The Governance of Innovation: vertical integration and collaborative arrangements in the Biotechnology industry

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Abstract

p. 237 This paper analyzes and compares the various governance structures through which new biotechnologies have been developed and commercialized over the past decade and a half. These governance structures include (1) forward vertical integration by new biotechnology firms (NBFs) from R&D into manufacturing and marketing; (2) backward integration by established firms from downstream industries into biotech R&D; and (3) various forms of collaboration between NBFs and established firms involving R&D, technology transfer, production and distribution.

I. Introduction

Technological innovation inherently involves linkages between a broad set of technical and commercial activities. The innovation literature has long recognized that successful innovation requires the coupling of some combination of R&D, product design and testing, process engineering, manufacturing and distribution. Historically, many of the activities required for innovation have been organized within the administrative hierarchies of firms, rather than through contractual mechanisms of markets. However, in many contemporary industries, joint ventures and other forms of inter – firm cooperation are playing an increasingly important role in the development, commercialization and diffusion of technical know – how. Decisions about what types of activities in the innovation chain to internalize and which ones to access through contractual arrangements are now a central element of technology strategy for both the entrepreneurial entrant and the established enterprise.

Collaborative arrangements between entrepreneurial firms and established corporations have become increasingly common over the past decade. Such collaboration raises interesting issues about the relationship between technological change and competition. In the Schumpeterian model of "creative destruction",

technological upheavals are characterized by protracted competition between new entrants and incumbents.

A major stream of research has focused on how technological change affects entry and the success of new entrants relative to their entrenched (and often larger) competitors. The competitive dynamics of an industry undergoing a major technological change will be different if new entrants and incumbents have and exploit mutually beneficial opportunities for collaboration. Rather than the new firms driving out the incumbents (or vice versa), the new and the old may co – exist in symbiotic supplier – buyer relationships. The factors generating and impeding opportunities for collaboration are therefore important for a fuller understanding of the relationships between technological change and the competitive environment.

To illuminate some of these factors, this paper examines the organizational evolution of the biotechnology industry over the past decade and a half.
p. 238 It analyzes the trend toward vertical integration of biotechnology R&D, manufacturing and commercial distribution of commercial products. While collaboration between biotech specialist firms and established corporate enterprise continues to be a very important mode of developing and commercializing biotech, this paper presents evidence that vertical integration has increased.

What is the economic rationale for vertical integration in biotech? It is this question which forms the central focus of this paper.

II. An Overview of the "New" Biotechnologies

Biotechnology can be defined as a body of knowledge and techniques for using live organisms in a particular productive process.

The commercial potential of biotech has been vastly expanded by a set of techniques that allows researchers to manipulate the genetic structures of micro – organisms used in fermentation and other biological production processes. These "genetic engineering" techniques form the core of a group of technologies sometimes reffered to as *third generation* or "new" biotechnologies. Through genetic engineering, researchers can "create" cells capable of producing specific proteins.

Because genetically engineered proteins are generally quite similar in molecular structure to the "natural" versions produced in the body, they have potential use as therapeutic drugs. Genetically engineered cells can also produce proteins for use in biomedical research, diagnostic products, drugs for animals and specialty

chemicals. Genetic engineering can be used to develop new breeds of plants or to create micro – organisms used directly in certain industrial processes, including waste treatment.

p. 239 The rate of introduction of new biotech – based drugs is expected to increase rapidly. In 1988 there were 400 biotech – based drugs in some stage of pre – clinical testing or human clinical trials.

III. The Emergence of Commercial Biotech R&D

Critical scientific foundations for the new biotech were laid by Watson and Crick's 1956 discovery of the double – helix structure of DNA. However, two scientific breakthroughs of the '70s were instrumental in triggering commercial R&D. In 1973, Herbert Boyer and Stanley Cohen discovered a technique for removinh specific genes from one organism and implanting them into the genetic structure of another. This technique, which has since become a basic tool of genetic – engineering, is known as recombinant DNA (r – DNA). The other basic genetic engineering method was invented in 1975 be Caesar Milstein and George Kohler. They fused antibody producing lymphocytes with malignant myeloma cells. This method for creating hybrid cells is known as cell fusion or "hybridoma" technology. It is used to form cells that produce monoclonal antibodies. The Milstein – Kohler technology was published and never patented. The Boyer – Cohen technique was patented in 1980, but Stanford University, the administrator of the patent, pursued a liberal licensing policy. Together these basic scientific advances provided a new set of tools in the search for commercially valuable chemicals. In this sense, biotech represents what Nelson and Winter call a "new technological regime" or paradigm.

Because the basic technologies underlying the new regime were largely public and widely diffused, new firms, many of which were founded by or in conjunction with university scientists, swarmed into the field of biotech R&D. In the earliest years of the industry (1976 – 1981), these new firms were the dominant source of biotech R&D.

Much of established firms' investments in biotech R&D were channeled to biotech specialist firms through R&D contracts, equity investments and joint ventures. In exchange for their support, they received rights to specific technologies or products that emerged from an NBF's R&D programs. Virtually every NBF, including those

that had attracted major venture capital investments, formed relationships with one or more larger corporate enterprises.

The role of established enterprises as investors in NBF's R&D is suggested by the fact that, between 1976 and 1985, they provided 56% of the total funds invested in NBFs.

p. 240 In the early phase of the industry, even two of the most established NBFs (Genetech and Cetus) depended largely on outside sponsors to support their internal R&D.

The biotech industry, in its early years, took on the characteristics of a specialized R&D supply sector. It could be argued that the biotech industry emerged as a market for R&D, with NBFs on the supply side and established chemical and pharmaceutical enterprises on the demand side.

The formation of a specialized R&D sector is somewhat unique within the context of other major industrial transformations. The semiconductor industry, for example, integrated R&D and production from its beginning.

Why did a market for biotech R&D form with NBFs on the supply side and established enterprises on the demand side?

For NBFs, there were two major reasons for supplying established corporate partners biotech know – how and products: (1) access to capital and (2) access to downstream capabilities in manufacturing, clinical testing, regulatory processes and distribution.

No NBF was able to raise enough capital from venture capitalists, private placements, debt, R&D limited partnerships or public equity markets.

Access to downstream capabilities, in most situations, was as much a rationale for collaboration as was access to capital.

For established firms, buying biotech R&D from the outside and focusing on commercialization had advantages. (1) These firms had in place valuable assets required for commercializing biotech. Control over these assets could be used to acquire access to the technology on attractie terms. (2) In addition, collaboration allowed the established firms to tap the specialized expertise of the NBFs. (3) Technology uncertainty also played a critical role in established firms' decision to contract out for biotech R&D.

p. 241 Scope economies in basic biotech R&D were critical in making the market for R&D an efficient way for both NBFs and established firms to share risks. Because

different commercial products were based on similar basic technologies, the cost (and risk) of developing the basic technologies could be shared by clients (including the NBF's own investors) with different commercial interests.

A combination of risk sharing, technological competence and economies of specialization helps to explain why established firms procured biotech from NBFs. Thus, partnerships between NBFs and established companies represented a division of labor whereby each could realized mutual gains through functional specialization.

IV. Vertical Integration

The vertical division of labor between NBFs and established firms that initially characterized the industry has not been stable. While NBFs and established enterprises continue to engage in collaborative arrangements, there has been a trend toward forward integration by NBFs into manufacturing and by established firms backward into biotech R&D.

IV.i Forward integration by NBFs

While biotech companies continue to complement their internal manufacturing capabilities with outside sources of manufacturing, data suggest that many biotech companies are not pursuing an "R&D boutique" strategy, but rather are developing into manufacturing enterprises.

Two indicators of vertical integration by NBFs are the ratio of R&D revenues to product sales and the ratio of R&D expenditures to R&D revenues. R&D revenues are typically generated by contractual agreements with corporate partners. A decline in R&D revenues relative to either product sales or R&D expenditures would indicate that biotech firms are holding onto a greater share of the downstream manufacturing and marketing activities.

p. 242 The decline in the ratio of R&D expenditures to R&D revenues suggests that biotech companies became less dependent on corporate partners to support their R&D programs; along with this greater independence comes the ability to hold onto a greater share of the manufacturing and marketing rights to products.

A possible alternative to either manufacturing in – house or selling manufacturing rights to a corporate partner is to use a contract manufacturer. However, the contract manufacturing segment of biotech is quite small and has not

been growing. There are only a few contract manufacturers, most of which are quite small.

By comparing the incidence of NBF development and marketing across products at different stages in the FDA (ο δικός μας ΕΟΦ) approval process, we can see that the newer products are no more likely to be marketed by NBFs than older products.

p. 243 The difference in extent of vertical integration into manufacturing versus marketing is also suggested by the incidence of different types of collaborative arrangements. It was found that marketing arrangements were the most common type of agreement being negotiated by biotech companies in 1989, while manufacturing agreements were least common[1].

IV.ii Integration by established enterprises into biotechnology R&D

There is also evidence that established enterprises from the pharmaceutical and chemical industries are vertically integrating backward into biotech R&D. Pisano[2] examined the biotech R&D sourcing decisions of 30 of the world's largest pharmaceutical companies. The latter were conducting R&D in – house in 43 of the 93 product projects in the sample. The analysis suggests that, at least in the pharmaceutical applications segment, established enterprises were conducting about half of their R&D projects in – house in 1986.

p. 244 The data presented above suggest that, in general, NBFs are less willing to play the role of "R&D boutiques" which service the pharmaceutical, chemical and agricultural sectors; likewise, established firms are less willing to limit themselves to the distribution of biotech products.

This trend warrants an explanation. It cannot be explained simply in terms of firms trying to increase their share of value – added. For example, if biotech firms are less capable of commercializing the fruits of their research than established firms, then verical integration by NBFs might actually damage performance over the long run.

Is there an economic rationale for vertical integration in biotech? Below, the author argues that there are economic benefits to vertical integration in biotech. By selectively vertically integrating, both NBFs and established enterprises are better

[1] The firms are vertically integrating into manufacturing but not into marketing!
[2] Pisano, G., 1990

able to avoid transactional problems which can be quite costly to the firm. In so doing, they can increase the appropriable rents from their core competencies.

V. NBF Integration into Manufacturing

For NBFs, whose core competence lies in R&D, in – house manufacturing is a way of avoiding transaction cost inherent in outsourcing manufacturing. In biotech, transactions cost in the market for manufacturing arise from: (1) the complexity of process development and scale – up; (2) the problems of protecting intellectual property rights; and (3) regulations which make it costly to switch manufacturers after conducting Stage III clinical trials (applicable only to the pharmaceutical segment).

V.i Process development and scale – up

Due to the novelty and complexitu of bioprocessing genetically engineered proteins, process development and scale – up are still somewhat of an art. While heuristics are evolving with experience, trial – and – error and learning – by – doing are inherent in these activities. In the absence of well – defined and well – understood sclae – up recipes, ensuring product integrity requires extensive interaction between the scientists.

Vertical integration of R&D and manufacturing may facilitate the requisite level of communication and coordination. Vertical integration allows firm – specific experience with scale – up to be accumulated over repeated projects.

V.ii Protection of proprietary know – how

p. 245 Process development and scale – up require intensive information exchange between product developers and process engineers. Much of the requisite information about the product and the process is highly proprietary, but cannot be effectively protected by patents.

Restricting the flow of information between the R&D and manufacturing organizations only adds to difficulties of scale – up discussed above. Vertical integration between R&D and manufacturing removes boundaries which can impede the flow of sensitive information.

By developing specialized capabilities in manufacturing, the NBF also raises the entry barriers in its product market. This is particularly important in biotech, because unlike the case of classic chemical products, the scope and efficacy patents

are somewhat uncertain. Thus, an innovator in biotech cannot be sure that its patents will imitators out of its market. Due to the difficulty of developing and acquiring bioengineering knowledge, manufacturing has become a key co – specialized asset in the biotech innovation chain.

V.iii Switching cost

In the U.S., if a firm were to change its source of manufacturing for a particular therapeutiv product, it would be obliged to repeat costly and time – consuming Stage III clinical trials. As a result of these regulations, a drug developer is locked – in to whatever manufacturer it used to produce materials for Stage III clinical trials.

The cost of switching manufacturers represent quasi – rents which can be extracted by the manufacturing partner during renegotiation. By vertically integrating into manufacturing, the drug developer avoids the hazards of *ex – post* opportunistic recontracting.

VI. Rationale for Vertical Integration into Distribution

The transaction cost rationale for vertical integration into distribution should vary by the product market. The exchange hazards will be lower for products which can be distributed be a potentially wide range of firms using existing channels. They are lower for the distribution partner because it does not have to invest in new distribution capabilities which cannot be redeployed in the event of contract termination.

They are also lower for the technology developer because it can more easily find an alternative partner in the event of contract termination. Under these conditions, the NBF does not need to control distribution through ownership of the distribution channel.

p. 246 In some markets, however, new channels must be established to distribute a specific product. Distribution of these products does not require a large sales force, but it does require the sales force to have very specialized knowledge of the product and close contacts with the leading regional specialists.

Contracting with a partner to distribute such specialized products involves transaction costs for both the distributor and the product supplier.

VII. Integration by Established Firms into Biotechnology R&D

R&D is an inherently uncertain activity regardless of the institutional arrangements under which it is performed. Howeverm when a firm procures technology via R&D contracts or licensing arrangements for R&D, it bears additional uncertainties related to the execution of the contractual agreement. Typically, at the time the collaborative agreement is signed, sufficient uncertainty will surround the project such that the following terms of trade cannot be specified with perfect clarity.

1. *Scope*: What product or process technologies are being developed and for what applications are they being commercialized?
2. *Form of "deliverables"*: In what form will the relevant technologies be delivered?
3. *Performance*: By what criteria will the contractual performance of each partner be evaluated?
4. *Timing*: When will specific "milestones" be met?
5. *Distribution of property rights*: Who owns the technology or technologies in question?

In most instances, collaborators leave open certain issues for negotiation or re – negotiation in the future. However, agreements to "agree in the future" can result in costly disputes due either to opportunism or to honest differences of opinion.

p. 247 As firms have gone further along the product development trajectory, much more of the know – how generated is idiosyncratic to the product and firm – specific. Such idiosyncratic knowledge can be difficult to transfer to a new R&D supplier (including an in – house R&D group). As a result, the sponsor cannot easily switch sources of R&D if it is unhappy with the contractor's performance or if the contractor cannot finish the project.

When switching R&D partners is costly, the value of the sponsor's R&D investment depends critically on the successful completion of the project by the initial R&D contractor. Having an in – house group working jointly with the R&D partner makes it easier to continue the project in – house if the agreement with the partner prematurely terminates.

R&D contractors will develop first – mover advantages in the future market for R&D services. Firms that procure R&D from a particular contractor today may be forced to procure additional R&D services from this same source in the future.

VIII. Conclusion

Despite the trend toward vertical integration, it is unlikely that vertical integration will completely replace all alternative organizational forms very soon. First, there are limits on the rate at which NBFs and established enterprises can expand their boundaries. For NBFs, capital constraints limit the rate of forward integration. For established firms, in – house experience with biotech will take time to accumulate. Rapid internalization of biotech R&D through acquisition of NBFs is unlikely to become a model for organizational change.

p. 248 Acquiring NBFs, or any entrepreneurial firm, is a dangerous strategy because it is difficult to guarantee that the key assets of the company, the people, will stay. Acquisition of NBFs may come, but only after established firms have accumulated significant in – house R&D experience.

A second reason why collaborative or market forms of organization will survive in biotech is that not all segments will be characterized by high transaction costs. Vertical integration is more likely to predominate where the innovation chain is characterized by uncertain property rights, transaction – specific assets and complex technology transfer.

Given that the extent of transaction cost will differ across application of biotech, firms are adopting hybrid organizational structures to source or commercialize technology. For example, a single NBF may use vertical integration, joint ventures and licensing to commercialize different technologies in different application segments.

Knowing when to integrate vertically, when to collaborate and when to license is likely to be a critical managerial skill required for both new and established firms to succeed in biotech.

Σημείωση: Στη βιοτεχνολογία, η τάση για καθετοποίηση είναι φυσιολογική, ξαθώς πρόκειται για νέα τεχνολογία. Έτσι έγινε αρχικά, π.χ., και με την αυτοκινητοβιομηχανία. Όταν έρθει η ωριμότητα και η σταθεροποίηση, ωστόσο, είναι πιθανή η επιστροφή στο μοντέλο των συνεργασιών, όπως και στην αυτοκινητοβιομηχανία.

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