Entrepreneurism in the Academic Setting

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"The future belongs to the entrepreneur."
Anonymous

INTRODUCTION
Entrepreneurism is a term not usually associated with a university, even though it is taught to students in its business, pharmacy(1), and other professional or graduate schools. Businesses and business men and women must have an entrepreneurial spirit to ensure their continued growth, but universities generally have not found it necessary to undertake such actions. However, the significant reductions in the income of universities brought on by the recent recession and other factors have triggered institutional entrepreneurial actions. Directed at academic, research, and service programs, such innovative actions have ranged from broad institutional initiatives to those of individual faculty members. This chapter will primarily review what is most often thought to be academic entrepreneurship—actions that are meant to increase individual or institutional profit or prestige through the development and marketing of research ideas or products(2).

DEFINITION AND HISTORICAL BACKGROUND
It is the author’s hope that each of the readers has had the privilege of participating in a snipe hunt. Some 40 years after my first and last snipe hunt, I agreed to collect a few books on the subject, entrepreneurism. That hunt helped me understand why most of the recent texts on the subject repeat the story first used by Peter Kirby in 1971(3). He, of course, got it from Winnie the Pooh. It is repeated here because it best explains the state of affairs in the precise use of entrepreneurism.

“The search of the source of dynamic entrepreneurial performance has much in common with the hunting of the Heffalump—a large and rather important animal hunted by many individuals using various ingenious trapping devices, but no one has succeeded in capturing him. Some hunters have used as bait their favorite dishes and have tried to persuade people that what they have caught was a Heffalump. Few are convinced and the hunt goes on.”

Derived from the French verb, *entreprendre*, meaning to undertake, entrepreneur has been used to name a wide variety of persons. In the 16th century, it referred to Frenchmen who organized and led military expeditions. Two centuries later, it was applied to contractors who built bridges and roads. As late as 1897, the *Oxford English Dictionary* defined it as manager of a public musical institution(4).

Jean Baptiste Say, in 1816, first used the term in an economic sense. However, a clear definition of the term was still not established. For example, in 1885, F.A. Walker suggested that “the control and the direction of capital and labor are so difficult that a distinct class is called into being in all advanced industrial communities to ‘undertake’ that function.”(5) Since the word English word “undertaker” had already been assigned to another important functional activity, we must assume that the French word, entrepreneur, as used in the 20th century by Cantillon(6) to define the new “employing class,” and by Schumpeter in establishing entrepreneurism as a vital process in economic development(7), has been impossible to replace in the English language.

Hebert and Link(8), in their text, *The Entrepreneur*, reviewed the several theories of entrepreneurism that have evolved since the late 1700s. Listed in their order of evolution, they are:

1. The entrepreneur is one who assumes the risk of uncertainty.
2. The entrepreneur is a pure innovator.
3. The entrepreneur is a combination risk taker and innovator.
4. The entrepreneur is a decision maker who allocates resources to alternate uses.

More recently, Carson(9) proclaimed that, for the most part, economists have surrendered the defining of entrepreneurial action to sociologists, psychologists, and political scientists. Some of his conclusions include:

1. Entrepreneurism appears as a personal quality

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1 Reprinted from the Academic Management Series, American association of Colleges of Pharmacy. Alexandria VA.
which enables certain individuals to make decisions with far-reaching consequences.

2. Entrepreneurs typically operate as a minority of one that is right, surrounded by a majority that is wrong.

Peter Drucker breaks the mold in his book, *Innovation and Entrepreneurship* (7). Peter Kirby and the Heffalump are not reinforced, but Drucker certainly puts it on the plate. As he points out, entrepreneurs “... create something new, something different; they change or transmute values... [they] see change as the norm and healthy... the entrepreneur always searches for change, responds to it, and exploits it as an opportunity.” He notes that, “Innovation is the specific instrument of entrepreneurship. It is the act that endows resources with a new capacity to create wealth.”

Many relate entrepreneurship only to the business world, but a number of authors point to the creation of the University of Berlin by Wilhelm von Humbolt as a major example of such an action. It gives us clues to the common threads that weave the fabric of entrepreneurial activity. The modern university (one that has been frequently copied) was created by Humbolt, a Prussian diplomat. He created the University of Berlin in 1809 to a backdrop of chaos and no resistance, when the traditional university of the 17th and 18th century had been destroyed by the French revolution and the Napoleonic wars. It was indeed innovative and resulted in the transfer of intellectual, scientific and political leadership from France to Germany.(10)

**CHARACTERISTICS OF AN ENTREPRENEUR**

The use of the word entrepreneur often engenders stereotypical visions of a brash, cigar-smoking man with an ego as big as his latest acquisition. But not all entrepreneurs are men or smoke cigars. The characteristics of such individuals have been identified by various writers. Taffi’s list(11) has been modified to contrast the positive and negative aspects to allow a manager to recognize entrepreneurial talent and hopefully to provide some tolerance to support the entrepreneurial activities of a subordinate.

**Positive**

**Planning.** A risk taker, but not an irrational gambler—contingency planning is six months ahead of subordinates. Can move right, left or reverse on a moment’s notice.

**Pragmatic.** Deals with the world as if it is not as they would like it to be. Above average intelligence. Can see the “big picture.”

**Mentally.** Has a high threshold of emotional stability. Tragedies managed to minimize impact on efforts.

**Physically.** Inexhaustible resources of energy. Only a severe illness will keep them from the work place.

**Other Characteristics.** Perseverant, creative, competitive, strong desire to succeed, great enthusiasm for product and service.

**Negative**

**Relationships to Others:**

**Superiors.** Demands tolerance, obstinate, and will not communicate freely, disruptive on purpose.

**Peers.** Exhibits an inability to work with peers, unwilling to surrender work environment.

**Subordinates.** Very demanding, high energy level, can be devastating to those who become part of the team.

**ENTREPRENEURISM IN THE UNIVERSITY**

Drucker(13) suggests that a university may need to be more entrepreneurial and innovative than for-profit businesses. His example suggests that rapid change is more of a threat, and yet represents greater opportunity, to a university or other public service institution than it does to the traditional business. But for the manager of such an institution, the caution flag is always out if we are to learn by history dating back to Humbolt’s innovation. Many real innovations that have been developed in the not-for-profit sector have come from outsiders and/or are accomplished in the vacuum resulting from a catastrophe. The recent drastic budget cuts present such an opportunity.

Entrepreneurship is often thwarted in a university by forces that are inherent to it. The many obstacles include:

1. **Its budget, rather than profit, is its measure of success.** Success is measured by budget size, results are difficult to quantify, tradition assures that we keep the old and add the new to keep the budget growing.

2. **It serves the masses.** This policy allows the university to have a multitude of constituencies to serve, thus striving to satisfy all and alienate none.

3. **It holds to a “do good” mission.** This serves a very high purpose with little or no need to define “better.” It gives a perfect defense for doing good whether it is a success or not. The notion of doing something else (innovation) is an attack on the basic commitment, values and beliefs of the institution (13).

The development of a set of policies that allows for change in a university may be one of the foremost political tasks of the generation. At first glance, the following list of policy statements appears to be a rehash of mission and goal statements that have been the manager’s milieu for the past three or four decades. Indeed the possibility exists that the average academic manager might be more comfortable with the preceding list of obstacle statements than the following:

1. **The Mission Statement**
   The focus is on the objective, with programs and projects as short-term means to an end.

2. **Realistic Goals**
   Goals should be stated in terms that will, lead to a statement that “the job is finished.”

3. **Accept Failure**
   Failure to achieve an objective is prima facia reason to question the validity of the objective. This is the exact opposite of what most of us have been taught and the practice in a university. “If at first you don’t succeed.”

4. **The Opportunity to Change**
   Viewing change as an opportunity requires that the organization has an ongoing search for innovation in the changing environment.

On the last point, Lew Lehr, retired chairman of the 3M Corporation, noted, “Innovators and their mentors are the key to renewal of an organization. And we don’t have to
look for them. They’ll find us if we let them.” This comment is a lead to an article by Leland R. Kaiser(14) that describes research and development programs in hospitals. It gives the hospital administrator and trustees an action plan for managing within a policy statement that declares, “Opportunity is Change.”

Universities generally have not been successful entrepreneurs, and a study by Louis, et al.(15) suggests that university policies and structures have little impact on faculty entrepreneurship. Their study of major research universities was based on surveys of faculty and administrators conducted in 1985. Key determinants of entrepreneurship revolve around the characteristics of the individual researchers. The authors noted that, “Many scientists still believe that the search for truth is inconsistent with any interest in profiting from ideas.” It is clear that the development of a strong entrepreneurial thrust by an institution must carry with it the commitment of its key faculty research leaders.

The evidence is also clear as the decade of the 1980s unfolded that an awareness of new opportunities was becoming evident. Alistar Brett, the director of technology management and transfer at Virginia Polytechnic Institute, Blacksburg, summed it up, “many universities are recognizing that their research base has more commercial value than they realized”(16).

FACULTY ENTREPRENEURSHIP

The paper by Louis, et al.(17) divided academic entrepreneurship into five categories. They form a useful outline for the subsequent discussions in this paper. The types include: large-scale science, earning supplemental income outside the university, industrial support for university research, patenting, and direct commercial involvement. Their data were for the 1984-85 academic year.

1. Large-Scale Science
   This category involves the obtaining of large, externally-funded research projects. The median level of direct costs was $195,000 per year. The top 20 percent of the faculty got $250,000 or more per year, while ten percent of the faculty got $3,000 or less.

2. Supplemental Income
   This related mainly to consulting, with a median income of $4,843, with 27 percent of the faculty consulting for profit-making companies.

3. Industrial Support for University Research
   Only 23 percent of life science faculty members received funding from industry, but it was noted that “scientists who obtain money from this source are more likely to select research problems because of their commercial applicability.”(18)

4. Patenting
   Since the mid-1980s, there have been some new “box scores” appearing in the media. While it has been usual to see the results of higher education’s efforts in the sports pages, these scores were reported in the financial sections:
   MIT 66
   Northwestern 10

They were the number of new patents issued during the calendar year. One year later the same newspaper reported the ten research universities that received the most patents in 1989(16).

They were:

- MIT 102
- U. Calif. 81
- Cal Tech 59
- U. Texas 51
- Stanford 43
- U. Florida 42
- U. Minn. 41
- Iowa St. 28
- U. Wise. 28
- Johns Hopkins 27

The survey by Louis, et al.(19) revealed that 19 percent of the faculty had applied for or had been granted a patent or had generated a trade secret. One of the events that stimulated the increase in patent applications was a change in the federal law that allowed universities to retain the rights to inventions that were developed from federally-funded research projects.

5. Direct Commercial Involvement

This category involves the formation of a private firm whose products are based on the university scientist’s own research. The Louis study noted that seven percent of the faculty in the top research schools held equity in such companies(2).

In the preceding decades before the 1980s, universities were, in general, only mildly positive about the role of faculty in technology transfer, and gave little support to fostering the notion of entrepreneurship that was directed toward private enterprise. The author’s first direct negotiation with industry occurred in 1968 when the Alza Corporation established the Alza Institute of Pharmaceutical Chemistry in Lawrence, Kansas, with Professor Takeru Higuchi as its director. At its time it was a remarkable event.

THE UNIVERSITY/INDUSTRY INTERFACE

Many words have been written on the rewards and risks of joining the two very different cultures of academe and industry. One seeks knowledge and understanding in an atmosphere of open and free dialogue, the other seeks market share and profit with trade secrets and patent protection. Some notable examples of joint ventures include:

1. University-Assisted Research Parks
   - The University of Utah coined the term “academic capitalism” and allowed up to 10 percent equity positions in new start-up companies and royalty arrangements for faculty involved in innovative technology transfer.
   - Boston University directly invested $49.2 million in Seragen Inc., a biotech start-up company.
   - The University of Florida used venture capitalists to form Pharmatec Inc., and located the corporation in its research park.
   - The University of Kansas Endowment Association started a bioanalytical service corporation, Oread Laboratories Inc., and located it in a university research park.
2. Entrepreneurial “Cherry Picking”
There are private entrepreneurs that, in the words of the business world, “cherry pick” among faculty innovators.

- Professional entrepreneur, Michael Wall(20), founder of 19 new ventures, started Centocor Inc. in 1979 using 30 university scientists to ensure a steady stream of diagnostic and therapeutic products based on monoclonal antibody technology. He started Alkermes Inc. in 1988 with five scientific collaborators. It was a corporation dedicated to products that deliver drugs across the blood brain barrier.

3. The Individual Deal
In some cases, it appears that the faculty member can be a part of both worlds.

- “The Man Who Made Millions by Marketing Monoclonal Antibodies”(21) reports on the sale of the Hybritech Corporation to Eli Lilly and Co. in 1986 for a reported $480 million. The entrepreneur retained his faculty position throughout the life of the company and the sale of the company.

ACADEMIC ENTREPRENEURIAL CASE STUDIES
As part of this review, the authors felt that it would be instructive to go beyond the rhetoric and collect a series of case studies which are representative of academic entrepreneurship in our colleges of pharmacy. These case studies were selected to go beyond the more common forms of academic entrepreneurship, such as consulting, industry-sponsored contract research, big science projects, transfer of technology (patenting) and other products of scholarship (copyrights). Examples include: (i) academic research and development or educational centers in cooperation with government and/or industry; (ii) revenue-generating units; and (iii) commercial corporate developments.

Not everyone was interested in sharing the details of their ventures—some because the road was rocky, and others because of confidentiality. It is important to note that, despite the pitfalls, many successful, revenue-generating ventures have been developed in our colleges (See Appendix).

CAUTIONS
There are many issues that must be faced for joint ventures between universities and industry to succeed. Some are related to general academic attitudes that consider the central work of the university to be teaching and research, not research and business; or that the traditional reward for the academic scholar has been peer credit for their recognized work, not dollars from economic gain.

Another stumbling block is that academic science and business do not mix because the ideas become proprietary and the central academic notion of free exchange of knowledge grinds to a halt. Other caution signs that have appeared include how profits are best distributed, faculty reward, and conflict of interest.

The often disparate goals of academic institutions and industry can lead to serious conflicts of interest. University faculty are generally considered responsible for finding new knowledge and making it available to their colleagues and to the public as quickly as possible. Any such information should be freely disseminated. Industry, on the other hand, has a responsibility to its investors to bring a product to market quickly, but generally requires secrecy in order to protect their intellectual property until their rights can be secured.

The specter of conflict of interest must be kept at arms length by a university policy that protects the independence of faculty research as well as its patent rights, while clearly defining academe-industry lineages in terms of investigator’s financial ties, equity limitations, royalty agreements, consultation relationships, and publication policies.

REWARDS
The rewards for closer relationships between academe and industry accrue to society, the university, the faculty member, and the industry itself. The economic development that can occur from such entrepreneurial action benefits all in the region. Newly-created technologies lead to new industry and job formation. Hullar(22) sums up the early 1990s by noting that, “This country’s economic health as well as its standing in an increasingly competitive world—depend on the expeditious development of basic research findings into commercial products and valuable products.” He and others proclaim that where the ties between academia and industry are by tradition much stronger, such as Japan and Germany, through special agencies and institutes, that the power of collaboration yields economic strength.

The generation of income for the institution helps to revitalize hard-pressed teaching and research facilities. The American research university has, since the 1950s, been expanded by a series of public, and to a limited extent, private support systems. The decade of the 90s begins with a nagging promise to reduce funding from the sources that are now looked upon by many as traditional—federal and state funds as well as the upward adjustment of tuition to offset increased cost and needs for expansion. But it comes to us on the heels of the 80s with its promise of profits from economic development and the increase of private industry funding. The benefits promised to both industry and the academic institutions may be as simple and straightforward as survival to high profit and great prestige in the world of private enterprise. The risks to the academic community are the loss of open and free exchange of ideas and the loss of collegiality, shifts in the measure of successful behaviors that break with theacademic tradition, and the stress of serving a new and very different set of clients.

SUMMARY
American universities have been engaged for the past decade or more in a shifting pattern of activity that extends the responsibility of its faculty and administration beyond the traditions of teaching, scholarship (the development of new knowledge) and service. Universities have been encouraged by both the public they serve and by private industry to promote the transfer of knowledge to the public in the form of new services, products and the creation of new jobs for the region that the institution serves.

The institutions and the faculties have responded to this call. The characteristics of the entrepreneur have been noted and several models of university responses have been detailed. As these activities have increased, so have the concerns about the definitions of conflict of interest.

In summary, it is obvious that the process is continuing,
the public is being served by improved and timely introduc-
tion of new products and services from the academic com-
munity. New jobs are being created. But as it continues, the
traditions of a conservative institution are being challenged
by the actions of “Academic Entrepreneurship” as an
increased number of faculty and institutions deliberately set
out to collect both profit and prestige by marketing intellec-
tual property in the form of products and services.


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APPENDIX. CASE STUDIES

FORMATION OF A PHARMACEUTICAL COMPANY

PHARMATEC

(University of Florida)

Pharmatec was incorporated under the laws of the State of
Nevada in December 1982 in order to commercially exploit novel
methods in drug delivery to the brain and central nervous system
(CNS). The core technology around which Pharmatec crystallized
was pioneered by Professor Nicholas Bodor of the University of
Florida’s College of Pharmacy. This technology involves the chemic-
ical manipulation of a drug to enhance its bidirectional movement
through the protective blood-brain barrier (BBB). The ostensibly
protective barrier system effectively excludes many potentially
useful drugs, including antibiotics and anticancer agents. The
chemical delivery system (CDS) methodology acts to non-invasively
circumvent the BBB, thereby increasing the efficacy of the drug
and, at the same time, reducing the toxicity of the agent. Subse-
quent to publication of the method and of the initial proof of
concept in the journal science, several venture capitalists ap-
proached the University of Florida to secure rights to the technol-
ogy in exchange for providing a capital infusion to fund research
and development. The results of these negotiations were that Loeb
and Company obtained rights for the technology and soon there-
after founded Pharmatec. Loeb and Company then transferred
the patent license to Pharmatec, in exchange for which Pharmatec
granted Loeb and Company a substantial equity position. Under
the License Agreement, Pharmatec was obligated to pay the
University a royalty of 3 percent of annual sales up to $20,000,000
and 2 1/2 percent of annual sales exceeding $20,000,000. In addi-
tion, Pharmatec promised to devote $6,000,000 to the develop-
ment of the CDS over a five-year time span. Of these monies,$1,000,000
was earmarked for unrestricted research at the University of
Florida College of Pharmacy. Pharmatec completed its initial
public offering on August 5, 1983, raising 3.3 million dollars.
Pharmatec fulfilled its obligation and funded further work at the
University subsequent to the first five-year obligation.

Since its founding, Pharmatec has been assiduously working
to develop the CDS. It has been successful in attracting funding
from the U.S. Government through the SBIR program and U.S.
Army, as well as from larger pharmaceutical houses such as Pfizer.
Burroughs Wellcome and Nova. The technology has developed to
the point that one of the CDSs, a system based on estradiol, entered
human clinical trials in 1988 and a variety of other systems are in
preclinical development. In 1992, Pharmatec entered into a merger
agreement with Pharmos, an Israeli-based formulations
development company.

Nicholas Bodor, PhD, DSc
Graduate Research Professor and
Executive Director
College of Pharmacy
University of Florida

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CENTER FOR BIOCATALYSIS AND BIOPROCESSING
(The University of Iowa)

This program developed as a result of a faculty-based interdisci-
plinary effort in 1983. The faculty group focused on the area of
biocatalysis and formed a discussion and seminar group. The group
developed state-of-the-art fermentation facilities, focused recruit-
mment in several departments, and received support for an endowed
professorship from the State of Iowa. Since 1987 the Biocatalysis
Research Group has grown to include 37 faculty members from six
departments (Biochemistry, Chemical and Biochemical Engineer-
ning, Chemistry, Civil and Environmental Engineering, Medicinal
and Natural Product Chemistry and Microbiology). In 1990 the
Iowa Regents recognized and funded the Center for Biocatalysis
and Bioprocessing in the State of Iowa. The Center is developing
an Industrial Affiliates program which is in the early stages of
growth and development. This group is central to the “technology
transfer” focus in Iowa and is expected to be funded in the order of
$2,000,000 per year by the State of Iowa in the next two years. This
will allow further facilities development and recruitment of an
executive director.

John P. N. Rosazza. PhD
Professor and Head, Medicinal and Natural
Products Chemistry and Director, Center
for Biocatalysis and Bioprocessing

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DIVISION OF PHARMACEUTICAL SERVICE
(The University of Iowa)

The Division of Pharmaceutical Service is one of the few Food
and Drug Administration-registered pharmaceutical manufactur-
facilities associated with a college of pharmacy in the United
States, and is the only such facility that actively produces most
types of pharmaceutical dosage forms for clinical use. It occupies
The current full-time staff includes four PhD scientists, four registered pharmacists, two bachelor-level scientists, an accountant, 17 technicians, and two clerical workers. Current part-time staff includes several graduate and undergraduate students. In association with the faculty of the College of Pharmacy, the Division offers the following pharmaceutical research and development services and clinical supply production capabilities:

Research and Development Activities
- Preformulation studies of the physicochemical properties of substances
- Studies of drug-excipient interactions
- Formulation and process development
- Packaging suitability
- Formulation stability testing
- Specialized dosage form development

Clinical Production Capabilities
- Sterile injectable solutions, emulsions, and suspensions
- Lyophilized preparations
- Topical and oral solutions, emulsions, and suspensions
- Ophthalmic and otic preparations
- Tablets (uncoated, and film or sugar-coated)
- Hard gelatin capsules
- Production of hazardous drug products in a special isolation facility
- Unit dose injectables and oral products
- Packaging of products for blinded or non-blinded studies

Gilbert S. Banker, PhD, Dean
College of Pharmacy
The University of Iowa

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THE HIGUCHIBIOSCIENCES CENTER OF EXCELLENCE
OREAD LABORATORIES, INC.
(University of Kansas)

In the Fall of 1983, the University of Kansas created a research center in bioanalytical chemistry in response to a then new state initiative for economic development. The funding from the state’s resources required a 150 percent cash match from a for-profit partner. The university turned to its endowment association for the creation of a for-profit corporation.

In the nine years that have intervened, both the university’s center and the for-profit corporation have transformed into separate and expanded activities. The model of the founder, T. Higuchi, has in a way been followed. He believed that a new creation will have good value if you let it grow naturally and are willing to assume a very flexible plan for its growth.

The university center of excellence is now called the Higuchi Biosciences Center. It is about to be housed in a new laboratory facility. It has several additional centers of activity in addition to its original bioanalytical center. It is still supported by the Kansas Technology Enterprise Corporation as a center of excellence for economic development in the area of biomedical and pharmaceutical technology.

Oread Laboratories now has over 100 associates and offers preclinical services to the pharmaceutical and biotechnology industry. The services include formulation, analytical, synthesis, and absorption, distribution, metabolism and excretion (ADME) services to the domestic and international pharmaceutical and biotechnology industry.

In summary, a small but innovative step to take advantage of a local economic development activity some nine years ago has created two separate and growing entities. Over 130 new positions have been established within the community that focus on pharmaceutical technology with a combined annual operating budget in excess of $10 million.

Howard Mossberg, PhD
Vice Chancellor for Research, Graduate Studies and Public Service
The University of Kansas

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NATIONAL CENTER FOR THE DEVELOPMENT OF NATURAL PRODUCTS (The University of Mississippi)

The Research Institute of Pharmaceutical Sciences of the University of Mississippi has more than a 25-year history of commercializing products derived from plants and exists as an excellence center of the University. It is seeking to form and lead a partnership with the federal government (U.S. Department of Agriculture), and the pharmaceutical and agrochemical industries by establishing the National Center for the Development of Natural Products.

BACKGROUND

The Center will use an integrated and interdisciplinary approach with its partners to develop and commercialize new pharmaceutical and agrochemical products from natural sources. This process will begin with the biological evaluation of natural product preparations, carry through to development and commercialization of products derived from natural sources, and finally come full circle by developing the plant sources of these products into alternative high-value crops for farmers. The importance of commercialization will be emphasized by a division in the Center that will attempt to ensure that marketable products and processes developed in the Center will be commercialized. The two broad research emphases of the Center will be: improved human health and safety and increased agricultural productivity. Specific foci within those research areas will be developed as the partners and their capabilities are identified.

CONSORTIAL CONCEPT

The realization of the potential of natural products as new chemotherapeutic agents and agrochemicals is dependent upon harnessing diverse activities for discovery, development, and commercialization of those substances. The formation of a partnership of university and federal laboratories, and the private sector can assure that sufficient strength in all the requisite activities, especially commercialization, will be available. The proposed consortium is viewed as the most effective mechanism to accomplish that goal.

The consortium will formalize the proposed working relationship between the Institute, the USD A. and the private sector. The relationship will assure a blend of fiscal resources to support the core activities of the National Center, and facilitate the commercial realization of the products of its research. Private sector support will come first for the development of specific products, and then, as more products are commercialized, larger proportions will be in the form of royalty income or equity position income from spin-off companies. Federal support will begin as direct appropriations and then come increasingly from extramural grant and contract support.

James D. McChesney, PhD, Director
National Center for the Development of Natural Products
The University of Mississippi

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RESEARCH BIOCHEMICALS, INC. (Northeastern University)

Professors John Neumeyer and Evelyn Friedman formed a business in 1980 to market four or five dopamine agonists and antagonists that Professor Neumeyer had developed at his Northeastern University laboratory. Research samples of these compounds had been distributed at no cost to fellow scientists, but the
demand for these products (specifically the dopamine agonist, NPA, N-n-propylnorapomorphine) became too great to continue that practice. Research Biochemicals, Inc. (RBI) was incorporated to supply the growing needs of the neuroscience community, and at the same time, sponsor the research of graduate students working in Neumeyer’s medicinal chemistry group at the university.

Within a year profits from RBI sales provided support for one graduate student, and by 1982, Friedman had left her teaching position to assume administrative responsibilities of the company and to become its first president. Neumeyer continued his academic duties at Northeastern while taking on new responsibilities at RBI as Chair and Scientific Director. During this time RBI licensed one of its first significant products from Ayerst Laboratories—the dopamine antagonist (+)-Butaclamol and its inactive (-) enantiomer.

The RBI strategy was, and is, to continually broaden its product line while maintaining the highest standards of product quality and purity. The first catalog was a single mimeographed page. By the end of 1984, the catalog had expanded to eight pages, and the company had three employees. The business had taken on a life of its own.

Research was conducted originally in space leased from Northeastern University, but gradually that space became too small. In 1986, 2000 square feet were leased, two more staff members were hired, and a small laboratory for quality control and organic synthesis was added. Additional expansion took place in 1990 when RBT moved into a newly-renovated area providing over 10,000 square feet of office and laboratory space. RBI now employs 40 full-time or part-time persons, and its 1992 catalog/handbook will contain a listing of over 800 products.

RBI has been successful in attracting government funding, especially Small Business Innovation Research (SBIR) Grants. Since 1986, RBI has received eight Phase I and six Phase II research grants from the National Institute of Digestive and Kidney Disorders, the National Institute of Neurological Disorders and Strokes, the National Institute of Alcohol and Drug Abuse, the National Science Foundation, and the Department of Energy. These grants have greatly facilitated the development of new products which have and will continue to play a critical role in studies dealing with the cause and treatment of disorders such as Alzheimer’s and Parkinson’s diseases, drug addiction, and basic brain research. More recently, RBI was awarded a major contract from the National Institute of Mental Health entitled “Synthesis of Chemical Compounds Relevant to the Field of Psychopharmacology.”

The success of RBI is at least partly due to its efforts to remain on the cutting edge of the growing area of neurosciences by offering unique and exclusive products required for neuroscience research.

John L. Neumeyer, PhD
Chair of the Board and Scientific Director

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FORMATION OF A REVENUE GENERATING FACILITY—NUCLEAR PHARMACY
(The University of Oklahoma)

In 1977, The University of Oklahoma College of Pharmacy established a fully licensed Nuclear Pharmacy Service. Governed by the Nuclear Pharmacy Professional Practice Plan, the nuclear pharmacy provides high quality radio-pharmaceutical services to 25 hospitals in the greater Oklahoma City metropolitan area and to 10 additional hospitals and nuclear pharmacies regionally and throughout the United States. The Nuclear Pharmacy Service occupies approximately 2,000 square feet in the College of Pharmacy building and is divided into four separate areas: dosage preparation and dispensing, receiving, waste storage, and radiopharmaceutical development. The staff is composed of a director, a manager, an accounting specialist, two staff pharmacists, three drivers, and between three to five interns. This unique facility, perhaps the only one in existence totally operated by a College of Pharmacy, serves as a significant revenue source for the college faculty engaged in its nuclear pharmacy teaching and research programs. Revenues from the nuclear pharmacy provide nuclear pharmacy faculty with salary supplements and serve as a source for graduate student support in the form of graduate assistantships and funding for graduate research programs. Faculty in the nuclear pharmacy program offer a series of nuclear pharmacy elective courses to undergraduate and graduate students not only in pharmacy but in other health-related programs within the Health Sciences Center. In addition to funding the nuclear pharmacy teaching and research components, the nuclear pharmacy has, whenever possible, provided funding to assist the College in unique acquisitions of capital equipment.

The nuclear pharmacy also provides a broad range of investigators within the Health Sciences Center the opportunity to take advantage of the unique facilities and expertise offered by the Department. Radiolabeling expertise, facilities and funding for both basic and clinical sciences in the College of Pharmacy and throughout the Health Sciences Center are provided through funds generated by this Service.

The unique nature of nuclear pharmacy education of this highly specialized area of pharmacy can be best accomplished with outside financial support either through the entrepreneurial efforts of the nuclear pharmacy faculty or by outside funding through the private sector. To be successful in this type of venture, it is almost mandatory that the entrepreneurial efforts of the nuclear pharmacy faculty generate revenues that can in turn be put back into the basic components of teaching and research.

Gross revenues in the range of $500,000-$1,000,000 in moderate-sized communities can provide essential revenue for the education and training of nuclear pharmacists and generate funding for unique and innovative research opportunities that are difficult to fund from more traditional sources.

Victor A. Yanchick, PhD
Stanley Mills, PhD
Dean, The University of Oklahoma
Director, O.U. College of Pharmacy
Regional Nuclear Pharmacy

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COUNCIL OF OHIO COLLEGES OF PHARMACY
Academic Entrepreneurship: A Consortial Approach

BACKGROUND AND MISSION

Only California, New York, Ohio and Pennsylvania have four colleges of pharmacy within their states. Nationally, Ohio exemplifies a unique model of cooperation through the consortial arrangement among its four colleges. The Council of Ohio Colleges of Pharmacy, non-profit educational consortium of the four colleges of pharmacy (the University of Cincinnati, Ohio Northern University, The Ohio State University and The University of Toledo) was established in 1966. The Council’s efforts are directed at the planning of professional activities and projects vital to the advancement of pharmacy in Ohio.

Specifically, it is the mission of the Council to:
1. Strengthen the ties between the colleges and the profession;
2. Eliminate the duplication of resources and effort among the four colleges of pharmacy by developing a coordinated and collective approach to the delivery of continuing education; and,
3. Develop a strategic approach for cooperation on issues which impact on pharmacy education and relate to the professional practice.

ORGANIZATION

The Council is organized on a voluntary, informal basis to undertake projects deemed mutually beneficial to the organization. Membership consists of the dean and a delegate from each of the
Dr. Martin’s experience with the tumor marker, carcinoembryonic antigen for monitoring his patient’s disease, and Dr. Thurston’s experience with development of radiation detectors soon led to the concept of using radioactively labeled tumor markers and a radiation-detecting probe to localize cancer that could not be seen or felt during the traditional surgical exploration. Soon after his release from the hospital, Dr. Thurston returned to Dr. Martin’s office with the first prototype of a probe detector, and the concept for an intraoperative diagnostic system was developed.

In 1983, Drs. Martin and Thurston founded the Neoprobe Corporation, based in Columbus, Ohio, on the doorstep of The Ohio State University where a major portion of the development work has been completed during the past ten years.

At the core of the RIGS system is a highly sensitive, portable gamma detection device, which has progressed through approximately twenty-five different versions before the currently-used computerized unit that signals when higher than normal levels of radioactivity are encountered, was conceived. Equally as important is the radioactive signal generator which must localize at the tumor sites in higher concentrations than in the surrounding normal tissues. Since neither the engineer nor the surgeon had any experience in the use of radioactive drugs, they turned to George Hinkle, RPh, MS, the nuclear pharmacist at The Ohio State University Hospitals. By mid-1982, the three, working with surgery fellows and a nurse, had tested the first RIGS system in tumor bearing mice using I-131-labeled baboon anti-CEA antibody prepared in the Nuclear Pharmacy of University Hospitals.

That initial research has led to a ten-year collaborative progression through a variety of radionuclide/antibody combinations, animal and human studies and other spin-off studies investigating other uses of the RIGS methodology, he Nuclear Pharmacy Services team effort included: the procurement of monoclonal antibodies, peptides and other biological markers; radiolabeling of these compounds; quality assessment testing; administration into patients; collection of patient samples for pharmacokinetic and clearance studies and the completion and maintenance of the many records required by the regulatory agencies monitoring the research. The team has also been instrumental in the multicenter clinical investigations for which radiolabeled antibodies used for the localization of cancer, myocardial infarction and infections are packaged and shipped.

Neoprobe Corporation is working toward obtaining FDA approval to market the radiolabeled monoclonal antibodies and other markers used in the RIGS system. Phase III trials are currently underway on the iodine-125 labeled CC49 monoclonal antibody at six different centers across the country and in Rome. The company hopes to gain approval to market the drugs used with the system as well as the device. Neoprobe Corporation and its team are committed to a common goal: to make the RIGS system accessible to surgeons and patients, worldwide—not only for the surgical treatment of colorectal cancer, but for all solid tumors. The company, still headquartered in Columbus, Ohio, occupies its own 20,000-square-foot office and production facility. It also has access to the facilities and broad-based resources available to The Ohio State University and at the new Arthur G. James Cancer Hospital and Research Institute.

George Hinkle, MS
Nuclear Pharmacist and Clinical Pharmacy Professor
The Ohio State University

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UNIVERSITY-INDUSTRY COLLABORATIVE RESEARCH ON DRUG DISCOVERY (PURDUE UNIVERSITY-THE UPJOHN COMPANY)

The discovery of better drugs for cancer treatment is a complex process. It requires the collaboration of outstanding scientists from diverse scientific disciplines within the chemical, biochemical, biological and pharmacological sciences. In 1988, the National
Cancer Institute issued a request for applications (RFA) for the establishment of “National Cooperative Natural Products Drug Discovery Groups” for new effective anticancer treatments for natural sources. In response to this RFA, Purdue University’s Natural Products Drug Discovery Group formed an interdisciplinary consortium consisting of two natural product chemists, two molecular biologists, and a pharmacologist to design new screening strategies which are centered around the selective modulation of signal transduction and gene expression. All phases of development for biochemical assays and physical/chemical methods leading to the efficient isolation, purification, and structure elucidation of novel active compounds can be performed at Purdue University. However, the development of new agents for clinical trial must rely on animal models for identifying and setting priorities. Therefore the Upjohn Company was invited to participate in this cooperative drug discovery effort.

Both Purdue University and the Upjohn Company have been extremely active in the discovery and development of anticancer drugs for many years. A combined effort from these two institutions will result in a highly synergistic effect toward the discovery of novel antitumor agents. The geographic proximity of the two institutions also ensures efficient communication and close collaboration. The project leaders from both institution and the NCI program directors have met three times each year to review research progress, improve experimental protocols, establish priorities for further mechanistic studies, and make recommendations for in vivo evaluation.

From Upjohn’s viewpoint, this cooperative research program will complement their overall anticancer research and development program. Upjohn reorganized the infrastructure of their Cancer Research Division so that most resources were directed toward clinical trials of several promising antitumor agents and almost all screening programs for new leads from natural sources were terminated. The collaboration with Purdue’s natural product research group allows the company to maintain access to novel and commercially attractive natural products and to have contact with research which may lead to the discovery of unexploited mechanisms that elicit selective toxicity against tumor cells.

For Purdue University, the collaboration provides a valuable addition to strengthen its research capability in testing the antitumor efficacy of biochemically interesting natural products. The contribution of intellectual and material resources from Upjohn Company has reduced the overall cost and makes this cooperative drug discovery group more competitive. Furthermore, this collaboration will facilitate the future preclinical and clinical development and marketing of new anticancer drugs.

This close cooperation has led to the second joint effort on the development of plant tissue culture biotechnology for the production of taxol to improve its availability for further clinical evaluation, and the isolation of novel taxol efflux blockers to overcome taxol-resistance problems. This research program is currently supported by the National Cancer Institute.

C.J. Chang, PhD
Professor of Medicinal Chemistry
Purdue University

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SOLID STATE CHEMICAL INFORMATION, INC.

In 1990, Solid State Chemical Information, Inc. (SSCI) was formed. This company provides short courses and consulting to the pharmaceutical industry in areas related to solid drug products. Areas included are polymorphs, solvates, amorphous forms, bulk drugs, control and regulatory issues. The main offering of this company is a two-day short course entitled “Pharmaceutical Solids.” This course addresses the areas described above by providing lectures and demonstrations. The course is taught by Stephen R. Byrn. Professor and Head. Department of Medicinal Chemistry and Pharmacognosy and Director of the Center for AIDS Research at Purdue University, and Ralph Pfeiffer, a solid state chemist who recently retired from Eli Lilly after 35 years of experience in the solids field. Both Drs. Byrn and Pfeiffer serve as consultants for SSCI.

To date, the Pharmaceutical Solids Short Course has been presented to seven pharmaceutical companies, twice at the Meadowlands in New Jersey as an open course mainly for companies in the New Jersey area who do not wish to have an “in house” course, at INUNIV in Puerto Rico, and at the FDA for reviewing chemists. In addition, Drs. Byrn and Pfeiffer will be participating in a Polymorphs and Solvates short course sponsored by the Royal Society of Chemistry in Bradford. England and Dr. Byrn will participate in a polymorphs short course taught by the AAPS in November of 1992.

In order to avoid possible conflicts of interest, Dr. Byrn is not president of SSCI and does not have any decision-making responsibility. Instead. SSCI is set up as an “S Corporation” with Sarah Rushmore-Byrn as the president. In addition, an effort is made to not compete with Purdue University. That is, SSCI does not conduct activities which could normally be carried out at Purdue University. In this way conflicts between Dr. S.R. Byrn at Purdue University and Dr. S.R. Byrn, Consultant, SSCI, are avoided as much as possible.

Both Dr. Byrn and Dr. Pfeiffer have found SSCI activities tremendously enjoyable. The participants in these activities are often very motivated and enthusiastic students. In addition, time is provided at the short courses for presentation of participants’ problems leading to an open-format, free-flowing problem-solving session which is intellectually stimulating and helpful to the participant. It is very rewarding to be able to assist scientists with real-life problems. Overall, participation in entrepreneurial activities such as this enhance the role of pharmaceutical sciences in the pharmaceutical industry and lead to quicker solutions to important drug development problems.

Stephen R. Byrn, PhD
Professor of Medicinal Chemistry
School of Pharmacy and Pharmacal Sciences
Purdue University

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THERATECH, INC.

TheraTech was founded in 1985 by William I. Higuchi, PhD, chairman of the board and distinguished professor and chairman of the University of Utah Department of Pharmaceutics; Dinesh C. Patel, PhD, board member, president and chief executive officer; and Sung Wan Kim, PhD, board member, chairman of TheraTech’s Scientific Advisory Board, and professor of Pharmaceutics and director of the Center for Controlled Chemical Delivery at the University of Utah. Drs. Higuchi and Kim are internationally recognized leaders in the fields of pharmaceutics and controlled drug delivery. TheraTech has a scientific staff of more than 51 full-time employees, including 15 PhDs and one MD, in a variety of related scientific technological disciplines. The company’s R&D efforts are enhanced through:

- close relationships with the University of Utah’s Department of Pharmaceutics and Center for Controlled Chemical Delivery;
- exclusive contractual relationships with preeminent consultants based in the United States, Japan and Europe;
- equity investments by four multinational pharmaceutical companies: Pfizer, Kali-Duphar, Inc. (a wholly-owned subsidiary of Solvay & Cie), Sam Yang (Korean company), and Syntax. The company’s early years have been devoted almost exclusively to a heavy emphasis on research and development in several fields of drug-delivery technology. This work has resulted in several issued patents, a number of pending patent applications and various products undergoing clinical testing.
Today, TheraTech is on the verge of significant growth, both in continued R&D of innovative technologies and in pharmaceutical product development and commercialization. The company, using its proprietary technologies as a base, intends to emphasize work in the field of absorption-enhancer technologies and polymeric drug-delivery technologies. It remains committed to the research, development and commercialization of unique pharmaceutical products capable of controlled, programmed, targeted and/or bioregulated delivery of therapeutic agents.

William I. Higuchi, PhD
Chairman of the Board and Professor
University of Utah

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FORMATION OF A PHARMACEUTICAL CORPORATION
(University of Wisconsin-Madison)

The University of Wisconsin-Madison will not directly participate in a commercial venture but has traditionally done so through a non-profit foundation, the Wisconsin Alumni Research Foundation (WARF). In more recent years, other indirect models have been tested, all of which have fallen short of direct involvement of the University.

In 1986, using technology developed at the University of Wisconsin-Madison, a start-up ophthalmic company, Insite Vision, was created. A venture capital firm provided $1,000,000 of seed money and the University Foundation received 100,000 shares or approximately two percent of the founding stock.

From 1986-1988 some unrestricted research monies ($50,000-$100,000 per year) were directed to the University from Insite Vision. Presumably the financial impact of the founding stock, more so than unrestricted research grants, is the real incentive in permitting faculty to participate in entrepreneurial activities. However, it should be noted that the level of stock given to the University was a gift, in contrast to a negotiated position. Clearly the University would benefit considerably from direct rather than indirect participation. It is expected that Insite Vision will go public in the near future and, at that point, the University will achieve some financial benefit.

Joseph R. Robinson, PhD
Professor of Pharmacology
University of Wisconsin-Madison