboration was mutually beneficial during the HP tomato research project, which lasted close to 10 years. The Zeneca biotechnology group learned much from Dr. Grierson's expertise in tomato physiology, biochemistry and genetics. From Zeneca, Dr. Grierson's lab learned current biotechnology methods, obtained research tools, and received scientific and material support to effect change in plant systems. Their combined R&D efforts helped bring both parties to the evolving frontier of biotechnology.[3]

By the late 1980's, the joint research program had identified and sequenced specific genes controlling PG expression. Because PG triggers tomato solid breakdown as part of the ripening process, the researchers sought technology to suppress expression of PG genes in the tomato. Antisense and gene suppression methods were applied to block expression of the PG gene and delay pectin breakdown.[4] Continued experiments successfully demonstrated that tomatoes could be altered to exhibit increased pectin and solids content. With this breakthrough, the R&D team began to focus on a strategy to develop a product to take advantage of the benefits of the HP tomato.

At this point, Zeneca began to provide some direct funds for the Nottingham research in exchange for exclusive rights to patented technology promising commercial viability. "Proof of concept" studies were then undertaken in a UK heirloom tomato variety, the "Ailsa Craig," a variety with which the university researchers were familiar. Moreover, Ailsa Craig is an especially soft variety of tomato, and therefore was a good variety with which to demonstrate the effect of PG suppression. However, the "Ailsa Craig" was not a commercially relevant variety, so Zeneca needed access to germplasm with complementary traits to make a commercially viable tomato. Once the "proof of concept" studies for creating a plant with value-added characteristics was accomplished, they decided to pursue marketing collaborations to bring the tomato to market (see section on "Supply Chain Integration and Marketing Strategy").

R&D funding

The R&D partnership with Zeneca was beneficial to the University of Nottingham's tomato research program. The University never received substantial R&D funding from Zeneca, whose contributions to the research effort were mostly in the form of materials, equipment and scientific support. However, funding mechanisms and grants were available in the UK to encourage research collaborations between public and private sector entities. The major source of funds came directly from the Biotechnology Directorate, part of UK's Science and Engineering Research Council. Nottingham also received grant money to fund PhD students, many of whom would later find employment in private industry. Overall, the University of Nottingham received close to £500,000in funding related to the tomato research collaboration. Modest royalty payments from sales of the HP tomato were also realized, but these payments probably totaled only thousands of pounds for reasons discussed in a later section ("Fate of the High Pectin Tomato").

Role of Intellectual Property Rights

This section examines the role of various IPR mechanisms in the development of the HP tomato. Patents and other IPR provide incentives for R&D by protecting new products from imitation and competition for a limited time. For example, expansion of patentable subject matter in the U.S. in the early 1980s to include multicellular living organisms created an incentive for firms to develop innovations in that field, and led to increased R&D

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[3] While we do not directly reference individual comments, we would like to acknowledge input from Dr. Donald Grierson, Dr. Wolfgang Schuch and Dr. Ed Green, which has been incorporated throughout the text.

[4] Gene suppression technology was used to develop the commercial tomato variety.

investment. Another advantage of patent protection and other IPR is that they require firms to register their discoveries, promoting the disclosure and diffusion of new technology. Without mandatory disclosure of patents, firms seeking to protect their intellectual property might rely extensively on trade secrets, which are disadvantageous in that they reinforce firms' incentives to conceal technological progress and resort to distortionary defensive practices.

Although IPR promote private sector investment in agricultural research and development, they also can have adverse consequences for innovating firms. Patents can impede research efforts if other innovators (including competitors and both non-profit and public sector research institutes) are denied access to patented research tools. Patents might also lead to excessive duplication of research effort as firms rush to win patent races. Competitive advantages, such as "lead-time" in establishing working partnerships and "know-how" in management and production experience, do not enjoy the same legal protection as patents, but nonetheless play an important role in protecting R&D investments. While the Zeneca case is only one example of how IPR affect the development and implementation of a new technology, it provides some insight into the results when IPR policy is implemented. This section describes the IPR and other intangible assets that were most instrumental in protecting the value of Zeneca's R&D investments, and then addresses their relevance to broader IPR issues.

Patents, Interferences, PVPCs and "Know-how"

Although facets of the research related to the development of the HP tomato began in the 1970s, the earliest relevant patenting activity occurred in the late 1980s and was related to gene identification, sequence and function. Later patenting focused on antisense technology to limit expression of the PG gene. At this point, the focus turned toward commercialization of the invention. However, the Nottingham/Zeneca research group was not the first research team to isolate the PG gene: Calgene had accomplished the same feat and applied for a patent (U.S. Patent 4,801,540) a short time earlier. To resolve this conflict of intellectual property rights, the parties pursued dispute resolution through U.S. Patent and Trademark Office interference proceedings. In the course of resolving the dispute, the researchers at Nottingham and Zeneca determined that the texture change gained through PG suppression technology had minimal commercial potential for fresh market tomatoes. They determined that the higher pectin content had potential benefits for tomato processing. Calgene, however, came to the opposite conclusion. As a result, a conclusion of the interference hearings was that Calgene would pursue applications of PG suppression in fresh market tomatoes while Zeneca would apply the technology in processed tomatoes. This resolution was reached mid-term in development of the HP tomato, further shaping subsequent R&D and commercialization efforts.

Utility patents were a primary vehicle for protecting IP. The Nottingham/Zeneca research group received several utility patents related to the HP tomato and similar technologies covering horticultural crops, particularly tomatoes (Table 2). Most of the patents were issued in the U.S., but Zeneca obtained additional protection through several European patents and one Japanese patent. Most of the patent claims cover the transformation of the tomato plants to limit expression of the PG gene that controls texture. Additionally, the threat that competing research teams, particularly Calgene, might patent similar technologies prompted Nottingham/Zeneca to gain priority by obtaining R&D results and patenting them as quickly as possible.

An instrument of IP protection that did not play a significant role was plant breeders' rights under the U.S. Plant Variety Protection Act (PVPA) instituted in 1970. The PVPA established protection for sexually reproduced seed varieties, and was subsequently amended to expand scope of coverage and limit farmers' rights to resell seed. However, it still contained exemptions for farmers' rights to replant saved seed, weakening developers' control over modified seed in a way that patents do not. Moreover, PVPCs are usually applied for after the successful development of a commercially viable variety. Because the scientific discoveries in need of IP protection were made before varietal development was complete, utility patents were more critical and deemed sufficient for protection of the HP tomato from imitators.

Investments in scientific and managerial expertise, or accumulated "know-how," are difficult and time-consuming to replicate, providing additional protection for early innovators. The ability of a follower to imitate the HP tomato would depend on the ability to link several of a complex series of business operations, an area in which Zeneca had gained considerable lead-time through various partnerships (see elaboration in the next section). Studies by Levin et al. (1987) and Cohen et al. (2000) stress the importance of lead-time for protecting intellectual property.

Technology licensing

During early collaboration, the University of Nottingham granted Zeneca the right to first refusal of exploitation rights. Although the outcome of the research collaboration was then unknown, in 1983 Zeneca signed an agreement with the University of Nottingham that granted Zeneca first rights to anything patentable. The parties also agreed that rights to joint discoveries from continued research would be negotiated in good faith. UK laws governing industry and university cooperation allowed the University of Nottingham and Zeneca to enter into a research collaboration.

Royalties and some details were not negotiated at the outset of the collaborative venture, but instead were left to be negotiated once the commercial potential of the research became clearer. The licensing arrangements eventually agreed upon by these parties demonstrate the flexibility with which these instruments can be employed. At the early stages of research, much of the cost and financial risk of the project were underwritten by research grants. Zeneca provided some material and research support at latter stages of the project, securing the option of first refusal to serve as a partner in commercialization. As Zeneca exercised this option at later stages of research, after the likely commercial benefits of the project became clearer, the parties extended their negotiations to include royalty payments to the University of Nottingham.

These flexible, cooperatively-negotiated licenses stood out in contrast to the narrow licenses negotiated with other companies for access to complementary research tools. To incorporate the high-pectin trait, Zeneca required access to specific enabling technologies or research tools that were known to be effective in facilitating R&D. Many of theses technologies were patented or otherwise owned by other firms. While the fundamental research that took place in Dr. Grierson's lab did not require the licensing of any technologies, technology licensing was critical for manipulating the plant genes and subsequent hybridization undertaken by Petoseed. Examples of patented technology utilized in the development of the HP tomato included Monsanto's 35S promoter, a gene for introducing desired traits into target DNA, Monsanto's kanamycin for use as a selectable marker, and DNAP's "Transwitch" (gene suppression) technology (Table 3). Zeneca finally obtained use of these technologies after negotiations with Monsanto and DNAP, overcoming both initial lack of experience in the biotechnology industry with technology licensing and the absence of established benchmark values.

Patents can also be used to block research as rival firms inhibit competing research outright by denying use of their patented technology. However, clearly defined IPR can facilitate R&D as firms create markets for licensing complementary technology. When IPR are uncertain, unclear or disputed, firms may find it harder to gain access to important enabling technologies and to agree on licensing terms.

For example, some of the first U.S. patents covering gene suppression (DNA Plant Technology's Patent 5,034,323) and antisense technologies (Calgene's Patent 5,107,065) were in direct competition with Zeneca's antisense patent (5,457,281). The subject matter of the Calgene and Zeneca patents are closely related. It is interesting to note that Calgene had an earlier filing date on their antisense patent, but Zeneca received their patent sooner. In the end, the patent claims were sufficiently different to allow separate patents to be granted. However, the close timing of this patent race illustrates the uncertainty, risk, and potential barriers arising from patent rights and competition in innovation markets.

So in one sense, patents facilitate the creation of a market in which technology licenses can be negotiated, and in another, patents can block further research. It is the opinion of Dr. Schuch (2000) that the proliferation of patented technologies in the emerging field of modern biotechnology has made research *easier*, not harder in the long run. Greater industry experience with research tools has facilitated technology development and led to the establishment of market rates for some technology licenses. This may have contributed to the supply of research tools and the reduction of transaction costs, creating more alternatives for attaining research goals rather than more barriers. In this regard, patents on enabling technologies not only establish a market for technology, but industry learning may also reduce the cost to participate in that market.

Supply Chain Integration and Marketing Strategy

The research on PG-suppression in tomatoes pioneered in the Nottingham/Zeneca laboratories culminated in the commercial introduction of pureed HP tomatoes in February 1996. Over the course of several years leading to commercialization, Zeneca oversaw not only the R&D process, but also the production and marketing phases of the product. In addition to its scientific contributions to the development of the tomato, Zeneca forged several key partnerships to form a supply chain capable of delivering the product to market:

- The **University of Nottingham** laboratory secured public funding and provided the fundamental knowledge and research on which the genetically altered tomato was based;
- **Zeneca** provided material and technical support to facilitate R&D, and oversaw efforts to obtain regulatory approval;
- **Petoseed** supplied elite germplasm with demonstrated desirable market traits for hybridization, transformation, germplasm development, breeding and production of seeds exhibiting the PG-suppression trait;
- **Hunt-Wesson** evaluated characteristics of PG tomato paste, contracted with California tomato growers and processed the tomatoes;
- **Safeway** and **Sainsbury** marketed and retailed the processed tomato in the UK under their respective own-store brands.

This section discusses the factors that led to the choice of partnerships at each step in the supply chain, specific challenges met by Zeneca in uniting these disparate entities, and ramifications of the decision to form strategic partnerships as a means of integrating the supply chain leading from university laboratory to retail shelves.

Establishing partnerships

The determination that high-pectin content was the most significant result of PG suppression in tomatoes – reinforced by the resolution of the patent interference hearings with Calgene – focused commercialization efforts on the processed tomato market. This decision determined specific links in the supply chain. Zeneca lacked the requisite skills, experience, and market presence in the tomato processing industry to successfully produce and market processed tomatoes, necessitating the formation of partnerships. Factors such as the location of growing, processing and hybrid development, as well as regulatory concerns and the need for strong supply chain links all determined Zeneca's choice of partners.

The first step that influenced partner choice was the selection of a growing location. Despite its intention to market the product in the UK, Zeneca chose the United States as the location to grow HP tomatoes. Zeneca chose the U.S. in part because scale requirements of tomato processing favored the large size of U.S. growing operations – particularly those in California – relative to their European counterparts, which were smaller and more scattered. California’s favorable climate and experience with growing tomatoes for processing was well known: in 1996, U.S. suppliers accounted for more than a third of processed tomato production worldwide[5] and a significant amount of U.S. supply originated in California.

[5] http://www.seedquest.com/processingtomato/marketdata/1996.htm

Another constraint on selecting a growing location was Zeneca's need to secure regulatory approval for field tests and cultivation of a genetically engineered crop. Even before recently heightened consumer rejection in Europe, considerable debate surrounded the desirability and benefits of genetically engineered crops. Contemporaneously with the first full-scale planting of genetically engineered varieties, regulatory authorities were designing and implementing guidelines and requirements. Furthermore, the environmental and human health questions posed by genetically engineered varieties crossed several areas of regulatory oversight. It is likely that an expectation of a more transparent regulatory process in the U.S. relative to Europe influenced Zeneca's decision to grow in the U.S..

In conjunction with the choice of growing location, Zeneca needed regionally favorable germplasm for hybridization. The "Ailsa Craig" variety in which the benefits of the HP tomato had been demonstrated was not a commercially viable variety for large-scale field production, nor was it well suited to the California growing climate. Zeneca partnered with PetoSeed to supply germplasm from which to breed hybrids with the HP trait. Petoseed was an established U.S. hybrid developer for fruits and vegetables, with several successful hybrid lines in the California processed tomato market. Also, PetoSeed possessed the facilities and human capital necessary for rapid and effective development of new genetically engineered varieties.

Once a supply of modified seed was arranged, a processor was necessary to take advantage of the special characteristics of the HP tomato. Zeneca chose Hunt-Wesson to process the tomatoes because of its broad range of tomato-related consumer products. Hunt-Wesson also arranged a supply of tomatoes through grower contracts in addition to performing processing operations, typical practice in the processed tomato industry.

Finally, Zeneca collaborated with Sainsbury and Safeway to market the tomato puree in the UK. Each chain possessed large distribution networks, and each had store brand names under which the HP tomato puree could be marketed.

Contributions by Zeneca

Along with the activities of its partners, it is important to recount specific contributions to the supply chain made by Zeneca. Foremost was the effective management of the international, cross-disciplinary and complex collaboration among many different entities. Aside from this management, oversight and joint development of the HP tomato with the University of Nottingham lab, some of Zeneca's other main functions were to secure regulatory approval (for field trials, commercial growing, and food use) and to establish the identity-preserved marketing channel leading "from seed to shelf."

Consumer acceptance of agricultural biotechnology was an important issue, and Zeneca treated it very seriously. Zeneca approached this issue largely within the regulatory framework. Zeneca pursued regulatory approval at all phases of product development in both the U.S. and the UK (see Table 1). It received permission to field test and commercially grow the crop in the U.S. and gained approval for food use in the UK and U.S.. Field trials of the HP tomato lines developed by Zeneca Plant Sciences and Petoseed were conducted under Animal and Plant Health Inspection Service (APHIS) permits during 1991-1993 and under notification in 1994. In 1995, the USDA ruled that it would no longer regulate the tomato, clearing the road to commercialization. At about the same time Zeneca received U.S. Food and Drug Administration (FDA) approval for food use of the HP tomato in the U.S., which was not a regulatory requirement *per se*, but which represented diligent effort by Zeneca to ensure product safety and to gain consumer acceptance. The HP tomato also received UK government approval for food use from the Advisory Committee of Novel Foods and Processes.

Another critical step in securing consumer acceptance was to clearly label the tomato puree as "genetically modified," selling it alongside other conventional tomato brands. Because the stores retailed the product under their own store brand, they effectively staked their reputation on the quality, safety and desirability of the HP tomato puree.

Strengths and weaknesses of the partnership strategy

This section elaborates on the strategic decision to implement the supply chain through many partnerships, rather than pursue a "go it alone," vertically integrated strategy. While ultimately the partnerships coordinated by Zeneca proved effective at bringing a commercially successful product to market, the strategy of taking on partners had its own strengths, weaknesses and challenges.

Perhaps the most important strength of the partnering strategy was that each partner possessed effectiveness and efficieny at their respective steps in the supply chain. For instance, the Grierson lab had expertise and experience at the forefront of tomato research. Petoseed and Hunt-Wesson operated in their respective markets from a position of competitive success, and Safeway and Sainsbury had competitive own-store brands in the retail grocery market. The strength of the individual components created a "first-best" delegation of duties to the partner best able to carry them out.

A primary demand on Zeneca management by pursuing the partnering strategy was the need to coordinate the activities of so many different processes and operations. This was especially true for many biotechnology applications, because of the many temporal and technical dependencies (or bottlenecks) involved. However, it is worth keeping in mind that the complex series of operations were not necessarily a result of the partnering strategy, but resulted from the inherent complexity of a project with scientific, technological, regulatory, and market components. In fact, the partnering strategy substantially facilitated Zeneca's ability to deal with the complexity of the project, because it provided Zeneca management with more experience and specialized knowledge than it possessed alone. Through partnership, Zeneca gained the ability to refine and streamline crop development despite the inherent complexity of biotechnology production. McElroy (1999) suggests that improving coordination between R&D and process development is a critical factor in remaining competitive in agricultural biotechnology innovation.

According to several sources involved with the project, one of the most valuable outputs of the project was the development of cross-cultural bonds and management skills arising from the coordination and integration of so many different business functions. The management skills necessary for successful commercialization of such a large, integrated enterprise were a key benefit that arose from collaboration on the HP tomato project. It is not an exaggeration to say the partnering strategy and leadership role of Zeneca enabled the successful development of the HP tomato. Without the leadership role provided by Zeneca management, individual partners acting alone might have lacked the incentive, skills and assets to undertake the entire project. Likewise, Zeneca depended on and benefited from the knowledge and expertise of its partners.

Individual partners gained valuable experience as well. For example, the University of Nottingham and Petoseed gained some of the following benefits:

- Integration of genetic manipulation and other new biotechnology techniques into research programs and with existing hybrid operations
- Management and project execution within a 3rd party/partnering relationship
- Establishment of working relationships with project partners, with the potential for future collaboration

Although not as intense as during the development of the HP tomato, a working relationship and continued collaboration exist between Zeneca and University of Nottingham scientists. Moreover, the University of Nottingham has received some royalty payments for their scientific contributions, in addition to BBSRC funding for related research.

A disadvantage of partnering was that the value chain was only as strong as its weakest link. For instance, Hunt-Wesson's contribution of benefits were limited because they used tomato processing techniques that are popular in the U.S.. The "hot break" processing method is typically used to deactivate the PG enzyme and thus maintain pectin integrity and desired product viscosity. The hot break method requires high temperatures (usually just below the boiling point of water) and concomitantly high energy costs. The advantage of the HP tomato in processing was that the PG enzyme was genetically suppressed, obviating the need for high temperatures used in the hot break method. Instead, the HP tomato would probably have yielded greater economic benefits had the "cold break" method been used. Using this method, processing can occur at lower temperatures, and thus lower energy costs, without sacrificing the desired product viscosity. Ultimately, the retooling costs of switching over from the hot break method undermined some of the economic benefits of the HP tomato for processing.

Consumer opposition to genetically engineered varieties exposed a weak link in the supply chain at the retail level. In the face of broad rejection of genetically engineered varieties, both Sainsbury and Safeway ceased to retail the HP tomato puree. Retailer concerns both for customer acceptance and the value of their store-name brands probably contributed to their decision to halt sales, although the threat of broad rejection of genetically engineered varieties was also a factor that probably imperiled any attempt to market the HP tomato in the UK.

A more onerous challenge of a partnering strategy is the need to negotiate and respond to the different cultures, incentives and requirements of the different partners. To illustrate this point, consider the interaction between the University of Nottingham and Zeneca laboratories. To facilitate a fruitful outcome from the partnership, both partners had to understand and consider the differences between university and corporate labs. While ultimately bound together by the culture of science and the possibility of a shared monetary gain for a commercially successful innovation, university and corporate labs almost certainly have different cultures and incentives. For instance, the incentive to publish results as early as possible in prestigious peer-reviewed journals is central to the university perspective, whereas intellectual property restrictions might encourage corporate labs to maintain confidentiality for a longer period The interaction between Zeneca and University of Nottingham labs probably was not the only instance in which different cultures and incentives of the various partners could have threatened the success of the partnerships. Handling these and other differences was surely one of the most important challenges that the various partners had to overcome.

Fate of the High Pectin Tomato

Commercial introduction of the HP tomato occurred in February 1996. The tomatoes were marketed as tomato puree in larger 170g tins under the Sainsbury and Safeway brand names and were clearly labeled as "genetically modified." The labeling was likely intended to pre-empt consumer concern about GMOs. The price was about the same as traditional tomato purees, but the HP tomato tins contained 20 percent more puree by volume.[6] The larger cans created a concrete impression of the greater consumer value compared to competing brands, a shrewd marketing tactic.

Initial acceptance of the HP tomato puree was high. The HP tomato puree had higher quality and was less expensive than conventional tomato puree. As a result, the HP tomato accounted for a 60-65% share of tinned tomato puree in 1998, which in turn constituted approximately 20-25% share of the entire tomato puree market. Pureed HP tomatoes achieved this market share just two years after introduction, indicating a very fast consumer adoption rate. Consumers were able to buy more tomato puree for the same cost (about 29 pence) without losing any tomato quality benefits. During this time, 1.6 million cans were sold.

However, consumer acceptance of the HP tomato evaporated along with consumer confidence in genetically engineered crops in 1998. Opposition to genetically engineered crops became widespread throughout the UK and Europe. Sainsbury pulled the product from its shelves, and Safeway sold out its remaining stock. Contracts for growing, processing and shipping more puree were not renewed. Furthermore, Petoseed halted seed production for the genetically engineered hybrid.

[6] http://www.monsanto.co.uk/news/98/June98/safeway4jun.html

However, Zeneca has not entirely abandoned the HP tomato and is now pursuing potential cultivation and processing in Europe. They are also developing other high-quality, nutrient dense horticultural crops based on technology, knowledge and experience acquired during their partnerships with the University of Nottingham, Petoseed and Hunt-Wesson.

Conclusions

The partnership led by Zeneca was successful in developing and introducing a new agricultural product into the marketplace. Accomplishing this feat required the partners to coordinate across cultural, technical and business arenas, to employ novel biotechnology applications and to gain new understanding of fundamental biological processes. Not only did they succeed at implementing the new technology, the product they introduced was – if only temporarily – commercially successful. Because of the short-lived support for the product, monetary benefits were probably modest (if any). From the publicly available market data, gross revenues from tomato puree sales were estimated at about £464,000 ($700,000). Revenues from HP tomato puree sales probably fell well short of compensating the management effort and other expenses that went into its research, development and production. However, the initial commercial success of the HP tomato indicates that the tomato might eventually have produced greater monetary benefits if consumer concerns had not forced the removal of the product from store shelves.

Although monetary gains from the project were minimal, it yielded several valuable non-monetary benefits. Overall benefits included improved management of research projects, establishing relationships with other companies, and access and use of biotechnology tools for developing horticultural crops. According to several of the parties involved, one of the most valuable outputs of the project was the management skills developed through the coordination and integration of so many different business functions. The management skills necessary for successful commercialization of such a large, integrated enterprise led to an exchange of ideas and expansion of R&D capacity. The close relationships required coordination of the actions of the various parties and created an opportunity for long-term collaboration among the individual partners going forward. The long term R&D and management relationships forged and the knowledge they generated were valuable. Finally, negotiating licenses and acquiring rights to use technology owned by parties outside the partnership was a skill with increasing importance in rapidly developing markets for biotechnology research tools.

The contrasting experience of competitor Calgene illustrates the benefits of pursuing a strategy based on partnerships. Despite the fact that its main comparative advantage lay in genetic technology, Calgene solely attempted to develop operational capacity at other steps in the supply chain, such as growing and distribution. Teece (1995) suggests that parties without assets complementary to their innovations most often fail to capture the added value. However, relying on internally directed operations precluded them from employing the skills and experience of the best providers of any given operational step. For instance, their lack of experience in agricultural operations led to as much as a 30 percent crop loss (Tally 1998).

As use of agricultural biotechnology becomes widespread, product life cycles are growing shorter and profit margins from successful innovations are eroding. McElroy (1999) discusses the need to integrate research efforts, process development and other business functions to streamline product introduction. To remain competitive, firms must closely coordinate R&D with regulatory processes, business operations, and consumer preferences. The integrated strategy pursued by Zeneca harnessed the talents of its partners to achieve necessary production steps simultaneously, although it did have its gaps. For instance, the product could have been more successful if they had incorporated the PG-suppression trait into a tomato hybrid under development rather than an existing successful hybrid already on the market. The short time in which the HP tomato was in production limited the extent to which it suffered from this obsolesence or "yield drag," but this example shows further room for streamlining new product introduction. Hindsight also reveals that further gains could have been achieved using different processing techniques.

A few remarks about intellectual property rights and science policy as they relate to this case study are offered in conclusion. First, firms that use outside technology can increase their “freedom to operate” by obtaining intellectual property rights to use in negotiation. However, freedom to operate can also increase when patents are awarded to other firms. Obtaining access to technology through licensing agreements was more difficult while patent applications were still pending. Licenses for patented technologies (such as selectable markers, kanamycin and gene suppression technology) could be negotiated more easily after patents for these technologies were issued. Furthermore, interference hearings as part of the patent application process played a role in clearly delineating intellectual property rights.

The close proximity of patent application filings by Zeneca and Calgene suggests that patents foster an intensely competitive research environment. However, the differentiation of the Zeneca and Calgene patents, as well as the two different paths (processing vs. fresh market) taken by each in commercializing their inventions, suggest that the duplication of research effort often ascribed to patent races may not be problematic. Finally, the role of public funding for "basic" science that later can be developed into "applied" science in the private sector is consistent with the example of the HP tomato. Public support played an important role in funding the fundamental work to identify the role of polygalacturonase (PG) in texture change and softening processes in the tomato, but Zeneca provided additional support and much of the financial resources necessary to transform that research into a retail product.

Table 1. HP Tomato Timeline.

1974	Don Grierson begins fundamental research on texture changes, ripening and softening processes in fruit
1982/83	Don Grierson (U. Nottingham) & Wolfgang Schuch (Zeneca) begin research on “gene-isolation technology,” on reducing levels of enzyme polygalacturonase.
1985	"Narrow use" in-licensing of kanamycin promoter from Monsanto
January 1989	U.S. Patent 4,801,540 "PG gene and its use in plants"; assigned to Calgene (Filed 2 January 1987)
December 1989	Zeneca and Petoseed begin collaboration on germplasm development
July 1991	U.S. Patent 5,034,323 "Genetic engineering of novel plant phenotypes"; assigned to DNA Plant Technology (Filed: 30 March 1989)
December 1991	U.S. Patent 5,073,676 “Tomato anti-sense pectin esterase”; the first of many patents awarded to Grierson and Schuch, assigned to Imperial Chemical Industries, PLC (Filed: 29 September 1989)
April 1992	U.S. Patent 5,107,065 "Anti-sense regulation of gene expression in plant cells"; assigned to Calgene (Filed: 30 August 30, 1988)
February 1995	UK government approval for food use, on recommendation of Advisory Committee of Novel Foods & Processes
March 1995	USDA approval for growing and processing
April 1995	FDA approval for food use
February 1996	Retail by Safeway & J. Sainsbury under store brand, labelled as GM, side by side with non-GM product
November 1997	Over 1.6 million cans sold in UK
June 1998	U. Nottingham receives first royalty payment from Zeneca
1999	Major UK supermarkets (Safeway, Sainsbury, Asda, Tesco, etc.) announce intentions to remove GM ingredients from their store brands

Table 2. U.S., European and Japanese Patents assigned to Zeneca

U.S. Pat.	U.S. Issue	U.S. Filing	Description
5073676	12/17/91	9/29/89	Tomato anti-sense pectin esterase
5254800	10/19/93	10/19/90	Tomato plants and cells containing pTOM36 antisense constructs
5296376	3/22/94	12/5/90	DNA, constructs, cells and plants derived therefrom
5304478	4/19/94	12/28/92	Modification of carotenoid production in tomatoes using pTOM5
5304490	4/19/94	8/23/91	DNA constructs containing fruit-ripening genes
5365015	11/15/94	3/16/92	Antisense constructs derived from pTOM13 plants and plant cells with reduced ethylene evolution
5387757	2/7/95	4/1/93	Tomatoes with reduced expression of polygalacturonase
5413937	5/9/95	12/7/93	DNA constructs containing segments from tomato polygalacturonase and pectin esterase genes
5442052	8/15/95	7/8/93	Expression of genes in transgenic plants
5447867	9/5/95	2/26/93	Recombinant DNA containing pectin esterase gene segments
5530190	6/25/96	10/12/93	DNA constructs containing the gene for ACC Oxidase, cells and plants derived therefrom
5457281	10/12/95	9/29/89	Dicot plants containing an antisense polygalacturonase gene segment
5569829	10/29/96	6/9/93	Transformed tomato plants
5659121	8/19/97	9/30/94	DNA, DNA constructs, cells and plants derived therefrom
5744364	4/28/98	2/28/95	PTOM36 constructs and tomato cells transformed therewith
5824873	10/20/98	4/10/96	Tomato ripening TOM41 compositions and methods of use
5908973	6/1/99	1/11/96	DNA encoding fruit-ripening-related proteins, DNA constructs, cells and plants derived therefrom
5942657	8/24/99	1/9/95	Co-ordinated inhibition of plant gene expression

EurPat.	EurIssue	EurFiling	Description
EP502995B1	7/31/96	11/26/90	DNA constructs, cells and plants derived therefrom
EP341885B1	8/23/95	5/2/89	Tomatoes
EP271988B1	8/16/95	11/6/87	Anti-sense regulation of plant gene expression
EP270248B1	3/16/94	11/3/87	DNA useful for the transport of foreign proteins to the plant cell wall

JapPat.	JapIssue	JapFiling	Description
JP1989116213	1/1/90	5/11/1989	Production of Fruit, Seed and Tomato Hybrid

Glossary of Biotechnology Terms

Antisense DNA: A method used to eliminate or reduce the expression of a gene in an organism. Antisense DNA binds to and alters a message of messenger RNA (mRNA) which transfers genetic information from DNA to cells. This cancels the genetic message by preventing cells from translating its instructions (e.g., blocks cells from making particular enzymes or proteins).

Gene Suppression: TRANSWITCH®, owned by DNA Plant Technology Corporation, is a "sense" technology that suppre sses the function of genes that may cause an unwanted effect (e.g., premature fruit ripening).

Promoter: Regulatory genes that control the functioning of other genes. More specifically, a DNA sequence promoting transcription of a gene to produce mRNA. The promoter controls where (e.g., plant part) and when (e.g., stage in plant lifetime) the gene is expressed. An example is the *Cauliflower Mosaic Virus 35S Promoter (CaMV 35S).*

Selectable Marker: Genes coding for specific characteristics, that when expressed, allows researchers to identify genetically transformed organisms from untransformed organisms. An example is the incorporation of genes into a plant to produce *kanamycin* (antibiotic) resistance. These kanamycin-resistant genes are linked to the gene that is transformed to express a selected trait in an organism. These plants are then cultured in media containing kanamycin and successfully transformed plants are able to grow.

Polygalacturonase (PG): An enzyme (e.g., present in tomatoes) that breaks down fruit tissue and causes ripening.

Source: This Glossary was constructed using information from Nill, Kimball R., the Food and Agricultural Organization and the Office of Technology Assessment.

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