

Prospects for Marine Biotechnology in Maine

Prepared for the
**Maine Department of Marine Resources
Maine State Planning Office
Maine Science & Technology Foundation**

**Charles S. Colgan PhD
Colin Baker**

**Edmund S. Muskie School of Public Service
University of Southern Maine**

November 2000

EXECUTIVE SUMMARY

Maine has recently focused a major effort at fostering economic development based on expanded research and development. The expectation is that Maine can develop the kinds of highly innovative, fast-growth firms that are typical of such regions the Research Triangle of North Carolina. Such regions have high levels of research and clusters of firms that interact with one another to achieve strong and sustained economic growth.

One of the elements of this strategy is the field of marine biotechnology, which involves a number of technologies that transform products from the ocean into new foods, drugs, chemicals, and other products. This report provides a detailed discussion of the conceptual basis for the growth of marine biotechnology and assesses the current state of marine biotechnology in Maine and considers the potential for this industry to grow to the kind of self-sustaining cluster of economic activity that characterizes many economically successful regions. The study was conducted by undertaking extensive interviews with private companies inside and outside of Maine and with a number of research institutions that may support marine biotechnology. The findings from these interviews and recommendations are summarized below:

Findings

- Marine biotechnology is inseparable from biotechnology as a whole. Development of the overall biotechnology field in Maine is the key to development of marine biotechnology.
- Biotechnology is a complex field with many different products and processes. It is comprised of industries with very different product development paths and market potentials. Each of these product areas must be understood and addressed separately.
- No single factor or group of factors explains Maine's current marine biotechnology companies. Maine is currently the home of a number of small companies that are located here for a wide variety of reasons.
- Maine currently supplies some ingredients for the success of firms developing marine biotechnology, but important ingredients are lacking. Capital and physical facilities do not appear to be a major problem, but finding a trained "mid-skill" work force and support from Maine marine research institutions are cited as issues.
- Competition to create marine biotechnology industries elsewhere are somewhat ahead of Maine, but have not yet achieved a level of success that would either limit Maine's future or clearly show the possibilities of success. The field of marine biotechnology is still wide open, and Maine has real opportunities that can be seized.

- Marine biotechnology in Maine today is primarily concentrated in the first of four stages of transition from research and development to cluster, with some transitions to the second. Firms are transforming research into products, and are creating new firms built around those products. But there is no “marine biotechnology industry” as such, and the transition to industry or cluster is still years away. It is thus far too early to tell at what point a critical mass of firms in marine biotechnology will be reached which can be a self-sustaining cluster of economic activity.
- Marine biotechnology is not likely to replace traditional fisheries as a driver of Maine's coastal economy in the foreseeable future. Its current size and long development horizon are two reasons. Another is that even if, for example, marine compounds with enormous market potential in the pharmaceutical industry are found, industry will likely try to synthesize these compounds in the laboratory rather than harvesting from the environment.
- The small size and long development road for marine biotechnology should not obscure the fact that Maine has a larger concentration of activity in this field than many other states and the field is still in its infancy with enormous. Maine has both strengths and weaknesses to work with as the industry develops, and there does not appear to be any insurmountable barrier to marine biotechnology and biotechnology as a whole becoming an ever-more important part of the Maine economy in the future.

Based on this assessment, two kinds of actions are required over the next decade. The first is to recognize that forces outside of public policy will play the major role in shaping the sector, and the public sector must closely monitor changes in marine biotechnology firms in Maine. At the same time, there clearly are actions that the public sector can take to assist the industry in its growth. These are summarized as:

Recommendations for Monitoring the Growth of Biotechnology in Maine

- *Expansion of existing companies in Maine and elsewhere.* Maine needs additional biotechnology companies, and existing companies must grow to larger scale production. Companies may not grow entirely within Maine; some will seek partnerships and changing ownership structures with companies outside of Maine. In the early years of this new industry, such growth should be seen as a sign of health and success even if it takes place partly outside the state.
- *Development of new entrepreneurial companies.* The number of new entrepreneurial companies in marine biotechnology and biotechnology as a whole should grow significantly as R&D expands. A doubling or tripling of the current group of about 20 marine biotechnology firms over the next ten years should be achievable.
- *Research activity.* The volume and sources of research activity must continue to expand at recent growth rates or even faster. Particularly critical will be expansion of

funding of research in the biomedical area, including expanding funding from the National Institutes of Health.

Recommendations for Supporting Growth in Marine Biotechnology

- *Enhance R&D in Maine.* Maine has already committed significant new funds to the University of Maine System and to other research organizations, and there are plans for further expansion. These commitments are critical, and must be maintained over the long term. The largest growth potential in biotechnology and marine biotechnology lies in the biomedical field, and efforts should be particularly expanded to create both the research and education infrastructure in this field if biotechnology is to succeed.
- *R&D Funding.* Maine has greatly expanded its direct funding of research and development through creation of the Maine Technology Institute. MTI, the Small Business Administration's Small Business Innovation Research (SBIR) program and categorical grant funding from the federal government are the critical ingredients sustaining much of the current marine biotechnology efforts in Maine. Growth in all of these areas is important, particularly the receipt of SBIR funds and categorical grant funding from federal agencies.
- *Organizing Biotech and Marine Biotech.* Interaction among the firms, research institutions, customers, and government organizations is the key ingredient of any cluster. While marine biotechnology is still highly fragmented, it can begin to realize some of the advantages of location in Maine through regular opportunities for interaction. Regular forums, perhaps jointly sponsored by industry and government, could aid the development of interactions, much as the Fisherman's Forum has been an important annual event for the fishing industry over the past two decades.
- *Setting Regulatory Policies.* Some aspects of marine biotechnology activities will inevitably and appropriately come within the purview of government regulation. An example is the development of safeguards for the raising of transgenic species, such as salmon. Developing clear and reasonable rules as early as possible to deal with these issues can encourage firms to locate and expand in Maine.

Table of Contents

<u>INTRODUCTION</u>	6
<u>THE PATH FROM R&D TO CLUSTER</u>	9
<u>ASSESSING MARINE BIOTECHNOLOGY</u>	17
<u>COMPANIES USING MARINE BIOTECHNOLOGY</u>	18
<u>FINDINGS</u>	21
<u>1. DEMAND CONDITIONS: THE BIOTECHNOLOGY COMMERCIAL ENVIRONMENT</u>	21
<u>2. FIRM STRATEGY AND RIVALRY</u>	29
<u>3. FACTOR CONDITIONS</u>	31
<u>4. RELATED AND SUPPORTING INDUSTRIES</u>	34
<u>5. CLUSTER DEVELOPMENT IN MARINE BIOTECHNOLOGY AND BIOTECHNOLOGY</u> <u>OUTSIDE MAINE</u>	38
<u>CONCLUSIONS</u>	43
<u>KEY FINDINGS</u>	43
<u>SUPPORTING GROWTH IN MARINE BIOTECHNOLOGY</u>	45
<u>MONITORING THE GROWTH OF BIOTECHNOLOGY IN MAINE</u>	49
<u>REFERENCES</u>	50
<u>AUTHORS</u>	53

INTRODUCTION

Over the past decade, the State of Maine has significantly increased its investment in research and development in the expectation that doing so would enhance the state's economy. Maine's approach to economic development based on enhanced research and development was formed after observing the success of such regions as the Route 128 Corridor around Boston, Silicon Valley in California, and the Research Triangle region in North Carolina. Each of these regions has been characterized by significant growth in high-wage jobs in technologically advanced industries and sustained economic success over long periods. Each was also anchored by universities in the region, which provided the research on which technological innovation was based and the educated workforce on which the growing industries of the region depend.

Maine's investments in research and development were directed at improvements in the University of Maine System, which has historically lagged well behind other public university systems in attracting research funding. Maine's funds have also been directed to assisting firms in a number of industries that have been identified as potential growth areas where Maine has potential competitive advantage.

In formulating an economic development strategy based on technological innovation, Maine has also explicitly adopted the concept of "clusters" as an objective. The idea of cluster-based industrial development derives from a long history of economic research on the factors that create successful regional economies. Clusters are groups of related industries that are located in the same region. (Porter, 2000) The industries are related by both vertical (supplier-customer) and horizontal (competitive) relationships among one another, and their co-location within a region gives each firm in the industry certain advantages that are not available in isolation. Advantages associated with a cluster include a critical mass of services, expertise and personnel that allows the component companies to be more competitive.

Among the industries on which Maine has chosen to focus attention are biotechnology, aquaculture and marine technology. Marine biotechnology serves both the biotechnology and aquaculture industries, and is considered to hold great promise as a source of innovations for a number of different commercial applications. Maine is seen as having a potential advantage in this area owing to its long coastline, a cold water-high tide environment that is unique in the eastern U.S., and its history of industries connected with the sea.

Many of Maine's traditional ocean industries have been under extreme pressure recently. This is particularly the case with the groundfish industry, where severe over-fishing and subsequent dramatic reductions in allowable catch under government management have reduced both output and employment. Loss of fishing jobs has increased dependence on lobster fishing for employment, making this industry more vulnerable to a downturn. There are also severe potential problems in the salmon aquaculture industry, the only marine industry that has seen real growth over the past

decade; potential conflicts with management of the wild salmon stocks may severely limit this industry's future. The strong dependence of many coastal communities on a relatively narrow set of fishing-related activities only reinforces the need for assessing potential alternatives.

Attention to marine biotechnology thus comes at a time of great hope that Maine may dramatically increase its technologically based industries and great fear about its traditional marine industries. The ability of marine biotechnology to play a role in a new economic foundation for Maine is something that will require careful monitoring to assure the best chances for success. The Department of Marine Resources, in cooperation with the State Planning Office and the Maine Science and Technology Foundation commissioned this study to explore the implications of cluster-based economic development in Maine and specifically what this idea means for assisting the growth of the emerging field of marine biotechnology in the state. Ideas for how marine biotechnology might become an important sector for Maine, especially in light of the troubles faced by traditional ocean sectors such as groundfishing, were also sought.

In response, this study lays out a framework to help understand the types of changes that will be needed for marine biotechnology (as well as other areas where the State has made significant investments) to form a new economic foundation for Maine. It also provides a "baseline" assessment of the marine biotechnology industry in 2000 based on an extensive set of interviews with people in marine biotechnology and related industries, and makes recommendations for enhancing the growth of this industry in Maine

The term "marine biotechnology" denotes a potentially wide variety of activities, which may be divided into the following broad categories (Colwell, 1984):

Genetically engineered marine organisms

Aquaculture is already a well-established industry in Maine, including Atlantic salmon, oysters and mussels. Genetic engineering is considered to have significant potential to enhance aquaculture through the use of recombinant DNA techniques that would yield faster-growing and/or disease-resistant varieties of fish or mollusks.

Manufacture of pharmaceuticals and nutraceuticals

Chemicals produced by or found in marine organisms have been shown to have a wide variety of applications as pharmaceuticals for humans and other animals. Uses have included antibacterial, and antiviral and anti-tumor agents. Particular attention has been paid to a variety of toxins formed by marine organisms. Nutraceuticals constitute a variety of substances used in the food supplement and "natural health" markets.

Industrial Chemicals

Marine organisms are the source of a variety of chemicals used in industrial processes. The best-known example in Maine is carageenan, extracted from seaweed and used as a thickener in ice cream and other foods and as a laboratory culture medium. A variety of other chemicals used both in food processing and other manufacturing processes have also been developed from marine resources.

Biofouling

Fouling of man-made structures, such as boats and piers, is a constant threat to a number of man's uses of the ocean. While inorganic chemicals (such as copper) have traditionally been used to limit biofouling, a number of marine organisms, including bacteria, are being studied for use in anti-fouling applications. These studies have also examined the biochemistry of adhesion of marine organisms, which may improve aquaculture in other applications.

Marine Pollution Control

The use of marine organisms to degrade pollutants introduced to the marine environment is considered feasible in numerous applications. Bacterial treatment of human waste is already common, and other wastes such as halogenated compounds have been shown to be susceptible to degradation by microorganisms. There has also been substantial research in using bacteria to degrade spilled oil.

The Path From R&D to Cluster

Maine has adopted a number of policies designed to enhance research and development in the state in an effort to achieve the kind of sustainable economic success that has been observed in regions such as eastern Massachusetts and Silicon Valley. The process of moving from research to an economic cluster of the type that Porter and others have defined is not well understood, but it can be broken down into four basic steps:

1. Research $\dot{\rightarrow}$ Products
2. Products $\dot{\rightarrow}$ Firms
3. Firms $\dot{\rightarrow}$ Industries
4. Industries $\dot{\rightarrow}$ Clusters

The elements of each of these steps are somewhat understood and so provide a kind of road map of the path that leads from research and development to clusters.

Stage 1 is referred to as the use of “science and technology” or the “research and development process”. Stage 2 is the “entrepreneurial” function. Stages 3 and 4 comprise “economic development”. Stage 3 may be thought of as a form of “traditional” economic development, while stage 4 recognizes that successful industries do not function in isolation, but depend on other elements in the regional economy.

1. Research and Development: From Research to Products

The process of transforming research into products is fairly well understood. Research may be roughly divided into basic and applied. Basic research investigates the fundamental principles of natural systems without any particular application in mind. Applied research refines the knowledge developed by basic research with specific uses of the knowledge in mind. Development transforms applied research into products that are ready for the marketplace. Development itself may consist of several different phases, including prototype development, product testing, testing for compliance with applicable government regulations, and preliminary market research.

From an economic development perspective, a major issue to be addressed is what organizations undertake the various stages of the process. Since each stage from basic research to preliminary market testing requires a different set of skills, it is often difficult for very small organizations to undertake all stages. Larger organizations will have specific groups assigned to specialize in each stage of the R&D process. The specialized nature of each step may thus constitute a barrier for small organizations.

2. The Entrepreneur: From Product to Firm

The transformation of ideas for a product into an actual product available in the marketplace is the fundamental function of the entrepreneur. The entrepreneur and the entrepreneurial function have been much analyzed and celebrated in economic development, particularly since the emergence in the late 1970s of a much more intense focus on small businesses as a prime mover in economic growth. Programs to assist entrepreneurs in commercializing their ideas have been a mainstay of economic development since that era, and a number of federal and state programs exist in Maine to assist small businesses with everything from writing a business plan to financing.

The entrepreneur's key role in the economy has been a central focus of much research. A number of authors, including Joseph Schumpeter who developed much of the modern concept of the entrepreneur, have defined the role of the entrepreneur as the person who:

- perceives a need
- undertakes (the literal definition of the entrepreneur) to fill that need
- deals with the substantial uncertainties surrounding any new venture.

The critical role of the entrepreneur is well understood, but what makes an entrepreneur actually decide to start a business is not. This is an inherently risky decision, and there is little agreement on the precise characteristics of individuals, or their environment, which leads some people to become entrepreneurs and others not. Yet this is obviously a critical question in the context of an R&D-led development strategy, for such a strategy relies on someone who will take the initiative to transform scientific research into commercial products.

Searching for explanations of entrepreneurship in the economy has focused on a number of factors. Early studies focused on personal traits such as alertness, aggressiveness, a high sense of personal control, low risk aversion, and a need for achievement. But these traits were also found in almost all business managers to one degree or another, and so the unique characteristics that lead to entrepreneurship had to include something besides personality. These additional characteristics include (Mokry, 1988):

Role Models Entrepreneurs have other people who have been successful entrepreneurs to look to. Often, these are family members; there is a high correlation between parents who have started a business and children who start a business. There are also cultures in which entrepreneurship is a valued trait and which thus produce a large number of role models.

Precipitating Events Often, the entrepreneurial function is undertaken following some specific event. In R&D-led growth models, such events would clearly include developments in either basic or applied levels of research. But other kinds of events can also be important. These could include changes in a person's

life circumstances, or in the organization in which he or she works. Some of these may be negative “pushes” such as a divorce or a layoff. Others may be positive “pulls” such as getting a contract to pursue a major line of R&D.

Supportive Environment To become entrepreneurs, people must perceive both the *desirability* and the *feasibility* of doing so. Desirability is detected from a number of sources (including the role models noted above). Feasibility must be found in the availability of financing and time and also perhaps additional labor or physical space. Many of the programs, such as incubator facilities, are directed at increasing the feasibility of entrepreneurship. Education of the entrepreneur in the many requirements for successful commercialization is also important to increasing feasibility. Other key characteristics of the supportive environment may be the features of a “cluster” which are discussed below.

Organizational Design and Management Sooner or later, if they are to be successful from an economic development perspective, entrepreneurs must form or function as part of an organization. The “backyard inventor” is certainly a part of entrepreneurship. David Hewlett and David Packard may have invented their first oscilloscope in a garage, but Hewlett-Packard did not become one of the world’s leading electronics companies by staying in the garage. With the transition to organization comes the transition from researcher to manager.

Entrepreneurship, whether R&D-based or not, must thus deal with a variety of issues, including characteristics of the individuals, of their surrounding society, of events, of the environment, and of the organizations within which they currently or come to function.

3. From Firm to Industry

A key change, from an economic development perspective, is when a collection of firms becomes an industry. Industries are typically defined by their products; an “industry” consists of many firms that produce essentially similar products. Industries are not defined by their inputs, yet the term “marine biotechnology” actually describes more of a production process with multiple possible products as the outcome. The outputs of marine biotechnology will appear in many different industries, including food processing, chemicals, and pharmaceuticals. Most of the products will be sold as intermediate inputs to other producers, though some (such as salmon or mussels) might be sold more or less directly to consumers.

An important element in marine biotechnology’s ultimate economic contribution will be how it affects existing or new industries in Maine. Maine has a well-developed food industry, which includes commercial seafood in both fresh and processed form, as well as a variety of processed and fresh agricultural products. Maine has a small chemicals industry, primarily involved in producing specialty chemicals for the pulp and paper industry or for other industrial processes. There is little pharmaceutical manufacturing in Maine. Marine biotechnology in the food industry could strengthen

many other firms in Maine. It could also play an important role in the chemical and pharmaceutical industries, but the effects on these industries may be more limited from a purely Maine perspective, at least in the near term. A key to the long term economic effect of marine biotechnology, therefore, will be whether it is able to expand beyond the food industry to provide a foundation for expansion and diversification in the chemical and pharmaceutical industries.

4. From Industry to Cluster

The concept of regional industrial clusters has emerged over the past decade as an answer to an important question about regional economies: Why do some industries seem to thrive in certain regions and not in others? Why do some regions do particularly well despite changes in the economy? The answer must go beyond simple location factors such as forests or a coastline, though the location of such natural resources will always be important. But other factors must be at work in developing such regional economies as those of eastern Massachusetts. The area inside Route 495 was a very weak economy in the years immediately after World War II, as the textile and clothing industries that had dominated the region moved to the South. But since the 1960's, eastern Massachusetts has seen several successive waves of industrial growth, each based in new technologies, to the point where it is now one of the strongest economies in the U.S.

Understanding the factors that make regions like eastern Massachusetts able to generate and sustain successive waves of economic development means understanding the concept of industrial clusters. Clusters are groups of industries located in the same region and which, by virtue of their interaction with one another, increase the capacity of firms to successfully compete in a global economy. Clusters are also centers of high degrees of innovation, since the firms in the cluster compete with one another to constantly improve their products and services.

The concept of clusters provides plausible answers to the questions of why some industries and regions seem to thrive together (Porter, 1998). The combination of these factors can have a powerful effect on firm and industry productivity, and thus on economic growth. A great deal of analysis of clusters has been done recently designed to identify what clusters exist in a region and what drives those clusters (Hill and Brennan, 1999; Feser, 1999). These studies have looked at the existing clusters rather than clusters that are just in process of forming. It is possible to identify the way in which a cluster functions, as Porter has done, and measure whether those functions are present in a given region. Porter's characteristics (the "diamond") include:

1. **Related and supporting industries**, which include suppliers and customers of the company, as well as competitors. These industries may share the benefits of location in the cluster, including access to a larger and better trained labor pool, enhanced transportation or other cluster assets.
2. **Factor conditions**, which includes all the characteristics of an area that affect the costs and timeliness of production, ranging from labor costs and availability to costs

of capital, raw materials and other requirements including taxes, training, research and development, and infrastructure.

3. **Local demand conditions.** Demanding local customers better prepare a company to compete in larger markets. According to this element, companies that can meet the high standards of local customers will be better able to compete elsewhere.
4. **Firm strategy and rivalry.** This includes the relationships that business have with each other, including rivalry and intensified competition, as well as opportunities to cooperate or collaborate on projects of mutual interest.

The challenge for Maine's R&D-led cluster strategy is to identify potential clusters and to support their development. Yet these potential clusters may not be easily recognized or clearly defined. There is an emerging body of research which seeks to identify the characteristics of regions where there are continuing sources of innovation. These have been called "learning regions" (de la Mothe and Pacquet, 1998). Learning regions are ones where the fundamental source of competitive advantage is continuous creation and improvement of knowledge, rather than on natural resources or physical labor.

Such regions have both knowledge-creating institutions and manufacturing industries. They also have support services such as adequate transportation and communications infrastructure, as well as the availability of appropriate financial resources. Most importantly, they are ones with abundant and skilled human resources from which firms may easily draw the skilled "knowledge workers" they need. (Florida, 1998) The importance of a large and highly flexible workforce is seen as one of the keys to understanding the success of Silicon Valley. (Saxenian, 1994)

Another strand of research concerning innovation looks at the flows of information upon which innovation can be based and the sources of innovative ideas from which new products and services can grow. The factors are described by Padmore and Gibson (1998). Information about new ideas can come from:

- Products
- Services
- Intellectual Property
- Human Capital

and each of these elements can be either developed in-house or acquired in the market. The spur to innovation can come from in-house developments, suppliers, peers, customers, or the public sector; all are elements of the surrounding environment of the innovative firm and implicitly characteristics of the regional cluster.

The idea of clusters is not as recent as might be suspected. Over a century ago, Alfred Marshall developed his idea of "industrial districts", In these districts, firms created external economies of scale rather than internal ones. Economies of scale exist

when a combination of specialization in the organization and size of output allow the average and marginal costs of production to fall over a wide range of output. Put another way, the larger the size of the production process, the more increases in output will actually cause production costs to fall rather than rise, at least up to the point at which the law of diminishing marginal returns takes over and causes first marginal and then average production costs to rise. Lower production costs mean that a product can be sold at a lower price and still make money, giving it an advantage in any competitive market.

There are two ways in which economies of scale can be achieved. The most common is *within* the firm. Firms that can bring together as much of the specialized inputs (land, labor, and capital) as possible and use technology (capital) to increase their output often enjoy economies of scale and the resulting lower costs, prices, and competitive advantage. However, it is also possible for the sources of efficiency to be *outside* the firm. When many smaller firms located near one another to share specialized inputs, such as labor, and because of their combined size within the same region, they also can achieve economies of scale. The idea that many small firms (or even many large firms) can increase the scale of their production, and thus lower costs and prices in a competitive marketplace, is a key underlying factor in the success of clusters.

Marshall's notion of industrial districts and external economies of scale assumes that mere co-location is sufficient for success. Porter's model elaborates on this concept by pointing out how the relationships among firms in a region build the conditions for external scale economies. These relationships are both competitive and cooperative, and are both upstream (supplier) and downstream (customer). In addition, other environmental conditions (factor conditions) such as the presence of research and education facilities that provide both knowledge and labor inputs are also important. The key is understanding who the actors are and how they interact.

These various elements come together to suggest the key ingredients in the transformation from R&D to cluster is to take place. These may be summarized as:

- A favorable array of conditions outlined by Porter in his "diamond"
- The institutional resources to support innovation
- The interaction among the various organizations in the region that makes the whole greater than the sum of the parts.
- The achievement of economies of scale both within organizations and within the region.

Identification of the ingredients of the process is a first but far from sufficient step. After all, ingredients are listed on food labels but the ingredients alone tell us nothing about how to mix them to get the results we want. Nor does the existing literature tell us much about the boundaries within which clusters develop. Porter's regions encompass everything from relatively small areas of eastern England (in the case of Grand Prix auto racers) to the entire country of Japan (in the case of fax machines). His businesses also vary, from household appliances in Germany to telephone services in

Omaha; the former is clearly an industry, while the latter is merely a technological input to many different industries.

Perhaps the most important issue from a policy perspective is the question of when each of these transitions takes place. Unfortunately, this is perhaps the least researched and thus the least well understood feature on the road from R&D to cluster. A conceptual model could analogize the interaction of the various actors (researchers, universities, entrepreneurs, firms, suppliers, etc.) in a given region to the interactions among atoms that form the basis for nuclear energy. At the earliest stages of the process of R&D evolution towards clusters, a number of individual actors interact with one another in much the same way that atoms of uranium do. There are a number of interactions among atoms which give off electrons (ideas, products, etc.) but the interactions are too few to be more than random. As more mass of uranium is brought together under the right conditions, interactions begin to occur more and more frequently, with the result that more and more energy (radioactivity in the physical case; products, firms, and industries in the economic case) is given off. Once a critical mass is reached, the process of fission becomes self-sustaining, at least until all the fissionable atoms are converted to another matter state, at which point more fuel must be added. In the economic world, the critical mass of firms, resources, and interactions creates a Silicon Valley or Research Triangle.

It is always dangerous to use physics as an analogy for the economy, since the economic world never obeys the same degree of precision as the physical world. But this analogy points to some useful questions that must be answered to fully understand the evolution from research to cluster. First, as with nuclear fission, it is necessary to identify the combination of ingredients in the right order and in the right amounts. As with uranium, simply throwing it together does not work. More uranium or more R&D plus more entrepreneurial support may yield the desired result, but it will be more through random chance than purposeful action. Second, it is relatively easy once you know the physics to calculate the exact size of the critical mass that will produce a sustaining fission reaction. However, it is not at all possible at this stage, even with some understanding of the theory, to calculate the “critical mass” of the cluster.

The absence of such critical information should not be considered fatal, however. After all, it took more than three decades of physics research between the time that the theory of fission was first worked out and Enrico Fermi successfully achieved the first sustainable reaction under the football stands at the University of Chicago. Like the physicists, economists and regional developers will have to do considerable experimentation in the creation of R&D-based clusters to determine what the right “recipe” is. It is also quite possible that there is more than one correct “recipe” for cluster formation.

The nuclear analogy also serves to reinforce the idea inherent in cluster theories that it is the relationships and interactions that matter, rather than the simple presence or absence of certain factors or their size of growth rates that matter. The “Geiger counter” of cluster formation, therefore, are the numbers and types of interactions that develop

over time within a region, just as the Geiger counter measures electrons escaping from the radioactive interactions. Research to assess the progress of cluster formation thus needs to focus on these interactions.

Assessing Marine Biotechnology

Analysis of the prospects for marine biotechnology requires developing detailed information about the industry, the companies and the research institutions in the region working with marine biotechnology. This section outlines the approach used to collect information, examines potential demand in the biotechnology industry, and presents results and analysis from the research and interviews. A close look at the companies and research institutions in the state provides insights on the obstacles facing marine biotechnology research and applications. A review of locations around the country that are potential or actual centers for marine biotechnology provides some further insights, and a look at a developing biotechnology cluster in the region shows some clues for successful cluster development.

The overall objectives for the survey were to profile the companies and research institutions that are currently engaged in marine biotechnology research and applications and describe the ongoing research and product development occurring there. Particular attention was paid to the types of institutional and/or business relationships that are important for organizations and businesses in this field, and the obstacles to growth encountered in Maine.

Information about biotechnology firms was gathered through a series of interviews with representatives of a variety of organizations both in Maine and elsewhere. A list of potential questions was developed to serve as a guide for identifying information needed for the analysis. Data was collected primarily through a set of in-depth interviews with CEO's of companies and/or directors of institutions or departments engaged in marine biotechnology related research, product development and/or commercialization. In the interviews, information was developed on:

1. The nature of the business or research occurring.
2. The short or long-term potential of the commercial product development or research.
3. The availability of funding and/or capital, and the effect on business or research strategy.
4. The types of partnerships, collaborations and/or customer/ supplier relationships that were most important to the company or institution.
5. The availability of specialized services such as patenting, accounting or technical support.
6. The type and nature of obstacles to growth of the company or growth in research effort.
7. Perceived general obstacles to growth of the sector in Maine.
8. Opportunities for development of an industry cluster in Maine.

This information was summarized for each interview; additional data was collected with follow-up phone conversations, emails or from other sources such as publications, or newspapers. Care was taken to avoid discussing proprietary information that was critical to research and/or company success. No sensitive financial data about profit, loss, debt load or salaries was collected. Instead general information on economic performance, financing, and financial obstacles was provided at the discretion of the CEO or director.

Companies and institutions contacted were primarily in Maine, but included some in other states and provinces. Given the small size of the marine biotechnology field in Maine, every effort was made to contact all individuals that worked in the field. Suppliers for the aquaculture industry were not included unless the company used biotechnology in product development or manufacturing. Companies that handled distribution or marketing of local marine biotechnology products were included as they provided important information on potential markets. Additional companies in Massachusetts and Canada were interviewed, but the number of companies working with marine biotechnology was small. The following companies and individuals were interviewed for this report:

Companies using Marine Biotechnology

Maine

BioWhittaker Molecular Applications, Rockland

Shawn Cavanaugh – Site Manager, - formerly FMC BioProducts, BMA has 80 employees engaged in manufacturing DNA testing gels and kits from marine agars or carrageenan

PhycoGen, Portland

Ike Levine, Ph.D. – Former CEO

Randall Alberte, Ph.D - President

Formerly Coastal Plantations, Phycogen has 8 employees and is currently in advanced product research and development of antifungal agents derived from seagrasses. As Coastal Plantations, the company undertook commercial nori cultivation as well as research on seagrasses throughout the 90's.

AquaBio Products Sciences, Portland

Bill Harris Ph.D., M.D.– President– APS, with a staff of six, is engaged in research and commercial development of growth enhancement technologies for aquaculture species.

SeaRun Holdings, Arundel

Evelyn Sawyer, Ph.D.– President– SeaRun, with a staff of four, manufactures serums from salmon blood for biomedical industry, and conducts research on potential biomedical applications for other fish derived products.

Capricorn Products, Scarborough

Jane Havey – President– Capricorn’s staff of eight manufactures and markets antibodies for the biomedical industry – Capricorn collaborated with and marketed products from SeaRun Holdings.

East Coast Biologics, North Berwick

Clark McDermith – President,– East Coast’s staff of three markets and distributes antibody agents and fish blood sera to the biomedical industry.

Coastside Bio Resources, Stonington

Pete Collin – President,– Coastside, with a staff of four, manufactures and markets nutraceuticals derived from sea cucumber for the human and veterinary markets.

VeriPharm International, Richmond

Bill Keleher – President - VeriPharm is a new spinoff company of Micro Technologies, a provider of fish health services for aquaculture operations in the U.S. and Canada. Veripharm supplies hormone implants for spawning control to the aquaculture industry.

Massachusetts

Associates of Cape Cod, Falmouth

Robert Novitsky, Ph.D. – President,– ACC, with 80 employees, is a leading research lab, manufacturer and distributor of blood extracts from horseshoe crabs for the biomedical industry.

A/F Protein, Waltham

Eliot Entis – CEO -- A/ F Protein, with 22 employees, conducts research and product development on fish derived antifreeze compounds for uses in the biomedical and food industries, and has developed transgenic salmon strains.

Phytera, Inc, Worcester

Nancy Wetherbee – Vice President, Business Development -, Phytera conducts screening of marine and terrestrial microorganisms for potential biomedical applications.

Canada

Aqua Bounty Farms, Prince Edward Island

Arnold Sutterlin, Ph.D., Manager, – Aqua Bounty is a subsidiary of A/F Protein and has successfully developed several strains of transgenic salmon that are currently undergoing testing.

Other Organizations and Research Institutions

Morse, Payson, & Noyes – Portland

Charleton Ames — With Charleton’s guidance, Morse Payson has invested venture capital in aquaculture and marine biotechnology companies since the mid 1980’s

Gulf of Maine Aquarium, Portland

Don Perkins - the Aquarium coordinates a number of research and educational projects in Maine, and plans to build a research center for marine biotechnology on the waterfront in Portland.

Department of Industrial Cooperation, University of Maine, Orono

Jake Ward– DIC handles all of UMO's patenting and commercial development of innovations produced from university research programs.

Department of Biochemistry Microbiology and Molecular Biology, U. of Maine, Orono

John Singer, Chair, Mike Vayda, Beth Van Beneden – the department, with 16 faculty members, is engaged in a number of research efforts in or related to marine biotechnology.

School of Marine Sciences, University of Maine

Bruce Sidell, Director, – the school, with over 40 faculty, is the largest research institution in the state for marine science and aquaculture, with expertise in a broad number of different fields.

Bigelow Labs, Boothbay

Sandy Sage, Director, – Bigelow, with 15 Ph.D research scientists, is reknowned for marine phytoplankton research, and is commercializing technical innovations developed there for potential use in the biomedical industry.

MDI Biological Laboratory, Bar Harbor

John Forrest, Director, – MDIBL, with over 56 Ph.D or M.D research scientists in residence during the summer, conducts biomedical research on marine organisms as analogs for human organ function.

FINDINGS

Porter's four elements for a successful cluster form a useful organizing framework within which to summarize findings from the interviews conducted for the project. These elements are:

- Demand Conditions
- Firm Strategy and Rivalry
- Factor Conditions
- Related and Supporting Industries

In this section we review marine biotechnology in Maine using this framework, and then consider the growth of marine biotechnology and biotechnology elsewhere for comparative purposes.

1. Demand Conditions: The Biotechnology Commercial Environment

In order to understand the potential growth of marine biotechnology, it is first important to understand the ways marine biotechnology contributes to the larger biotechnology, biomedical and aquaculture industries. This is critical because interviews with companies made it clear that the term “marine biotechnology” is misleading. Companies view themselves as part of the much larger biotechnology industry, and they face the same research, technical and financial obstacles as other companies in the biotechnology field. Some companies such as PhycoGen and Associates of Cape Cod that utilize marine related biotechnology no longer use the word “marine” in describing the company product development activities. The interviews revealed that the term “marine biotechnology” creates perceptions of a specialty market or field when in fact their products are targeted for the same markets as other biotech companies. Marine biotechnology has direct outputs to the pharmaceutical, agricultural and industrial chemical industries, just as the larger biotechnology industry does (Figure 1 - Industry Structure)

Demand in the Biotechnology Industry

Biotechnology is playing larger and larger roles in product development for several industries in the biomedical, chemical and agricultural sectors. Large multinational corporations such as Merck, Monsanto, and Archer Daniels Midland all have biotechnology divisions developing new products, and there are new companies being formed at a rapid pace. Revenues for the biotechnology industry in the U.S. reached \$20 billion last year (Ernst and Young, 2000), and venture capital investment in biotechnology rose from \$667 million in 1998 to \$1.04 billion in 1999 (PriceWaterhouseCoopers, 2000). The industry is small compared to the pharmaceutical industry (annual revenues of \$107 billion) but it places an increasingly important role in drug development.

While biotechnology is actually used in a number of industrial processes, it has become synonymous with genetic engineering of new products, from new strains of herbicide resistant corn to new forms of drugs produced by genetically modified bacterial cultures. Genetic science (or ‘genomics’) is an area with great potential for finding solutions to human disease, and this field is growing rapidly. While genetic engineering for disease treatment or prevention are welcomed, other areas of genetic engineering, such as grain and produce crops genetically modified for herbicide treatment, face an uncertain future as public unease over unknown consequences of genetic manipulation continues to rise.

Demand in the Healthcare Sector

This sector includes a wide range of services and products ranging from human disease detection and genetic research, to health care services, medical products, instruments and pharmaceuticals. Inclusion of animal health products and veterinary applications adds additional breadth to this sector. Biotechnology plays an increasing role in developing and producing new products, particularly in the pharmaceutical industry. With health care revenues totaling \$838 billion (Business Week, 2000), this sector is larger than most others in the national economy.

Product development pathways for biomedical applications vary considerably, depending on whether the product is used directly in the human body, outside the body, or in the laboratory for research purposes only. Products used in the body, such as drug treatments or surgical instruments, face the most rigorous, time consuming and expensive process. Products used outside the body (lab diagnostics, some medical supplies) face a less rigorous but still demanding process. Products used for research purposes only (lab supplies, equipment, genetic samples or tests) face the least rigorous process, and can be developed, tested and marketed in much shorter time periods.

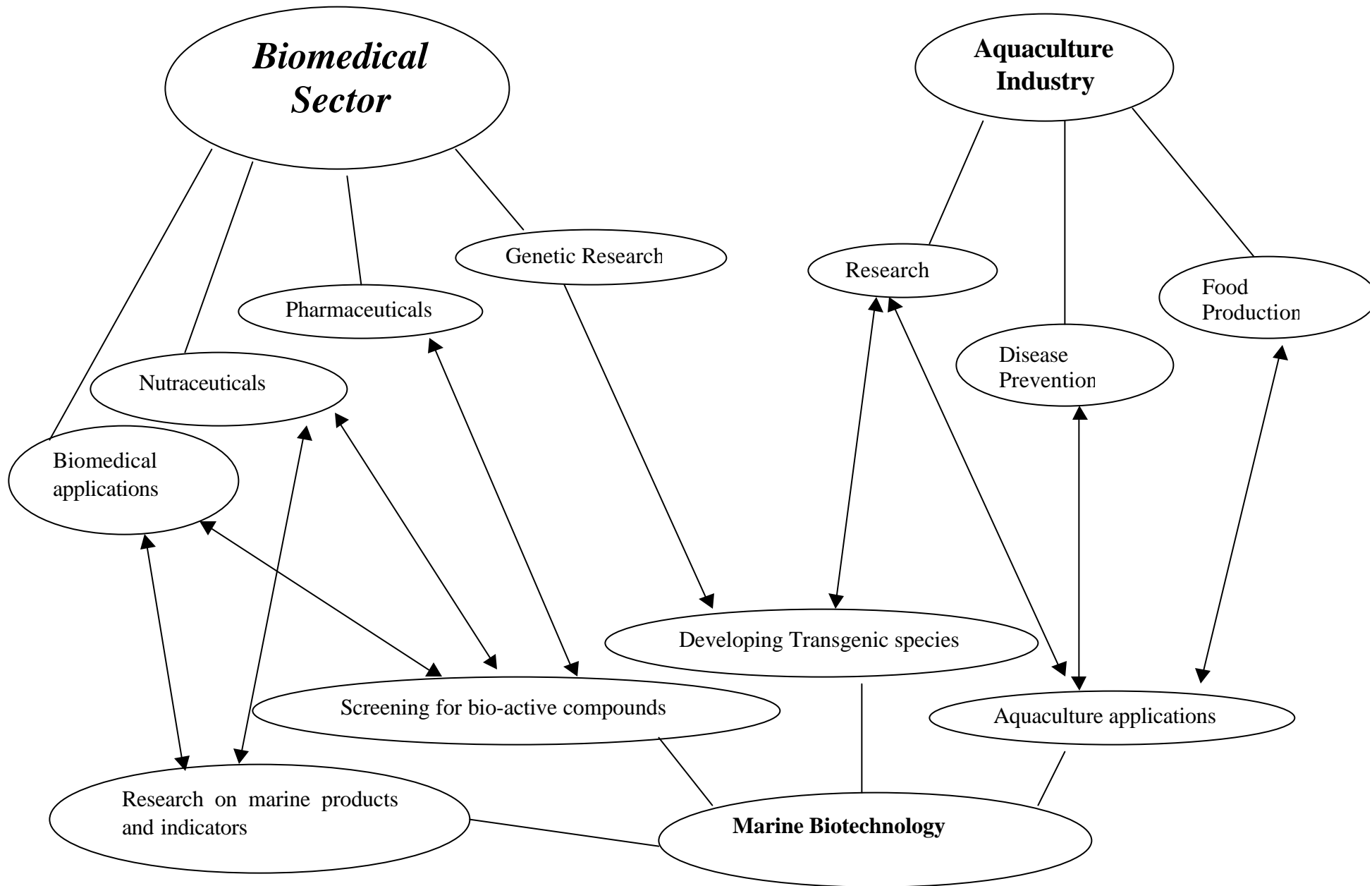
The scope of this sector and the range of product development pathways provide many opportunities for entrepreneurial activity. Sea Run Holdings, Coastside Bio Resources, Capricorn Products, East Coast Biologics and BioWhittaker Molecular Applications here in Maine, as well as A/F Protein, Phytera and ACC in Massachusetts are developing and/or marketing products for the biomedical sector.

Demand in the Pharmaceutical Industry

In the last few years, interest in the ocean as a source of bioactive compounds and drugs has increased dramatically, as many of the most useful compounds from the terrestrial ecosystems have been commercialized (for example, penicillin, actinomycin, cyclosporin, and streptomycin are all derived from terrestrial microbes). While identification of compounds from terrestrial plants (i.e. tamoxifen and others) receives much publicity, in fact the unidentified reservoir of bioactive compounds from microbes and higher life forms in marine systems is considered to be much larger than terrestrial systems, and remains largely unexplored. (National Academy of Sciences, 1999)

The demand for new drugs for the U.S. and global markets is very strong, and the outlook is for continued growth over the next five years. The value of industry shipments for the U.S. drug sector was \$107.7 billion in 1998, an increase of 13.1% from 1997; the global market for prescription and nonprescription drugs is estimated at \$300 billion, with a growth rate of 7% per year (U.S. ITO, 2000). Research based U.S. pharmaceutical companies increased R&D expenditures from \$18 billion in 1998 to an estimated \$24 billion in 1999, a 33% increase. The biotechnology industry has received

Figure 1 - INDUSTRY STRUCTURE



an increasing share of these expenditures as pharmaceutical companies look for new types of drugs and new ways of producing them. (U.S. ITO, 2000)

This demand for new drugs has created opportunities in marine biotechnology. There are several new companies such as Phytera in Worcester and Oceanix Biosciences in Baltimore that operate primarily as screening and inventory operations for marine microbes and related compounds, with the major pharmaceutical companies as their primary clients. These companies provide high volume automated testing of marine derived compounds for antiviral, antibacterial and anticancer properties, among others.

Research institutions such as Scripps Oceanographic Institution in California have also responded to this demand, creating a new research center (Center of Marine Biotechnology and Biomedicine) jointly with the University of California-San Diego Medical School to expedite discovery and testing of potential bioactive compounds. Harbor Branch Oceanographic Institution in Florida has had a research division devoted exclusively to identifying potential new compounds for several years, with funding support from several pharmaceutical companies.

Identification of a potentially useful compound is but the first step in a long and expensive process of product development in the drug industry. With each potential chemical compound of interest, costs must be estimated for additional research and testing, and balanced against the potential returns from the market for an approved pharmaceutical targeted toward specific illnesses. The vast majority of identified and patented compounds do not pass this test and are never developed further. Extensive additional testing and regulatory approval is necessary through laboratory, pre-clinical, and Clinical Phase 1, 2 and 3 trials before a FDA approved product is ready, a process which can take from 5 to 7 years. The major drug companies estimate average costs to produce an approved drug approaches \$200 million.

The time and cost of developing new products in the pharmaceutical industry has led the industry to concentrate development efforts on those compounds that can be artificially synthesized. Thus, simultaneous with testing of a potential drug, industrial processes must be developed that can synthesize, extract or purify sufficient quantities of the relevant compounds. The industry is concerned that dependence on a supply of the compound of interest from a solely marine source may not be economic, since marine resources and ecosystems are often too variable to meet production needs and thus can not readily be scaled-up to meet potential high volume demand. Some compounds can be extracted from microbial cultures grown in bioreactor vessels, and transgenic techniques may permit production of compounds by cells that do not naturally produce it. Other compounds may be synthesized using complex multistep chemical processes that take years to perfect. Compounds that cannot be produced in commercial quantities are destined to be archived for potential later use.

While the technical and regulatory issues in producing successful pharmaceuticals are formidable, the resources and capabilities of the industry have expanded to meet this need. With single drugs such as Lipitor, a cholesterol lowering drug, capable of

producing revenues in excess of \$1 billion, the potential returns for investment in research are enormous and can justify high levels of risk. Of the surveyed companies, Coastside Bio Resources here in Maine, as well as A/F Protein and Phytera in Massachusetts have tapped into the strong potential demand for bioactive pharmaceutical compounds.

Demand in the Nutraceutical Industry

This industry includes the growing market for nutritional supplements, herbal or “natural” remedies and other forms of non-traditional medicine. This industry has grown dramatically in the last five years as a number of companies have developed and expanded the mass market for nutritional supplements and "natural" remedies. The alternative medicine market has grown to nearly \$30 billion in the U.S. in 1999, with \$14.7 billion spent on nutritional supplements alone. (Nutrition Business Journal, 1999)

This market has considerable attraction from a business perspective due to its potentially high profit margins, the immature or unconsolidated nature of the market, and the opportunities for direct marketing through the Internet. In addition, the reduced testing requirement for naturally derived nutritional supplements and herbal remedies can expedite product development and marketing. Nutritional supplements do not require FDA approval and can be brought to market in a year or less.

Natural nutritional supplements, a rapidly growing market, are by definition derived from natural terrestrial or aquatic sources, and so, unlike some pharmaceutical products, are dependent on a good supply of the natural resource. Coastside Bio Resources is successfully marketing both human and veterinary nutraceuticals using chondroitin derived from sea cucumbers, and an adequate harvest of this species is important for production.

Demand in the Agricultural/Industrial Chemical Industries

A separate but also very important source of demand comes from the agribusiness and specialty chemical industries. This includes pesticides, herbicides, specialty chemicals and additives, and a number of other applications such as adhesives. This market is large and diverse, and has a number of areas such as pesticides that are research intensive and are tightly regulated.

While the global pesticide market, with \$31 billion in sales in 1998 (U.S. ITO, 2000), is not growing rapidly, there are a number of changes occurring in the market. The U.S. EPA is restricting the use of an increasing number of pesticides and herbicides that have been mainstays for the agricultural chemical industry, and few new pesticides are available that do not have undesirable side effects. This creates opportunities for new products such as the non-toxic antifungal agents developed by PhycoGen from seagrasses. Testing and development of bioactive marine derived compounds for the agricultural/industrial industries is an area of potential demand that has been tapped by PhycoGen and A/F Protein in Massachusetts.

Demand in the Aquaculture Industry

Aquaculture is a growing industry worldwide, with gross revenues of \$46.3 billion on a global basis in 1996 (UNFAO, n.d.). U.S. production was valued at \$978 million in 1998, according to the USDA Census of Aquaculture. The industry is highly competitive in certain areas such as salmon, catfish and shrimp, where there are a large number of producers around the world. Salmon, the mainstay of Maine's aquaculture production, is dominated by a few multinational corporations with production facilities in Canada, Chile, Norway and other countries. U.S. imports of salmon rose 24% in 1999, to \$629 million, with \$231 million imported from Canada alone. As with other commodity producers, these companies compete aggressively on price and supply, and the long-term stability of the industry in Maine is not assured. Additional threats to the industry in Maine include listing of salmon as an endangered species, difficulty in obtaining leases, and water quality impacts of intensive fish farming.

In commodity industries, economic advantage is gained through reducing production costs and maximizing production. Innovations, such as the development of transgenic salmon with very high growth rates pioneered by Aqua Bounty Farms, seek to dramatically reduce production costs and thereby capture significant market share. As such, the role of innovation is significantly different in aquaculture than in the biomedical or nutraceutical industry, where competition is not driven by price but by technology, specialization and the potential value of applications for human health.

Development of transgenic fish with accelerated growth rates or special culturing characteristics is occurring for a number of aquaculture species, including salmon and tilapia. While these innovations offer the promise of much lower production costs, there are a number of regulatory issues that companies such as Aqua Bounty Farms must overcome for salmon, including potential escape and interbreeding with wild stocks, as well as stringent testing for food product safety. Concerns about the interaction between transgenic and natural stocks may lead to transgenic stocks being grown entirely within closed cycle systems that may have little or no connection with the ocean and coastal locations. In addition, public acceptance of genetically engineered food products is highly variable, with Europeans developing increasing distrust of these products. Whether U.S. consumers develop this aversion remains to be seen.

Product development pathways in aquaculture are not well defined as with the biomedical industry. Research funding, while available, is generally in small amounts that cannot support major research labs or staff. Bill Harris of AquaBio Products Sciences points out that should a new product or licensable discovery be made, there are few intermediate size companies waiting to purchase the rights and invest large sums in development and marketing of an improved product for the aquaculture industry. Full scale production and marketing must often be undertaken by the entrepreneur, a formidable task for small research and development ventures. The only consumers of products from the marine biotechnology sectors tend to be small operators, who have little capital, and large multinational corporations engaged in seafood production and

aquaculture. The competitiveness of this industry means that margins are low and funding from these companies is limited for innovative but risky projects. Successful new products, such as VeriPharm's hormone implants for spawning control, are targeted toward reducing costs for producers. Companies developing and/or marketing products for the aquaculture industry include AquaBio Products Sciences and VeriPharm here in Maine, and Aqua Bounty Farms in Prince Edward Island.

Summary

The biomedical, nutraceutical and agricultural chemical industries present attractive opportunities for startup companies that have the capabilities and specialized knowledge to take advantage of the demand for new products for both mass and specialty markets. (Table 1) There are several reasons this industry has attracted so much investment, including:

- Potentially very high profit margins, particularly in the biomedical and nutraceutical industry, with large potential returns for investors
- The ability to tap into specialized markets for goods in which consumers will pay premium prices, and/or tap into very large global markets with potentially high demand
- The ability to license discoveries, processes or products to mid-size or large multinational companies that have the financial resources, expertise and/or marketing skill to fully capitalize on the potential for these new products.

Of the 12 companies contacted for this report, most are working on products for the pharmaceutical, nutraceutical, biomedical or agricultural/ industrial chemical industries.

The aquaculture industry presents opportunities for startup companies such as VeriPharm or AquaBio Products Sciences in aquaculture biotechnology, but the potential market is more limited. While demand exists for innovative solutions to problems in culturing and disease prevention, the potential markets for these solutions may be relatively small or dependent on outside factors. Enhanced production techniques targeted toward reducing costs, including accelerating growth rates, offer the best opportunities for commercial development. The use of genetically modified organisms such as transgenic salmon faces a high degree of uncertainty due to regulatory concerns as well as public perceptions and acceptance of products.

2. Firm Strategy and Rivalry

Maine has only a handful of companies engaged in marine biotechnology, but has as many research ventures as some coastal states with much larger populations. These small companies, each with its own special niche, are not yet competing with one another and so this characteristics of a cluster is not yet present. Rather, their competitors are found throughout the United States and the rest of the world.

Of the small companies interviewed, all had revenues of less than \$1 million per year, and most were less than \$500,000 per year. All were engaged in research and development, though some companies derived their revenues from marketing and distribution of products. Most companies had relied on grants for support of some research activities over the last five years. Some companies such as A/F Protein, with 22 employees, report no revenues from products or licensing, and are financed solely through venture capital.

The key role of the entrepreneur was discussed earlier, and some key characteristics identified. The interview process did not allow sufficient time to explore the nature of events that precipitated starting the companies, but some general observations can be made. For research-based companies such as PhycoGen or AquaBio Products, the founders often had extensive educational backgrounds in the health or natural sciences, often from top universities around the country. Advanced degrees in multiple disciplines were not unusual, and partners or senior staff was highly trained as well.

Founders for all companies also had considerable experience in the field prior to starting their own enterprise, and through this experience were well informed as to risks and opportunities in the industry and the feasibility of starting a successful business. The previous work experience was often important for motivating the founders to go into new and sometimes uncharted waters. For research-based companies, dependence on “soft” money was high, but this is typical for companies engaged in product development where revenue streams from products have not been established. The interviews revealed a high level of self-confidence and self-determinism typical of many entrepreneurs.

It is not clear if Maine provides a culture conducive to entrepreneurship or if the Maine firms are here as a result of purely personal or largely random factors. The role models here are not abundant. Funding and financing are available but are not easily obtained, especially for startups. There is not a large consolidated research community, nor is there a large business community of potential customers. Knowledge of the requirements to successfully develop and market products is particularly important, but many potential entrepreneurs here in Maine lack this experience. Development of programs or systems of networking among businesses to get this knowledge into the hands of new entrepreneurs could be particularly useful.

Almost all companies and research institutions contacted were interested in the concept of cluster development. The benefits of cluster development, including enhanced

networking, exchange of ideas, better access to trained personnel, and opportunities for collaborations or partnerships, were recognized as very attractive to both companies and research institutions. Interactions for many companies are of necessity heavily oriented toward customers and suppliers, and opportunities for exploration of new ideas or potential commercial ventures can be few. Several companies interviewed relied on publications and conferences in their specialty for new ideas, information on technical breakthroughs and potential new customers outside of Maine.

In an industry that is currently dominated by very small companies, the presence of some larger companies in the region is important. Thus, the recent growth of biotech companies and research institutions such as IDEXX and Maine Medical Center Research Institute is seen as especially important, providing potential sources of innovation, as well as potential trained employees. The planned Gulf of Maine Aquarium research center for marine biotechnology was also an important factor for some companies, as the center has the potential to draw researchers from across the country. Portland also can provide good access to expertise on marine engineering and vessels suitable for research use.

The context for firm strategy and rivalry encourages investment and upgrading through vigorous competition between local firms and speaks to the choices that each company makes about how to respond to competitive conditions. Most of the Maine companies are primarily engaged in securing their competitive position through the research and development process to create new products that will find their own position in the appropriate markets. With the exception of such established firms as BioWhittaker, the principal strategic focus of the Maine biotech companies is establishing themselves as viable, ongoing operations. As such, they share the problems and potentials of small companies in all industries, with the added burden of working in a very high cost research field.

Critical strategic choices for these companies will come in the future once they have established themselves. Two key choices will likely arise. Firms that demonstrate a high degree of market success may find themselves targets for acquisition by larger firms, most likely located elsewhere. Whether to choose to be acquired, and thus possibly relocate operations elsewhere, will be a very important choice, particularly for those companies where personal factors have played a key role in deciding on a Maine location.

The second set of strategic choices will come for those companies that produce a successful product that is ready for the market. Either they must dramatically scale up a production process for such a product, or license the product to another company for production and marketing. Research companies such as PhycoGen or AquaBio may license their discoveries to others, while companies such as Sea Run or Coastside may undertake production themselves. Production at a much larger scale will involve a company choosing whether to build their own facilities, and where to build them. In today's much more flexible business environment, it is also possible to contract out or license production to other firms, which may be located nearby or around the world. The availability of production capabilities in the state will determine whether Maine remains a

location for small-scale research or large-scale biotech manufacturing along the lines of BioWhittaker in Rockland. These choices lie some time in the future, and will be among the most important in determining whether marine biotechnology will evolve into a cluster in Maine.

3. Factor Conditions

Locational issues

The type and focus of entrepreneurial activity varies widely across the companies contacted in this survey. Generally, marine biotech companies such as Sea Run Holdings or Coastside Bio Resources that are closely tied to continued supply of a resource from aquaculture or harvesting are located further Down East, while those that depend on good access to networks, personnel, access to Boston research universities/ hospitals and good air service are located in the southern part of the state. Sea Run Holdings has locations in both eastern and southern Maine to address both needs. AquaBio Products Sciences relocated from MDI to Portland due in part to the isolation, poor air service, and lack of access to research resources.

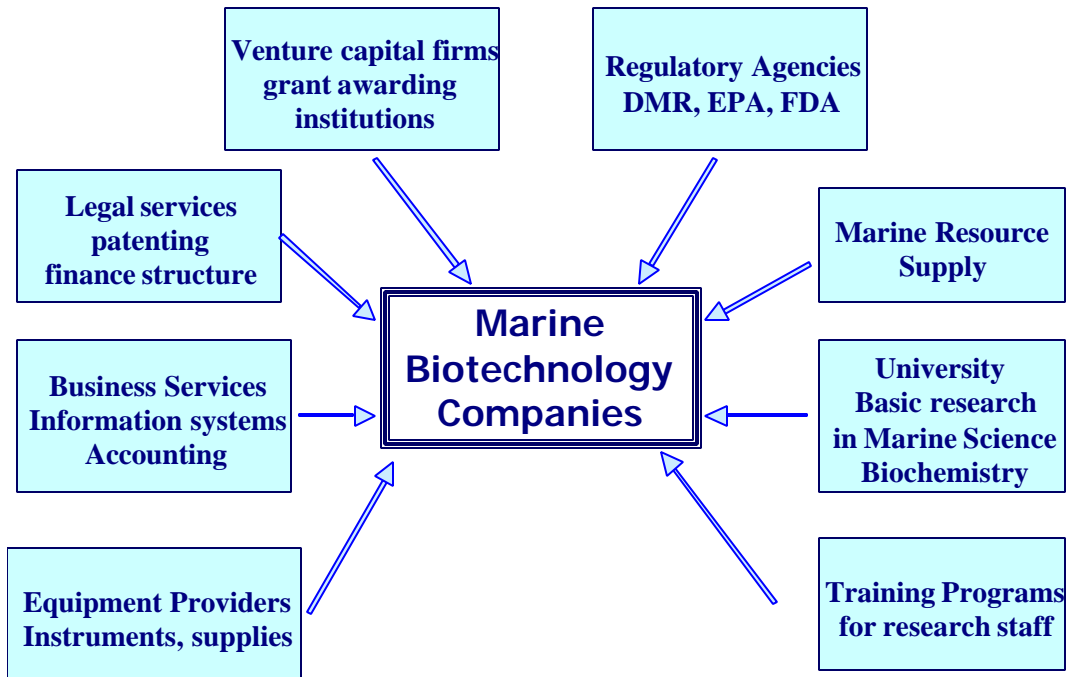
The availability of good air service from Portland or Boston is also an important factor for companies that serve national or international markets. Also important was the availability of legal and financial services, general business services, and local suppliers or vendors. The proximity to Boston's research centers, biotech companies, equipment vendors and service companies was considered important as well. Companies located in southernmost Maine, including SeaRun Holdings and East Cost Biologics; saw UNH at Durham as an important asset with its research libraries and supply of graduates.

Grant Funding

Most companies in marine biotechnology in Maine are engaged in research and development, either as a primary focus or as part of their continuing development of new product lines. For companies in early stages of new product research and development, the level of research activity depends to a significant degree on accessing grant funding. Small Business Innovation Research and Maine Technology Institute funding plays a very important role here for companies heavily engaged in marine biotechnology research, and several of the surveyed companies had obtained both SBIR and MTI grants.

Research on commercial applications for marine biotechnology related to the health sciences can tap different sources of grant funding unavailable to aquaculture, including the twelve Institutes of the NIH, Department of Defense and numerous large foundations devoted to funding biomedical research. This funding is often in larger amounts, and can support larger research efforts with more staff for longer periods of time.

Factor Conditions or Inputs



Access to capital

Companies located in southern Maine apparently have good access to established networks of investors in the area. Obstacles to obtaining financing, while often significant in terms of time and managerial energy, are usually resolved successfully. For companies such as PhycoGen or AquaBio Products Sciences that have products in development that have clear market potential and have well thought out business plans and strategy, venture capital seems to be available, often through a network of “angels”. Charleton Ames of Morse, Payson & Noyes indicated that venture capital is available for well planned aquaculture related ventures, but may not be available in amounts over \$500,000 unless the company has an excellent track record. Almost all of the companies surveyed reported that raising capital required significant time and effort, and that a high degree of persistence was often necessary to be successful.

Labor supply

The research companies in southern Maine also do not report problems attracting and retaining research personnel they need. Ph.D. scientific staff are reportedly drawn by the ability to pursue research interests without constraints imposed by other more urban locations, such as high housing prices, congestion or poor schools. Spouses, often highly educated, can find numerous opportunities for meaningful employment.

However, some companies such as Capricorn Products indicated that finding well-trained laboratory staff was difficult; increasing amounts of time were required for

employee training. The tight labor market in southern Maine was partly responsible, but local university educational programs were also not considered adequate. The increasing number of companies in the area working in the biotechnology field will increase the pool of employees, though salaries are increasing and competition for personnel can be an issue. Sea Run holdings reports continuing problems finding lab technicians for its Eastport operations. Local residents generally lack any of the necessary training, and getting potential employees to relocate to the area is very difficult.

Companies located in the mid-coast such as BioWhittaker Molecular Applications may be able to attract research personnel, but the isolation and lack of alternatives for employment for spouses was a recurring problem. BMA recently transferred its research staff from Maine to its headquarters in Maryland as part of a reorganization. BMA also reports increasing difficulty in recruiting entry-level workers, in part due to competition for these workers from MBNA.

Infrastructure

The type of physical facilities needed for marine biotechnology varies widely. It may include wet lab space for culturing, or specialized lab space may be required for biochemical procedures and testing. Equipment needs are determined by the area of specialization for the company; DNA sequencers may be needed for genetic testing and manipulation; costly analytical equipment may be required for chemical analyses; bioreactors may be required for microbial culturing. These expensive equipment needs and the technical staff to run them can be significant barriers to startup companies entering the business. Considerable capital is required to start operation, and years of research may be needed prior to producing any sort of product or licensable discovery.

Currently each company in marine biotechnology in Maine has its own lab facilities, or contracts for outside lab work. Opportunities for centralization and sharing of facilities and analytical equipment could produce significant benefits. The proposed Aquarium research center includes plans for shared analytical equipment and instrumentation, with separate lab and office space for each commercial venture. This facility will provide a significant resource for the kinds of small companies doing research that are critical to marine biotechnology in the near future.

Regulatory issues

The regulatory issues raised by companies varied widely. Sea Run Holdings was concerned about state regulation of private hatchery facilities. Ike Levine and Coastal Plantations spent large amounts of time and effort in the mid 1990's addressing regulatory concerns about non-native nori species that it proposed to cultivate in Cobscook Bay. Companies such as Aqua Bounty Farms in PEI faces a number of regulatory obstacles in commercialization of transgenic salmon.

In general, those companies engaged in aquaculture-related marine biotechnology faced the most regulatory issues, with transgenic species development being particularly

difficult. Aqua Bounty Farms in PEI has done all of its production of transgenic salmon in closed aquaculture systems, which reduced some regulatory concerns. They are currently focused on getting FDA approval for their transgenic salmon strains, which may be the first living organism to receive FDA certification. This process uses protocols reserved for pharmaceuticals, which are very expensive and time consuming. Even with approval, the economic outlook for transgenic foods is not clear.

The factor conditions affecting Maine biotechnology firms are positive, but not uniformly so. Some, such as capital availability are positive, and expected to remain so, but the availability of certain types of labor, and somewhat uneven access to key resources in different parts of the state make for a mixed picture.

4. Related and Supporting Industries

Access to business services

In addition to obtaining funding, small startup companies in marine biotech may face hurdles in the growth of small business common to all new ventures, including concerns on patenting, legal services, and business management. A number of services are available in Portland, and most of the large law firms located there now offer a full range of services from patenting to permitting. However, several companies indicated that effective patenting for biotechnology discoveries often required specialized and costly patenting services from law firms in Boston, New York or Washington.

Companies such as East Coast Biologics or Coastside Bio Resources, which are located in more rural locations, may not have easy access to business services. Business and legal issues can be handled better when networks are established among companies in the industry for formal and informal advice on legal issues, patenting and financing. The Biotechnology Association of Maine currently plays an important role in advocating for the biotechnology industry, and provides some of these networking functions. The Center for Innovation in Biotechnology and the Maine Technology Institute can provide advice on patenting and financing issues as well.

Issues of patenting and product development also pose obstacles for research institutions such as Bigelow Labs that are beginning commercialization of technical breakthroughs developed at the Lab. Formation of commercial ventures poses particular challenges for basic research institutions. Development of separate organizational structures is usually necessary to separate commercial research from nonprofit research activities, an approach that Bigelow is using for its commercial development activities. UMO uses its Department of Industrial Cooperation for this purpose.

Research infrastructure

Attempting to create a cluster around a group of technology industries such as marine biotechnology must rely to a very great extent on the institutions and infrastructure for both basic and applied research within the region. For marine

biotechnology, this requires assessing both the current state of related research in Maine and the possible future.

With the exception of aquaculture, the companies contacted generally did not view Maine's research infrastructure, including the University of Maine, as an asset. While individual researchers from the institutions had on occasion provided assistance on a number of technical issues in aquaculture, food science and marine science, the general perception remained that the research institutions were currently not significant assets.

There are a number of explanations for this view. Most important is that the mission of the three research institutions differs from the goals of the entrepreneurial companies. Bigelow Labs and Mount Desert Island Biological Labs are private nonprofit institutions organized primarily for the purpose of basic research, with education as a distant secondary purpose. The University of Maine, with its Department of Biochemistry and the School of Marine Sciences (SMS), is also organized for basic research, but education and public service are equally important to its mission and command a significant portion of its resources in staff and facilities.

The state marine research institutions maintain a high degree of independence from each other, and while collaboration occurs between individual researchers at all the institutions, the missions are different for each and a number of obstacles to large-scale institutional collaboration remain. Projects such as the Gulf of Maine Ocean Observing System (GoMOOS) have brought the institutions such as Bigelow and SMS together because they provide significant research benefits and additional funding to the both institutions that would otherwise have not been available. Successful industry clusters in other locations around the country found ways to encourage entrepreneurial activity at supporting universities, with faculty fully engaged in application of technologies. Projects such as GoMOOS may offer opportunities for development of this entrepreneurial spirit.

In addition, locational issues play a big role in the perceptions of institutions as assets. The geographic separation of these research centers from each other and from the business centers in southern Maine is a factor in their ability to collaborate with each other and with private commercial ventures in the state.

Although there are a number of issues in linking today's marine research capacity in Maine with the emerging field of marine biotechnology, it should be recognized that the marine research institutions do comprise a significant foundation for the future. Despite its small size, the **Bigelow Laboratory** is one of the top marine research stations nationally, and is highly successful in capturing large grants from the National Science Foundation, the Office of Naval Research, and the National Oceanic and Atmospheric Administration. With 15 Ph.D. research scientists, it is small compared to other marine research centers that have 50 to 100 researchers. It has recently begun the process of commercial development of a technology developed at the Lab. This technology has application in marine science but also for the larger biomedical industry, and Bigelow has successfully formed a partnership with a biomedical manufacturer to develop and market the technology. Following an approach used very successfully by MIT, the commercial

development activities will be undertaken by a separate foundation created for the purpose.

The **University of Maine's School of Marine Sciences**, the largest marine research institution in the state, consistently brings in \$5 to \$6 million in research funds from outside sources each year, primarily from NSF, ONR, and NOAA, with lesser amounts from NASA, Sea Grant and NIH. Development of aquaculture applications, disease prevention and cooperative research with and for the aquaculture industry have been a key focus for a number of years, and have provided a number of benefits to the aquaculture industry. While one researcher in the department has been successful in capturing NIH funds, it unlikely to become a large part of the SMS research effort.

Mount Desert Island Biological Laboratory's (MDIBL) annual revenue of \$1.6 million (1998) is considerably smaller than the other marine research centers, though the shift to year round operations may change this. What is also unique about MDIBL is that much of its research is oriented toward addressing questions pertaining to human organ function and health. With principal investigators drawn from prominent medical schools and universities around the country, MDIBL draws the majority of its research funding from the National Institute of Health, the American Cancer Institute and other funding institutions for biomedical research. The only other institutions capturing NIH dollars are Jackson Labs, with over \$50 million a year in grant funding, and Maine Medical Center Research Institute, which has in excess of \$7 million in NIH funding. Neither of these institutions has a strong interest in marine biotechnology.

Funding sources and awards for research in the state were profiled in *An Initial Review of Maine's Academic and Non-Profit Research Assets (State Planning Office, 1998)*. The funding picture in 2000 remains very similar. Funding for basic research in marine science comes primarily from the National Science Foundation and the Office of Naval Research, with lesser amounts from NOAA and NASA. NSF funding is highly competitive, with 1 in 6 applications receiving funding on a national basis. Maine as a state does considerably better than the average, with 1 in 3 applications to NSF receiving funding, and some institutions such as Bigelow Labs receive funding on up to 70% of their submitted proposals.

The NSF annual budget in 1999 was \$3.9 billion, with almost all distributed as research grants. This funding is projected to grow to \$ 4.2 billion in 2000, after several years of slow growth in the NSF budget. Maine is also receiving more Office of Naval Research funding through projects such as GoMOOS, as the ONR seeks a wider research base of institutions. Both NSF and ONR have had program initiatives in the last 10 to 15 years targeted toward expanding research in marine biotechnology, though other programs in physical sciences are much larger. Randy Alberte, president of PhycoGen in Portland, was formerly the ONR national program director for marine biotechnology for much of this period, and brings extensive expertise to the state in this area.

NOAA marine research funding is much more limited, and grants are generally far smaller than NSF or ONR grants. The pressing problems in fishery management have

generated some additional research funds, but much is targeted toward economic relief for the fishing industry. NASA also is an important source for funding, especially for development of remote sensing research using satellite imagery. MSTF has played a key role in the fostering basic research lately with its grant programs for both infrastructure and research.

Biomedical Research Funding

Considering all the funding sources, the dollars available for basic marine research are considerably less than those available for research in the biomedical sector. The National Institutes of Health had an annual budget of \$17.9 billion in 2000, up 15% from 1999, and over four times the budget of NSF. While a small portion of this funding goes to NIH's own research facilities in Maryland, most of the funding goes via the twelve National Institutes to major universities, teaching hospitals and laboratories engaged in basic and applied biomedical research. The Republicans in Congress have been pushing hard for doubling of the NIH budget in the next five years, while the President is proposing a budget of slightly less than \$19 billion for 2001.

NIH funding in Maine is primarily to Jackson Labs, which captured in excess of \$50 million in grant funding last year. MMCRI captured \$7 million last year and will be increasing that this year with their new facility; UM also brings in a small amount (\$300K). The ability to capture larger portions of NIH funding for research in Maine will be critical for the growth of the biotechnology industry, including marine biotechnology

Maine's competitive position in marine biotechnology is limited by a number of different conditions, including geographic dispersal of research and commercial activity, availability of adequately trained biotechnology staff in certain areas, and a small and/or fragmented research infrastructure. Maine's vast ocean resource provides some advantage for research, but for some of the largest growth industries such as pharmaceuticals, production of marine related biotechnology products is not necessarily dependent on proximity to the ocean. If Maine is to be a competitor in this field, a key factor for Maine's success in marine biotechnology and biotechnology generally will be the strength of its research and education infrastructure in biotechnology and biomedicine.

Maine competes successfully for funding in marine science, but the sources of funding such as NSF lack potential for significant growth, and reliance on these agencies for growth in research dollars is risky. Funding for biomedical research via NIH is much more promising, with a potential doubling of the NIH research budget in the next five years. Currently, the majority of funding is captured by Jackson Labs, and the only other institution capable of attracting funding is MMCRI. If Maine wishes to improve and expand its research infrastructure, it is essential that ways be found to expand biotechnology research and education, and improve collaboration among Maine's research institutions to capture new biomedical research dollars.

5. Cluster Development in Marine Biotechnology and Biotechnology outside Maine

Marine biotechnology has attracted attention from several state governments and research institutions across the country as a possible focus for economic development efforts. A few coastal cities and states have sought to capitalize on established university programs and proximity to marine resources to establish centers for marine biotechnology. At least two marine research centers have made development of marine biotechnology applications a primary focus of their research programs, and are actively seeking corporate partners for collaborative research. Several centers around the country were examined to determine if clusters of marine biotechnology companies were developing in the area. These institutions have functioned as centers for marine biological and biotechnology research, some for many years, and have attracted top researchers in the field. These include:

- Marine Biological Laboratory in Woods Hole
- Center of Marine Biotechnology in Baltimore
- Harbor Branch Oceanographic Institute, Fort Pierce, Florida
- Scripps Institute of Oceanography, La Jolla, California.

Other marine research institutions with the potential for moving into marine biotechnology, but which have not yet done so in a significant way include the Rosensteil School of Marine Science at the University of Miami, Friday Harbor at the University of Washington, and the University of Delaware.

The Marine Biological Laboratory in Woods Hole

MBL seemed a particularly promising candidate, as it has been the center for some of the most important research in marine biology over the last 50 years. A number of prominent scientists working there have made discoveries that were highly influential in the fields of biology and medicine. With a worldwide reputation for excellence, hundreds of research staff, and a location adjacent to both Woods Hole Oceanographic Institution and the National Marine Fisheries Research Center, MBL enjoys numerous advantages. MBL is a private nonprofit institution unaffiliated with any university, and receives all of its funding from research grants, fees, and endowment.

Surprisingly, the only spin-off company identified in the area was Associates of Cape Cod in Falmouth, which was founded in the late 70's. ACC is a major processor of horseshoe crab blood to make products used for testing for bacterial contamination in the products manufactured by the biomedical industry. The lack of spin-off companies is in sharp contrast to the field of marine technology, which has seen over a dozen companies develop in the Woods Hole-Falmouth area in the last two decades. The president of Associates of Cape Cod, Robert Novitsky, suggested several reasons for the lack of a marine biotechnology industry in the area, including:

- the culture at MBL and WHOI, where excellence in basic research was the priority and commercial applications were not highly valued,
- for biomedical applications, the importance of proximity to university research hospitals (ACC staff traveled frequently to Boston for this reason), and
- location in the area only provided advantages for companies such as ACC that were dependent on continued harvesting of a marine resource (such as horseshoe crabs). Companies that could produce synthetic equivalents did not have this requirement.

The Center of Marine Biotechnology in Baltimore

COMB is one of four research centers in biotechnology established by the state government and the University of Maryland in the late 80's and early 90's for the purpose of research and economic development. The center, built as part of the \$160 million Columbus Center, includes 14 full-time faculty. The facility, located adjacent to the National Aquarium in downtown Baltimore, contains state of the art facilities for culturing of marine bacteria, DNA sequencing and a full range of equipment for biochemical analysis. A separate aquaculture facility at Fells Point includes state of the art facilities for culturing marine organisms.

Approximately 25% of the center's budget of \$8.1 million comes from federal research grants, and industry and foundation grants provide another 14 %. The remainder is funded by appropriations from the state. Each year the Legislature questions if the funding is actually producing any economic development. A large portion of COMB's grant funding is heavily oriented toward basic research funded by NSF, so expectations of a high level of commercial development from this work may be unrealistic. A considerable percentage of COMB's research is also geared toward aquaculture applications, an area that, as discussed previously, offers numerous challenges for large-scale commercial development. Biomedical research is not a large portion of the research program at COMB, and the lack of connections to medical research centers and the associated NIH funding may have curtailed potential development of biomedical applications. This would also limit potential collaboration with the booming biotech industry in the Washington-Baltimore corridor. This area is one of the hottest areas for biotechnology, with numerous companies locating in the area due to proximity to other biotech and pharmaceutical companies, as well as the National Institutes of Health in Rockville, Maryland.

The center has produced a number of discoveries in aquaculture including development of the first transgenic fish in the U.S., the discovery and manipulation of hormones controlling spawning in fish and development of marine based adhesives. However, the center has spun off few successful commercial enterprises, and only one remains in the area. One technique developed at COMB is hormonal implants in fish for control of spawning. This technology, patented as Reproboost, has been licensed to VeriPharm in Richmond and is being successfully marketed to the salmon aquaculture industry.

Scripps Institute of Oceanography in La Jolla, California

Scripps is a good example of a marine research center deliberately creating a connection to biomedical research. Scripps has recently formed the Center for Marine Biotechnology and Biomedicine (CMBB) to promote drug development from marine organisms. For a number of years Scripps has been a leader in research on the life forms associated with the extreme environments of deep sea hydrothermal vents, and some of the unusual bacteria from these environments have provided unique biochemical models useful for pharmaceutical development. Scripps also began research on the biomedical potential of a number of Pacific invertebrates, including soft corals. Scripps has expanded this program to work directly with UC-San Diego School of Medicine to identify and test promising chemical compounds found in marine organisms, and has attracted funding from pharmaceutical companies for this research. The Scripps Research Institute, a separate entity from the Oceanographic Institute, is also a significant asset, with over 230 research scientists working on basic research in the biomedical field. These assets are complemented by a strong biotechnology industry in the La Jolla- San Diego area.

Scripps has spun off several companies from its marine research over the last 15 years, mostly in biomedical related research. Agouron Pharmaceutical of La Jolla, CA, now a subsidiary of Pfizer, started with commercial development of discoveries in bioluminescence in the 1980's. They have since diversified and have a number of promising AIDS and anticancer drugs, but the link to marine biotechnology has long since faded. Neptune Pharmaceuticals was started by Scripps oceanographer William Fenical to do commercial screening of marine derived compounds. Neptune has since been bought by Phytera, of Worcester, Massachusetts, which screens marine and plant samples for potentially useful pharmaceutical applications. Scripps research on Pacific marine organisms is paying dividends; eleutherobin, a compound identified from soft corals, has been licensed to Bristol Meyers Squibb for development and testing as an anti-cancer agent.

Harbor Branch Oceanographic Institution

HBOI is another example of a private, nonprofit ocean research institution notable for emphasis on biomedical applications for marine biotechnology research. Scientists at the HBOI Division of Biomedical Marine Research have identified and patented over 50 promising chemical compounds from marine sponges and other organisms in the last 15 years. One compound, discodermilide, has proved to be particularly useful for cancer treatment and has been licensed to Novartis Pharmaceuticals. While a number of drug companies are collaborating on research at HBOI, to date no spin-off companies have emerged from this work. This may reflect the very high costs for drug development and testing programs, which are best undertaken by large well-capitalized corporations.

HBOI has also invested heavily in development of potential aquaculture applications, including culturing of shellfish and ornamental fish (tropical fish). The

development of commercial enterprises for aquaculture has been more difficult. Harbor Branch is currently investigating forming its own company to do commercial work on culturing of tropical fish for aquaria, as it has been unable to find outside companies with the capital or capabilities.

A brief review of several well known centers of marine biological research shows that, with the possible exception of Scripps, most have not functioned as centers for development of industry clusters in marine biotechnology. Those centers that have good track records for commercial development of promising discoveries, such as Scripps and Harbor Branch, have aggressively pursued the market for potential biomedical applications.

The absence of clusters in marine biotechnology may be due to a number of factors:

1. An immature industry – research in this area only started 15 years ago, and the intense activity in pharmaceutical development has only been in the last 5 years,
2. A heavy focus on basic research in marine biology from the academic community, rather than seeking potential applications in medicine, agriculture or specialty chemicals,
3. The highly diverse nature of research in marine biotechnology, ranging from drugs to bioremediation to aquaculture, which leads to fragmentation and dispersion of research efforts,
4. For potential biomedical applications of marine biotechnology, companies are drawn not to marine research centers but to centers for biotechnology and biomedical research which have the resources and facilities for research, development and clinical testing of potential products,
5. A poorly funded research effort for aquaculture biotech, and a poorly developed and financed market for applications from that research.

Biotechnology Cluster Development

While marine biotechnology has not developed definable clusters, biotechnology as an industry has several successful clusters around the country, including Worcester and Cambridge in Massachusetts, the Washington Baltimore corridor, and the San Diego area. In a few cases the local economy developed into a cluster based on a concerted effort by industry, government and academic institutions. It is useful to examine how this effort was organized.

One of the best examples of successful cluster development in biotechnology is Worcester, Massachusetts, a city that is similar to Portland in size. In the 1980's Worcester was in the depths of a significant economic downturn prompted by collapse of its traditional industries and was forced to reinvent itself from scratch. Largely through an effort driven by leaders in the local business community, but supported by local and state government and the university system, Worcester has become home to dozens of

biotechnology companies. Some of these companies grew from local startups and industry-university collaborations, and other companies have been drawn to the area by the benefits and opportunities available.

The effort to develop the biotechnology industry in Worcester was not strictly based on the theory of cluster development. Yet the business community had a clear understanding of what was needed to transform Worcester into a hub for the biotechnology industry. They were able to convince government and educational institutions of the need for a major sustained initiative to transform the area's economy, and to obtain the commitments of resources needed to start the effort. Considering that the successful outcome of these efforts was by no means assured, there was a significant level of risk associated with this endeavor, but the commitment to make a sustained effort was made.

The effort has been action oriented from its beginnings in the 1980's, and the area has now started to see the benefits of years of hard work. The effort has focused on several key areas, including:

- Expanding educational and training programs at Worcester Polytechnic and other area universities
- Establishing local biotechnology research programs tied to the University of Massachusetts Medical School, Clark University and other institutions
- Creation of an industry government organization (Massachusetts Biotechnology Research Institute) to facilitate obtaining funding and needed infrastructure improvements
- Establishing a center for the industry- Worcester Biotechnology Park has now grown to four complexes housing numerous companies
- Attracting biotech companies and suppliers to the area – there are numerous companies, including the headquarters for BASF Biosciences division that were recruited to the area.
- Creation of streamlined regulatory standards for biotechnology companies, from zoning standards to waste disposal
- Establishing forums, including biotechnology conferences, to bring together participants in the biotech cluster

Through this effort Worcester has established itself as a nationally known biotechnology center. This is a significant accomplishment considering the city started with very few companies and is located in the shadow of the Boston metro, with its well established industry clusters along Rt. 128. Fifteen years after beginning this effort, Worcester is still working hard to expand its biotechnology industry, but it has made significant progress. The Worcester Biotechnology Park now is home to dozens of companies, including the headquarters for BASF BioSciences, one of the larger biotechnology companies. Efforts continue to encourage the growth of this cluster, as the industry is dynamic and competitive, and there are numerous other areas in the country that are now seeking to develop their own industries.

Conclusions

Marine biotechnology is still at an infant stage in Maine and elsewhere, and as such it is many years away from forming the kind of cluster of economic activity that are observed in the Maine fishing or forest products industry. Yet it is an area with enormous potential for growth. The markets that it will serve are high return industries with significant growth potential. Indeed, the real potential for growth in many of the markets, such as pharmaceuticals, still lies in the future. The future success of marine biotechnology in Maine will depend on several factors, only some of which are within the control or influence of the current companies or of state government. However, state policy can play a role if it is based on a realistic view of the industry and its potential.

In this section, we summarize our key findings regarding the current and potential state of marine biotechnology in Maine, and make recommendations about specific actions that can be taken to support the growth of this industry and to monitor its growth.

Key Findings

Forming state policy towards marine biotechnology should be based on several key findings from the assessment conducted here:

1. *Marine biotechnology is inseparable from biotechnology.*

Using marine organisms or materials as inputs to new biotechnology products is an important innovation. But the marine environment is but one among many possible sources of materials and innovation in the rapidly evolving biotechnology field. The firms in the marine biotechnology field are only parts of the larger area of biotechnology since that larger set of industries is where the markets lie.

2. *Biotechnology is a complex field with many different products and processes. It is comprised of industries with very different product development paths and market potentials.*

There is a spectrum of development possibilities within the industries served by marine biotechnology. At one end lies the very high profit, high volume and high risk pharmaceutical industry. This industry is characterized by intense product specialization, which gives the successful firms very high market potential. At the other end is the salmon aquaculture industry, which is now essentially a worldwide commodity industry with very low levels of product specialization and low profit margins.

At the same time, the pharmaceutical industry is subject to the most extensive, and expensive, product development process, which can stretch the time from idea to product to a decade or more. At the other end, the aquaculture industry is subject to a much less regulated and less intensive product development process.

There are also large differences between the two extremes of the market spectrum in terms of the types of firms. The pharmaceutical (and to some extent the industrial chemical) industry is composed of large, highly organized, worldwide corporations, many with their headquarters outside the United States. The aquaculture industry is composed of some small firms and a few large multinational corporations; with consolidation an increasingly common occurrence as economic advantage goes toward large-scale producers. Currently internal research and development capacity is limited.

Marine biotechnology developments may have very different impacts on the two ends of the spectrum. In the pharmaceutical/nutraceuticals industries, marine biotechnology may create both dramatically new products and new production processes. The result could be significant profits for companies that, for example, develop a major new drug.

At the aquaculture end, marine biotechnology will primarily be used to improve production processes. Innovations such as transgenic fish that grow to market size much more rapidly may simply increase the supply of fish in an already competitive market, with the result that prices are further depressed and more pressure put on smaller companies. This is not to deny that firms that first deploy such technologies as transgenic fish may realize significant first-mover advantages with dramatically improved prospects. But these advantages may be limited to a very small number of firms, while other firms in the industry may lose market share.

3. No single factor or group of factors explains Maine's current marine biotechnology companies.

Maine's current marine biotechnology companies have arisen from a variety of personal and organizational circumstances. It is thus difficult to pinpoint a set of factors upon which future support policies can be confidently based. Maine's current marine biotechnology companies have assembled the elements of their current success from a variety of resources both in state and out of state. For example, funding has been obtained from both public and private sources, and from a variety of federal agencies.

While the ocean waters of Maine are an important source of material for research and development, it is unlikely to be the production source for compounds of interest in the pharmaceutical or specialty chemical business. Industries such as nutraceuticals, however, may need a well managed resource for sustained production of natural products.

4. Maine currently supplies some ingredients for the success of firms developing marine biotechnology, but important ingredients are lacking.

Marine biotechnology firms report access to important business support services, particularly those located in southern Maine. Financial barriers to innovation have been reduced by the availability of funding for commercialization from MTI. The state has considerable research resources in aquaculture and marine science. But some of the important sources of locational advantage for firms in marine biotechnology appear to be

absent in Maine. The University is not currently a major source of the advanced education of people in the firms that serve the biomedical sector, and several firms report difficulty obtaining trained personnel. The University also does not serve as a major source of research and innovation in the biotechnology field. Private and public research efforts are geographically dispersed and fragmented.

5. Competition to create marine biotechnology industries elsewhere are somewhat ahead of Maine, but have not yet achieved a level of success that would either limit Maine's future or clearly show the possibilities of success.

Looking at other centers or potential centers for marine biotechnology in Massachusetts, Maryland, Florida, and California, it is apparent that no region has yet achieved the kind of distinct regional advantage in this area that has been achieved in other areas of biotechnology or electronics. However, other states, notably Maryland and California, have devoted significant resources to establishing such centers.

Based on these findings, it is possible to revisit the model of cluster development laid out at the beginning of this study. There, four transitions were identified as the key mileposts along the road to a successful regional economy based on technologically innovative industries:

1. Research \dot{y} Products
2. Products \dot{y} Firms
3. Firms \dot{y} Industries
4. Industries \dot{y} Clusters

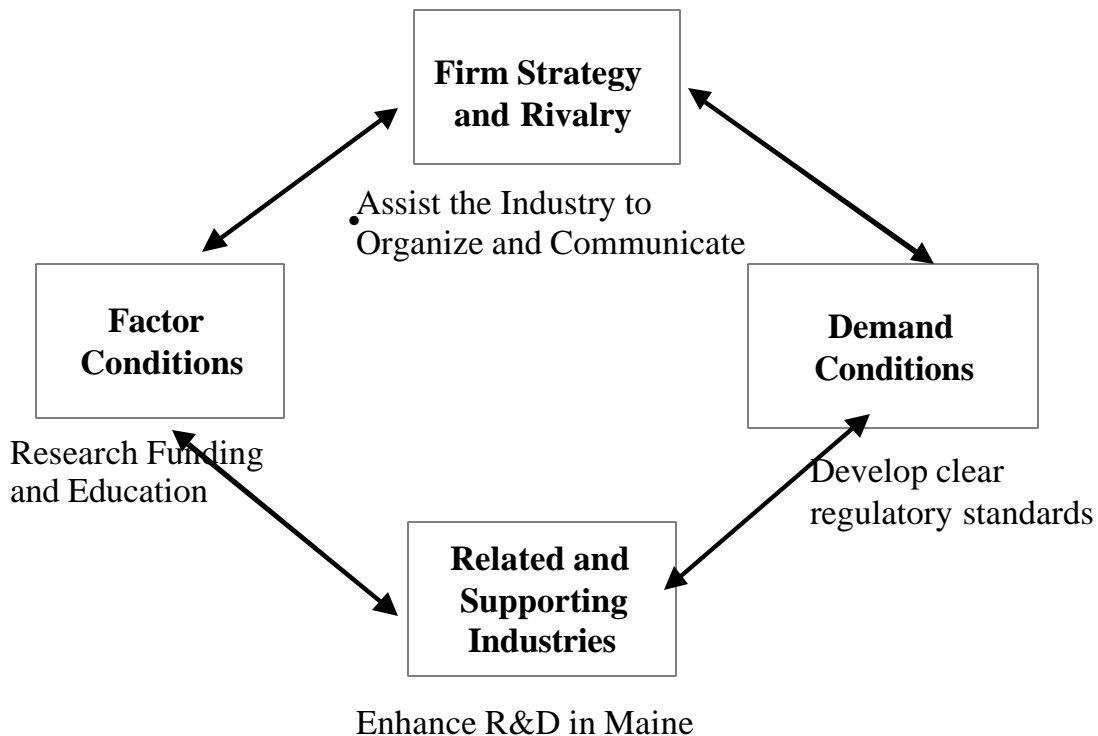
It is apparent that marine biotechnology in Maine today is primarily concentrated in the first stage, with some transitions to the second. The transition to industry or cluster is still some time away. Because of this, it is too early to tell at what point a critical mass of firms in marine biotechnology will be reached that will create a self-sustaining cluster of economic activity. However, it is possible to point some general directions that may be used to shape and assess future development in this field.

Supporting Growth in Marine Biotechnology

The evolution of the current activity in marine biotechnology into a self-sustaining cluster will take place over a number of years. While we cannot be precise about when critical mass will be reached (and may never know until after the fact), the evolution will take place over the next two decades. The rapid development of new knowledge and technologies in this field may speed the process to some extent. State support can help the process to some extent. The suggestions below are framed again in

the Porter “diamond” framework. We also re-emphasize that marine biotechnology should not be treated separately from biotechnology in general. Our recommendations can just as easily apply to the larger field of biotechnology development even though they are presented in marine biotechnology context.

Enhancing Marine Biotechnology in Maine



Enhance R&D in Maine

Despite dramatic growth in state dollars in research and development over the past five years, there is no doubt that Maine, as a small state, cannot invest in research at the same level as larger states such as Maryland and California. Maine continues to lag other states in research funding, so much remains to be done. Some gap will always exist, but it is essential that Maine sustains the current level of effort and further expands it. Large investments in research funding are best made during periods when state revenues exceed expenditures for other programs. Proposals are under consideration for presentation to the next session of the legislature that will continue the commitment that has been made

Current marine biotechnology firms indicate that the University of Maine is not a major source of either research or personnel. This is not surprising, since marine research at the University of Maine has been focused on other areas of the marine sciences. To the

extent that it has been connected with marine industries in Maine, it has been connected to traditional fisheries concerns of biology and physical oceanography. This is entirely appropriate and must be continued.

If the University of Maine, and the University of Southern Maine are to play an expanded role in support of marine biotechnology, it must be through expansion of existing programs through hiring new faculty. This point cannot be over-emphasized. Scientific research in any field is by its nature highly specialized and can only be undertaken by people who themselves are highly specialized by training and experience. The freedom to research in one's chosen area is also essential to successful research enterprises. It is this freedom that motivates people to work in areas of personal interest and to pursue research through the many failures that mark the progress of any research endeavor. The ability to work in areas of personal interest was one of the key factors cited by marine biotech entrepreneurs in their decisions to come to Maine and start their own companies. It is thus both very difficult, and usually counterproductive, to simply direct that existing resources be redeployed to new areas. The path to expanding research in new areas in the university is to hire the best and most promising researchers and provide them with the tools to do the job.

It is also important that new resources be for faculty, not only for "soft money" researchers. The interaction between teaching and research is particularly critical in the natural sciences and equally critical to creating *both* the research and the trained workforce that together comprise essential ingredients to a cluster. Effective research is a team endeavor between the senior researcher/faculty member and the junior researcher/student. This team approach is the foundation for much of the success of the modern American university. Researchers who are teachers are also essential because Maine must expand the pool of skilled labor in the biotechnology fields if it is to have any hope of establishing itself in the biotechnology and marine biotechnology fields.

Currently biotechnology is the only one of the State's targeted growth industries that has no training program through the Quality Centers. Our results suggest that the current supply of trained personnel is inadequate to meet the potential growth in the biotech industry in the state. No specific recommendation about dollars or personnel or even specific fields is made here. These are matters for discussion among university and state officials.

We also note that the one area of worldwide marine biotechnology that does not appear to be present in a major way in Maine is research on biofouling. It may be that Maine's cold waters and harsher climate (which encourages boats to be removed from the water for the winter) limits the local demand for research in this area. Biofouling is generally a much more significant problem in warm waters, and much of the research takes place there. However, this may be an area where Maine's colder waters might provide a specific niche for research which might be encouraged.

R&D Funding

Our research indicates that both the Maine Technology Institute and the federal Small Business Innovation Research (SBIR) program are playing a key role in fostering the growth of entrepreneurial companies that use marine biotechnology, as the majority of companies surveyed have accessed funds from one or both programs. Sustaining and increasing access to these programs is essential, particularly SBIR grants, an area in which Maine lags the rest of the country. With support through such organizations as FAME and the Small Business Development Centers, Maine has an array of support services for small businesses in general and for firms involved in technology development in particular. Again, sustaining these efforts is essential.

It is also clear that the National Institutes of Health are, and will be for some time, the single largest source of potential funding for research in this area. Outside of Jackson Laboratories, which is not a player in the marine biotechnology field, Maine is not significant recipient of funding from this major source. Any significant expansion of R&D efforts should explicitly address both this deficit and the means to reduce it, while recognizing that Maine is not likely to become the home of a new medical school, which is elsewhere the single largest factor in attracting NIH funding.

Organizing Biotech and Marine Biotech

All companies contacted for this report were interested the concept of cluster development, particularly because of potential opportunities for idea exchange and collaboration. It could be beneficial to enhance opportunities for interaction between entrepreneurial companies, through support for local forums or conferences on marine biotechnology or biotechnology innovations. As the interviews showed, the pressures of operating a small business combined with the specialized markets that current firms serve, makes it difficult for existing companies to interact with one another. Forums can provide ways for entrepreneurs to gather information on a variety of subjects, such as the requirements for commercialization of products in business fields in which they lack experience. The Biotechnology Association of Maine (BAM) or the Center for Innovation in Biotechnology (CIBT) could play a key role in this regard. It may also prove advantageous to establish working groups for marine biotechnology that can facilitate networking and business attraction activities.

Setting Regulatory Policies

Biotechnology remains a young field, and there is much that is unclear about what the needs for government regulation will be in the future. As Porter (2000), points out, however, in his studies of economic clusters, the key to government regulation's role in economic development is its predictability. Whatever the rules are going to be, set them early and stick to them. There is at least one area, and possibly more, where early state regulation might be important to expansion of marine biotechnology in one area. This is in the field of transgenic species, particularly the use of transgenic fish in aquaculture. Concern over the possible contamination of the natural gene pool with genetically altered species has led some governments, notably Canada, to impose strict rules requiring the

isolation of research processes involving transgenic species. It may be in Maine's interest to investigate the Canadian or other experience with the development of appropriate safeguards for transgenic marine species research and/or production and adopt the appropriate regulatory frameworks as early as possible.

State government has also worked effectively with a number of industries in developing regulatory structures and approaches that do not hinder commercial growth while achieving regulatory goals. This approach will be particularly important in marine biotechnology and biotechnology, which are highly dynamic and must respond quickly to the rapid technological changes occurring in this field. Working proactively with groups such as the Biotechnology Association of Maine on impending issues such as transgenic species and genetically modified organisms may be important to define effective and flexible regulatory strategies. Given the strong public reaction to the idea of genetically modified foods, it will almost certainly make for more considered and effective regulation if regulatory development takes place accompanied by an extended and extensive period of public education and discussion, rather than in the potentially heated atmosphere that often surrounds a specific proposal.

This report has summarized both the strengths and weaknesses of marine biotechnology in Maine today. There is a long road ahead before marine biotechnology, or biotechnology in general, reaches any kind of sustainable size in the Maine economy. But the small size and long development road for marine biotechnology should not obscure the fact that Maine has a larger concentration of activity in this field than many other states and the field is still in its infancy with enormous potential ahead of it. Maine has both strengths and weaknesses to work with as the industry develops, and there does not appear to be any insurmountable barrier to marine biotechnology and biotechnology as a whole becoming an ever-more important part of the Maine economy in the future.

Monitoring the Growth of Biotechnology in Maine

The fate of marine biotechnology in Maine cannot be separated from the biotechnology industry in Maine. Marine biotechnology in Maine will remain a field of isolated and small companies if the biotechnology industry in Maine does not grow. Because of the small number of firms involved in marine biotechnology, it is unlikely that these companies by themselves will be the answer to job creation in Maine. The larger biotechnology industry in Maine, with 70 companies and annual revenue growth of 20% per year (1997, CIBT) plays a major role in the creation of high wage jobs in the state.

Biotechnology is also in its infancy, with a number of firms and organizations still in the early stages of establishing their presence in this fast-changing field. Maine is also undertaking a number of initiatives to advance biotechnology in Maine, including new centers of research at the University of Southern Maine and support for biotechnology companies through the Maine Technology Institute. Tracking growth in biotechnology in Maine as a whole will shed much light on the growth of marine biotechnology.

Expansion of existing companies in Maine and elsewhere

The fate of the current nucleus of marine biotechnology companies in Maine should be monitored. In particular, the success and growth of these companies will determine whether Maine becomes known in the biotechnology community as a place to do business, particularly when marine inputs are needed. When appropriate to the company's strategy, movement towards large-scale production of goods and services will be important. This may be measured in part by employment growth. It will obviously be preferable from Maine's point of view if employment growth associated with production takes place in the state. But it may be just as important for the future of biotechnology and marine biotechnology in Maine that early entrants are seen as successful firms even if production does not take place in Maine. Success breeds success, and in the early years it is more important that Maine firms be successful (including getting to the point where they are acquired by non-Maine firms) in order to inspire additional growth.

Development of new entrepreneurial companies

The current pioneers of marine biotechnology must be followed by others. There does not appear to be any single factor which will, in the near future, assure that this takes place. Over the longer term (five years or more), the various investments in these areas by the state and university will begin to bear fruit and begin to be evaluated. It is not possible to definitively identify a minimum rate of growth of new firms, but the current number of smaller biotechnology firms in Maine specializing in or making a major commitment to using marine inputs should at least triple over the next 5-10 years if this field is to become an established part of the Maine economy.

Research activity

The flow of research dollars into Maine to support additional basic and applied research related to marine biotechnology is the single best short-term indicator of future potential. Some funds may be monitored when they come from public sources such as NSF, NIH, or MTI. Other funds will come from private sources and cannot be easily monitored except through regular contact with firms in the field. Attracting private research dollars is another key indicator, since private dollars are usually subject to risk/reward calculations. Expanding private research investments, whether measured in absolute dollars or relative to the amount of public dollars, will be another key indicator of evolving success.

REFERENCES

Business Week, 2000, 1/10 Industry Outlook – Healthcare <http://www.businessweek.com>

Center for Innovation in Biotechnology - <http://www.cibt.org/news.htm>

Colwell, Rita. 1984. "Biotechnology in the Marine Sciences" in Colwell, Sinskey, and

Pariser, *Biotechnology in the Marine Sciences*. New York: John Wiley.

de la Mothe John and Gilles Pacquet, 1998 “Local and Regional Systems of Innovation as Learning Socio-Economies” in de la Mothe and Pacquet. *Local and Regional Systems of Innovation* Boston: Kluwer.

Ernst and Young, 2000 *The Economic Contributions of the Biotechnology Industry to the U.S. Economy*, May 2000, <http://www.bio.org/news/ernstyong.pdf>

Hill, Edward W. and Brennan, John F. 2000. “A Methodology for Identifying the Drivers of Industrial Clusters: The Foundation of Regional Competitive Advantage”. *Economic Development Quarterly*. Vol 14 No. 1, 65-96.

Feser, Edward J. 1999. *Regional Growth and Industry Clusters in the Scranton-Wilkes Barre-Hazleton (Pa.) Metropolitan Statistical Area*. Chapel Hill, N.C. Batelle Memorial Institute.

Florida, Richard. 1998. “Calibrating the Learning Region” in de la Mothe and Pacquet.

Mokry, Benjamin W. 1988. *Entrepreneurship and Public Policy: Can Government Stimulate Business Startups*. New York. Quorum Books.

National Academy of Sciences, 1999. “Marine Derived Pharmaceuticals and Related Bioactive Agents” in *From Monsoons to Microbes: Understanding the Oceans Role in Human Health*, National Academy Press, Washington D.C.

Nutrition Business Journal, January 1999, *Complementary and Alternative Medicine*, <http://store.yahoo.com/nbj/jan19comalme.html>

Padmore, Tim and Hervey Gibson. 1998. “Modeling Regional Innovation and Competitiveness” in de la Mothe and Pacquet.

Porter, Michael, 1998. Clusters and competition: New agendas for companies, governments and institutions. In M. Porter *On Competition* (pp.197-287). Boston: Harvard Business School Press

Porter, Michael, 2000. “Location, Competition and Economic Development: Local Clusters in a Global Economy” *Economic Development Quarterly*, Vol. 14 No. 1

PricewaterhouseCoopers, 2000. *Moneytree Report: Venture Capital Investment in the U.S. 1999*. <http://204.198.129.80/pdfs/reportq499.pdf>

Saxenian, Annalee. 1994. *Regional Advantage: Culture and Competition in Silicon Valley and Route 128*. Cambridge: Harvard University Press.

State Planning Office, 1998 *An Initial Review of Maine's Academic and Non-Profit Research Assets*

United Nations Food and Agriculture Organization, *Trends in Global Aquaculture Production, 1984-1996* <http://www.fao.org/fi/trends/aqtrends/aqtrend.asp>

U.S. ITO 2000. *Industry and Trade Outlook, 2000*. McGraw Hill Publications, NY, NY

Authors

Charles S. Colgan is Professor of Public Policy and Management and Chair of the Graduate Program in Community Planning and Development in the Edmund S. Muskie School of Public Service. He served as Director of Economic and Natural Resources Policy and State Economist in the Maine State Planning Office in the administrations of Governor Joseph Brennan and Governor John McKernan.

Colin Baker is a Maine native and recent graduate of the Masters program in Community Planning and Development at the Muskie School. He worked for a number of years in planning and engineering in Massachusetts and Colorado, and is currently working on economic development projects here in Maine. He resides in Freeport.

