research can be sold, and the risk reward realized, only after long years of regulatory review.

Patent Term Restoration and the Small Company

We have spent millions of dollars on research and development at Genentech, and the level of those expenditures is increasing as the company grows.[7] We have been in existence for more than five years but, owing to the recognized and understandable necessity of obtaining regulatory approvals, we have yet to sell an ounce of product to end-users. The promise of patent protection lets us raise capital to sustain the company in these dry years. By licensing a portion of that technology to others, we can also earn the revenue needed for operations on an expanded front until our first products can be sold directly. The available levels of both types of funding are, naturally, influenced by perceptions of the ultimate worth of our proprietary position. To the extent the patent reward is made more meaningful, as by restoring the full term envisioned by earlier Congresses, the opportunities for start-up companies like Genentech to continue to fund life-giving research will be enhanced.

Patents and Competition

We believe that patent term restoration will enhance competition, not diminish it.

Every opponent of patenting chooses the pejorative term "monopoly" as the cornerstone of his argument. The argument from "monopoly" overlooks a fundamental precept of the patent

system. Rather than taking away from the public something it earlier enjoyed, patents produce to the public understanding, and ultimately to its own enjoyment, something the public might otherwise never have had, or had only after long years. The only "monopoly" the patentee gets is a monopoly over his own creation, and then for only a limited term. Those who endure the risk of innovation ought to receive in full measure the reward for success.

S.255 will not extend the patent for any product for which regulatory approval has been given in the past, and therefore will not influence its price in the future. And we believe enactment will lead to lower prices for the products of the future by increasing competition in two ways.

1. Competition between products. When the courts look at a monopolization charge, they first define the relevant market. They look not at monopolization of any single product, but instead at the whole constellation of different products that compete with one another because they exhibit what the judges call cross-elasticity of demand. In this philosophy, cellophane competes with wax paper, plastic wrap with both, and aluminum foil with all three. The new products of innovation, when they are better, exert downward pressure on the prices of the different but cross-elastic products that predate them. Legislation that enhances the climate for new product innovation enhances the climate for this most meaningful form of competition.

2. Competition between companies. Competition is also a function of the number of companies operating within a given field. The fewer the entrants, the less occasion there is for competition. And yet many studies have shown that since 1962 the number of firms engaged in the manufacture and distribution of pharmaceutical products has markedly declined. Some have predicted that the tendency toward market concentration will continue as a result, among other things, of the costs imposed by the regulatory environment and the inability of small companies to maintain the research and development efforts required to provide new patents.[8] But the new revolution in biotechnology offers ground for optimism. Genentech was only the first of the dozens of new firms that have formed around this technology, all seeking a formula for survival and growth in research and in the development of a proprietary position. Restoring the full term of patents can help these new market entrants to sustain themselves. Capital is more easily raised when research and regulatory costs can be recouped from marketing revenues over the full term of an issued patent. Where the remaining patent term has not been foreshortened by regulatory delays, economics will more often justify the small company's defense of its patent (and its market) in expensive litigation brought to "break the patent", oftentimes by breaking the patent owner. And to the extent the full measure of patent protection is made available through restoration of term, start-up companies can get greater value from licenses they grant to meet interim cash needs. In every respect, the

restoration of the full term of patent protection can be expected to enhance competition.

Patent Term Restoration: An Ideal Adjustment of Regulatory Mechanisms

The genius of the legislation before this Committee lies in its simplicity, flexibility and automatic adaptation to a host of different circumstances. The useful life of a patent is restored in every different case only as the period of regulatory review in that case requires. The more a new product departs from past practice, the longer will be its review period, the longer will be its patent term restoration, and the more will the patent reward be assured for those who take the greatest risk in departing from the tried and true. But we do not believe passage of the legislation before this Committee will in any way encourage regulatory delay. The greatest incentive will remain for eliminating delays in new drug approvals: the need to get safe and effective drugs to people who are sick.

I should add that in the case of each of the new products of our research now undergoing clinical testing, our experience with the Food and Drug Administration has been encouraging. We have found that Agency both professional in its attention to its important mission and receptive to the potential of our new technology. FDA's attitude to the present time has been both forthcoming and cooperative. It is quite possible that regulatory clearance will come before any basic patent issues

to Genentech.[9] Our concern is accordingly not one of focus on products now in testing, but rather on the future conditions under which our young company and others like it will seek their full maturity.

The Need for Patent Term Restoration Relating to Processes

S.255 makes no provision for restoring the term of patents on new processes for making old substances. Although a limited number of new substances have already been produced by gene splicing techniques, by far the greatest efforts to date have been expended in creating practical means for the industrial production of substances that are old in the sense that they are already made in the body. Until Genentech devised a process for biosynthetic production of human insulin that substance, though old and of known composition, had never been available in quantities suitable for the treatment of diabetics.[10] Until Genentech devised a method for the biosynthetic production of human interferon that substance, though old in nature, was available for the treatment of cancer patients only in low purity, minute quantities and at a price that effectively put it beyond reach of the people who might need it. Until Genentech devised a method for the biosynthetic production of human growth hormone, that substance, though old and of known composition, was unavailable to the great majority of children suffering from dwarfism because of critical limitations in raw material sources.[11] One can anticipate that a great number of additional materials, until now unavailable or in short supply, will become available through

the development of other such methods, if the full patent incentive for such developmental work can be restored.

The present position of the Food and Drug Administration is that an old substance, even one hitherto approved for treatment when gotten from conventional sources, will be treated as a "new drug" when made by genetically engineered microorganisms.[12] If the product that FDA regards as a "new drug" is in fact old and hence cannot be encompassed within the scope of the patent, as required by Section 155(a)(1) of S.255, then the Act will not be available to restore patent term lost through the "new drug" regulatory review period that FDA will impose.

The genetic engineering example is only one of many that might be imagined. Frequently, occasion will arise for protracted regulatory review before an invention of great value can be commercially practiced, even where the invention relates not to a new thing, or a new method of using a thing, but rather to the first practical method of making that thing. Innovation in the science of making "old" things in better and more economic ways should be encouraged to the same extent the bill in its present form would encourage the making of new things. Most particularly should this be done when regulatory agencies bid fair to treat products that are "old" in the patent sense as "new products" for purpose of regulatory review.

We believe S.255 should be amended to provide for the restoration of patent term where "old" products are subjected to regulatory review because manufactured by a new and patentable process. I will be happy to assist the Committee's staff in its efforts in this regard.

FOOTNOTES

1. Diamond v. Chakrabarty, 447 U.S. 303.

2. Jewkes, Sawyers and Stillerman, The Sources of Invention, St. Martins Press (1958).

3. "The Position of Applied Research in Nonindustrial Laboratories," an address by Sir Ernst Chain, May 1976, in Biotechnological Applications of Proteins and Enzymes, Zvi Bohak and Nathan Sharon, eds., Academic Press, N.Y. (1977), at 15. Sir Chain holds the Nobel Prize for Physiology and Medicine.

4. Hearings on Regulation of Recombinant DNA Research before the House Subcommittee on Science, Technology and Space, 95th Congress 1st Sess. 55 (1977). (Testimony of Paul Berg). In 1980 Dr. Berg was awarded the Nobel Prize for Chemistry.

5. Testimony of Phillip Handler, id at 27.

6. Address by Thomas J. Perkins, President, National Venture Capital Association, before the San Francisco Bay Area Council Outlook Conference, January 13, 1981. The Supreme Court's confirmation of patents on genetically engineered microorganisms preceded the October 14, 1980 public offering of Genentech stock by several months. The October 14, 1980 banner of the San Francisco Examiner declared "Genentech Jolts Wall Street", a reaction that suggests the investing public agrees with Mr. Perkins.

7. Five years ago Genentech had one employee. Today it employs 230 and is seeking more.

8. F.H. McKim, "Will Your Company Survive the Economics of the '80s?" in Pharmaceutical Executive 1, 50-55 (April 1981).

9. Examination of related patent applications was suspended pending resolution of the threshold question addressed by the Supreme Court in Chakrabarty, supra n. 1.

10. Previously, only animal insulin was available to diabetics.

11. Until recently, human growth hormone could be extracted only from human remains.

12. "The statutory definition of new drug (21 USC §321(p)) is 'any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience . . . as safe and effective.' Until drugs made by recombinant DNA techniques become 'recognized [by] experts . . . as safe and effective' they will be treated as new drugs." Statement of Henry Miller, M.D., M.S., Medical Officer, Bureau of Drugs, Food and Drug Administration before the Industrial Practices Subcommittee of the Federal Interagency Advisory Committee on Recombinant DNA Research. Minutes of 4th Meeting, December 16, 1980, pp. 3-4.

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STATEMENT OF

DONOLD K. LOURIE

PRESIDENT AND CHIEF EXECUTIVE OFFICER

LESCARDEN LIMITED

submitted to the

SUBCOMMITEE ON COURTS, CIVIL LIBERTIES,

AND THE ADMINISTRATION OF JUSTICE

U.S. HOUSE OF REPRESENTATIVES

concerning

PATENT TERM RESTORATION ACT OF 1981

My name is Donold K. Lourie. I am President and Chief Executive Officer of Lescarden Limited, a New York corporation engaged in pharmaceutical research and development. The Company was established and began work in the early 1960's. Its original stockholders were Dr. Leslie Balassa and Dr. John F. Prudden.

Dr. Balassa holds a Ph.D. in biochemistry from the University of Vienna and has many patents for inventions in the chemical and pharmaceutical fields.

Dr. Prudden is a graduate of Harvard Medical School, a board-certified surgeon and a doctor of Medical Science. He served on the faculty of Columbia Presbyterian Medical School for many years as Assistant Professor of surgery. In addition to his management duties with Lescarden, he has actively practiced medicine and surgery for over twenty years in New York City and been deeply involved in pbarmaceutical research. Dr. Prudden has published more than fifty articles on his cartilage research in widely read medical and scientific journals including the Journal of the American Medical Association and Lancet. Dr. Prudden is here with me today.

The Company's research has been principally directed towards the extraction and development of pharmaceutical products from animal and fish cartilage. Prior to Lescarden's work, cartilage had been recognized as possessing some biological activity, but these properties had never been well defined or documented. As a result of its investigations and research, Lescarden has developed a constellation of pharmaceutical products derived from cartilage,

as well as processes for manufacturing these products and methods for using such products in the treatment of several diseases.

The most interesting and potentially important product developed by Lescarden, and the one on which our testimony will focus, is referred to as Catrix. Catrix is produced from an acid-pepsin digested cartilage powder, obtained from bovine trachea. Preliminary work by Dr. John F. Prudden (who is now Chairman and Scientific Director of Lescarden) provides evidence that some forms of Catrix may be effective in the palliation and treatment of certain human cancers. Catrix is unusual in that it appears to exert its anti-cancer effects without being toxic to surrounding organs or other cell systems in the body. The therapeutic effects of Catrix have been observed for several years by Dr. Prudden in his research laboratory and in his clinical practice as a physician and surgeon.

More than a dozen U.S. patents (and more than fifty foreign patents) covering Lescarden's pharmaceutical products and various methods of using such products in the treatment of human diseases have been obtained by Drs. Prudden and Balassa and have been assigned to the Company. The first of these, the basic patent on Catrix, was issued in September 1968 and will expire in 1985. The New York patent law firm of Darby and Darby P.C. has represented the Company for more than ten years and Mr. Peter Ludwig of that firm (who serves as patent counsel to Lescarden) is here with me today.

We are very grateful to have the opportunity to testify before this Subcommittee. H.R. 1937 is of vital concern to pioneering, innovative companies like Lescarden. Important and prolonged

testing requirements of regulatory agencies seriously threaten the economic survival of small research and development companies whose initial progress necessarily depends on risk capital. These companies are often willing to undertake high risk, long term projects that larger companies consider less attractive due to the variety of lower risk, shorter term alternatives available to them. Evaluation of risk/reward ratios by big companies on a large list of opportunities often relegates high risk projects to a low priority. Whatever its size, a company has limited resources. It is obliged to use those resources on its most attractive, i.e. most economically beneficial, projects. In the entrepreneurial plunge into a project shunned by its larger competitors, a small firm must rely heavily on patent protection to secure the rights to its innovations and more importantly to attract risk capital. Even then, the entrepreneurial waters are cold and risky.

The work of Drs. Prudden and Balassa makes possible, but not necessarily probable, the eventual marketing of Catrix as a low cost, easily available medication of minimal toxicity for certain diseases including some cancers. To protect themselves, their Company, and their product, Drs. Prudden and Balassa invested large portions of their own and Lescarden's funds in patenting their inventions. Patents seemed to them the only real protection for a small company with novel, but as yet unproven products. Patent protection seemed essential for at least three reasons:

1) As protection against encroachment on their inventions by competitors;

2) As a potential means for acquiring income (either by licensing or sale of their inventions to third parties; and

3) As an inducement for the venture capital required to continue their research and bring their inventions to market.

During the last twenty years the Company has invested more than one-half million dollars in patent protection. It has raised more than $2,000,000 in risk capital investment.

Lescarden has also been active on the regulatory front. Between 1971 and 1977, the Company filed a number of INDs, the most important of which, from the point of view of human suffering, was directed to the investigation of Catrix in the treatment of cancer. This IND was filed in 1977.

During the period from its inception in 1960 to the mid-1970's the Company was engaged in developing and analyzing various uses for its new drug products and in performing the preliminary laboratory and animal work necessary for securing an IND. In past years the Company tried repeatedly to interest larger pharmaceutical companies in acquiring licenses of its technology. The Company's experience in this respect illustrates the often expressed view that large companies are unwilling to become involved in a high cost, high risk project when the underlying basic patent rights might well expire before necessary regulatory clearances can be obtained.

For instance, in 1975 the Company granted an option to one of the largest pharmaceutical companies in the world to acquire a license to manufacture and sell Lescarden's Catrix products. The agreement provided that both companies would collaborate during

an initial period and do joint research to identify the active principle in Catrix. Lescarden successfully collaborated with this firm for approximately two years in further investigating and developing the Catrix product. At the conclusion of the initial joint research period, the company elected not to exercise the option to acquire a license, although many of its scientific and management personnel were enthusiastic about the medication's potential for success.

It was later learned that a major factor in this decision was that the risk-to-reward ratio for commercialization of Catrix was too high. More specifically it was reasoned by the company's FDA experts that it would require at least four or five years to obtain an NDA for the product and that this would involve staggering costs. By the time the NDA had been granted, either the basic patents on the product would have expired or their terms shrunk to the point where they would not provide a period of exclusivity sufficient to justify the investment required to obtain the NDA.

The Company's efforts to interest private investors at this time were also largely frustrated by the same circumstances. Although many were skeptical about the inventions and their usefulness, investors generally regarded Lescarden's products as interesting and commercially viable, but were put off by the fact that it would take many years and dollars to obtain the FDA approvals required to market Catrix. By the time such approvals were at hand, even using the most optimistic estimates, the Company's basic patents would be close to expiration. Some small funds were raised from time to time but by early 1981 the Company was insolvent.

Both then and in prior years, the Company had in fact lacked funds sufficient even to commence the enormously expensive testing required by its INDs. As a result, Lescarden was obliged in 1979 to withdraw all but its cancer IND. A hold was put on clinical testing under this IND pending appropriate response to a number of deficiencies found by the FDA in the application. Proof of lot-to-lot consistency, animal efficacy, and a complete toxicity summary all required moneys and skills the Company did not have due to its inability to attract risk capital.

I first became acquainted with Dr. Prudden in 1980. Based on my conversations with him and other physicians and scientists, the patent work that had been done, my discussions with his patients and a review of his treatment records, I became convinced that Catrix was in fact a safe and efficacious medication for the treatment of certain minor and major diseases, including cancer. I believed that in spite of its then insolvency, Lescarden could be refinanced, reorganized, and a business strategy designed to give the Company a last chance for survival and success. I felt qualified to make this analysis and forecast. In addition to legal, financial, and business experience, I had, in the years from 1968 to 1977, participated in the founding, financing, and management of a seed-venture technical company whose annual sales ultimately exceeded $100 million.

I agreed to become Lescarden's Chief Executive Officer if Dr. Prudden would give up the major part of his medical practice to become the Company's scientific director and if investment bankers could raise, with our help, enough money to survive for

a year-and-a-half. We estimated we would need one-and-one-quarter million dollars to perform the basic work required to commence testing under Company INDs and to carry out the vital scientific research needed to raise the much larger funds necessary for completion of clinical testing. On the advice of experts, we concluded that Lescarden's cancer IND and at least one other IND could be reactivated.

· As discussed above, Lescarden had been unsuccessful in its efforts to license Catrix to large pharmaceutical companies in the United States. A major effort of the Company, however, will be to license abroad, particularly in Southern Europe, Asia, and Latin America, where the regulatory processes are shorter and less costly than in the United States. Another corporate effort may be to develop Catrix, the same composition believed to be useful in treating serious organic disease, as a cosmetic cream. Cosmetics do not require the same lengthy premarket tests and analyses as drug products and Catrix has shown some cosmetic effect.

Neither John Prudden nor I have much interest in foreign licensing or in developing Catrix as a cosmetic. These are, however, essential alternatives that were reluctantly adopted to satisfy the sophisticated investor who demands some reasonable possibility of an early return on his investment.

Even with these alternatives, even with new evidence on the efficacy of the medication, many knowledgable investors have turned us down. The Company raised less than it needed and had hoped for. The most often repeated criticism of the venture was, "Why invest in a company whose basic composition patent will expire in four years, when large scale clinical testing on that composition has not yet even begun? Assuming the medication is efficacious, why won't the big companies simply produce and market the drug when the patent expires, taking advantage of whatever research and testing you've been able to accomplish with our money?"

When these questions first arose, S. 255 had not yet passed the Senate. If the Patent Term Restoration Act of 1981 had been law, I am certain we could have attracted more venture capital, even though the Act will not restore that portion of the patent term lost in the regulatory process prior to the Act's effective date. We see this as a weakness of the Act particularly harmful to a small and vulnerable company like Lescarden, laboring so long before the FDA to bring an almost totally non-toxic invention to the thousands, even millions of people who suffer from the diseases it may alleviate. I believe, however, that if the Act does become law, even in its present form, it will greatly enhance our opportunities for raising vital additional funds in our next round of financing.

The act will benefit other entrepreneurial companies. For what I've said here has been confirmed by investment bankers of solid reputation in the financial community, who are engaged in

raising risk capital for innovative technology. They assure me that the scissors of federal regulation cutting deeply into patent-protected marketing life cut deeply as well into essential fund-raising. Young companies with exciting new products just never get started or start with so little capital as to be almost certain to fail. It is not imitation and cost-cutting that has given the United States its great economic strength. It is, and should continue to be, inventiveness and innovation. When these qualities are not expressed in the marketplace, what products are there to imitate or produce at lower costs?

The Company has never received federal, state, or local governmental financing or assistance. The Company has paid its own way for research and patents, as well as all business activities. Rather than having its entrepreneurial efforts encouraged and rewarded by government policy, the opposite has occurred.

The rationale of the patent system is based on the concept of disclosure in return for a limited period of exclusivity in the marketplace. While Lescarden has kept its part of the patent bargain, disclosure, the regulatory process has stripped away any reasonable period of exclusivity in the marketplace. In retrospect the Company might have been better off keeping its inventions in secret and not applying for patent until the eve of commercialization. Instead, the Company is now caught between the Scylla of an expiring patent and the Charybdis of the Food and Drug regulatory process.

If seventeen years of effective patent life is an equitable measure, and if enlightened federal regulation is in the public interest, which we believe it is, action should be taken so that

the patent protection afforded a new product or treatment is not unfairly and inadvertently shortened by the regulatory process. If this Committee believes that the kind of innovation represented by Lescarden's discovery should have a fair chance for clinical testing and for economic survival, the Patent Term Restoration Act of 1981 should become law.

S U M M A R Y
OF
STATEMENT OF
NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION
BEFORE THE
SENATE JUDICIARY COMMITTEE
APRIL 30, 1981

The National Agricultural Chemicals Association (NACA), a trade association of 115 companies which manufacture or formulate virtually all of the pesticides produced in the United States, fully supports S. 255 and urges its enactment.

The bill would:

- Restore the full measure of patent protection intended by Congress for products subject to the federal registration process.

- Help maintain the incentive needed for agricultural chemical companies to continue to invest long-term high-risk capital in pesticide research and development.

- Help reverse the current trend of fewer and fewer new pesticides reaching the marketplace due to the increasing time from discovery to full commercial use. That time is averaging almost eight years while research and development costs for a new product range from $20 to $25 million. (See diagram indicating research and development expenditures vs. new products being registered by EPA.)

- Help assure the availability of safer new pesticides considered indispensable for doubling food production by 2030 to feed a world population of 8 billion.

(Full Statement Follows)

STATEMENT OF
NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION
BEFORE THE
SENATE JUDICIARY COMMITTEE
APRIL 30, 1981

I am Nicholas Reding, a Group Vice President of Monsanto Company and appear here today in my capacity as Chairman of the Board of Directors of the National Agricultural Chemicals Association (NACA). I am accompanied by Dr. Jack Early, President of the Association.

The National Agricultural Chemicals Association is a nonprofit trade association representing a total of 115 companies which manufacture or formulate virtually all of the agricultural pesticides produced in the United States. We use the word "pesticides" to include various kinds of agricultural chemicals, such as insecticides, fungicides, bactericides and herbicides or, in other words, those chemicals used to protect crops from destruction by various insect, disease and weed pests.

Mr. Chairman, we appreciate this opportunity to contribute NACA's views and indicate our support for S. 255. We believe the Patent Term Restoration Act would help to maintain the incentive needed for pesticide research and development. It will help to restore to pesticide patent holders a portion of their patent rights which are lost as a result of the federal registration process. Importantly, it is not a broad or automatic extension of patent rights. It doesn't give companies any unusual or unfair advantage. It does not require additional government bureaucracy.

Congress intended that a seventeen-year patent be awarded to promote the development of new technology, thereby encouraging

the early disclosure of an invention while affording protection for the inventor. Since the adoption of the patent incentive system in 1790, there have been tremendous changes in scientific knowledge in general and in the field of agriculture specifically, and developments will continue to be made.

Pesticide chemicals require scientific evaluation of potential toxic effects to assure public health and safety to the consumer, worker and the environment. As a result, there has been an ever-increasing review of pesticides. Regulatory review is certainly proper for the protection of our citizens. However, the regulatory review process has caused an unforeseen erosion of the patent system. A recent study over a six-year period, conducted by the industry, has determined that the average time for registering a pesticide is five to seven years from initiating a major health test until first registration of a label. During that time, the patent term continues to run. By the time that a company has obtained its registration and enters the market, a significant portion of the patent term has been lost. An imbalance has been created, and clearly the time has come when the incentives of the patent system need to be restored.

During the past forty years, the agricultural pesticide industry, through chemical and field research, has been very creative and innovative. For example, the invention of pre-emergence herbicides has created a technical revolution in the production of corn, soybeans, cotton and many other grain crops throughout the world. Yield increases resulting from weed control with these chemicals can range from as little as ten percent

to as much as fifty percent or more, depending on the weed intensity in the production area. A high percentage of the U.S.-grown corn and soybeans are treated with pre-emergence herbicides for weed control. This technology is utilized on almost 150 million acres of cropland. If the value to the farmer is calculated (yield, quality, dockage discounts, mechanical efficiency, etc.), the total dollar improvement to the U.S. farm economy from this one concept would be in excess of $5 billion per year ($35/acre x 150M ac.).

Continued innovation, however, must be supported by adequate return on investment in research and development from sales of patented products. On an average, it now takes over eight years and some $20 to $25 million to bring a new product from discovery through registration. Normally, the construction of new and unique chemical plants to produce the technical grade chemical is also required, at a cost of an additional $40 to $70 million.

Only a limited number of companies in our industry are able to invest this kind of long-term and high-risk capital and resources necessary for the major discovery and development of entirely new technical grade pesticide chemicals.

The technical grade pesticide is the chemical which is processed into formulated retail products for application to specific crops under specified environmental conditions. Each use of a given chemical must be separately registered with the Environmental Protection Agency (EPA), and extensive test data must be submitted to the agency to demonstrate its safety to man, animals and the environment. A single pesticide chemical may have a wide variety

of crop or pest uses when formulated, and each use requires review and approval by the EPA based in part on test data specific to that use.

The Federal Environmental Pesticide Control Act of 1972 (FEPCA) and its 1978 amendments dramatically increased the time and cost of developing new chemical products for agriculture. The time from discovery of pesticidal properties of a compound to full commercial registration increased on an average from fifty-eight months in 1967 to ninety-two months in 1979, and is still increasing.

To assist the Committee in developing an even greater appreciation of the problem, we have included a diagram and explanation (see Appendix A) depicting the chronological development of a herbicide from initial synthesis and discovery of biological activity to the first commercial sales.

Because the process is rather complex, we have included with the diagram an explanation of the scientific and regulatory steps which must occur between discovery of a new pesticide and its entry into the marketplace. Rather than take the Committee's time now to review the chronology outlined in the diagram, we would encourage you and members of your staffs to study it carefully at your convenience. However, at a glance, you can see why many years of a new product's patent life are absorbed during the federal regulatory process.

Below is an example of the schedule for an actual chemical candidate, which demonstrates the time constraints imposed by federally required pre-market testing and regulatory review and

which erode the benefits of the patent. If everything goes right and there are no unforeseen delays, the following timetable is anticipated:

1. Discovery of biological activity - 1979
2. The patent is applied for - May 1981
3. The domestic patent issues - May 1983
4. Long-term health studies begin - September 15, 1982
5. Earliest completion date of long-term studies - February 1986
   The two major studies, mouse and rat, require 24 and 30 months, respectively, to complete. At least an additional 12 months is required for analysis of the animals; e.g., histopathology, sectioning, review of data by toxicologists, preparation and auditing of report to be submitted to EPA and submission of the report.
6. Full registration package to be compiled and submitted to EPA for review by June 1986 (includes both mouse and rat studies).
7. Scientific review and regulatory actions within EPA from twelve to twenty-four months from submission date - June 1988.
8. First tolerance and approved label allowing commercial sales by June 1988. If too late for seasonal use, then first sales will be delayed until spring of 1989.

In the above actual example, it is highly possible that first commercial sales would not take place until at least six years following the issuance of the patent. The loss of patent life

(six years) allows the owner of the patent only eleven years to enjoy the fruit of his innovation. The six-year period of regulatory testing and review disallows earlier market development and delays the time when the consumer can benefit from the product. It then takes many years after first commercial use to reach the full market penetration and total product utilization that result in maximum sales benefits. These years of market development use up an additional part of the patent life. As a consequence of the regulatory process, the last several years of patent protection that is available for non-regulated products - a time of maximum sales - have been cut off for the regulated product.

If the company has an extremely unique and innovative product concept, it has only the remaining time of the patent life to develop market strategy, develop environmental compliance procedures, recoup the invested capital and regain all other costs and expenditures, and generate sufficient return to continue in the business. In contrast, with a simple non-regulatory controlled patented product, the patentee enjoys the fruits of his patent from the first day the patent is issued.

In 1979, NACA surveyed members who manufacture pesticides on questions relating to the impact of patents and government regulation on their research and development (see Appendix B). Nearly all companies indicated that a favorable patent position was a critical factor in determining whether to invest in new product development. The survey also indicated that availability of patent protection is a highly important element in long-range research planning and funding. Respondents reported that the uncertainties,

cost and delay caused by government regulations have forced a reduction in research efforts. These companies favored restoring to patent owners the term of patent protection set by Congress. Without fully adequate patent protection, our member companies cannot continue to undertake the increasingly costly and time consuming research involved in discovering and developing new pesticide products and still compete with other companies who can copy their successes without the heavy cost of research and development. And copiers provide the public with nothing new.

The unchecked erosion of patent protection can only serve to discourage continued innovation. When protection is devalued, much of the incentive to invest long-term high-risk capital in innovative pesticide research goes with it. This is, perhaps, best illustrated by Appendix C which shows the trend of increasing research and development cost, yet a decreasing number of pesticides being registered.

The accomplishments of American agriculture comprise one of the most gratifying success stories in the annals of world history. Food production has increased in this country by 200-fold since the turn of the century. Today only three percent of the U.S. popuulation feeds us and much of the rest of the world. In 1980, exports of agricultural products contributed almost $40 billion to our balance of payments.

Let me remind the Committee that throughout the world, losses of food to pests are enormous. Estimates of loss (U.S. Department of Agriculture, Agricultural Research Service, Handbook No. 291) have ranged as high as forty-five percent of production in countries

where pesticides are not readily available. Even when pesticides are readily available, insects, disease and weeds are major contributors to the destruction of food and fiber. Agricultural pesticides significantly reduce but do not eliminate pest losses. The use of pesticides not only increases the quantity of our food, but also improves its quality, reduces disease to humans, increases the farmer's profits, aids in solving his labor problems and improves his cash flow. These achievements are due in large measure to the agricultural chemicals industry's long-term commitment to innovation.

Nobel prize winner, Dr. Norman E. Borlaug (who received the Nobel Prize for Peace for his outstanding contribution to alleviation of world hunger through the development of improved wheat varieties) warns that food production must double by the year 2030 to feed a world population of eight billion. "We can't feed the world with old technology. And we can't feed it without insecticides, fungicides, herbicides, and good machinery," says Borlaug.

A recent study (Department of State Bulletin, Fall 1978) pointed out that increased productivity, not increased land, is key to augmenting the world's food supply. Most of the increases in food required to meet the projected increases in demand over the remainder of this century must come from raising the productivity of land already in cultivation. Achieving significant increases in land productivity requires capital inputs and use of technology on a massive scale. Pesticides, fertilizers, improved seeds, farm implements and user education are major factors in increasing crop productivity for the foreseeable future.

Obviously, doubling food production -- the need identified by Dr. Borlaug -- will require sustained incentive and innovation on a scale never before seen in worldwide agriculture. The U. S. pesticide industry, to remain a dynamic contributor to development of such new technology, must be encouraged to retain its position of worldwide preeminence. We cannot afford through patent devaluation to risk the loss of innovation through government institutionalized interference with American ingenuity, whether intentional or inadvertent.

The innovative organizations in our industry regard the patent system as a prime motivator for undertaking costly programs in the high-risk area of new pesticide research and development. Thus, we are understandably concerned whenever these important incentives, provided by that system, are eroded.

There is an obvious need to reconcile the patent system with the federal regulatory process. We believe S. 255 will effectively meet this need.

Thank you.

88-310 O—82——34

APPENDIX A - 1

Chronology of Pesticide Development

The following explanation of scientific and regulatory steps indicates the time frame required to bring a potential pesticide candidate from synthesis to commercial sale (diagram attached).

Point I identifies the time of synthesis. Point II shows the time for bioevaluation. As will be related below, after the initial bioevaluation (II), and if biological activity is of sufficient interest, patent actions may be initiated at Point III. Bioevaluation screening tests are designed to reveal activity of a compound. It could have commercial potential as a herbicide, plant growth regulator, fungicide, insecticide, etc., any of which activity may be useful in solving a problem in agriculture.

When the kind and degree of biological activity of a compound is sufficient to suggest commercial utility, a broader and more intensive testing program is carried out, usually followed by limited, small-scale outdoor field tests. Obviously, these require a full growing season; i.e., one crop year. If results of the first year studies are promising, small field tests across wide geographic ranges are carried out during the second growing season. If results from this broader testing still appear favorable, a decision is made to continue toward commercialization of the compound.

At that time, indicated by Point IV, a very lengthy and expanded research and development effort is launched. This includes generation of technical data which ultimately are used to support the registration of that commercial candidate chemical (IV). General kinds of information are depicted in rectangles. The longest run of time is five years minimum, a period now dictated by the toxicology testing requirement. The latter is a test series in prescribed sequence

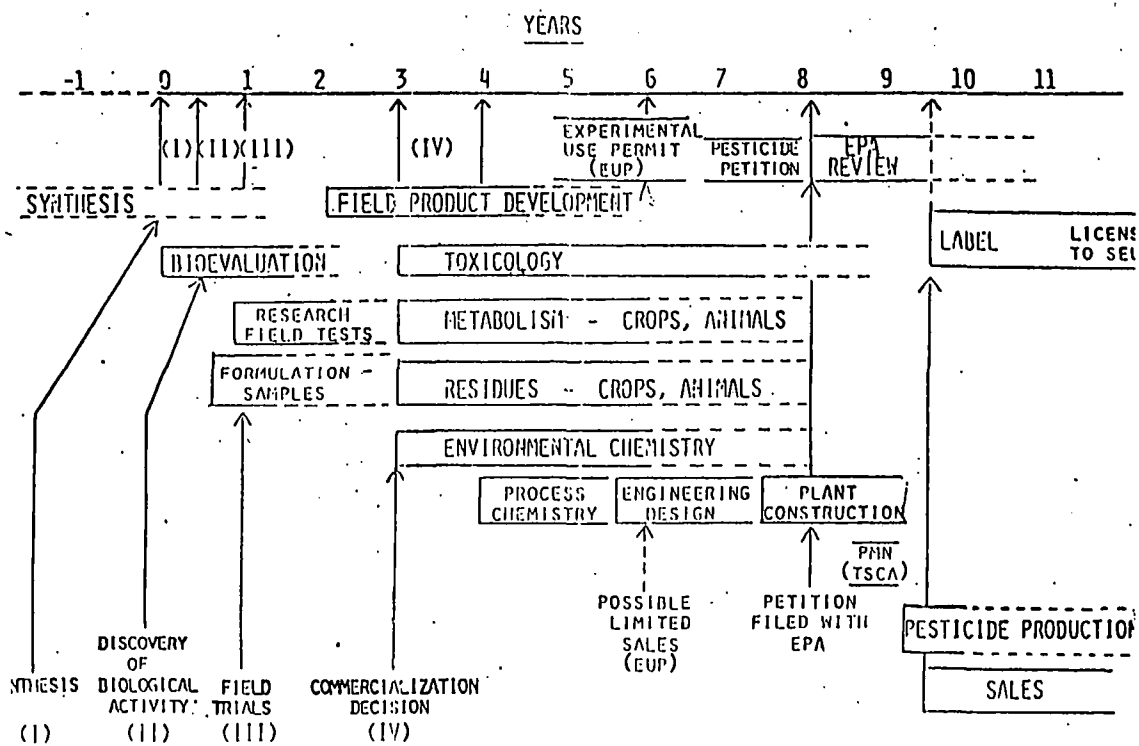
to define dose-response levels for the chemical in laboratory animals. After the feeding phase of a chronic study (1.5 - 2.5 years), about one year is required to complete full examinations of all animals and to prepare the final report. Therefore, the toxicology sequence requires about five years elapsed time for completion. And the trend now is for an even longer time.

All of the other kinds of information identified in the rectangles of the diagram can be obtained within that five years. However, this is the minimum accelerated time for a well-resourced organization. The small developer cannot afford to take a risk of that magnitude. At commercial decision time (start of Point IV), toxicology, metabolism, and environmental chemistry studies are initiated. The extended field studies and other major programs are started at the onset of the next growing season. Ancillary programs such as formulation, process chemistry, process/environmental are started as resources become available. The steps leading to a manufacturing plant are carried out in that five-year period encompassing the toxicology sequence. Final manufacturing plant construction, start-up, and actual production will normally coincide with the EPA review time of 1.5 years. Ideally, sufficient inventory of the proposed new product can be prepared to meet first year market sales by the time the label is granted by EPA, provided, of course, that premanufacturing notice (PMN) requirements for the manufacturing process have been satisfied under the Toxic Substances Control Act. The new candidate pesticide cannot be sold until a conditional or full registration is granted and an acceptable label has been approved by EPA.

Patent activities normally commence whenever significant biological activity of a given compound is projected to have commercial

utility in agriculture (III). This initiation of patent action can follow observations in greenhouse studies and a patent covering the compound and/or use of this compound may issue within 2-3 years after the initiating action. As is apparent from the diagram, this can result in loss of five or more years in the 17-year patent life.

PESTICIDE DEVELOPMENT CHRONOLOGY
FROM DISCOVERY TO SALES



APPENDIX B - 1

NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION

PATENT QUESTIONNAIRE

TOTAL NUMBER OF RESPONSES: 35	Yes	No	No Answer
1. Do you have a research program which includes the synthesis of novel compounds and the screening of the compounds for utility as pesticides?	29	6	
2. Is a favorable patent position a mandatory element in making the decision to commit capital to new products ("new products" includes new uses of compounds)?	22	13	
Always		7	
Generally		6	
3. If your company commits research funds primarily with the aim of developing a superior product or to fulfill a gap in consumer need, is a secondary aim to develop patented procedures?	32	1	
Did not understand question.			1
If the word "procedures" means processes for manufacture, the answer is	1		

Brief Statement if answer is "no":
"We are primarily interested in R & D efforts toward establishing product position."

Statement with a "yes" answer:
"We consider patented chemicals and procedures to be automatic in our research, i.e. we don't debate if we should try - we expect it".

4. If research expenditures constitute a commitment of capital for your company:
   A. To what extent are patent considerations weighed in long-range research planning and funding?
      Always 28
      Generally 6
      Seldom 1

   B. If patent protection is sought on "basic" products being developed, do you also consider expanded patent positions to enlarge the parameters of research (i.e.,cost reducing process patents, novel formulations)? 35

5. How important is a favorable patent position at the following stages in a research program?

	Essential	Major Importance	Slight Importance
A. Early Idea	7	14	13
B. Bench Development	11	18	6
C. Pilot Plant	19	14	1
D. Plant Design	23	11	

Note: One responded only to question "B"

APPENDIX B - 2

NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION

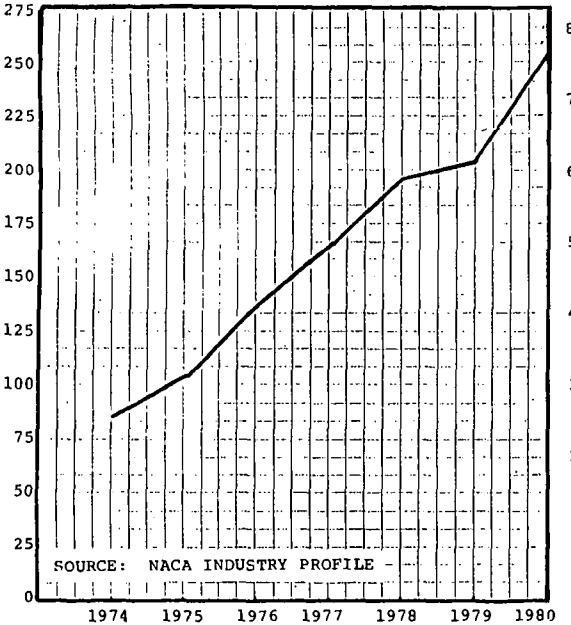
PATENT QUESTIONNAIRE

		Yes	No	No Answer
6.	Do you consider foreign patent protection when committing capital for:			
	A. New Products	33	2	
	B. New Processes	33	2	
7.	Does the discovery of the existence of third party patents tend to direct research into areas which:			
	A. Are chemically related, but patently distinct?	33	2	
	B. Entirely chemically unrelated?	19	14	2*
	*no relevance to third party patents			
8.	Do you know of instances where your patents have spurred competitors to further research?	30	5	
9.	Do you know of specific instances where the existence of government regulations has reduced research efforts in a specific area?	33	2	
10.	If the answer to question 9 is yes, is the reduced effort substantially the result of regulations causing long delays to obtain product registration?	29*	4	2
	*Comments "but also give much weight to the uncertainty of getting product registration". "but also due to expanded test requirements".			
11.	If the answer to question 10 is yes, do you favor a patent term for a new agricultural product to commence at time of product registration for a stated period of time, rather than the present term of 17 years from time of patent issuance?	29	3	3*
	*Comment: Extend patent life by number of years needed to get registration.			
12.	If the answer to question 11 is yes, but there is the possibility of providing the first opening to compulsory licensing after the following number of years, how would you answer?			
	All blanks accounted for			
	Five Years	1	16	18
	Ten Years	8	14	13
	Fifteen Years	23	3	9
		32	33	40

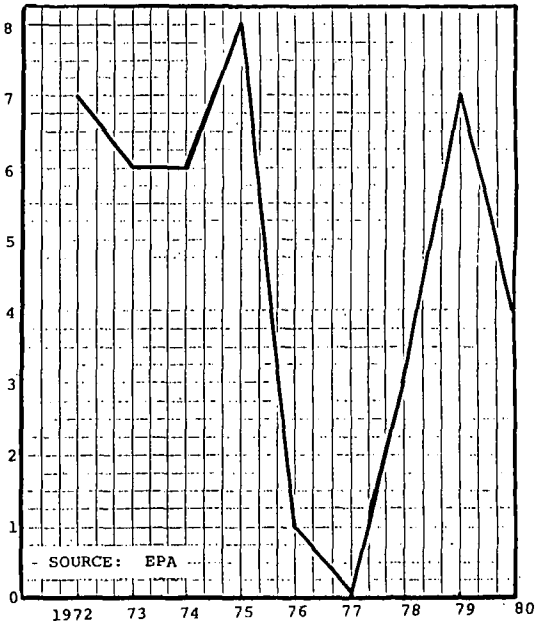
Explanation for 32 Yes replies to only 28 Yes answers in question 11:

2 Yes answers checked both 10 and 15 years
1 No answer checked 5 and 10 years as Yes
1 Yes answer checked No for 5, 10 and 15 years

R&D COSTS OF NEW PRODUCTS IN MILLIONS OF DOLLARS (TOTAL PER CALENDAR YEAR)



NUMBER OF NEW AGRICULTURAL CHEMICALS REGISTERED ANNUALLY*



*First registrations for products containing new active ingredients never before registered and available on the market to agricultural producers for use on either food, feed, fiber crops and tobacco but excluding uses on ornamental crops, forests, and rangeland.

STATEMENT

of the

NATIONAL RETIRED TEACHERS ASSOCIATION

and the

AMERICAN ASSOCIATION OF RETIRED PERSONS

on

H.R. 1937

THE PATENT TERM RESTORATION ACT OF 1981

Submitted to the

HOUSE COMMITTEE ON THE JUDICIARY

SUBCOMMITTEE ON COURTS, CIVIL LIBERTIES,

AND THE ADMINISTRATION OF JUSTICE

October 1, 1981

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The National Retired Teachers Association and the American Association of Retired Persons, representing 12.5 million older Americans, have a strong interest in encouraging innovative research and development, especially in the pharmaceutical industry. We, therefore, appreciate the opportunity to submit our views for the record on HR 1937, the "Patent Term Restoration Act of 1981."

Background

Older Americans have a keen interest in patent term restoration as it would affect the prescription drug industry. Our Associations believe that everyone--including pharmaceutical manufacturers--is entitled to, and should receive, fair and equal treatment under the patent laws. For this reason, we can support the provision of HR 1937 that would restore the term of a patent grant for the period of time that nonpatent regulatory requirements prevent the marketing of a patented product but in no event for more than seven years. We believe that such protection is essential to the encouragement of innovation and the introduction of major new drug therapies.

The elderly have a direct interest in expanded and more meaningful research and development activity. However, other factors and considerations that fall outside the scope of HR 1937 as drafted cause us considerable concern.

Those over the age of 65, while today representing only 11.3% of the population, account for over 25% of all expenditures for prescription drug products. On a per capita basis, they spent $133 in CY 1978 on drugs and drug sundries, nearly double the $68 spent by all age groups. More significant perhaps, prescription drugs represent approximately 36% of total out-of-pocket health care expenses for this group. And in meeting the ever-mounting burden of drug costs, the elderly find that they must pay for 84% of total expenses from their own financial resources, with only 7.9% being financed by private insurance and 8.4% by the public sector (e.g., Medicare, Medicaid). This situation is compounded by other ominous trends; namely, the increasing incidence of chronic debilitating conditions among the elderly, the relatively greater utilization of multiple prescription drugs, and an increased tendency among physicians to over-prescribe prescription drugs or to do so with less than adequate knowledge of their patients' current consumption patterns and experiences. It is also germane to the present discussion to note that some 70-75% of drug misuse among the elderly is due to under-utilization, most often because they cannot afford the medicine that has been prescribed.

Clearly, older Americans, often subsisting on relatively fixed incomes, have much at stake in the current debate over patent restoration. In a larger sense, our Associations are also very much interested in working toward drug regulatory reform so as to devise a means to achieve the essential purposes of regulation in a way that is affirmative and supportive of innovation yet does not deny the most dependent and needy segments of our society access to prescription drug products because the price is too high. Within this context it would be fallacious to characterize patent restoration as embodied in HR 1937 as a "cure-all". There is a pressing need for changes in the attitudes and value systems of both the Food and Drug Administration (FDA) regulators and the drug industry.

Our Associations strongly support increased emphasis upon drug research, development and innovation, because it is all too evident that the absence of certain drug therapies is effecting a cost. The real question for us, however, arises as to the level, direction and nature of drug innovation. We are concerned about the effect patent restoration would have on competition in the drug industry, particularly price competition, and whether the benefits of patent term restoration are commensurate with the costs such legislation would necessarily entail. The impact of reduced competition and patent restoration on aged persons dependent upon prescription drugs can not be discounted. We, therefore, believe that the Congress would be well advised to examine very closely whether extended patent

protection would, in fact, likely lead to significantly more research, development and innovation. The importance of patent restoration and its long-term impact on drug prices behooves the Congress to examine a multitude of causal factors--some exogenous in nature--which have led to a slow-down in innovative research and development in the drug industry. We would hope that patent (term) restoration, if enacted, would lead to new real R & D spending by the industry as well as more new major breakthroughs and new chemical entities that can be profitably marketed. We can be sure that additional years of patent protection will result in very real income transfers from elderly consumers to large brand-name manufacturers. The elderly should not be asked to accept the worth of these substantial transfers on faith alone or for that matter the assertion that "competition" from new products generates downward pressure on the price and market share of old products.

We do not deny that the drug industry is entitled to profits from their investment of high-risk capital in drug R&D, nor deny the cost effectiveness of many types of drug therapy when compared to higher cost alternatives (e.g., acute care hospitalization, nursing home care). Should HR 1937 be enacted, we sincerely hope that the new age or renaissance in research productivity and actual innovation, which the industry proclaims, is fully realized in the near term.

The FDA Drug Approval Process

For the most part, the FDA has developed an excellent new drug review process. However, this regulatory process does need to be reformed. While there should be no lowering of the statutory standards of safety and efficacy, there is clearly a need to assess those factors needlessly delaying new drug approval and to subsequently remedy the situation.

A great deal of debate continues as to the existence of a "drug lag" in this country. Without becoming sidetracked on this issue, we would state the obvious--that lengthy approval times can add substantially to the cost of developing a drug. However, to the extent that a "drug lag" does exist, our Associations would equate it with greater consumer protection and a substantially improved and more thorough drug approval process.

The gains from the FDA approval process are primarily reflected in today's quality drug development process. Yet the clinical phases of the new drug approval process now average 5 years, and the NDA , or New Drug Application phase, at least 2 years, with an additional 1-3 years of pre-clinical (IND) investigation, for a total of 8-10 years. The development and approval of minor chemical variants or innovative dosage forms take, on the average, only about half this time. In a major report issued in May of 1980, the General Accounting Office (GAO) cited several factors affecting drug approval time. It was

the opinion of the GAO, which we share, that both the FDA and the drug industry contribute to the time it takes to approve new drugs--often needlessly. This happens due to a number of factors, including: imprecise FDA guidelines which are subject to varying interpretations; scientific and professional disagreements between the industry and FDA; slow or inadequate FDA feedback to the industry on deficiencies in applications; incomplete new drug applications and industry's slow rate of resolving deficiencies; communication problems and an adversary relationship; and limited time spent by FDA reviewers actually examining drug applications, along with an uneven workload. Such deficiencies have resulted in 76% of all NDA's having to be resubmitted for additional data one or more times by the sponsor (with 85% being approved after the second or third review cycle).

The drug industry has asserted that there has been a rapid and progressive decline in the introduction of new molecular entities. While we do not deny a long term downward trend that needs to be addressed, data from the FDA indicates that, despite some up and down movement, over half of all new molecular entities introduced in the U.S. in the past decade are considered by the FDA to have provided "significant medical gain". Furthermore, any comparison of the risks of delay in the introduction of new drugs presents serious difficulties. The assumption that reduction in the risk of adverse effects from

drugs must be accompanied by an increase in the time taken for their introduction is not necessarily valid. Labels for regulatory systems, such as "fast" and "strict", should be used cautiously. To the extent such system comparisons are possible, however, we would note that of the four new chemical entities introduced in the United Kingdom since 1964, which were subsequently withdrawn due to unacceptable toxicity, three (ibunefac, practolol, and alclofenac) were never introduced in the U. S. Largely on the basis of preliminary toxicology data, the FDA postponed a decision about the drug practolol, for example. This wait-and-see attitude turned out to be well advised since, during the FDA review process, the suspected tumorigenic quality of the drug was confirmed with the discovery of severe adverse reactions in Britain.

Another factor that may be impinging upon truly innovative drug R&D, and the decline in productivity of R&D investment, is what seems to be a change of strategy by the industry. There has been a sharp drop in the portion of total R&D funds expended on basic research. From 1968-1978, this spending fell from 15.4% of total R&D outlays to 11.4% and became narrowly targeted toward more economically significant diseases (e.g., cardiovascular drugs). This tendency of companies to concentrate research efforts in a relatively small number of fields which

appear promising from a commercial point of view has, quite naturally, led to crowding in some areas of research and neglect of others. The outcome has been a plethora of closely related "me-too" drug products. Instead of limiting their efforts in introducing new drugs that are qualitatively and quantitatively superior to those already available, many drug companies expend considerable effort in copying or modifying successful therapeutic principles, with the result being the introduction of numerous analogous drugs--quite commonly accompanied by exaggerated claims of efficacy. Examples would range from closely related penicillin and cephalosporin derivatives to diuretics, topical corticosteroids and minor tranquilizers. We would contend that some measure of self-restriction on the part of research-based pharmaceutical companies in this regard would contribute significantly to improving the credibility of their arguments for patent restoration. We would also add that, for the most part, we agree with the many experts in this field who have claimed that it has become increasingly more difficult to discover drugs of major therapeutic importance.

Former FDA Commissioner Kennedy repeatedly referred to the relationship between the FDA and medicine as "creative tension". Perhaps this is an ideal description of the

relationship that could be developed between the drug industry and the FDA. Such tension should be acceptable as long as it is not only negative but also has positive side effects that are visible in the quality of the drug approval process. We strongly believe that there is little to be gained at this point in time from imposing additional restraints upon industrial drug research and development. At the same time, the industry should accept the statutory requirements that serve the purpose of substantiating the efficacy and safety of a drug within reasonable time limits. Industry protests as to unnecessary regulatory practices and redundancy should be fully substantiated with convincing data.

Comments on HR 1937 - The Patent Term Restoration Act of 1981

With respect to HR 1937 we have a number of specific comments to make. First, we would note that patent restoration is not likely to accelerate the IND (pre-clinical) and NDA (clinical) approval process. The industry has to bear some of the responsibility for the lengthy delays in drug testing and the submission of data to FDA. To quote from the Heritage Foundation report, Mandate for Leadership, "care must be taken in any restructuring of the patent laws to avoid creating disincentives to sponsors' proceeding as rapidly as possible with their research programs." We hope this concern will be addressed by the Committee either in the context of HR 1937 or in other patent restoration legislation, especially since the FDA is now in the process of making major revisions in its IND and NDA guidelines in order to improve and expedite the drug approval process.

Second, because of its limited scope, HR 1937 would have little impact on research and development efforts aimed at "orphan drugs" or drugs with limited marketing potential. Our organizations continue to support "flexible patents" for such drugs for which the clock should start ticking at the time they are approved and not when they are first patented as a molecule. Patents for orphan drugs could thus be extended two to three times the standard 17 year period. Realistically, however, we would concede that such extended patent protection may produce only marginal improvement in such new drug discovery if projected sales are

well below a threshold the company has established for marketing purposes. This seems to us one area where the Federal government needs to involve itself more intensively in new drug research and development given the somewhat logical reluctance of the industry to devote its resources to meet these special needs.

Another issue of major importance that ought to be addressed but that falls outside the scope of HR 1937 as drafted is what we refer to as the "de facto" patent protection afforded brand name manufacturers by brand name loyalty and entrenched prescribing patterns. Indeed, with no limitations being placed on the exclusivity of brand names and the drug industry's continuing persistence in litigation aimed at competitors who utilize similar product size, shape and color, trademark protection may be more important to the brand name manufacturer than patent protection in extending monopoly pricing and market shares. Data from recent studies clearly indicate that neither generic nor brand name manufacturers have met with much success in capturing significant market shares from original brand name manufacturers. A 1978 study of 12 major drugs (including Librium and Darvon) revealed that not one of these original products had less than 92.4% of their market five to eight years after patent expiration and that the average share in 1978 was 96.1% of the drug store market.*/ Other examples of this experience would

*/ Presentation by Meir Statman, Rutgers University, at Conference on "Drugs and Health: Economic Issues and Policy Objectives", American Enterprise Institute (AEI), November 15-16, 1979.

include Orinase - which still retains 97% of its market (tolbutamide) - and Persantine (dipyridamole) - which maintains 99% of its market 1½ years after patent expiration. Pioneer producers do not necessarily maintain market share by reducing prices (upon patent expiration). Prices generally continue to increase over time as even large, research - based drug companies have a difficult time entering these markets in a meaningful fashion. It is a very gradual and protracted process, more often than not, whereby a major drug product coming off patent loses its grip on its market.

The Patent Term Restoration Act HR 1937 proposes to provide an extension of patent protection for a new drug sponsor equal to the marketing time "lost" in the "regulatory review period". It is our understanding that this additional protection could not exceed 7 years and would include drugs already in the pipeline but exclude those which have already received NDA approval for marketing. And, as we have already noted, the drug would retain patent protection from the time it is patented as a molecular entity throughout the FDA review process.

Our Associations cannot object to the goal of treating all patent holders equally in terms of patent protection. But we do not believe that the Congress should consider patent term restoration in isolation. While we support equitable treatment of industries such as pharmaceutical industry and the medical devices industry, we would suggest that patent restoration be

limited for the vast number of me-too product reconstitutions that provide little if any new therapeutic value and which are often accompanied by higher prices. Also, the deregulation of early clinical research and reform of the FDA drug approval guidelines should be allowed to precede any form of patent restoration. Companies receiving patent extensions should also be required to demonstrate to the Congress and Commissioner of Patents a "real" increase in total R&D spending in at least the relevant therapeutic category of the drug in question. So as not to delay competition once the extended patent period of a particular drug product has expired, we would also recommend that as a condition of patent restoration all safety and efficacy (or testing) data be made available to the public sometime during the period of restored patent protection, perhaps after three years. We would note in this regard that the NDA (new drug) approval process with its confidential documentation has to date actually provided better protection than patents for many new drugs. At this point, we would note with approval the recent announcement of HHS Secretary Schweiker that he has lifted the previously imposed "stay" on so called paper-NDA's. This action should greatly facilitate the competitive movement of both brand name and generic manufacturers into the marketing of certain well-established prescription drugs (approved after 1962) as they come off patent. Not requiring new entrants

into these markets to repeat already published studies demonstrating the safety and efficacy of a particular drug helps save valuable scientific (research) resources, lowers drug prices through increased competition, and avoids ethically questionable repetition of clinical trials in human subjects.

We also think there is need for a specific provision, mandating the prominent use of a drug's generic name in labeling and advertising. Furthermore, we would hope that brand name manufacturers would drop their litigation aimed at generic manufacturers who produce products of a similar size, shape, and color (to off-patent pioneer drug products). These legal actions, in the absence of Congressional action, have seriously hampered the development of competition. We would also suggest that this problem could be addressed through an effective consumer education effort on the part of the FDA and other interested parties and would urge such action.

Finally, our Associations recommend that alternative approaches to furthering drug research, development and innovation be explored with the aim being to find alternatives to prescription drug prices as a means of financing R&D. One approach we find particularly attractive, especially in light of its broader applications, is the amending of our tax laws to provide accelerated depreciation and capital investment in research facilities and equipment. The U.S. lags too far behind its foreign competitors in this area. If this nation is to remain competitive in pharmaceutical innovation investment in R&D must be effectively encouraged by our tax

laws. In such a manner the financial burden of providing for increased and ostensibly more targeted drug R&D would be distributed more equitably throughout all segments of our society.

Summary

Older Americans have a direct and continuing interest in the researching and development of truly new and innovative drug products. At the same time this Committee should be fully aware of the direct financial burden older Americans are bearing as a result of their dependency on prescription drug products. With the vast majority of incurred expenses coming out-of-pocket, the elderly have much at stake in seeing that competitive forces in the drug industry are encouraged.

To repeat, our Associations are supportive of equitable treatment of all industries under the patent laws. We therefore, can support HR 1937 restoration of the patent grant for the period of time - not to exceed seven years - that nonpatent regulatory requirements prevent the marketing of a potential product. We fully realize that the FDA new drug approval process is in need of reform and that this process is inflicting a very real cost on the industries subject to its review as well as consumers. In this regard we must also note that the elderly are already spending 44% more on out-of-pocket health expenses than the non-elderly and that per capita drug expenditures for this group are twice that of the non-elderly. In these times of sustained

high rates of inflation which are particularly burdensome on older Americans we would hope that this Committee and the Congress would closely examine suggestions for improving or expanding the scope of (HR 1937) or developing additional but separate legislation.

The suggestions we have offered as to how HR 1937 could be expanded to make it more equitable and to lessen its impact on the elderly we believe deserve serious consideration. We would also counsel further caution and suggest that the major revisions in FDA's IND and NDA guidelines be implemented before patent restoration legislation is acutally implemented. These revisions will probably not be available until next year.

The pharmaceutical industry claims that lengthy new drug approval times have resulted in fewer new drugs and higher prices. For the most part this is probably true. As such, it points to the pressing need for Congressional action to effect necessary drug regulation reforms. However, our Associations do not believe that Americans would benefit from undue haste in judging the acceptability of new chemical entities or from lowering statutory measure of safety and effectiveness.

Enactment of patent restoration will likely result in additional increases in the elderly's expenditures for prescription drugs. It is our sincere desire to see the industry utilize these income transfers in the development of new and innovative drug products and therapies. Our Associations sincerely urge the Congress to consider the suggestions and concerns we have raised before moving to restore patent protection.

Statement of
Robert H. Thorner, P.E.
Farmington, Michigan
Regarding H.R. 6444 *

Mr. Chairman and members of the Committee:

I am a professional engineer-inventor and have worked on my own projects as an independent for over 30 years. I am one of the few pioneers of cruise-control for cars, and the major manufacturers purchased my patent rights directly or indirectly. This paper is based on notes for a book I plan to write on inventions, inventors and their backers, and the patent system including reform.

I urge that you pass the Patent Term Restoration Act (HR 6444) for very important reasons, now to be discussed. The American patent system until about 20-25 years ago was one of the most important factors which made our free-enterprise system so highly productive, reaching a peak in about the first decade after WW II. Our patent system was once far superior to any foreign patent system. In addition to the motivation for creating new products (which also creates useful jobs), an important public benefit of the patent system during its useful period was that the limited patent-monopoly acted to prevent commercial monopolies. This was done by providing an incentive for the formation and growth of small firms, which often resulted from the work by individual inventors. With the help of realistic patents, these individuals and small firms could then compete successfully with established firms. And in this manner the patent monopoly helped the anti-trust laws to foster real competition and prevent commercial monopolies.

However, because of some of the gradual changes in our patent system during the past 25 years, culminating with the maintenance fees for the first time in 200 years, the patent monopoly is now working against the public interest and in opposition to the anti-trust laws by fostering commercial monopolies in large firms. These large firms can handle comprehensive patent programs while small firms can no longer do so as they could before --- all because of the many changes which have reduced incentives for investors and independent risk-takers like myself.

The main purpose of the patent system has always been to benefit the public by offering incentives for people like myself to make a decision to assume the high risks of pursuing inventions

by investing considerable funds and time. So when people like me decide that the risks are now too great, and can no longer assume these risks, the number of patents issued reduces; and they have indeed reduced in recent years because of the drastic loss of incentive, all while our population increased. In my own case, I have been compelled to reduce my patent program except for relatively simple projects. I have several fine inventions which must remain in my files because of the gradual increase of patent risks resulting from the slow but steady reduction of incentives over the years.

I believe, respectfully, that one of the main causes of this tragic loss of incentive is what Congress has done in recent decades. One important factor is the selection of people from whom the Congress received advice which appears to have been followed and which has led to the reduction of incentives; these people comprise primarily patent attorneys along with the Commissioner.

Whenever people want to get something done on any subject, they of course always seek out those who really have full responsibility and power to make decisions. Then they try to influence these decision-makers. The heart of the patent system is to influence people like myself to decide to undertake these great risks and develop the inventions which produce the public benefit. Therefore, in order to reverse the reduction of patents issued, it is imperative that committees of Congress seek out and influence the real decision-makers in the patent system to increase their investment in patent programs.

It is a fact -- not opinion -- that patent attorneys never make these decisions to invest in patents. In 28 years, my patent attorney never has made a single decision for me to invest in my various programs; I of course always make these decisions. No Commissioner of Patents has ever made these decisions and never will. And of course, "consumer advocates" never make these decisions in the patent system and they are never consulted by patent investors. But it appears that these people are the ones considered most important by the Congress in patent hearings and whose advice has been followed. It has been primarily a "negotiation" between the Patent Bar and the Commissioner. Patent attorneys have appointed themselves to speak for people like me without authorization.

They are paid up to $100 per hour or more for every hour from the start regardless of the outcome of their client's patents, so they take no risks. Patent attorneys can never speak for people like me; they are just not qualified because there is far more to the investment-decision than patents.

The Commissioner has some real problems, but there are other ways to solve his problems than by reducing the effectiveness of the patent system as has been done. The job of the Commissioner is only to execute the patent system -- not to decide or negotiate on how the patent system should be constructed. This should be solely the responsibility of the contracting two parties to the patent system -- the public (represented only by Congress) and inventors plus their financial backers who make all the risk-investment and decisions therefor. I mean no disrespect to the Commissioner, but these are the simple facts which apparently have been ignored. The Patent Commissioner is no different from the IRS Commissioner, whose sole job is to collect taxes but never to set the taxes; again this is done only by the Congress, to be discussed further.

Patent attorneys and the Commissioner not only have no decisions in patent investment but have no direct influence on those like myself who make these decisions. The incentives or lack of incentives has only an indirect influence. So if the Congress wants to find out why people like me decide the way we do, and further to influence more people like me to take these high risks which produce the public benefit, they must seek out and listen to the advice of the real decision-makers; and it appears in recent years that this has not been done.

In patent hearings in the past, I corresponded with the Chairmen of the subcommittees on patents. I was sent copies of all hearings and received detailed letters from the Chairmen and others; I believe my efforts had some effect. Today it all appears to be different. When I recently wrote Congressmen responsible for patent legislation, I first had great difficulty even finding the subcommittees handling patents and had almost no response to my letters. Only by a recent call to the local office of a Michigan member of a House subcommittee was I able to find any response to

my views as a professional engineer-inventor. I never before encountered this lack of response. It is understandable with a partial subcommittee on patents in the House and no subcommittee on patents in the Senate. It is even more understandable with all the various PAC and other pressures on members of Congress which interfere with proper consideration of basic and truly important legislation. The patent system and the free-enterprise system is of basic importance if this nation is to survive. But this pressure is the main reason that full subcommittees on patents should be restored, as they existed for most of the life of the patent system.

This paper is only a cursory discussion of what can be done to restore the former enormous effectiveness of the patent system. But the intricacies of patents requires much time for proper consideration; and just because legislators in a multi-subject committee understandably cannot take the necessary time does not change the fact that much time is required to do what is necessary.

For most of the life of the patent system when it was dynamic, the Congress had subcommittees only on patents. The patent system has been a wealth-creating institution in the past. The elimination of subcommittees only on patents is an example of false-economy which has helped to reduce incentives and the enormous public benefit of the American Patent System which served to create our unusual wealth in past years.

A few of the changes in the patent system which discourage incentive can only be mentioned here. One of the worst changes that discourages investment is the "goal" of issuing patents as fast as possible, "so the public gets the benefit quickly and to spur other inventors", according to the logic. However, there is a serious problem to "revolving-door" patents which opposes public benefit; it causes real problems for inventors and others taking these high risks, thereby reducing incentive. However, the explanation is too involved for this paper. But it is suffice to say that when people like me decide to curtail our patent activity (which has happened according to the reduction of patents issued), then the public never gets the inventions that remain on the shelves. And I have some fine projects which I was forced to decide will remain on the shelf.

Another problem for inventors is basing the cost of fees on inventors paying 50% of the cost of the patent system. This decision is founded on several erroneous premises. But again, this problem is too involved to discuss in this paper. However, I can say now that if the public has not benefitted in the past by at least 25-100 times the benefit to inventors, the patent system should have been closed long ago. The patent system did benefit the public by these ratios in the past, and in many cases much more. The public should assume a proportional share of the true cost of the patent system. The total facts are even more startling. Because of R & D and attorney costs in addition to patent fees, inventors actually assume about 80-90% of the cost to bring an invention to market. So the public receives about 20 to 100 times the benefit to inventors (or greater) at only 10-20% of the total cost. Hence, the "50%" premise is not accurate.

There is another very real problem for inventors in obtaining the best organization of patent claims, with the Patent Office now striving to rush out patents as fast as possible. This problem has made it much more difficult and risky for inventors, especially if the patents end up in court. Again this problem favors large firms to help the patent monopoly foster commercial monopolies. There are solutions to this problem which do not destroy incentive but also help solve some of the Commissioner's concerns. However, they are too involved to explain in this paper.

These problems and others can be discussed thoroughly in the future if the Congress shows a real indication of turning around this long destruction of the patent system, such as by passing the Patent Term bill as a small but important first step. And a second important step would be to restore subcommittees on patents --- we cannot afford not to do this.

Another very important problem for investors like me has been the short life of patents, especially in view of the difficulty in development, patenting and marketing an invention. I have had several fine inventions patented after long development time at great cost which are good examples of this problem. When only 8-9 years remained for these patents, manufacturers were understandably reluctant to take a license. If manufacturers are faced with

about $300,000 for development, tooling and promotion costs which may take 4-6 years before recovery, they just end up financing and teaching their competitiors who can copy everything at no cost just a few years later. The same loss of patent time often is produced because the development time is completed after 8-10 years of patent-life.

Of all the "creative arts", inventions are by far the most difficult and costly to obtain protection for, and are the most difficult to enforce in court. Composers and authors have the benefit of copyrights. In Jan. of 1978, the new law extended the term of copyrights. Also, copyrights were made much easier to obtain, and the cost is only $10 --- just once, and without maintenance fees. While copyright infringement is fairly easy to prove, patent infringement is extremely difficult to prove and the cost is enormous. The term of copyrights has been extended to the life of the "creator" plus 50 years. While the legal term of a patent is 17 years, the effective term is very often only 7-10 years for reasons explained above. The new copyright law extends all copyrights obtained before the new law to the new term, as I understant it.

As an example, I now have an excellent invention all developed which required 10 years to perfect, and is a particularly useful device; but this invention is becoming difficult to place because of the $300,000 tooling and promotional cost with only about 10 years of patent-life remaining. My patents for this invention happen to be very basic which is rare. It is difficult to express the sickening feeling after so much work, cost and time and finally obtaining strong patents at great difficulty --- only to lose it all if these patents are not placed within a year or two. It is even more sickening because it is such a useful product and in view of the long term of copyrights.

Also, some years ago, I wrote a book, "Aircraft Carburetion", published by John Wiley & Sons in New York. The book royalty was 12%. Patent royalties average 2-4%. The effective life of the patents just described is about 8-9 years, but the public now continues to pay these much higher royalties for all books, recordings, etc., for the creator's life plus 50 years. The enormous inequity in the "creative arts" is crystal clear.

The important point is that compared to the term of copyrights, the effective patent-term is too short, particularly in view of the greater difficulty and high cost for obtaining patents and for asserting infringement. Actually, from an equity standpoint, patents should have a longer term than copyrights. I found the work in patent programs to be more difficult than writing my book. There are many ways the patent term can be improved so that incentives for the high risk-investments by inventors and small firms will be dramatically increased. Older patents might even be extended only for the original inventor, as was done by the new copyright law.

It appears that "consumer advocates" now oppose the Patent Term bill because it "extends the royalties paid by the public". These people should be asked whether the term of copyrights should be reduced because "too many royalties" are paid to authors and composers for their entire lives plus 50 years. The advocates should be made to understand that patents are so much more difficult to obtain and enforce, and the development work is more difficult and costly than for books and recordings, and that royalties for books and records are about 4-10 times the percent royalties for inventions. I understand that book royalties are about 15%, and income from sheet music and recordings are much higher, even up to 50%.

However, the worst error in the thinking of consumer advocates is to <u>assume</u> that these inventions will <u>always come forth</u> and be agressively pursued by inventors and their financial backers --- even though incentives have been drastically curtailed in recent decades. They just <u>take it all for granted</u>. But the <u>fact</u> is that <u>decision-makers</u> like me have <u>chosen</u> to curtail patent activity because the risks have been made so great in recent years, as proven by the reduction in patents issued while the population has increased. And patent-investors <u>never</u> discuss their decisions to invest with consumer advocates, nor do activists have any influence in our decisions

I can give a good example of the "penny-wise-pound-foolish" advice of consumer advocates in relation to what I was compelled to do because of increased risks. I had an improved cruise control partly developed a few years ago, but was forced to drop the project

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because it was too involved in view of all the increasing risks, and I decided to work only on projects less costly and less complex. The improvement would have reduced the cost to the consumer 25-40%. With the present enormous sale (50% of all cars), a 25% cost-reduction would save the consumer at least $200,000,000 per year --- year after year, which is far more than I would have been paid in royalties. And the sale is expected to increase to 90% of all cars. This is only a small example, but it shows the erroneous thinking of consumer advocates.

The glaring error in the reasoning of consumer advocates is this: They focus only on what I might receive in royalties, and not what my invention might have done for the public, which in this example is far more than the 100 to 1 ratio discussed above, even if the patent term were increased as for copyrights. The result is that the public will never receive this invention, at least not from me. The motivation of people like me to reduce patent activity is hardly the way to improve our technology, as we hear discussed so often as a "goal".

The enormous risk-investment and high cost for the decision-makers in the drug industry would be just as great and no different from the high risks for the decision-makers in any other industry. Hence, all the arguments presented here also apply to the drug industry.

Some of these considerations are difficult to base on facts. It is somewhat like "proving" that automotive turn-signals and cruise-controls really save lives (as they do) by "statistics" of accidents that never happen --- we can see trends, and we just know by the nature of these devices that a net gain in safety will be produced. Similarly, we see a definite reduction in the number of patents issued while our population has increased. We also see a clear decline from our former position as the outstanding industrial and technical leader of the world; and this decline occurred during the same period as for the decline of the patent system.

In the drug industry, it is particularly tragic for the elderly and chronically ill who might be denied a helpful drug because the risk-takers were forced to decide (and they do decide) not to invest in the enormous costs of research and development,

tooling, manufacturing and marketing because the effective patent-life is too short.' The main focus should be on the larger benefit to the public which is always many times larger than what the public pays the inventor and the financial backers.

But there is a far more important consideration than all the foregoing. There is no need to defend or even to prove to anyone that incentive is the major factor requiring "restoration" action by Congress to save the patent system. It is a fact that in the early years of this Republic, one of the first acts of our founders was to establish an institution to encourage citizens talented in the "creative arts" (writers, composers, inventors) to come forth with their contributions for the benefit of the public. This public-benefit is the sole basis for the only legal monopoly in our society --- copyrights and patents --- as an incentive for these talented people. The copyright incentive was recently improved by the Congress, so copyrights are considered to be working properly for the public benefit.

Except for the last few decades, the incentives resulting from the patent monopoly did indeed provide a public benefit beyond the expectation of our wise founders, even with the short term compared to copyrights. But now the patent monopoly opposes the public benefit in important ways discussed herein, while incentives have been reduced which has resulted in less patents issued with increased population.

Hence, incentive was indeed the major "force" utilized by our founders to bring forth enormous benefit to the public ---- and it has worked --- a fact. So if the existing degree of incentive made us the envy of the world, as it did at one time, then it is certain that an increase in this incentive factor will provide a proportional or some increase in the benefit to the public, because the "benefit-curve" does not suddenly flatten out. Since it did work for the nation so well in the past, the burden of proof resides in any doubters; they must prove that in view of the fact that incentive has worked so well in the past, that increasing the incentive suddenly will have no further effect.

As mentioned, the Commissioner's function is to execute the patent system according to the intent of Congress. I must add that in my long experience with patents, the Patent Office has done a good job of what it is supposed to do. Recently, I wrote the Patent Office for the latest rules and regulations. They also sent a copy of a paper presented by the Commissioner to the Patent Law Association of Chicago on Jan. 20, 1982 regarding the changes in the patent system including the new fees he is seeking. His problems indeed are real; in fact they may get far worse than he suggests just in the next 10-15 years.

Hence, dramatic and innovative solutions to his problems are essential. But his "cure" is worse than the disease. The reasoning is based entirely on several erroneous premises, which are too detailed to discuss here. The Commissioner's paper is further evidence of the assumption that policies of the patent system are primarily established by a joint effort of the Patent Bar and the Commissioner --- and indeed it mostly has been done this way in the past. The Commissioner's conclusions highlight the tragedy of this very real problem of a proper perspective of the patent system. His statement on page 18 of the report follows:

> "Given the funding constraints throughout the government, the only realistic alternative to the increased fees is a PTO program well below the present unacceptable level". (emphasis mine)

After all these years, respectfully, is this really the best that can be offered, wherein the "solution" tends to destroy the heart of the patent system --- incentives for the only people who must decide to take these great risks? Of course the statement implies that all other alternatives have been considered, which, respectfully, just cannot be correct. Surely it indicates incomplete consideration at the very least.

Congress should seek realistic solutions from the real parties to the patent system, who mostly are highly creative and talented people and are the only real decision-makers. As only one participant, I can assure you that all alternatives have not been considered. If the purpose of the patent system is to provide jobs for Patent Office employees and provide work for patent attorneys and to reduce the "backlog" --- then no changes are necessary. If the

purpose is to benefit the public by increasing incentives to invest, then drastic changes are necessary. The Congress should soon consider the overall perspective of the patent system to seek major reform to restore and increase incentives, especially in view of the other creative arts.

I now have a project which is simple enough that I have decided to proceed with a patent application. According to the fee schedule set forth in the Commissioner's paper(pages 13 and 18), the filing fee alone would amount to about $1500 if the application is prepared properly (not including attorney fees and development costs). I have had as many as 14 pending applications at one time. Small firms and independent inventors could never handle a comprehensive program like this with such high costs; but large firms would have no problem, so the patent monopoly favors these large firms.

An example of one cause of the deterioration of the patent system is the incentive-destroying maintenance-fees to be applied for the first time in the entire history of the nation. In the Commissioner's paper (page 18), he sets forth the intended maintenance fees --- $400 after 3½ years, $800 after 7½ years, $1200 after 11½ years or a total of $2400 for only one patent just for "maintenance". Some of my projects of medium complexity required a good plurality of patents for proper coverage.

The filing fee of my new and fairly simple application mentioned above would be about $1500, for a total of about $4000 for only one patent! I may need several patents. And this cost does not include the higher attorney fees plus the large costs of development and marketing. This reduction of incentive is tragic consideringg that only 17 years ago and for the life of the patent system the total cost of all fees was $30!

The new rules will indeed close the door to small and medium firms plus independent inventors whose efforts with the help of patents can provide real competition for large firms and conglomerates. And all of this has been done for the sole problem of "backlog" and Patent Office cost based on the erroneous 50% division of costs, when there are indeed positive and incentive-producing ways to solve these problems. We should do everything possible to encourage risk-investment in patents --- not to make it more difficult.

But the most startling statement in the Commissioner's paper and somewhat offensive to people who have risked so much, is as follows:

> "The calculations assume a "mortality rate" of 25%, 50% and 75% for the three payments; i.e., the calculations assume that those percentages of patent owners would not pay the required maintenance fees."

In other words, an average of about 50% of the maintenance fees will not be collected because the excessive cost has forced inventors to forefeit their patents --- as though this is good. For my one product mentioned above with many years to perfect and about 10 years of patent-life remaining, if I must be a part of the "mortality rate", I must forfeit any chance for recovery of my large investment in addition to the problems of the short remaining patent-life discussed above. This is hardly the way to motivate investment in patent programs of such high risk. Only large firms can handle the total patent costs, so the patent monopoly will encourage commercial monopolies even more than at present. Individuals and small firms could never handle many applications at one time with the new rules, which is often necessary for proper coverage; so the new rules act as an obstacle to investment.

Also, if the maintenance fees apply to any patent filed before the new fees are published, it is a breach of our patent "contract". I decided to file in these cases only with the representation of having the full term at the cost agreed upon when filed. No contract should be changed after it is agreed upon.

I have already curtailed my patent activity, as many small firms and independents will do. So the Commissioner will indeed "solve" his problems by "increasing" motivation --- motivating risk-takers to decide not to file applications. This will help to "reduce the backlog", but it will also reduce the public-benefit of the patent system. These are the very people who should be motivated to increase their patent activity. In order to increase incentives, inventors and small firms should have no maintenance fees.

For the entire life of this nation, Congress rejected maintenance fees as used in foreign patent systems. The "battle-cry" by advocates of maintenance fees and other causes was to "catch up" with the rest of the industrialized world. The Commissioner's

paper is filled with charts showing foreign facts supporting this argument. At one time, America was the envy of the "industrialized world", but only during the period when we had a truly dynamic patent system. We indeed have "caught up" with foreign countries --- we have "caught up" with lower productivity, inflation and all the other proplems, all with the help of incentive-destroying changes in our patent system. We should and can be the envy of the world again --- by not blindly imitating what others do, but doing what we should do to restore our former superiority. And this can be done only by restoring and increasing the incentives that gave us this superiority and made us so much more productive in the past.

A very dangerous present trend in our society is the conglomeration of large firms buying up small firms to produce concentration of industrial power. In future years, with proper reform, the patent monopoly could be a major factor to help retard and reverse this dangerous trend; it can motivate talented risk-takers to form and operate small firms based on patents which then compete successfully with "divisions" of conglomerates. So one of the most important functions of the patent system in the future could again be for the patent monopoly to prevent commercial monopolies -- but only if incentives are restored and increased, the very opposite of what is now being done.

This all indicates that the main consideration of patent-system reform is only to solve the Commissioner's problems and to consider the interests of patent attorneys, which are not the same as for the "decision-makers". The real intent of the patent system only appears to be incidental, and secondary at best --- which is to motivate people like me to decide to invest in patent programs.

The cruel truth ---a fact--- is that patent attorneys have never been and never will be a party to the contract comprising the patent system. And Patent Commisioners, respectfully, have never been and never will be a party to the contract comprising the patent system.

The patent system is indeed a contract --- between only the public and any citizen who chooses to be an inventor along with their financial backers. And that's the real patent system. The issued patent is the contract; it "teaches" the public the inventor's

new thing as his contribution, and the public agrees to a period of time for the exclusive "right to prevent others" from using the new thing. Patent attorneys and the Commissioner are only agents for the contracting parties. The "end of the line" for the public in this negotiation should be the subcommittees for patents.

The real and only purpose of the patent "contract" is for one party (the public) to influence the other party (investors) to decide to spend their time and funds at high risk on patenting, developing and promoting their inventions. Patent attorneys and the Commissioners never make these decisions and are never parties to this patent contract. This is the most important single statement that could be made to the Congress regarding the patent system.

Conclusion

The foregoing discussion only mentions some of the problems which have dramatically reduced incentives, particularly for small firms and inventors with their financial backers. When these people decide to reduce or not to pursue their patentable projects, as I have decided in recent years, the public never gets the inventions that remain on the shelves. Then the public loses the benefits they might have had and which are always many times more valuable to the public than the benefits to the inventors. Since mostly large firms can still cope with comprehensive patent programs, the patent monopoly now works against the public interest by fostering commercial monopolies in larger firms.

It has taken about 25 years to destroy the effectiveness of our once-vital and unique patent system. So I was surprised to learn of the Patent Term bill, even though it only affects one special industry. It is a first small step that could turn around the 25 year decline of our patent system. This concept can be expanded with even more benefit to the public in the near future.

This Patent Term bill appears to be a small thing in view of our present problems. But it represents something very important in solving these problems, and hence should be above politics. We are all "riding in the same ship", and the ship has holes in it. If we don't plug the holes, the ship will sink. No one can predict whether the next generation will choose to reduce or increase the large expenditures for our social programs by "transferring" wealth.

But whatever they decide, they had better be sure not to destroy our wealth-creating institutions like the patent system. Water cannot be "transferred" from an empty glass. Our once-powerful free-enterprise system was the major factor which created our unusual wealth, and our unique patent system was one of the rocks upon which the free-enterprise system was built, and which has been so productive in the past. Hence this bill is more important than it appears. Restoration of the patent term is a good first small step. The next step should be the restoration of the patent system itself --- by holding new hearings for major reform.

But the restoration of the patent system is impossible, in view of the enormous pressures on members of Congress, unless the full subcommittees on patents are restored. There indeed are innovative improvements which not only can solve all the Commissioner's problems for the next century, but can restore and dramatically increase the incentives which can double or triple the real benefits to the public. Respectfully, the Congress must either address these problems in their proper perspective or this wealth-creating institution will be gone. And wealth must be created before it can be transferred.

I urge you to pass this bill without delay as only a first small step to restore and improve the incentives which produce the public benefit of the patent system.

THE INDUSTRY VOICE

The National Agricultural Chemicals Association (NACA) is the National Association of the manufacturers and formulators of pest control products employed in agricultural production. NACA membership is composed of the companies which produce and sell virtually all of the technical pesticide materials (active ingredients), and a large percentage of the formulated products registered for use in the United States.

TYPES OF PRODUCTS

Chemical products produced or formulated by members of NACA include: herbicides, insecticides, fungicides, rodenticides, defoliants, miticides, nematocides, desiccant, plant growth regulators, and other related agricultural chemicals.

PURPOSE OF THE ASSOCIATION

NACA was organized in 1933 to promote the interests of manufacturers and formulators of agricultural chemicals.

The primary purpose of the National Agricultural Chemicals Association is to provide a collective industrial force to advance the level of public understanding of the value of pesticides in the production of food and fiber, to foster legislation which will promote the safe and proper use of Industry products and encourage continuing research of new products.

The Association staff is located in Washington, D.C. Activities of the Association are developed through a committee system composed of volunteers from members companies, and represent a wide range of technical expertise. Committee members serve without remuneration, and provide a collective industrial force to:

1. Stimulate research to improve the quality of pest control materials and techniques, to encourage the development of improved chemicals, the discovery of new chemical tools and uses which will contribute to an improvement in the ability of American agriculture to produce food and fiber.
2. Encourage better methods of application of crop protection chemicals with special emphasis upon safety and efficacy of the techniques employed to control pest populations.
3. Cooperate with state and Federal agencies, agricultural groups, industry scientists and other scientific bodies to further scientific pest control strategies.
4. Assist in the development of reasonable regulatory controls governing the use of agricultural chemicals, and to support sound legislative proposals in the public interest which will contribute to practical and economical regulations for all concerned.
5. Inform the members of the Association and the public about significant developments in the field of scientific pest control which have special application to agricultural production.

ORGANIZATION

NACA is incorporated under the laws of the State of Delaware as a non-profit organization. The Board of Directors is elected by the membership and is responsible for establishment of policy, setting budgets, and providing general policy guidance to all Association activities. The 30 members of the Board represent all sizes of companies, and all sections of the United States. The Board usually meets at least 3 times a year.

The Executive Committee is the working arm of the Board, meeting to deal with matters of policy. It is composed of the Chairman, Vice Chairman, immediate Past Chairman, President, and seven members of the Board.

COMMITTEE COMPOSITION

Through active participation in Association committee work, members involve themselves in making and carrying out NACA policies. The various committees advise and report to the Board of Directors on matters covered by their particular area of special competency. When necessary they may implement policies which have been approved for action programs.

All member companies have an opportunity to indicate an interest in representation on committees of their special interest. The Chairman of the Board of Directors appoints Committee Chairmen who in turn appoint members to their respective committees.

Standing Committees include:

Annual Meeting Planning, Executive, Foreign Affairs, Formulators, Good Environmental and Operating Practices, Industry Statistics, International, Law, Membership, Nominating, Occupational Safety and Health.

Patent Law, Pest Management, Public Relations, Regional and State Association Policy Advisory, Regulatory, Research Directors, Toxicology, Transportation and Distribution, and Washington Representatives.

Ad hoc Committees are also formed as the need and occasion dictate to deal with specific shortrange objectives.

TASK FORCES

The Association assists members with interest in one product or a group of products which are related by sponsoring the formation of such producing companies into Task Forces. This distinguishes and separates their activities from regular Association committee work.

RESOURCE LIST

The Association maintains a resource list of over 400 experts in 24 different categories relating to agricultural pesticides, their use, and manufacture. Some of these areas complement ongoing activities of standing Committees and Subcommittees, but there are several areas in which expert advice and counsel may be desirable and which are not being studied as a regular function of a committee.

MEMBERSHIP ELIGIBILITY

Any company is eligible for active membership if it produces or formulates any Industry product within the United States or its possessions.

Membership as an associate is available to those companies which are conducting research and development programs reasonably expected to lead into the marketing of pesticides, and to commercial research organizations regularly conducting work in the field of pesticide chemicals.

Application for membership in the Association is made in writing on forms available from the Association office.

COST

Active membership dues are based on a rate of assessment against sales. The rate is determined annually by the Board of Directors. Associate membership dues are also determined annually by the Board. Annual reports of member company sales are made to a Bank Trustee on a strictly confidential basis.

SERVICES

A number of special services are provided to company members, and include:

Bulletin services: Issued to keep NACA members abreast of important developments in legislation, regulation, public relations and information, and other areas of interest to the industry.

Special publications: These are publications containing information of value to the industry. Such information is generally not available from any other source.

Committees: All Association members have opportunity for representation.

Legislative—Regulatory: NACA members are represented in state and Federal matters by assigned staff and designated committee members.

ANNUAL MEETING

The annual Meeting of NACA serves as a common meeting ground for Industry members, state and Federal officials, and representatives of groups interested in the broad field of agriculture and pest control.

SAFETY INFORMATION AND EDUCATION

The NACA is actively supporting and participating in programs designed to promote the safe and judicious use of its members' products. A number of special communications techniques have been employed to develop packaged materials which lend themselves to easy delivery of safety messages to large groups, small groups and individuals.

The Association is actively involved in cooperative efforts with such groups as the National Safety Council. The National Clearinghouse for Poison Control Centers, National Poison Prevention Week and many others.

PUBLIC RELATIONS

The Association maintains a high level of public relations activity designed to promote the safe and judicious use of agricultural chemicals, and to develop a better understanding and appreciation among a broad range of publics of the role of Industry products in protecting the food and fiber production of the United States.

UNIFIED EFFORT

By working through the NACA, manufacturers and formulators of crop protection chemicals contribute to the advance of scientific crop protection and to the progress of the Industry. Companies which participate actively in the programs of the Association contribute not only to their own future, but to the future of modern agriculture and the opportunities which are ahead.

FURTHER INFORMATION

If you would like more information about the organization or operation of the Association, membership qualifications, or any of the specific programs being conducted, write to: President, National Agricultural Chemicals Association, 1155 15th St. N.W., Washington, D.C. 20005, Tel. (202) 296-1585.

American Chemical Society

OFFICE OF THE
PRESIDENT

Albert C. Zettlemoyer
President-Elect, 1980
President, 1981

1155 SIXTEENTH STREET, N.W.
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September 11, 1981

The Honorable Robert W. Kastenmeier
Chairman
Subcommittee on Courts, Civil Liberties,
and the Administration of Justice
Committee on the Judiciary
House of Representatives
Washington, D.C. 20515

Dear Chairman Kastenmeier:

The American Chemical Society firmly believes that technological innovation underlies and supports modern society and that its management should be a matter of national policy. An indispensable factor in promoting innovation is a strong patent system. Accordingly, the Society has repeatedly supported efforts to improve our patent system and its practical utilization.

Last year Congress took several major steps toward improving the patent system with the enactment of P.L.96-517. The Congress has the opportunity this year to take another positive step in this direction, through the enactment of H.R.1937, "Patent Term Restoration Act of 1981." The position of the American Chemical Society on the issues addressed in this bill has been set forth in the attached statement submitted to the Senate in connection with S.255.

The Society encourages you to take the necessary steps toward completion of Committee action on H.R.1937, and toward passage by the House. If we can be of additional assistance to you and the Subcommittee as it works on this bill, please call on us.

Sincerely yours,

Albert C. Zettlemoyer

Albert C. Zettlemoyer

Enclosure

ACS 81-010

STATEMENT

OF

DR. ALBERT C. ZETTLEMOYER

on behalf of the

AMERICAN CHEMICAL SOCIETY

to the

COMMITTEE ON THE JUDICIARY

UNITED STATES SENATE

on

S.255, PATENT TERM RESTORATION ACT OF 1981

Mr. Chairman and Members of the Committee:

My name is Albert C. Zettlemoyer. I am President of the American Chemical Society, and I appear before you today with the authorization of the Society's Board of Directors. Accompanying me is Dr. Willard Marcy, immediate past Chairman of the Society's Committee on Patents and Related Matters. The American Chemical Society welcomes this opportunity to comment upon S.255, the "Patent Term Restoration Act of 1981".

The patent system has served our country well. The basic principles supporting a patent system continue to apply in the modern world, and are ever more forcefully recognized by technologically advanced countries throughout the world. Yet the progress of science and technology has, inexorably, diminished the originally contemplated incentive value of the patent system. The legislation before us, S.255, is designed to compensate for the changes in the patent incentive for chemical science and technology by the simple method of restoring some of the incentive which has been lost. It seems quite logical that the patent laws keep pace with the progress of science and technology and adjust to new externally imposed constraints - specifically those of the regulatory process. The American Chemical Society believes that this bill is a positive step in that direction.

Although the proposed legislation does not treat the often overriding factor of the high cost of compliance with these regulations, it does address the time delays associated with the regulatory process. A corresponding restoration of the patent term could provide a logical and vital means to foster innovation. The American Chemical Society believes that investment in fundamental research - the foundation of innovation - would be encouraged by changes in the U.S. patent laws which would make more definite the period during which the investment might be recouped and a reasonable return on the investment might be realized. This belief is based on observations which

concern the ACS, namely that R&D resources are being diverted from new products, that small chemical enterprises are disappearing, and that students are seeking careers in fields other than chemistry.

Until the recent advent of prolonged regulatory procedures for chemical products, especially in the health and environmental areas, the 17-year period of exclusivity afforded under the present United States patent law appeared to provide a workable balance between investment incentives and the public interest in access to technology. This balance is skewed where the lack of government approval significantly delays the chemical inventions. In effect, the federal government is shortening its own grant of patent rights.

It is important to the nation, and to society as a whole, that the chemical research structure in this country retain its strength and vitality. Applied science and basic science go hand in hand, each supporting the other, each leading the other to further insights and useful applications. The ACS believes that S.255 is a necessary corrective measure to an ever-growing problem - the diminished incentive to innovate in this country.

The growth of chemistry and its impact on society has reached extraordinary fruition only recently. From a science dealing largely with laboratory curiosities, chemistry has evolved into one of the major technology-based enterprises in the nation and has made untold contributions to the quality of our lives. Chemistry and chemists have contributed in large measure to such progress as:

- new compositions for new applications not previously known or imagined, such as in contact lenses and transistors, to other practical applications, such as fabrics to clothe an increasing population;
- new structural materials, including high strength metal alloys, polymers, adhesives and heat resistant ceramics such as those used for reentry vehicles in space exploration;
- complex biologically active compounds, to prevent or treat diseases of humans and animals;
- agricultural chemicals that have helped make U.S. agriculture a major supplier to the world; and,
- all of the advances in photography, lasers, spectroscopy, solid and liquid fuels, and so many other things the public now takes completely for granted, but were undreamed of 100 or even 50 years ago.

The enormous diversity and challenge of chemistry is such that there are more scientists in the United States engaged in chemistry than in any other scientific discipline. A vast industry has grown around the technological applications of chemical science. This industry not only provides employment for several millions of people, but also contributes to the technological leadership of the United States. Chemical science, while enhancing the material qualities of life, continues to lead the human mind and spirit into new and challenging areas.

Most products of the chemical industry are new compositions not occurring in nature; thus, the full range of their properties is largely unknown without experimentation. Recent experience has shown that our environment has a limited ability to tolerate many such chemicals, either because they do not decompose under ordinary conditions, or because the very properties which make them useful for certain purposes may cause them to be detrimental under other circumstances. Scientists now can detect residues that would have been undetectable only a few years ago; they know that low-level ingestion of some substances may have long range harmful effects, and that the release of certain materials into the environment may have undesired consequences. Chemists have been in the forefront in developing much of the knowledge that has made it possible to have this information.

The American Chemical Society has continually supported appropriate legislation and regulations designed to enhance human health and safety, and to protect the environment. However, the Society is acutely aware that the advent of new technology, the safety requirements aimed at employees and consumers, and the implementation of the three major laws enacted to ensure the safety of chemical products - the Toxic Substances Control Act (TSCA); the Fungicide, Insecticide and Rodenticide Act; and the Food, Drug and Cosmetic Act - have led to requirements for complex, expensive, time-consuming testing, and a very thorough review of data and claims. Much of this testing and review is carried out after any patent protecting the product or its use has been issued, and the clock measuring its term has started to tick.

New technology, coupled with these laws, has changed the way chemicals are handled, developed, and used. While these laws have increased the cost of new developments, it also appears that they have reduced the commercial introduction of those products which cannot bear the increased costs. The impact of new technology and these laws, in general, goes far beyond that which can be reached by a change in the patent incentive. However, there appear to be some areas of chemical progress where a significant portion of the diminished incentive can be recovered by the simple expedient of restoring that portion of patent life which is lost due to self-imposed restraint and to the regulatory process, both requiring extensive testing for the safety of humans and animals, and review by government agencies. There is sufficient experience with these regulations, as applied to pesticidal and pharmaceutical products, to document the time and cost involved in compliance. For other chemicals, which are subject to TSCA, there is still insufficient experience to assess the full impact of the law. It appears, however, that to the extent that a regulatory agency may require proof that a certain chemical is safe in a human environment, the time and cost associated with compliance to TSCA may be extensive.

The importance of maintaining reasonable controls over substances entering our environment is recognized. It also is important, however, that the regulatory process not unduly reduce the incentive to invest in and conduct the research that will lead to useful new discoveries. It is important that the incentives to innovation which helped make this country preeminent in technology be preserved. To the extent that they have been diluted by ever-more time-consuming regulatory procedures, these incentives must be restored, where possible, so that they can continue to fulfill the objective of promoting "progress in science and the useful arts," as stated in the Constitution of the United States.

It is argued by some that, since the problem results from delays arising associated with the regulatory process, the solution should lie in making the regulatory process more efficient, not in restoring to the patent term the time lost in this regulatory process. The ACS certainly favors improvements in regulatory procedures that would minimize delays. To the extent that such improvements are achieved, there would simply be a corresponding shortening of the period that needs to be restored to the patent term under this legislation. There is nothing in the concept of patent term restoration that precludes seeking and implementing ways to make the regulatory process more efficient. However, it should be recognized that not all of the present delays result from inefficiencies on the part of the regulatory agencies; a chronic toxicity study will still consume approximately three years or more, no matter how efficient the agency.

The United States patent system was provided for in the Constitution, and the first patent law was enacted in 1790, almost 200 years ago. While chemical science has evolved beyond man's imagination, the patent system has been remarkably stable, not only in its philosophical basis, but also in its basic legal aspects. The American Chemical Society urges passage of S.255 so that the patent laws may keep pace with the progress of technology, and in order for the patent system to adjust to externally imposed constraints that are inherent in many regulatory procedures.

To acquaint you with the American Chemical Society, we would like you to note that ACS is an individual membership organization composed of approximately 120,000 chemists and chemical engineers reflecting a broad spectrum of academic, governmental, and industrial professional pursuits. Approximately 60 percent of the membership is employed by industry, 25 percent by academic institutions, and 15 percent by governmental and nonprofit insitutions. The Society's interest encompasses both the basic science aspects and the many practical applicatlons of chemistry.

The ACS, founded in 1876, was chartered as a nonprofit scientific and educational organization by an act of Congress signed into law on August 25, 1937. Under its National Charter, the Society is charged with the responsibility to encourage in the broadest and most liberal manner the advancement of chemistry and the promotion of research in chemical science and industry, "thereby fostering the public welfare and education, aiding the development of our country's industries, and adding to the material prosperity and happiness of our people."

The Charter imposes an obligation on the Society to provide assistance to the government in matters of national concern related to its areas of competence. Since one of the objectives of the ACS Federal Charter is the promotion of research, the Society appreciates the opportunity that has been given it today to comment upon S.255, the "Patent Term Restoration Act of 1981."

88-310 O—82——37

APPENDIX 2.—CORRESPONDENCE

A. John Conyers, U.S. Representative (Michigan)

B. R.D. Cosgrove, President, Ohio Medical Products

C. Benjamin Elder, President/Chief Executive Officer, Metropolitan Savings

D. Larry J. Eriksson, Vice President-Research, Nelson Industries, Inc.

E. James E. Hopkins, President, Hopkins Agricultural Chemical Co.

F. Robert A. Jerred, Research Products Corporation

G. R.H. Leazer, President, Ohio Medical Anesthetics

H. Jack Olshansky, Division Vice President/General Manager, Cutter Medical, Cutter Laboratories, Inc.

I. James A. Pittman, Jr. Dean, University of Alabama

J. Kenneth Preston, Jr. Vice President/General Counsel, TRW, Inc.

K. James H. Sammons, M.D., Executive Vice President, American Medical Association

L. Roth S. Schleck, Chairman of the Board/Chief Executive Officer, First Wisconsin National Bank of Madison

M. Robert W. Schumann, Vice President, Nicolet Instrument Corporation

N. George Schwartz, Executive Director, Milton A. Bass, General Counsel, National Association of Pharmaceutical Manufacturers

O. George W.F. Simmons, Chief Patent and Trademark Counsel, Rohm and Haas Company

P. Joel Skornicka, Mayor, City of Madison

Q. Sherman E. Unger, General Counsel, United States Department of Commerce

JOHN CONYERS, JR.
1ST DISTRICT, MICHIGAN

COMMITTEES:
JUDICIARY
CHAIRMAN
SUBCOMMITTEE ON CRIMINAL JUSTICE
GOVERNMENT OPERATIONS

WASHINGTON OFFICE:
2313 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, D.C. 20515
PHONE: 202-225-5126

DETROIT OFFICE:
642 FEDERAL BUILDING
231 W. LAFAYETTE
DETROIT, MICHIGAN 48226
PHONE: 313-226-7022

Congress of the United States
House of Representatives
Washington, D.C. 20515

September 29, 1981

Honorable Robert W. Kastenmeier
Chairman, Subcommittee on Courts, Civil Liberties, and
Administration of Justice
2137 Rayburn HOB
Washington, D.C. 20515

Dear Mr. Chairman:

I understand that the Subcommittee on Courts, Civil Liberties, and Administration of Justice is scheduled to hold hearings on Wednesday and Thursday of this week on the Patent Term Restoration Act. Allow me to share with you some concerns I have about its impact on consumers, especially the elderly.

The pyramiding of chemical, use, and process patents often provide the name-brand pharmaceutical companies with a monopoly over drug products for over 17 years, the statutory maximum life for a patent. An extension of this effective patent life for an additional 7 years would further delay and possibly preclude entry into the market by generic manufacturers and result in steeper health care costs. The burden of higher prices would fall disproportionately on the elderly, who already expend 36% of their total health care costs on prescription drugs.

Our aged can not afford to bear this burden. Elderly Americans now constitute the fastest growing segment of the poverty population. More seniors joined the ranks of the impoverished during 1979, the latest year for which figures are available, than any single year since 1959 when the Census Bureau first compiled such statistics. The average cost of health care for an elderly person is expected to rise to almost $3,900 by 1984. To the extent that Federal funds help to finance the purchase of needed drugs, the costs of extending patent protection would be borne by the Federal treasury.

The companies which stand to benefit from such legislation are among the most profitable multinationals, which retain a market share of 80%-90% of important drug products even after their patents expire. The Office of Technology Assessment has concluded that research and development has not suffered because of generic competition, available evidence does not support the claim that patent extension will increase innovation, and patent extension will raise prices and increase profits for the big drug companies.

In the interest of developing a full record on the issue, I respectfully urge you to consider the adverse effects patent extension could have on competition, prices, and health care costs at the hearings this week.

Sincerely,

John.

John Conyers
Member of Congress

Ohio Medical Products 3030 AIRCO DRIVE • P.O. BOX 7550 • MADISON • WISCONSIN 53707
TELEPHONE: 608-221-1551

September 23, 1981

Honorable Robert W. Kastenmeier
U. S. House of Representatives
Washington, D.C. 20515

Dear Mr. Kastenmeier:

Ohio Medical Products, a division of Airco, Inc., manufactures and distributes life support equipment in the United States, Canada, and worldwide to hospital, clinic, and paramedic personnel. Ohio Medical Products has been located in Madison, Wisconsin, since the acquisition of the Scanlan-Morris Company in 1945, and currently employs 1,063 people locally and 2,303 people nationwide.

We have noted a definite trend toward many firms expanding into the Sun Belt, with a resulting decrease in the number of persons employed in the greater Madison area or in the state itself. It is, therefore, important to encourage growth and expansion in research and other areas of industry in Madison and the State of Wisconsin.

Your Patent Term Restoration Act attempts to establish additional incentives for research and development. That bill, H.R. 1937, should be supported WITH AMENDMENT by all Wisconsinites. The bill will result in more research, but it should be IMPROVED to cover the few products which have completed the regulatory review period but which are unable to benefit under the bill's current language. We have been unable to market a new product, formerly under Ohio Medical Products but now under our new sister division, Ohio Medical Anesthetics, during review by the Food and Drug Administration, which has lasted for approximately ten years.

We are appreciative of the close cooperation you are giving to the Greater Madison Chamber of Commerce and to the research arms of Wisconsin for Research and The Wisconsin Alumni Research Fund. Our company supports your attempts to expand Madison as a research center, and we look forward to working closely with you in the future.

Sincerely,

R. D. Cosgrove
President

RDC-nlp

BENJAMIN L. ELDER
President
Chief Executive Officer

September 14, 1981

Honorable Robert W. Kastenmeier, Chairman
Subcommittee on Courts
Civil Liberties and the Administration of Justice
Committee on the Judiciary
U. S. House of Representatives
Washington, D.C. 20515

Dear Mr. Kastenmeier:

I am writing to you to ask your support for a matter to come before your Subcommittee dealing with the extension of patent protection. It is my understanding that the Senate has already passed the bill, S. 255 and it is now before the House of Representatives.

As an investor in a firm which has spent much time and effort in the research and development of a patented medical device, I cannot tell you how important the stretching out of patent protection to cover that investment in time might be. It has been of continuing concern to us that the extended period of development has used up much of the precious patent life of what we hope to be a contribution to the medical field. Your support of this measure is earnestly requested.

Very truly yours,

BLE/js

31550 NORTHWESTERN HIGHWAY / FARMINGTON HILLS MICHIGAN 48018 · TELEPHONE 313 851-5300

NELSON INDUSTRIES, INC.
P.O. Box 428
Stoughton, Wisconsin 53589
U.S.A.
(608) 873-4373
Telex 26-5433

October 1, 1981

The Honorable Robert W. Kastenmeier
U. S. House of Representatives
Washington, DC 20515

Dear Mr. Kastenmeier:

As a local manufacturing firm with an active technical program, Nelson Industries, Inc. is very interested in any measures to improve the federal patent process. During the forty-two years Nelson has been in business, continuously headquartered in Dane County, we have acquired a large number of patents covering a wide range of product inventions. Occasionally these inventions do require a regulatory review of some type before they are commercialized. We strongly support your efforts to improve the patent process in this area through your bill H. R. 1937.

However, concern has been raised that this bill could be improved by making some provision for also extending the patent life for products that have been through a lengthy regulatory review process but are ineligible for patent term extension under the present bill. We support a change along lines that would allow some degree of patent extension for these existing products.

Thanks for your interest in this area.

Sincerely,

NELSON INDUSTRIES, INC.

Larry J. Eriksson
Vice-President, Research

/ps

Hopkins

HOPKINS AGRICULTURAL CHEMICAL CO.
P.O. Box 7532, Madison, WI 53707
(608) 222-0624 • TWX 910 286 2731

October 7, 1981

Honorable Robert W. Kastenmeier
U.S. House of Representatives
Washington, D.C. 20515

Dear Mr. Kastenmeier:

Your sponsorship of HR 1937, the Patent Term Restoration Act, has been brought to our attention. We applaud your support of this legislation and your considerable efforts on behalf of PL 96-517, which was of such great potential importance to Madison. A small technologically based company such as ourselves must from time to time seek out the expertise of the University community as an aide to our development of new and useful products for agriculture.

PL 96-517 may someday be very instrumental in enabling us to make the investment required to bring ideas developed at the University into the marketplace.

Regarding more specifically HR 1937, we urge you to support the effort to amend the bill to cover unexpired patents on products which have completed the regulatory review period prior to enactment of the bill. We have had experience with the government regulatory process in our field, and know that the process can be not only expensive but of extended duration. If it is fair to restore the statutory term for patents covering products subjected to the regulatory process during or after enactment of the bill, and we believe it is, equal considerations of fairness would require that patents for products which have in the past been subjected to the same regulatory delays that have given rise to your sponsorship of HR 1937 should receive equal treatment.

I appreciate your consideration of this matter, and more generally, the close cooperation and interest you have shown to the Greater Madison Chamber of Commerce, Wisconsin for Research, Inc. and WARF relative to the concerns and hopes of the Madison technological community.

Sincerely,

HOPKINS AGRICULTURAL CHEMICAL CO.

James E. Hopkins

James E. Hopkins
President

JEH:nb

RESEARCH PRODUCTS CORPORATION

1015 EAST WASHINGTON AVENUE • P.O. BOX 1467 • MADISON, WISCONSIN 53701 • 608/257-8801
CABLE ADDRESS: RESEARCH - MADISON (USA)
TWX: 910 286-2781 (RESEARCH MDS)

PRESIDENT

October 7, 1981

The Honorable Robert Kastenmeier
U.S. House of Representatives
2232 House Office Building
Washington, D.C. 20515

Dear Congressman Kastenmeier:

Research Products Corporation has for many years been engaged in the design and manufacture of products to improve environmental air quality and other related products in the Madison area. Our company is technology-oriented and we feel that a strong, viable patent system is essential to our continued growth and expansion. We have supported the considerable efforts by the Greater Madison Chamber of Commerce and the University of Wisconsin as a member of the Industrial Liaison Council, College of Engineering, University of Wisconsin and a charter member of Wisconsin for Research, Inc., to develop a strong working relationship between the skilled scientists of the University and technology-based research and manufacturing organizations located within the Madison area or interested in locating here in the future.

We believe that an economic climate which is favorable to technological research, development and manufacturing is essential to the future desirable growth of Madison. In that respect, we support your past efforts to improve the patent system, particularly your work in obtaining passage of PL 96-517, which was so particularly important to the Madison community. We additionally support your sponsorship of the Patent Term Restoration Act, HR 1937. However, we feel that in the interest of equity and fairness, HR 1937 should be improved to cover unexpired patents on products which have completed the regulatory review period. We are aware that some Madison companies and the University have been and will be deprived of the benefits of their patents for a portion of the patent term because of the time their products were subjected to regulatory review. We believe it is only fair to substantially restore the effective term of those patents to the full statutory period. We think that all of the arguments which support your present bill apply equally to unexpired patents covering products which have been fortunate enough to have completed burdensome regulatory review periods.

We thank you for your attention to our concern, and express our support for your efforts to assist the Madison community in improving the economic climate for innovation and the development of Madison as a research center.

Sincerely,

Robert A. Jarred

Robert A. Jarred

emt

Ohio Medical Anesthetics 2005 WEST BELTLINE HIGHWAY • MADISON WISCONSIN 53713 • TELEPHONE 608-221-1551

September 22, 1981

Honorable Robert W. Kastenmeier
U. S. House of Representatives
Washington, D. C. 20515

Dear Mr. Kastenmeier:

Ohio Medical Anesthetics is a newly organized division of Airco, Inc., and formerly operated as the Anesthetics Department of Ohio Medical Products in Madison, Wisconsin. Ohio Medical Anesthetics manufactures and distributes inhalation anesthetics in the United States and Canada.

We have noted a definite trend toward many firms expanding into the Sun Belt, with a resulting decrease in the number of persons employed in the greater Madison area or in the state itself. It therefore is important to encourage growth and expansion in research and other areas of industry in Madison and the state of Wisconsin.

Your Patent Term Restoration Act attempts to establish additional incentives for research and development. That bill, H.R. 1937, should be supported WITH AMENDMENT by all Wisconsinites. The bill will result in more research, but it should be IMPROVED to cover the few products which have completed the regulatory review period but which are unable to benefit under the bill's current language. We have been unable to market one of our new products, Forane, during review by the Food and Drug Administration which has lasted for approximately ten years.

We are appreciative of the close cooperation you are giving to the Greater Madison Chamber of Commerce and to the research arms of Wisconsin for Research and The Wisconsin Alumni Research Fund. Our company supports your attempts to expand Madison as a research center, and we look forward to working closely with you in the future.

Sincerely,

Dick Leazer

R. H. Leazer
President

RHL:mj

Cutter

CUTTER LABORATORIES, INC.

2200 POWELL STREET
EMERYVILLE, CALIFORNIA 94608
(415) 420-4000

August 25, 1981

Robert Kastenmeier
2232 Rayburn Street
House Office Bldg.
Washington, D.C. 20515

re: Patent Term Restoration Act of 1981

Dear Representative Kastenmeier:

Cutter Laboratories, Inc., as a manufacturer of biological and medical products, urges the Patent Term Restoration Act be extended. We also urge that the term of patents which fall within the products covered by the U.S. patents which have not expired prior to the effective date of the above Act also be extended for a period of time equivalent to the regulatory review period.

The literature is replete with additional requirements introduced by the FDA Act of 1962 and such requirements have prolonged the period prior to product release. This delay has shortened the effective period of unexpired patents, and an extension of the Act to cover such products would provide a more equitable basis for return on the investment of companies such as Cutter Laboratories.

Sincerely,

Jack Olshansky
Division Vice President and
General Manager
Cutter Medical

JO/br

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ICS IPMWBWB WSH

SUSPECTED DUPLICATE: 4-005935S279 WBA 010 ICS IPMBNGZ CSP

2059345391 TDBN BIRMINGHAM AL 181 10-06 0841A EST

PMS CONGRESSMAN ROBERT KASTENMEIER RPT DLY MGM

2232 RAYBURN HOUSE OFFICE BLDG

WASHINGTON DC 20036

BT

DEAR CONGRESSMAN KASTENMEIER

THIS IS TO ENDORSE HR1937 OR S-255 WHICH INCREASE THE DURATION OF PATENT PROTECTION FOR NEW PHARMACEUTICAL PRODUCTS. THE CURRENT LAW GIVING PROTECTION FOR 17 YEARS FROM TIME OF INCEPTION IS INADEQUATE AND PROVIDES TWO SHORT A TIME FOR APPROPRIATE RETURN TO THE COMPANY TO STIMULATE RESEARCH AND DEVELOP ON NEW CHEMICAL AGENT FOR THE TREATMENT OF HUMAN DISEASE. THE LAW IS ANTIQUE AND OUTDATED FOR MODERN SOCIETY AND NEEDS REVISION TO PROMOTE RESEARCH BY AMERICAN PHARMACEUTICAL COMPANY.

ONE CREDENTIAL OF MINE WHICH MAY BE OF INTEREST TO YOU IN THIS CONNECTION IS THAT I WAS THE PRIMARY AUTHOR OF THE RESOLUTION PROMULGATED BY THE NATIONAL ACADEMY OF SCIENCES IN 1975 URGING CHANGES IN THE STATE-ANTISUBSTITUTION LAW TO PREMIT PHARMACIST TO UTILIZE CHEAPER GENERIC BRANDS OF EQUIVALENT DRUGS. SUCH CHANGES HAVE NOW BEEN MADE IN MOST STATES. ONLY BY AN ACCOMPANYING CHANGE IN THE FEDERAL LAW PROVIDING LONGER PATENT PROTECTION AND ADDED INCENTIVE TO PHARMACEUTICAL COMPANIES TO PURSUE RESEARCH ON NEW DRUGS WILL SUCH RESEARCH BE ACCOMPLISHED.

I URGE YOU TO CHANGE THE FEDERAL LAW ACCORDINGLY.

SINCERELY

JAMES A PITTMAN, JR, MD, DEAN UNIVERSITY ALABAMA SCHOOL OF MEDICINE
UNIVERSITY STA
BIRMINGHAM AL 35294

TRW

EXECUTIVE OFFICES

October 2, 1981

The Honorable Chairman Peter W. Rodino
United States House of Representatives
Washington, D.C. 20515

Subject: Patent Term Restoration Act of 1981
H.R. 1937 - Counterpart of S.255

My dear Mr. Rodino:

We, at TRW Inc., have been following the development of the legislation dealing with the above-captioned matter and believe that in its present form the legislation does not fully serve the best interests of the public.

As presently written, the Patent Term bill does not extend the restoration of patents covering processes for the production of certain products whose issuance has been delayed by nonpatent regulatory requirements. As currently under consideration, the bill limits its applicability to patents of products and method of use thereof.

It is our view that Government regulatory review is involved with new processes as well as new products and uses, and therefore this bill should provide benefits for processes as well as for product and use patents. To leave this gap in the applicability of the term of restoration will tend to result in inequities to the developers of such processes, leaving them without the benefits of the Act unless they also happen to hold patents to the products and methods of use as well.

The interest of TRW in this bill resides in the fact the delay imposed by new regulatory requirements in the issuance of patents may result from various governmental agencies other than those dealing with parmaceuticals.

We urge that the bill be amended to include the classification of patents covering manufacturing processes.

Very truly yours,

Kenneth G. Preston, Jr.
Vice President and Assistant
General Counsel

KGP:mm

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO, ILLINOIS 60610 • PHONE (312) 751-6000 • TWX 910-221-0300

JAMES H. SAMMONS, M.D.
Executive Vice President
(751-6200)

July 31, 1981

The Honorable Robert W. Kastenmeier
Chairman
Subcommittee on Courts
Judiciary Committee
U.S. House of Representatives
2137 Rayburn House Office Building
Washington, D.C. 20515

Re: Drug Patent Reform.

Dear Representative Kastenmeier:

The American Medical Association takes this opportunity to inform you of our support of H.R. 1937, your bill to amend U.S. patent law to restore to the term of a patent grant the period of time that non-patent regulatory requirements prevent the marketing of a patented product or method. We would appreciate this letter being incorporated in the record of the July 22, 1981 hearing on this legislation.

In the literature and recent debate on the desirability of U.S. regulatory and patent reform with respect to pharmaceutical products, we have noted that there is uncontradicted evidence that pharmaceutical innovation is not keeping pace with its performance in earlier decades. The Center for the Study of Drug Development has reported, for example, that there was a dramatic decline in the number of new chemical entities introduced in the U.S. between 1966 and 1977. The Center highlighted the fact that the effective patent life of these chemicals after New Drug Application (NDA) approval by FDA had fallen from a thirteen-to-fifteen-year average to a ten-to-twelve year average by 1977 due to regulatory requirements of the FDA. Additionally, between 1962 and 1976 the average cost of a new product for the pharmaceutical industry rose from a research and development investment of $12 million to more than $55 million, according to the Center's estimates. Recent industry estimates have placed that figure as high as $70 million.

Testimony of the pharmaceutical industry has illustrated the investment dilemma faced by those firms dedicated to pharmaceutical innovation. On a worldwide basis, the low rate of return on the millions of dollars of invested capital is not adequate to justify the risk inherent in pharmaceutical research and marketing.

We are in accord with those who have argued that action must be taken by this Congress, including the restoration of patent time lost as a result of premarket regulatory review, in order to provide incentives to the research-oriented firms that may reverse the decline in pharmaceutical innovation. We would hope that patent reform efforts will also encourage the Congress to examine the existing regulatory morass that faces pharmaceutical and medical researchers in this country every day. In addition to pharmaceutical patent reform, there is a pressing need for revisions to the law and regulations governing clinical research on drugs and medical devices.

The American Medical Association stands ready to work with you and your colleagues in the House, as well as with those in the Food and Drug Administration, who have the authority and responsibility to assure that today's citizens and future generations have available to them the highly cost-effective medical care that pharmaceutical products can provide.

Sincerely,

James H. Sammons, M.D.

JHS/kt

FIRST WISCONSIN • MADISON

ROTH S. SCHLECK
CHAIRMAN OF THE BOARD
AND CHIEF EXECUTIVE OFFICER

August 25, 1981

The Honorable Robert W. Kastenmeier
2232 Rayburn Building
Washington, D.C. 20515

Dear Bob,

I attended a meeting recently with Bob Brennan and was pleased to learn of the excellent work you are doing in regard to introducing and supporting the Patent Term Restoration Act of 1981, H.R. 1937. I understand also that you are favorably considering the improvement on the bill by extending patent life on those products which are still under patent but which have completed the regulation review period. I think that the legislation outlined in the basic bill and the improvement of extending the term of those that are still under patent will be extremely meaningful to Madison and to the whole State of Wisconsin. The University and a number of local businesses are very interested in being able to work under the complete package.

Best regards.

Sincerely,

Roth

NICOLET
INSTRUMENT
CORPORATION

September 24, 1981

The Honorable Robert W. Kastenmeier
U. S. House of Representatives
Washington, D.C. 20515

Dear Mr. Kastenmeier:

Nicolet Instrument Corporation is a Madison based manufacturer of scientific and engineering instrumentation. We were founded in Madison 15 years ago, and we now have 500 employees in the Madison operation.

For ourselves, and for the community as a whole, we consider it of major importance that the economic environment for high technology companies be enhanced. Among other things, we dislike seeing so many talented University of Wisconsin graduates leaving Wisconsin for the South or Southwest, for lack of opportunity in research and development, or business management, in this area.

We think your bill, H.R. 1937, is a significant step in helping research oriented companies, particularly companies such as Ohio Medical. We certainly approve of the bill, but we do believe it should be amended to include products which already have undergone regulatory review.

Your support and help to the Greater Madison Chamber of Commerce, WARF, and the Alumni Research Fund is appreciated.

Very truly yours,

Robert W. Schumann
Vice President

RWS:rg

5225 Verona Road
Madison, Wisconsin 53711
Telephone 608/271-3333

NAPM

National Association of Pharmaceutical Manufacturers

747 Third Avenue, New York, New York 10017 • (212) 838-3720

GEORGE DOWDEN
President

MILTON A. BASS
General Counsel

GEORGE SCHWARTZ
Executive Director

September 22, 1981

Honorable Robert W. Kastenmeier
Judicial/Courts Subcommittee
U.S. House of Representatives
Washington, D.C. 20515

Re: H.R. 1937

Dear Congressman Kastenmeier:

The undersigned, National Association of Pharmaceutical Manufacturers, respectfully requests that this statement be made part of the record relative to the hearings and consideration of H.R. 1937.

The National Association of Pharmaceutical Manufacturers is a trade association of manufacturers and distributors of prescription and OTC drug products. This is the largest national association of generic manufacturers in the United States. We primarily represent the smaller pharmaceutical manufacturers who have an important interest in the proposed patent extension bill.

We agree with the philosophy and public interest in stimulating innovation and experimentation by granting a monopoly for a period of years. Balancing this public interest is a very great public interest in stimulating competition and in providing life-protecting essential drug products at a reasonable cost. This is particularly so for the elderly, the poor, and the incapacitated.

In fact, the city, state and federal governments are now major purchasers of pharmaceutical products and have an important stake in the cost of essential drug products. We agree that there are instances in which extensive delays in government agency review have adversely affected a specific patent right for an excessive period of time. We also believe that in any given case a company may not recoup a reasonable profit for a particular drug. We do not believe, however, that any limited examples of this nature should lead to a drastic change in the present patent provisions. In fact, it is our fear that a very broad brush may be used to ameliorate a limited problem.

88-310 O—82——38

The government wishes to stimulate research, but the government is not an insurer that a company must make a profit. The government does not issue insurance policies. In addition, we believe that a very careful study must be made of the statistics that are being submitted relative to this Bill. We all know that there are many ways to write and analyze statistics. It is our belief that if statistics are taken of the actual sales and profit for a specific drug, we will find that the overwhelming majority of real innovative drugs have realized very significant profits for the innovating company.

We believe that any consideration of patent extension, because of time spent in the FDA for clearance, must be carefully written so as to prevent misuse. In this regard, there has been a great deal of discussion as to when the time should run for such extension. It has been proposed that the time should commence on the date that the first clinical trials in the United States are initiated. Another suggestion has been made that the time begin to run when the IND is filed or when pre-clinical animal tests are started. We believe that any patent extension time should not begin with any of the above-mentioned suggestions. There is no logical reason for beginning the extension on the date that clinical trials are initiated or the date that an IND is filed or animal tests are commenced. Even if there were no FDA clearance required, a company will certainly have to conduct animal tests and clinical trials before it markets a product to the public. Adequate and proper testing would most assuredly be conducted by any responsible company before putting a product on the market. This is one example of what we mean when we mentioned the attempted use of a broad brush to meet a limited problem. To the extent that any patent extension is considered, most assuredly the date should be one that addresses the problem which has been raised.

We understand the complaint to be that in some cases an extensive or unnecessary period has occurred in a review of an NDA and prior to approval. It would thus seem to be appropriate to provide for some relief where an unnecessary period of time is involved, and not the total regulatory review time. In this regard, we would suggest that the appropriate time would be a date such as 12 months or 18 months after the date that the NDA is filed. In addition, the relief should be predicated upon delay caused by the agency and not delay caused by the company.

We submit that the earliest possible date to commence any extension should be at least 180 days after the filing of the NDA. This would be in accordance with the period for review provided for in the Food and Drug Act. The reality, however, is that 180 days would not be adequate for any significant innovative drug. It is our view that the extensive argument about the various commencement dates illustrates the transparent nature of this attempt

by the larger pharmaceutical companies to obtain extensive patent extension totally unrelated to the alleged reason or cause for their request.

As noted above, we would respectfully ask any pharmaceutical company whether they are seriously suggesting to this Committee that if we did not have an NDA approval requirement, that they would market a drug to the public without doing adequate and well-controlled clinical studies before selling their product to the public.

This reflects one of the problems involved in a consideration of this most serious subject of monopoly extension and consequent high prices for pharmaceutical products which are not a luxury to the public but a necessity and in fact a life-saving necessity in many cases. The interests of small business must be considered not only because of the well-being of such small companies and their importance in the American enterprise system, but also for the important function they perform in providing necessary competition and consequent lower drug prices for the consumer. If the real reason for the present request is the unnecessary or improper time that has been taken in reviewing an NDA application, then most certainly the relief herein to be applied should be tied to that problem. As noted above, we suggest that this is a very limited area involving very few drugs which have had inordinate time delays and a failure to realize significant profits for the monopoly period.

Another subject that should be considered in any patent extension bill is the question of compulsory licensing. We can provide for reasonable royalties and an initiation date that compensates a company for innovation and experimentation.

We further submit that there has been a very misleading statistics game played with this Bill. There has been a great deal of discussion about averages as to costs of research and recouping of investment. We would like to initially state that a study of the annual reports of the leading pharmaceutical companies may shed very interesting light on just how much profits these companies are making and how much relief they may require. This is not a Chrysler Corporation problem where help is needed to survive. We believe pharmaceutical companies are probably among the leaders in this country in terms of profits.

We agree that there must be a carrot of reward to stimulate research but not a guarantee that all research will be successful. If a company conducts research that is not successful, that is the free enterprise system at work and it must bear the loss. However, when research is successful, we agree that the company should receive an attractive return for its research and investment. We believe that the facts will show in their own financial reports, that they have realized significant and very

material returns for their research on real innovative drugs. Many drugs are not real inventions. They are combinations of old drugs or new-use extensions that are merely devices to extend the monopoly period under the present law.

We of the NAPM respectfully repeat and submit that we support legislation which would attempt to correct a problem, but we do not support, and in fact strongly oppose the attempt that is being made at this time to use a limited problem as an excuse for broad monopoly extension. It is the consumer, small business and the city, state and federal governments who stand to lose if this attempt is successful.

Respectfully yours,

NATIONAL ASSOCIATION OF
PHARMACEUTICAL MANUFACTURERS

George Schwartz
Executive Director

Milton A. Bass
General Counsel

MAB:GS:sf

INDEPENDENCE MALL WEST PHILADELPHIA, PA. 19105, U.S.A. TELEPHONE (215) 592-3000
CABLE ADDRESS ROHMHAAS TELEX 845-247
REPLY TO:
PATENT DEPARTMENT
CABLE ADDRESS: ROHMHAAS

ROHM AND HAAS COMPANY

October 2, 1981

Bruce Lehman, Esq.
Committee on the Judiciary
2137 Reyburn Building
U. S. House of Representatives
Washington, D. C. 20515

Dear Mr. Lehman:

In accordance with our discussions on Monday, September 28, this will confirm that I am proposing a technical amendment to S. 255, the Patent Term Restoration Act of 1981. In particular, I recommend that the definition of "regulatory review period" set forth in sub-paragraph (c)(4)(B) be amended by inserting after "first registered", in the last line of said section, the words "to any party". Attached is a xerocopy of S. 255 with the amendment entered in red.

There are several instances in which more than one company may obtain a patent and apply to register a specific pesticide. Such instances occur when one company has a generic patent, i.e., a very broad patent covering many, many compounds and the other company has a narrow patent claiming only one or two specific compounds. Another instance is where both parties independently develop and claim the same compound. In this case, an interfernce will be set up in the Patent and Trademark Office. While ultimately only one party will end up with a patent, the one ultimately determined to be the first inventor and entitled to the patent may not be the one who first applied to register a particular pesticide.

One purpose of the Patent Restoration Act is to reward the diligent developer of pesticides by extending the patent term by a period directly related to the government's regulatory delay rather than the inventor's delay. The fact that a patentee would have been the second to apply to register a product is evidence that the patentee has been tardy in finding the commercial product and in developing it for use by the public. The proposed change will see that any patent restoration is not enlarged by the period of the patentee's own delay.

If you have any questions, please let me know.

Sincerely,

George Simmons

George W. F. Simmons
Chief Patent and Trademark Counsel

GWFS:jd
Attachment

Effective Date

The regulatory review period does not commence for purposes of the Act until an applicable patent is granted. If a regulatory review period has commenced prior to the effective date of the Act, the period of patent extension will be measured from the effective date of the Act.

VIII. Changes in Existing Law

In compliance with paragraph 12 of rule XXVI of the Standing Rules of the Senate, changes in existing law, made by the bill, S. 255 as reported, are shown as follows (new material is printed in italic and existing law in which no change is proposed is shown in roman):

TITLE 35, PATENTS

Chapter 14.—Issue of Patent

Sec.
151 Time of issue of patent
152 Issue of patent to assignee
153 How issued
154 Contents and term of patent
155 Restoration of patent term.

* * * * * * *

"§ 155. Restoration of patent term

"(a)(1) Except as provided in paragraph (2), the term of a patent which encompasses within its scope a product, or a method for using a product, subject to a regulatory review period shall be extended by the amount of time equal to the regulatory review period for such product or method if—

"(A) the owner of record of the patent gives notice to the Commission in compliance with the provisions of subsection (b)(1);

"(B) the product or method has been subjected to a regulatory review period pursuant to statute or regulation prior to its commercial marketing or use; and

"(C) the patent to be extended has not expired prior to notice to the Commissioner under subsection (b)(1).

The rights derived from any claim or claims of any patent so extended shall be limited in scope during the period of any extension to the product or method subject to the regulatory review period and to the statutory use for which regulatory review was required.

"(2) In no event shall the term of any patent be extended for more than seven years.

"(b)(1) Within ninety days after termination of a regulatory review period, the owner of record of the patent shall notify the Commissioner under oath that the regulatory review period has ended. Such notification shall be in writing and shall:

"(A) identify the Federal statute or regulation under which regulatory review occurred;

"(B) state the dates on which the regulatory review period commenced and ended;

"(C) identify the product and the statutory use for which regulatory review was required;

"(D) state that the regulatory review referred to in subsection (a)(1)(B) has been satisfied; and

"(E) identify the claim or claims of the patent to which the extension is applicable and the length of time of the regulatory review period for which the term of such patent is to be extended.

"(2) Upon receipt of the notice required by paragraph (1), the Commissioner shall promptly (A) publish the information noticed in the Official Gazette of the Patent and Trademark Office, and (B) issue to the owner of record of the patent a certificate of extension, under seal, stating the fact and length of the extension and identifying the product and the statutory use and the claim or claims to which such extension is applicable. Such certifcate shall be recorded in the official file of each patent extended and such certificate shall be considered as part of the original patent.

"(c) As used in this section:

"(1) The term 'product or a method for using a product' means any machine, manufacture, composition of matter or any specific method of use theeof for which United States Letters Patent can be granted and includes the following or any specific method of use thereof:

"(A) any new drug, antibiotic drug, new animal drug, device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act;

"(B) any human or veterinary biological product subject to regulation under section 351 of the Public Health Service Act or under the virus, serum, toxin, and analogous products provisions of the Act of Congress of March 4, 1913;

"(C) any pesticide subject to regulation under the Federal Insecticide, Fungicide, and Rodenticide Act; and

"(D) any chemical substance or mixture subject to regulation under the Toxic Substances Control Act.

"(2) The term 'major health or environmental effects test' means an experiment to determine or evaluate health or environmental effects which requires at least six months to conduct, not including any period for analysis or conclusions.

"(3) The term 'statutory use' means all uses regulated under the statutes identified in sections (c)(4)(A)-(D) for which regulatory review occurred for the product involved.

"(4). The term 'regulatory review period' means—

"(A) with respect to a food additive, color additive, new animal drug, veterinary biological product, device, new drug, antibiotic drug, or human biological product, a period commencing on the earliest of the date the patentee, his assignee, or his licensee (i) initiated a major health or environmental effects test on such product or a method for using such product, (ii) claims an exemption for investigation or requests authority to prepare an experimental product with respect to such product or a method for using such product under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Act of Congress of March 4, 1913, or (iii) submits an application or petition with respect to such product or a method for using such product under such statutes, and ending on the date such application or petition with respect to such product or a

method for using such product is approved or licensed under such statutes or, if objections are filed to such approval or license, ending on the date such objections are resolved and commercial marketing is permitted or, if commercial marketing is initially permitted and later revoked pending further proceedings as a result of such objection, ending on the date such proceedings are finally resolved and commercial marketing is permitted;

"(B) with respect to a pesticide, a period commencing on the earliest of the date the patentee, his assignee, or his licensee (i) initiates a major health or environmental effects test on such pesticide, the data from which is submitted in a request for registration of such pesticide under section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act, (ii) requests the grant of an experimental use permit under section 5 of such Act, or (iii) submits an application for registration of such pesticide pursuant to section 3 of such Act, and ending on the date such pesticide is first registered, either conditionally or fully;

"(C) with respect to a chemical substance or mixture for which notification is required under section 5(a) of the Toxic Substances Control Act—

"(i) which is subject to a rule requiring testing under section 4(a) of such Act, a period commencing on the date the patentee, his assignee, or his licensee has initiated the testing required in such rule and ending on the expiration of the premanufacture notification period for such chemical substance or mixture, or if an order or injunction is issued under section 5(e) or 5(f) of such Act, the date on which such order or injunction is dissolved or set aside;

"(ii) which is not subject to a testing rule under section 4 of such Act, a period commencing on the earlier of the date the patentee, his assignee, or his licensee—

"(I) submits a premanufacture notice, or

"(II) initiates a major health or environmental effects test on such substance, the data from which is included in the premanufacture notice for such substance,

and ending on the expiration of the premanufacture notification period for such substance or if an order or injunction is issued under section 5(e) or 5(f) of such Act, the date on which such order or such injunction is dissolved or set aside;

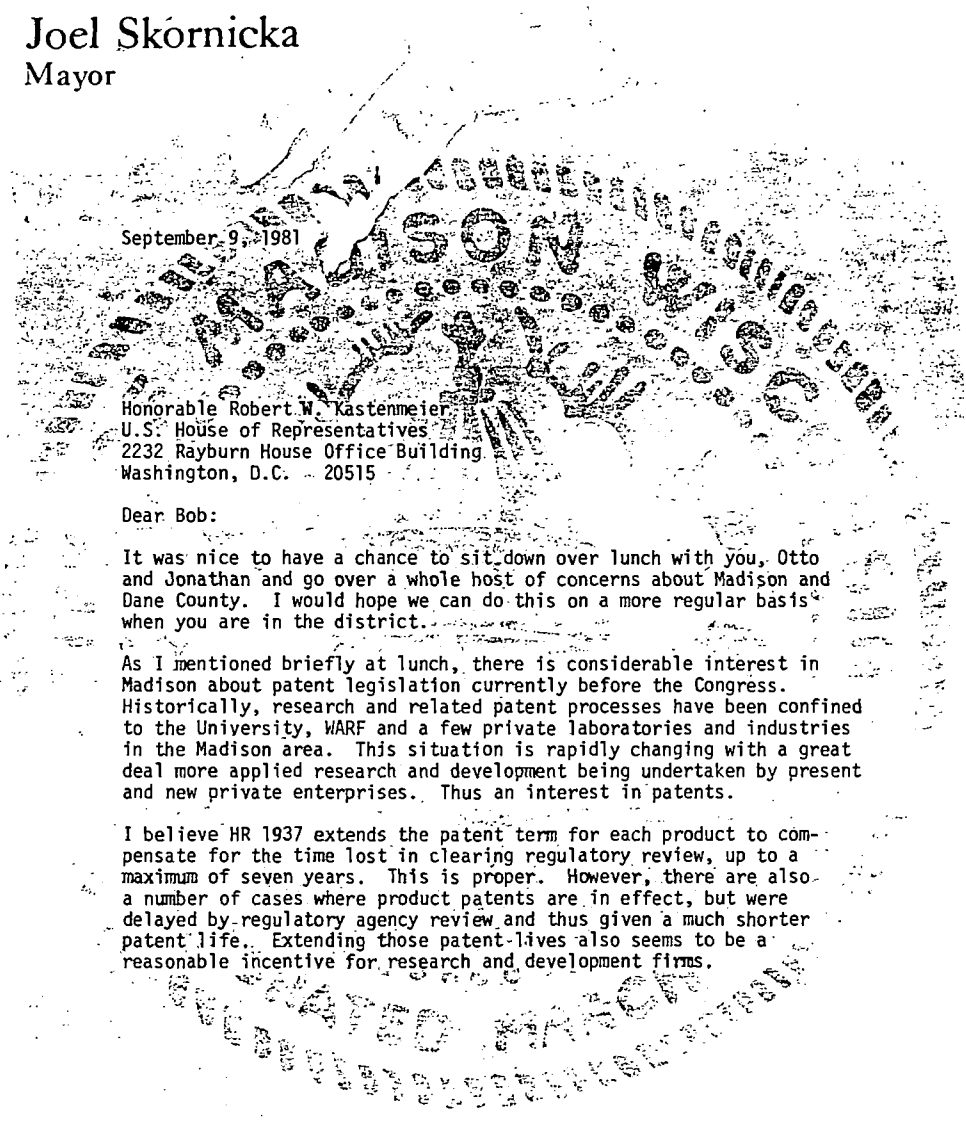
"(D) with respect to any other product or method of using a product that has been subjected to Federal premarketing regulatory review, a period commencing on the date when the patentee, his assignee, or his licensee initiates actions pursuant to a Federal statute or regulation to obtain such review prior to the initial commercial marketing in interstate commerce of such product and ending on the date when such review is completed,

except that the regulatory review period shall not be deemed to have commenced until a patent has been granted for the product or the method of use of such product subject to the regulatory review

period. In the event the regulatory review period has commenced prior to the effective date of this section, then the period of patent extension for such product or a method of using such product shall be measured from the effective date of this section.

* * * * * * *

Joel Skornicka
Mayor



September 9, 1981

Honorable Robert W. Kastenmeier
U.S. House of Representatives
2232 Rayburn House Office Building
Washington, D.C. 20515

Dear Bob:

It was nice to have a chance to sit down over lunch with you, Otto and Jonathan and go over a whole host of concerns about Madison and Dane County. I would hope we can do this on a more regular basis when you are in the district.

As I mentioned briefly at lunch, there is considerable interest in Madison about patent legislation currently before the Congress. Historically, research and related patent processes have been confined to the University, WARF and a few private laboratories and industries in the Madison area. This situation is rapidly changing with a great deal more applied research and development being undertaken by present and new private enterprises. Thus an interest in patents.

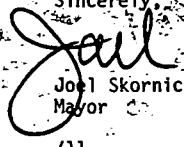
I believe HR 1937 extends the patent term for each product to compensate for the time lost in clearing regulatory review, up to a maximum of seven years. This is proper. However, there are also a number of cases where product patents are in effect, but were delayed by regulatory agency review and thus given a much shorter patent life. Extending those patent lives also seems to be a reasonable incentive for research and development firms.

City of Madison
Wisconsin 53709 608 266-4611

Thanks for the opportunity to express these views.

Best wishes,

Sincerely,



Joel Skornicka
Mayor

/ll

cc: Jonathan Barry

GENERAL COUNSEL OF THE
UNITED STATES DEPARTMENT OF COMMERCE
Washington, D.C. 20230

JUL 27 1981

Honorable Robert W. Kastenmeier, Chairman
Subcommittee on Courts, Civil Liberties,
and the Administration of Justice
Committee on the Judiciary
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

The Department of Commerce wishes to express its support for enactment of H.R. 1937 which would add a new section 155 to title 35 of the United States Code to provide for an extension of the patent term for patented products, or methods for using products, that are subject to regulatory review pursuant to federal statutes and regulations before they are permitted to be introduced for commercial use.

This Department strongly supports the objective of the bill, which is to permit adjustments of the patent term to compensate for the loss of a certain period of commercial exclusivity caused by Federally mandated testing and regulatory review requirements. It is, of course, crucial that new products brought on the market be safe for public use and not adversely affect the environment. As a consequence, adequate testing for safety, efficacy and environmental effects is in the public interest. There is no reason, however, why the protection of these public interests must be at the expense of new products on the market. Although Federal statutes enacted for the purpose of reducing the patent term of a regulated product, the practical effect has been just that. Curtailed patent protection lowers the incentive to innovate and the inevitable result is fewer new products in the market place.

As you know, a hearing on H.R. 1937 was held before the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce, on April 1, 1981. Although this Department was not asked to testify at that hearing, Rene D. Tegtmeyer, the Acting Commissioner of Patents and Trademarks, presented our veiws on S. 255, the companion bill,

at a heraing before the Senate Judiciary Committee, on April 30, 1981. In his testimony, Acting Commissioner Tegtmeyer noted the direct relationship which existed between shortened effective patent terms for new innovation rate in these industries. Statistics provided by the affected industries at both hearings show the extent to which patent terms may be curtailed. In the early 1960's, for example, it took an average of about two years of carry out testing and development procedures to fulfill approval requirements of the Food and Drug Administration for the marketing of a new drug. Today, the average regulatory review procedure takes somewhere between seven to ten years.

The effective term of pharmaceutical patents, as a consequence of regulatory review, dropped from 16 years in 1960, to about 13 years in 1970, to about nine years today. The agricultural chemical industry today can expect an effective patent term of only about twelve years. This is far less than the 17 year patent term available since 1861 to inventors involved in other technologies.

In 1960, new pharmaceuticals were introduced at an average rate of 50 annually. Only about a dozen new medicines were produced in 1980. From 1954 to 1958, new drugs were introduced to the U.S. market by 51 different companies. During the period between 1972 and 1976, however, only 41 companies introduced new drugs. Although a shortened effective patent life is not the sole reason for this decline, industry has identified the lack of an adequate patent term as a major factor.

Given the enormous costs, efforts, and risks involved in pharmaceutical and chemical research, effective patent protection is a necessary prerequisite. As noted above, the pharmaceutical and agricultural chemical industries have been adversely affected by the diminution of patent terms for their inventions. No enterprise can be expected to make huge investments without some reasonable chance of being able to recover its expenses and to make a fair profit. Patents provide that chance and will remain the stimulant for investment in research as long as protection is not unfairly shortened. Enactment of H.R. 1937 will go a long way toward alleviating the unfairness of artificially-shortened patent terms caused by Federal premarket regulatory review requirements.

I am enclosing for your consideration our detailed comments on the provisions of H.R. 1937. We will be pleased to provide you with any additional assistance.

We have been advised by the Office of Management and Budget that there would be no objection to the submission of this report from the standpoint of the Administration's program.

Sincerely,

Irving P. Margulies
for Sherman E. Unger
General Counsel

DETAILED COMMENTS ON H.R. 1937

Extension of the patent term is to be granted on the basis of a notification, which the owner of record of the patent must submit to the Commissioner within 90 days after termination of a regulatory review. The details which such notification must contain are specified in section 155(b)(1)(A) to (E). Subparagraph (D) requires that the owner of record "state that the regulatory review referred to in subsection (a)(1)(B) has been satisfied". To avoid any question about the meaning of this subparagraph, we suggest that the following language be inserted in subparagraph (D), after the word "satisfied":

> "and commercial marketing of the product for the statutory use is no longer prevented".

Section 155(b)(1)(E) refers to information which has to be supplied regarding the patent to be extended. For purposes of clarity, we would suggest that the first line thereof be amended as follows:

> "(E) identify the patent and any claim thereof [or claims of the patent] to"

Section 155(b)(2) now requires the Commissioner of Patents and Trademarks to issue automatically to the patent owner a certificate of extension of the patent term upon receipt of a notice from the owner. We believe, however, that where a notice contains an obvious and significant discrepancy, the Commissioner should be able to require the owner to clarify and to correct that discrepancy before the Commissioner issues an extension. In suggesting that the Commissioner have discretion to grant an extension of a patent term after reviewing the accuracy and completeness of the patentee's notification required under section 155(b)(1), we do not contemplate any system of verifying the alleged facts contained in the notice, nor do we suggest that any inter partes hearing procedures be established in which other interested persons could take issue with the facts alleged in the notification. Rather, a simple inquiry would be conducted to correct apparent errors only. Since in the vast majority of cases the Commissioner would simply accept the notification proffered and issue the certificate of extension, the financial implications of implementing this bill are expected to be of a minor nature. In order to grant the Commissioner such discretion, the following change of section 155(b)(2), page 3, lines 15 to 24, is suggested:

> "(2) Upon receipt of the notice required by paragraph (1), the Commissioner shall promptly [(A)] publish the information received [noticed] in the Official Gazette of the Patent and Trademark Office [, and (B)].

"(3) Unless the Commissioner believes that the requirements of this section have not been met, he shall issue to the owner of record of the patent a certificate of extension, under seal, stating the fact and length of the extension [and], identifying the product or method for using a product, and the statutory use therefor, and specifying any [the] claim [or claims] to which such extension is applicable. Such certificate shall be recorded in the official file of [each] the patent so extended and [such certificate] shall be considered as part of the original patent."

Section 155(c)(4)(D) would extend the possibility of patent term extension to any product, or method for using a product, that cannot be marketed or used without the authorization of a federal regulatory agency. Although in the areas of pharmaceuticals, medical devices and agricultural chemicals, ample evidence exists that relief is badly needed to offset the long time periods taken from the patent term by federal regulatory premarketing review, we have no evidence that such open-ended relief as that provided by section 155(c)(4)(D) is needed. Accordingly, we do not support providing a remedy for a problem which has not been demonstrated.

The following suggested amendments are of a technical or editorial nature only. First, reference is made throughout the bill to "a product, or a method of using a product, subject to a regulatory review period". As the product or method is more properly subject to regulatory review, we believe that the word "period" should be deleted in several instances. Further, while the bill is intended to extend the term of a patent encompassing a "product, or a method for using a product", this language is not consistently used throughout. Accordingly, the following language changes are suggested to correct these perceived deficiencies:

Section 155(a)(1), page 2, lines 4 to 6:

"method for using a product, subject to [a] regulatory review [period] shall be extended by the amount of time equal to the regulatory review period for such product or such method for using a product if--"

Section 155(a)(1)(B), page 2, lines 10 and 11:

"(B) the product or method for using a product has been subjected to [a] regulatory review [period] pursuant to statute..."

Regarding the last sentence of section 155(a)(1), page 2, lines 16 to 20, we have already suggested above a change in language, because of its possible lack of clarity. Should this suggestion not be adopted, we would offer the following technical amendments:

> "The rights derived from any claim [or claims] of [any] a patent so extended shall be limited in scope during the period of [any] extension to the product or method for using a product subject to [the] regulatory review [period] and to the statutory use for which [regulatory] such review was required."

The preamble of section 155(b)(1), page 2, lines 23 to 25, and page 3, lines 1 and 2, should read as follows:

> "(b)(1) Within ninety days after termination of a regulatory review [period], the owner of record of the patent shall notify the Commissioner under oath that such [the regulatory] review [period] has ended. Such notification shall be in writing and shall:"

Section 155(b)(1)(C), page 3, line 7, should read:

> "(C) identify the product or method for using a product, and the statutory use for"

Section 155(c)(4)(A) could be simplified to read more clearly if the following amendments were made on page 5, lines 8 to 25, and page 6, lines 1 to 9:

> "(A) with respect to a product or a method for using a product, which is a food additive, color additive, new animal drug, veterinary biological product, device, new drug, antibiotic drug, or human biological product, [a] the period commencing on the earliest of the date the patentee, his assignee, or his licensee (i) [initiated] initiates a major health or environmental effects test thereon [on such product or a method for using such product], (ii) claims an exemption for investigation or requests authority to prepare an experimental product [with respect to such product or a method for using such product] under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Act of Congress of March 4, 1913, or (iii) submits an application or petition [with respect to such product or a method for using such product] under such statutes, and ending on the date such application [or petition with respect to such product or a method for using such product] is approved [or], the product is licensed, or a regulation petitioned for becomes effective, under such statutes. [or, if] If objections are filed to such

approval, [or] license, or regulation, such period shall end [ending] on the date such objections are resolved and commercial marketing is permitted or, if commercial marketing is initially permitted and later revoked pending further proceedings as a result of such objections, such period shall end [ending] on the date such proceedings are finally resolved and commercial marketing is permitted;"

The last two sentences of section 155(c)(4), page 8, lines 16 to 23, should read as follows:

"except that the regulatory review period shall not be deemed to have commenced until a patent has been granted for the product or the method [of use of such] for using the product, which is subject to [the] regulatory review [period]. In the event the regulatory review period has commenced prior to the effective date of this section, then the period of [patent] extension of the patent involved [for such product or a method of using such product] shall be measured from the effective date of this section."

As an editorial suggestion, we would propose that the words "United States Letters Patent can be granted", appearing in section 155 (c)(1), page 4, line 4, be changed to "a patent may be obtained".

APPENDIX 3.—ADDITIONAL MATERIALS

A. N. Boyd Ecker, Manager-Government Relations Exploration & Producing (US) and Research & Development, Mobil Oil Corporation--White Paper

B. Lescarden Limited, Business Plan, June 1, 1981

C. The Journey, John F. Prudden, M.D., Med.SC.D.

D. Stanley Stringer, Chief, Product Coordination Staff, New Drug Evaluation, Bureau of Drugs, Department of Health & Human Services, Drug information Graphs

Mobil Oil Corporation

SUITE 620
1100 CONNECTICUT AVENUE, N.W.
WASHINGTON, D.C. 20036

August 11, 1981

Bruce A. Lehman, Esq.
Chief Counsel
Subcommittee on Courts, Civil
Liberties and Administration
of Justice
2137 Rayburn House Office Building
Washington, DC 20515

Dear Mr. Lehman:

At our recent meeting, we indicated that we would be preparing a white paper regarding inclusion of process patents in the Patent Term Restoration Act (H.R. 1937). Please find enclosed a copy of that paper dated August 7, 1981.

We would be happy to discuss the paper further if you wish.

Sincerely,

N. Boyd Ecker
Manager - Government Relations
Exploration & Producing (US)
and Research & Development

NBE:BJS:cce
Attachments

August 7, 1981

The Patent Term Restoration Act of 1981 (H.R. 1937) is an expression of the Congress' desire to restore to the patentee the full seventeen (17) year period of patent exclusivity. A portion of that term may be presently lost because of patentee's compliance with various Federal regulatory requirements. However, the legislation is not applicable to all patents, namely it excludes process patents. The exclusion of this area of patent protection, which has historically been part of the patent system in the U.S. since its inception, is not based on any legal, logical or philosophical precepts. United States process patents do not cover the product made by such process. Therefore the inclusion of process patents in this legislation would not enlarge the rights of product patentees beyond the scope of rights granted to them by the original version of this legislation, so long as the restoration of patent term for all patents is granted only if the patentee is precluded from commercial exploitation of his patented invention by Federal regulatory requirements.

H.R. 1937 seeks to resolve a conflict between two apparently opposing public policies affecting the U.S. patent system. On the one hand, the U.S. patent laws entitle a patent holder to a seventeen (17) year period of exclusivity during which the patentee is entitled to the use of the U.S. court system to preclude anyone from using, making, or selling the patented invention. On the other hand, various environmentally and health-oriented laws passed by Congress in recent years force the patentee to comply with a number of regulatory requirements. Compliance with such laws may take from two (2) to welve (12) years and at least a portion of the time necessary to comply with such laws is during the time of the patent exclusivity. Thus, in effect, compliance with Federal regulatory requirements may deprive the patentee of a portion of his seventeen (17) year period of exclusivity. H.R. 1937 attempts to restore to the patentee the full seventeen (17) year period by adding to the end of the patent term the time lost, up to seven (7) years, in complying with the Federal regulatory requirements.

The remedial scope of this important legislation should cover all patents whose commercial exploitation was impeded or delayed by compliance with Federal regulatory requirements. The loss of a

APPENDIX

EXAMPLE OF FEDERAL REGULATORY REVIEW AFFECTING PROCESS PATENTS

If one desires to construct a plant incorporating a patented process for producing synthetic fuels from unconventional sources of hydrocarbons, such as coal, the presently existing Federal regulatory requirements (namely, the Clean Air Act and the National Environmental Policy Act-NEPA) require the collection for a minimum of twelve (12) months, and usually for eighteen (18) months, of field data information, i.e., information on the existing air quality, and of baseline data information, i.e., data on every aspect of natural condition, in the area before construction of the plant may be commenced. Following the collection of the data, the holder of the patent, or his licensee wishing to build the plant, must prepare an Environmental Impact Statement (EIS), including a draft and a final version thereof, and give the public about six (6) months for comments on the EIS. The entire process of preparing the EIS, including the comments period, takes at least twenty-four (24) and usually twenty-four (24) to thirty-six (36) months. Finally, a U.S. agency designated by NEPA makes a decision based on the EIS as to whether or not the construction of the plant may proceed. The decision making process takes at least six (6), and usually six (6) to eight (8) months. Thus, the total time of delay imposed by the various regulatory requirements is at least four (4) years and may range of up to eight and a half (8 1/2) years or longer.

LESCARDEN LIMITED

Business Plan

June 1, 1981

Section I. Background

Lescarden Ltd. is engaged in research, testing, and development of a medication for the control and cure of various diseases, including hemorrhoids, psoriasis, arthritis, and cancer. The beneficial dynamics of the medication known as Catrix® are not yet completely understood, but fall within the burgeoning science of immunology. (A Brief Description of Immunology is attached as Appendix A of this Plan.) A Rationale for the Use of Catrix in Cancer (attached as Appendix B) may provide insight into the dynamics of Catrix therapy in other diseases as well.

A processed cartilage powder, Catrix was originally patented in 1968. Dr. John F. Prudden, surgeon and Doctor of Medical Science, then at Columbia Presbyterian Medical Center in New York City, first used the medication as a wound-healing agent in his laboratory and in his private practice. He subsequently discovered that certain other diseases were beneficially treated by Catrix in either its topical, injectable, or ingestible forms. Dr. Prudden's history of these discoveries and a review of his results accompanies this Business Plan and is entitled The Journey. (Dr. Prudden's resume is attached in Appendix C.)

A component of Catrix, polymeric-N-acetyl glucosamine, called Poly-NAG®, has been used successfully by Dr. Prudden in connection with wound healing. It can be used to accelerate wound healing in such surgical adjuncts as sutures, sponges, non-

woven mats, and prosthetic devices. Poly-NAG is an asset of the Company that should be further developed, since products containing it appear to possess significant advantages over corresponding products currently in use. Strategies with respect to its development and marketing are not, however, discussed in this Plan.

The Company was founded by Leslie L. Balassa, a Ph.D. in Chemistry (resume attached in Appendix C), in September, 1960 to further the work of Dr. Prudden. Dr. Prudden did not become a stockholder of the Company until three years later when, due to the difficulty of obtaining funds, he began to make significant financial contributions.

Method, process, and composition patents have been issued or applied for in the United States and abroad. Darby and Darby have been patent counsels to Dr. Balassa since 1948 and became the patent counsel to the Company in 1960 when it was formed. The enforceability of patent claims, particularly abroad, is difficult to estimate without case-by-case analysis of the patent, the infringement, and applicable law. A Darby and Darby outline of United States and foreign patents (attached as Appendix D) therefore must be considered an information document and not in itself determinant of ultimate protection against any particular infringement. Some of the earlier foreign patents were obtained by another law firm and their description is not included with that of Darby and Darby.

The Company has never been adequately capitalized. Capital requirements were not accurately estimated and costs and duration

of the regulatory processes governing new drug development have risen astronomically since 1960. (Estimates range from $7 million to $20 million and three to seven years from the start to finish of the FDA regulatory processes.)

Since 1960 Drs. Prudden and Balassa have invested approximately $.75 million of their own funds in Lescarden's activities. More than $1.75 million has been invested by others. These funds have been used primarily for salaries, toxicity studies, consultants, and patents. (A review of the Sources and Uses of Funds since 1960 is attached as Appendix E.) Funds from the February, 1980 Private Placement, closed in May, 1980, for $375,000 were used primarily for research, legal and consulting fees, and supplies. (Specific uses of the proceeds from that financing are listed in Appendix F.)

Section II. Business History and Condition

1. Management

Until recently the Company's only full-time officer was Dr. Leslie L. Balassa. Dr. Prudden continued his private practice, following the business and technical affairs of Lescarden in the time available to him. In November 1980 Prudden became Chairman of the Company. Concurrently with the raising of new funds Dr. Prudden will sign an employment agreement with the Company (substantially in the form attached in Appendix G) for the full-time performance of the Chairman's responsibilities and those of Director of Medical and Scientific Research. He will also be a member of an Executive Committee of the Board of Directors.

With the raising of new funds Mr. Donold K. Lourie will become President and Chief Executive Officer of the Company in accordance with the terms of an employment agreement (substantially in the form attached in Appendix G). He will be Chairman of the Executive Committee of the Board and act as Treasurer until a successor is elected. Mr. Lourie was one of the founders of Bradford National Corporation and has had extensive experience with the legal, financial, and administrative aspects of business. (His resume is attached in Appendix C.)

Mr. Lourie has had no experience in the pharmaceutical business. His primary responsibilities will be to bring business discipline to the affairs of the Company, raise additional

funds, and hire suitable pharmaceutical and other qualified personnel to carry out the Company's objectives.

One of the Company's major objectives is to obtain FDA approval for the testing and ultimate marketing of Catrix and its derivatives. Experienced and mature personnel are needed for that purpose. Some will be consultants, some employees.

When new funds are raised Dr. Roberts M. Rees will become a Director and consultant to the Company. His major responsibility will be to conceive and carry out appropriate plans for the issuance of IND's and NDA's for Catrix and its fractions. (See Section VI.) Dr. Rees has been a Director of Clinical Research for Internal Medicine at Hoechst Pharmaceuticals, Director of the Medical Research Divison at the Sterling-Winthrop Research Institute of Sterling Drug, Inc., and Corporate Medical Officer of Sterling Drug, Inc. (Dr. Rees's resume is attached in Appendix C. The Company's arrangements for the services of Dr. Rees are described in an Agreement attached in Appendix G.)

Dr. Balassa will be a member of the Executive Committee of the Board. He will also be Vice Chairman of the Board and will undertake special projects for the Company as needed. He will not be a full-time employee.

Mr. Chester Ross, counsel to the law firm of Cole and Deitz, is presently the Company's corporate counsel and its Secretary. His legal and business experience is expected to be important in the Company's future. (Mr. Ross's resume is attached in Appendix C.)

For the last four months Mr. Roben Seltzer has assumed

important responsibilities for Lescarden in connection with the review of aspects of its past corporate activities and the organization of its documents and files. Mr. Seltzer is presently Assistant Secretary of the Company. He will become Vice President and Assistant Treasurer on the raising of additional funds. He will assist Mr. Lourie and Dr. Prudden in the performance of their responsibilities. (Mr. Seltzer's resume is attached in Appendix C.)

Mr. Herbert Wahle, retired Vice President for International Affairs of Norwich Pharmacal Company (resume attached in Appendix C), is experienced and knowledgeable in both international and domestic licensing. He has agreed to assist Lescarden's effort in the development of licensing arrangements in the United States and abroad. (The Company's anticipated agreement with him is attached in Appendix G.)

2. Directors

It is expected that the present outside Directors of the Company, Mr. Norman Short, Dr. Jules Haberman, and Mrs. Carla Prudden (whose resumes are attached in Appendix C), will be of substantial assistance to the Company. All three have been Directors of the Company for over one year, and are familiar with the affairs of the Company. Guardian Growth Financial Services Ltd. of Canada, of which Mr. Short is President, holds 40,000 shares of the Company's stock. Mr. Short's business experience has been of great help to the Company in the past. As Assistant to the President of University Patents, Inc., Dr. Haberman brings to the Company a great deal of experience

in both licensing and medical research.

Mr. Peter Hager, a Goldman Sachs limited partner and a professional director and stockholder of a number of successful new companies (resume attached in Appendix C), has agreed to serve as a Director of the Company when a new financing is achieved. His contacts in business are extensive and it is believed that his services will be of great benefit to the Company.

3. Financial

As of May 31, the Company had a negative working capital of $26,428 and, as of April 30, an accumulated development deficit of $2,309,715. Certain creditors and warrantholders of the Company recently released the Company from some or all of its monetary obligations to them in return for shares of stock of the Company. A minimum of new funds will be used for the Company's past indebtedness. (A balance sheet as of April 30, 1981, is attached as Appendix H.)

4. Shares Outstanding, Stockholders, Warrantholders

As of May 31, 1981, there were 1,759,580 shares of Lescarden stock issued and outstanding. In connection with the arrangements made with certain creditors and warrantholders of the Company referred to above, it is anticipated that prior to the new financing there will be approximately 2 million shares outstanding. Assuming the new financing contemplated by this Business Plan is fixed at $1.25 million and shares are issued at a price of $2.50 per share, the Company's issued and outstanding stock after the financing will increase to approximately 2.5 million

shares (including 25,000 shares as part of a fee paid for services in connection with the raising of the funds).

Of these shares approximately 250,000 can be traded publicly, 100,000 having been registered in 1968 and approximately 150,000 freed under Rule 144 of the Securities Act of 1934. Approximately 900,000 shares have been held for more than two years and will become eligible for public trading if owners who desire to sell can meet the other requirements of Rule 144.

It is difficult to estimate when and to what extent shares eligible for public trading under Rule 144 will in fact reach the market. The Company intends to publish and distribute an Annual Report for the fiscal year ended May 31, 1981, a prerequisite for the sale of letter stock. After the publication of the 1980 Annual Report only a small portion of eligible shares reached the market in spite of a market price for the shares as high as $18.

Assuming the arrangements with creditors and warrantholders referred to above are concluded, there will be approximately 700,000 warrants issued and outstanding for the purchase of unregistered shares of the Company's stock. On June 24, 1981, 295,875 warrants with exercise prices of $4 or $5 per share will expire and not be renewed by the Company. The remaining approximately 400,000 warrants expire between April 15, 1982 and January 15, 1985. Their exercise prices range from $1.25 to $10. After the new financing contemplated by this Business Plan, there will be an additional 262,500 two-year warrants with an exercise price of $10 per share. If all of the warrants

were exercised the Company would receive approximately $4 million and approximately 3 million shares of the Company's stock would be issued and outstanding by the year 1985.

The Company estimates that prior to the financing there will be approximately 350 shareholders and 60 warrantholders.

5. FDA

In order to carry out third-party clinical (human) testing to prove the degree of efficacy of a medication, application for an Investigational New Drug (IND) must be made to the Food and Drug Administration. If within thirty days of the filing of the application the FDA has not responded, the applicant can proceed with the extensive clinical testing described in the application. IND's for dry sockets (1971), hemorrhoids (1972), pruritis ani (1973), psoriasis (1973), and acne (1975) were filed with the FDA. These IND's included the results of toxicity studies made by Food and Drug Research Laboratories and Leberco Labs.

The FDA requested additional material and correction of purported deficiencies with respect to these filings. On September 14, 1977 the Company filed an additional IND for the treatment of cancer. This IND includes teratogenicity and carcinogenicity studies by Foster D. Snell Laboratories. FDA attention became more sharply focused on Lescarden after this filing and requests with respect to all of the filings became more numerous and burdensome.

The cost of providing additional material for each of the earlier IND's plus the cost of going forward with their protocols

(testing procedures) was so onerous that in December of 1979 the Company terminated the earlier IND's with an option to refile, in order to concentrate its management and financial resources on the cancer IND. Cost considerations have been responsible for failure to remedy the so-called deficiencies cited by the FDA.

Briefly summarized, the FDA insists with respect to the cancer application that its form be changed, the results of the earlier toxicity studies be included, lot-to-lot consistency be shown for the Catrix material used in the toxicity studies, and animal efficacy data be provided. The Company's response has been that Dr. Prudden's extensive patient research has proven both efficacy and nontoxicity and that clinical testing by others under the protocols described in the application ought to be permitted in a competent institution (an "institutional IND).

Dr. Prudden has continued to administer Catrix. He and the Company believe that as a licensed physician he has a right to treat patients with whatever medication he and his patient agree to be in the best interest of the patient. When Lescarden's cancer IND was filed in 1977, FDA investigators spent several days with Dr. Prudden. The investigation did not result in a denial of his right to treat patients with Catrix, though it was and still is conceivable that this right could be denied in the future. The Company would contest such a ruling. The issuance of an IND will permit other investigators to use Catrix under the protocols established.

6. Research

Dr. Prudden has believed for many years that there are at least two active components (fractions) in Catrix: an inhibitory factor which controls and reduces the growth of unwanted cells, and a stimulatory factor that promotes the growth of healthy cells. Dr. Prudden believes these effects are achieved through modulation of the immune system of the body. (See The Journey and Appendix B of this Business Plan.)

These suppositions appear to have been confirmed during the last two years in the laboratory of Dr. Alan Walton (resume included in Appendix C) at Case Western Reserve University. Dr. Walton's results may soon be published, and it is expected that new funds raised by the Company will accelerate his work.

The fractions produced by Dr. Walton will be tested in animal pharmacologic studies. It is planned that this work will be carried out by Dr. Wayne Tompkins at the University of Illinois (see Section V below). Dr. Charles Denko is currently testing one of the Catrix fractions at Fairview General Hospital in Cleveland for its anti-inflammatory effects. (The resumes of Drs. Tompkins and Denko are attached in Appendix C.)

Mention should be made here of the work done under the auspices of the National Cancer Institute (NCI). In 1978 Dr. Prudden presented the results of his work with Catrix to the NCI. The then Deputy Director of the Cancer Therapy Section sent samples of Catrix to the Istituto Mario Negri in Milan to determine the extent of Catrix's immunological activity.

In February 1979 the Deputy Director reported that Catrix

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had shown significant immunological effects and that the Milan institute wanted additional Catrix powder. A series of errors on the part of the Istituto Mario Negri, Lescarden, and the NCI resulted in a report by the Institute that Catrix not only contained an impurity but showed less powerful immunological activity than in the previous tests. Dr. Prudden made a detailed analysis of this second report and discovered significant errors in the statistical treatment of the data. Dr. Prudden's analysis was sent to the Deputy Director, who agreed that there were questionable statistical comparisons in the report. For these and other reasons it was decided by the NCI and by Lescarden that no further work on Catrix would be done by the Istituto Mario Negri.

Despite Dr. Prudden's instructions to the contrary, the NCI meanwhile had tested Catrix in its standard chemotherapeutic screen. This is a standard testing panel to assess the efficacy of compounds as chemotherapeutic agents. Since Catrix does not function as a chemotherapeutic agent, the negative reported results are considered by Dr. Prudden to be irrelevant. The Deputy Director (now Deputy Director of the NCI itself) continues to be interested in Catrix and in Dr. Prudden's clinical results. He has received the writeup of Dr. Prudden's fifty-one cancer patients (see The Journey) and recently expressed his interest in reviewing Dr. Prudden's more recent cases.

Additional research was performed by Eli Lilly and Company during the years 1975 through 1978. The research resulted in abundant small animal and in vitro confirmatory evidence.

Following laboratory confirmation of Catrix activity, Lilly undertook fractionation studies. When one of Lilly's leading products unexpectedly required the attention of the fractionation team, the Catrix project slowed to an unacceptable level and was discontinued. Lescarden received the Lilly raw laboratory data upon discontinuation of their work and Dr. Walton has used some of their findings as a point of departure for his fractionation efforts.

7. Patents

As mentioned above, patents and applications for patents have been filed in the United States and abroad. An application will be filed shortly to seek protection for certain biologically active fractions derived from Catrix in Dr. Walton's lab at Case Western. The Company's basic composition patent on Catrix was granted in 1968 and expires in September 1985. While there are numerous process and method (patient treatment) patents (see Appendix D) which expire at later dates, the Company believes that its patent position will be measureably enhanced if this most recent application is successful.

Due to lack of funds, very little investigation has been done by the Company to determine current infringement of its patents in the United States or abroad. At present it is believed that Rumalon, an unpatented arthritis medication which is the product of Robapharm Ltd., Basle, Switzerland, is the only product that contains cartilage being sold (only in Europe) for any of the diseases covered by Catrix. On the other hand, it is known that considerable research on the use of cartilage derivatives in

the medical field is currently being done by both American and foreign corporations and institutions. (See the following item of this section.)

8. Competition

The Company intends to research its competition thoroughly. It is difficult to obtain up-to-date information on the success of such products as Interferon and other known medications that treat some or all of the Catrix diseases. There is presently a burgeoning interest in drugs that affect the immune system. Immunological medications for cancer and arthritis as well as many other diseases are being developed throughout the world. For example, it appears that immunomodulators are generating sales of $150 to $200 million for anti-cancer applications in Japan. Interferon is presently being used in clinical tests under an approved IND. However, its toxicity levels and cost are still high and its efficacy with respect to some types of diseases including certain types of cancer seems problematic.

The Company understands that due to publications on beneficial effects of cartilage, corporate and academic research is expanding in the United States and abroad. As mentioned above, an unpatented cartilage product, Rumalon, is presently sold in Europe to treat arthritis. In addition, Monsanto has financed a Harvard and MIT project that includes studies being made by Dr. Judah Folkman on suppression of tumor vascularization using a cartilage component. It is believed that this work has not yet included clinical tests.

Section III. Markets

Markets, market penetration, profitability and profits for Catrix should be but have not yet been estimated. Obviously, corporate resources should be directed toward the most rewarding return. Given a product such as Catrix, with its still unexplored fractions, corporate economics must be approached with great caution for many reasons, including the following:

1. The size of the markets for Catrix and its fractions cannot be accurately determined. It is not known with accuracy what population in the world suffers from the diseases Catrix may beneficially affect. It is estimated, for example, that there are at least 30 million cases of osteoarthritis in the United States. The cases reported by the Arthritis Foundation, however, are only 16 million, probably due to the methodology the Foundation has used to arrive at this figure. Psoriasis and cancer patients are estimated to number in excess of 6 million and 1 million respectively. If the population of patients with other diseases for which Catrix appears therapeutic (hemorrhoids, pruritis ani, viral infections, plant allergies, dry sockets, wound healing) are included, the markets in the United States alone would seem so large as to make precise economic analysis extremely difficult.

2. Market penetration is even more difficult to

estimate. If only cancer, osteoarthritis, and psoriasis are considered and if Catrix treatment for them only approximates the efficacy that Dr. Prudden's results would indicate, penetration could be a high percentage of the market. Also, competition is a determining factor in marketability.

Currently approved therapies (methods and medications) for treating cancer, arthritis, and psoriasis seem not to have the efficacy of Catrix therapies shown in Dr. Prudden's practice. The pharmaceutical therapies for cancer now in vogue have been shown, without exception, to have serious side effects. This makes their use hazardous with many patients on an extended basis. Catrix, on the other hand, has shown no undesirable side effects even after many years of continuous administration.

3. Profitability and profits are hard to measure when estimates of such factors as cost of production, cost of competing products, cost of sales, potential markup, etc. contain large margins for error.

The table on the last page of this section represents an attempt to estimate conservatively the revenues that might be derived from the sale of Catrix in the United States for psoriasis, osteoarthritis, and cancer. It is based on Dr. Prudden's indicated dosage, a five percent penetration of markets, and a cost of approximately sixty percent of the price Lescarden now pays for Catrix powder. (See Section IX below.) It assumes a psoriasis, osteoarthritis, and cancer population of 6 million, 16 million,

and 1.2 million respectively.

It is anticipated that, after further investigation of factors affecting estimated revenues and earnings, the Company will be able to refine its assumptions and those estimates. Progress in the various efforts described in Sections V through VII below should aid the Company in that effort. It appears valid to assume that large revenues and earnings can be realized from the production and sale of Catrix and its fractions. So far as the fractions are concerned, such conclusions will depend largely on their susceptibility to synthesis (e.g., recombinant DNA techniques) or other forms of production. The Company's present position is that the past work of Dr. Prudden and current and likely future conditions of the marketplace adequately justify the research and management effort contemplated by this Plan.

Annual Estimates--Catrix Capsules

Disease	Number of Patients[3]	Catrix Volume(kg)[4]	Revenues (in thousands)[1,2]
Psoriasis	300,000	985,500	$ 492,750
Osteoarthritis	800,000	2,628,000	$1,314,000
Cancer	60,000	197,100	$ 98,550
TOTAL	1,160,000	3,810,600	$1,905,300

[1]Assumes a Catrix cost of production of $100 per kilogram

[2]Assumes 500% markup of Catrix cost

[3]Assumes 5% penetration of estimated U.S. patient populations of 6 million (psoriasis), 16 million (osteoarthritis), and 1.2 million (cancer)

[4]Assumes Dr. Prudden's present treatment regime for each disease

Section IV. Corporate Problem and Strategy

The problem of Lescarden Ltd. has been variously defined as insufficient funds, failure to obtain an American IND, inability to license, and other frustrations which once resolved would lead to corporate success. Concentration on these and other problems such as patent applications, multiple IND filings, and possible inadequacies of the FDA, while not unreasonable, has sapped the Company's limited funds and misdirected its efforts. The promise that one medication might control, cure, and possibly prevent diseases as seemingly unrelated and widespread as psoriasis, arthritis, and cancer has bred scepticism, both medical and pharmaceutical. Not adequately investigated even by those closest to him, Dr. Prudden's claims have been accepted on faith by some, and rejected out of hand by others.

Simply defined, the immediate corporate problem is how to develop evidence that will confirm Dr. Prudden's clinical results. In the past the Company has maintained that such confirmation would best be obtained by clinical testing of Catrix under an FDA-approved IND. In adopting this position, the Company has failed to acknowledge that, in almost all cases, the FDA relies on complete laboratory and animal pharmacology in assessing the credibility of an IND application. The Company now recognizes that overly regulated and inadequately staffed government agencies and the not illogical tendency of large pharmaceutical companies to favor their own past investments and "in-house" priorities

are factors that must be taken into account, however reluctantly, in any new corporate strategy for Lescarden.

With fresh funds and a new management effort, Lescarden's strategy to obtain recognition and use of Catrix and its derivatives in its indicated markets must be:

1. to obtain objective third-party confirmation of Dr. Prudden's results by laboratory and animal pharmacology; and
2. to array all supporting evidence in proper form for publication and presentation to the medical profession, regulatory authorities, and prospective licensees.

Achievement of these near-term goals will permit the flexible application of additional funds and management to an effort on three fronts: FDA approval, foreign or domestic licensing, and the production and sale (with others if required) of a topical or cosmetic application for Catrix.

Confirmation of Dr. Prudden's results will require a significant portion of new funds. These funds should be spent on the animal pharmacology proposed by Dr. Tompkins at the University of Illinois and the continuing fractionation work of Dr. Walton. Completion and possible publication of their results, coupled with the publication of Dr. Prudden's findings, should put the Company in a better position with the FDA and possible licensees both in the United States and abroad.

With confirmation, corporate strategy and the use of funds will be more specific. Some non-clinical confirmation in labora-

tory and animal tests, with both Catrix and its fractions, has been obtained in the past but never systematically documented. Sections that follow describe the people and activities to be involved in the general corporate strategy leading toward the production and sale of Catrix and its derivatives. The mix of these efforts and the funds devoted to them will depend on their progress as well as the impact of outside forces, such as changes in regulations, competition, etc. (See Section XII below.)

Section V. Research Strategy

The long-range future of Lescarden probably will depend significantly on the fractionation work of Dr. Alan Walton. As mentioned above, Dr. Walton's research appears to substantiate Dr. Prudden's belief that Catrix contains at least two active components. A patent application with claims to these fractions is in preparation, and continued pharmacological studies for efficacy of the fractions will be a top priority of Lescarden during the coming year. Written proposals of Drs. Walton and Tompkins (attached in Appendix I) can be described briefly as continuing the isolation and identification of the active fractions of Catrix coupled with in vitro and in vivo testing of their effects. Prior to this work, Dr. Tompkins will be doing the animal pharmacology with Catrix for the FDA referred to in Section VI below. Additional research effort may be made on Catrix and the fractions by Dr. Denko of Fairview General and others. Drs. Prudden and Rees will coordinate this research.

The end result of Dr. Walton's fractionation would appear to be the production of at least two new chemically well defined entities, one inhibiting cellular growth, the other promoting it. Whether Catrix's unique efficacy depends on these fractions in combination, or whether they can be used separately for treatment of specific diseases is problematic. Much more will be known after the coming year's research effort; but it is anticipated that the total effort will require several years and considerably more money.

A prospect of Dr. Walton's work is that the active ingredient(s)

may be susceptible to synthesis by recombinant DNA techniques (or other processes). This would involve "sewing together" the components of the fraction, first in the laboratory and then in a consistent production process. An advantage of such a process would be product consistency and the avoidance of the variations inherent in "natural" products. The products of these new processes could be cheaper per unit of biological activity than Catrix.

In addition, Dr. Tompkins will undertake (perhaps in conjunction with Dr. Denko) the animal pharmacology required to show the efficacy of Catrix in animals, and thereby confirm Dr. Prudden's clinical results. The FDA has required animal pharmacology as a precedent to an IND and clinical investigation of Catrix by physicians other than Dr. Prudden.

It is believed that all of these studies will require a minimum of one to two years. The budget in Section XI below includes only one year of effort by Drs. Walton and Tompkins. Results and circumstances may require expansion of the first year's research effort with the use of funds presently allocated to some other project that can be postponed during the first year.

Section VI. FDA Strategy

As mentioned above, the Company filed a cancer IND on September 14, 1977. The FDA has responded that the filing was unsatisfactory in numerous respects, which can be generally categorized as its form, incomplete toxicity findings, insufficient animal (efficacy) data, and failure to show lot-to-lot consistency.

A large effort will be made by Drs. Prudden and Rees to meet the objections of the FDA. Dr. Rees believes that it is possible to respond to FDA comments in such a way as to obtain the agency's approval of controlled human testing in an academic setting. It is not possible, however, to accurately estimate the time and expense involved in obtaining such approval. The Catrix pharmacology referred to in Section V above may be a fundamental condition for such testing. On the other hand, it is Dr. Prudden's and Dr. Balassa's view that institutional human testing, approved by the FDA, should be permitted to proceed simultaneously with the animal testing because of Dr. Prudden's effective clinical work in cancer with approximately one hundred cases. Fifty-one of these cases have been filed as an addendum to the cancer IND.

The question whether earlier IND's (for dental dry sockets, pruritis ani, psoriasis, hemorrhoids, and acne) should be revived or an application for an arthritis IND filed is being considered by the Company. The fact that there is no known effective treatment for psoriasis might augur well for a prompt IND approval.

Psoriasis cannot be induced in animals, precluding requests for animal pharmacology for efficacy. Concentration of effort seems advisable in dealing with a regulatory agency such as the FDA.

Efforts with respect to other diseases might well be more effectively undertaken through foreign pharmaceutical companies under licensing agreements or joint ventures. The vital question of what IND's to file in addition to the cancer IND will be one of the most important and immediate issues to be resolved by the Company after the raising of interim funds.

The question whether to file for a topical therapeutic application or avoid the necessity for filing such application by marketing a cosmetic preparation is discussed in Section VIII below.

Section VII. Licensing Strategy

There is great variation in the cost and the time involved in the pharmaceutical regulatory processes abroad. Certain Southern European and Latin American countries require considerably less efficacy testing than the United States, Japan, the United Kingdom, West Germany, and Sweden. Even the more "sophisticated" countries have still not imposed the regulatory standards that have been the subject of increasing criticism in the United States. At the same time it would appear that there are a number of foreign pharmaceutical companies, doing business throughout the world, that might be interested in licensing Catrix or Catrix derivatives for development and marketing abroad.

During the last fifteen years management has attempted to obtain both foreign and domestic licensing agreements. Under such agreements, the licensee would agree to test and eventually produce and market Catrix or its active fractions depending on the results of the testing. Payments would be made to Lescarden in the form of royalties, with various combinations of limited time periods and penalty payments for the licensee's failure to go forward.

Considering Lescarden's size as well as its patent position (see Section II, Item 7 above), properly negotiated license agreements could be of significant assistance. Properly arrayed and documented confirmation of Dr. Prudden's work, evidenced by the objective third-party results discussed in Sections IV and V

above, will be of much assistance in concluding such agreements. In addition, the Company must have access to potential licensees. Two of Lescarden's Directors, Drs. Balassa and Haberman, have had experience in licensing both in the United States and abroad. Mr. Herbert Wahle (referred to in Item 1 of Section II above) has many business relationships in the foreign pharmaceutical field. He has agreed to work on Lescarden's behalf to find and negotiate with specific companies for specific parts of the international market. Mr. Wahle has agreed in principle to a company-by-company approach to this work.

Again, the cost and duration of this part of the Company's plan will depend on initial progress in negotiation, success with the FDA effort described in Section VI above, and the cost and success of the essential confirmation effort referred to in Sections IV and V.

Section VIII. Topical Applications

Management and funds have been insufficient to adequately study and plan for the production and sale of cosmetic applications of Catrix. Dr. Prudden's own practice, and tests performed over a five-week period with 391 airline stewardesses of various ages indicate that a Catrix face cream is cosmetically effective. (A summary of the results of the cosmetics tests is attached as Appendix J.)

In most countries, including the United States, cosmetic applications that make no curative claims are not subject to extensive regulation by the FDA. It is conceivable, therefore, that Lescarden, to develop early revenues and cash flow, might produce and market (alone or with others) a face cream or skin lotion.

It also seems likely that Catrix cream could be used as a base for steroid or other creams presently sold over the counter for acne, allergy, and other skin problems. This method would probably require little or no regulatory action since no therapeutic claims would be made. Results of sales and consumer acceptance then could be monitored to determine if the Catrix base had had an enhancing effect on the activity of the approved medication. The Company has good reason to believe that it would.

The Company will also explore the possibility of an FDA filing for a topical application. Catrix creams, suppositories,

and ointments have shown excellent results with diseases such as herpes, allergies such as poison ivy and poison oak, hemorrhoids, and burns. The regulatory process might well be shortened both in the United States and abroad by such a filing. The ultimate question of markets, profits, and cash flow will affect the Company's decision to make such filings.

Section IX. Catrix Supply

The Company depends for its supply of Catrix powder on Canada Packers in Toronto, an approved FDA supplier. Canada Packers is under no obligation to produce Catrix for Lescarden. The Company has no other source of supply, and the cost of the powder is still high despite considerable increases in the volume of the orders.

The Company's founders believe that Catrix powder can be produced by Lescarden itself or by others at a considerably lower cost than the Company presently pays. Additional volume, however, may further reduce the price Lescarden pays Canada Packers.

Studies were made some years ago of the cost of building facilities to produce Catrix, with estimates of the cost of its production in those facilities. (At that time it was believed that Catrix could be produced in a $3-million facility for $50 per kilogram, approximately one-third of the present cost of Catrix. There are no present plans to spend funds for this purpose.)

Such considerations as volume, supply of cartilage, FDA production approvals, exclusivity rights, and the possible production of Catrix fractions (see Section V above) will influence decisions with respect to product supply. Licensing negotiations might well include negotiations for the production of Catrix, especially where the prospective licensee has a source of

cartilage (such as a packing company subsidiary) and is a licensed FDA manufacturer. A variety of efforts with respect to lowering the cost and assuring the supply of Catrix powder must be a continuing activity of Lescarden during the coming year.

Section X. Cancer Clinic

Dr. Prudden's results with cancer patients are sufficiently positive to require the Company to give serious consideration to the commencement of a small and reputable clinic for the treatment of cancer patients in another country. Obviously such a clinic could not be commenced without such country's regulatory approval, and such approval would probably be conditioned on some or all of the third-party confirmation discussed above. Equally apparent is the necessity for treating patients with all of the methods presently considered medically appropriate, including radiation, chemotherapy, and surgery. In his own practice, Dr. Prudden has invariably recommended known methods for the treatment of cancer prior to the institution of Catrix therapy.

While "hard-headed" pharmaceutical and medical specialists might well disagree, failure to treat terminal patients with a medication that has proven beneficial, and possibly even curative, has an implication of immorality that might have a negative effect on all facets of Lescarden's future. Such a clinic would be operated at cost, results would be rigorously documented, and would then be made available to all interested regulatory agencies, medical institutions, and individual scientists.

The amount of time and money spent on this effort should be relatively small until all of the work discussed in Sections IV through VIII has been undertaken and results achieved. The feasibility of establishing such a clinic, however, should be investigated promptly.

Section XI. Costs and Duration

The ultimate goal of Lescarden is to make Catrix available to those who need it in a fashion that will produce reasonable profits and growth for the Company. To minimize the time and cost of the steps necessary to achieve that goal, a prudent course must be steered between two unlikely extremes: an attempt to become a world-wide pharmaceutical producer and marketer, or an effort to license all of Lescarden's rights, products, and patents to a multi-national pharmaceutical company.

The indicated optimum course would be to license certain applications, and to keep some domestic efforts solely under the control of Lescarden. Topical cosmetic applications, which would have beneficial side effects on allergies and other diseases that affect the skin, must be seriously considered as a means of developing product acceptance and cash flow in a short time and at low cost (see Section VIII above).

Estimates of expert pharmaceutical personnel vary so drastically on the likely costs and time involved to obtain the final New Drug Approval required to produce and market Catrix that management cannot now give any precise estimate of that cost and time period. Based on past results and success, cost and time would certainly seem to be less than the most pessimistic estimates, but considerably more than logic or those results might indicate. It is expected that when the third-party objective confirmations are obtained (referred to in Sections IV and V

above), and after several additional meetings with the FDA concerning the current cancer IND (Section VI above) the Company will be better able to determine the specific course of its management effort and the times and costs required to achieve results from those efforts.

In no way, however, can the capital requirements for the introduction of a new pharmaceutical such as Catrix be underestimated. Capital costs can be reduced by licensing agreements, but the loss of control under such agreements has to be reckoned with. While a more specific estimate of required funds will be made during the first year's effort (described and budgeted in the following Section), it seems likely that at least $10 million to $15 million will be required to assure a five-year effort to carry out the necessary research to obtain IND's and at least one NDA. Furthermore, it will be important that such minimal funds be available to the Company without the usual fund-raising uncertainties.

One of the basic objectives of the Company will be to attract good personnel, particularly a Chief Operating Officer skilled in the pharmaceutical business. It is doubtful that the proper kind of person can be attracted to the Company without assurances of large capital funds for the conduct of Lescarden's business. Research and IND panelling cannot depend too heavily on the vagaries of capital financing.

Section XII. First Year Budget

A budget to cover one year of the work described in Sections V through X is set forth on the next page of this Section. As indicated earlier, mix and cost of each effort will depend on the progress of each effort and other circumstances.

While the budget calls for an expenditure of $1,116,000, it is unlikely based on the uncertain starting dates of portions of the work (such as Dr. Tompkins' work on fractions) that more than $1 million will be spent in the first year after the raising of new funds. During that year plans will of course be effected for the raising of the additional funds required for the continuing efforts of the Company, especially IND panelling (clinical testing) and further fraction testing. Money saved or monies raised over and above the budget will be available for any FDA-approved panelling and additional research.

It is believed that the following minimal results can be achieved by the use of the funds listed in the budget:

1. The integration and control of Lescarden's records, offices, research efforts, and FDA applications.
2. The acquisition of a management group, including the services of a skilled pharmaceutical administrator who will be prepared to join the Company as Chief Operating Officer.
3. A more detailed long-range business plan, based on results of the work done in the first year.

Budget for One Year's Effort

Salaries	$ 210,000
Employment Contracts--Prepayments	70,000
Travel and Entertainment	50,000
Consulting--Research	260,000
Consulting--FDA	100,000
Consulting--Cosmetic	25,000
Consulting--Licensing	25,000
Legal	130,000
Auditors	20,000
Rental	56,000
Office Expenses	64,000
Administration	17,500
Special Expenses--Personnel	22,000
Insurance	57,500
Fees and Expenses--Directors	9,000
TOTAL	$1,116,000

4. A specific capital program geared to the long-range business plan.

5. Preliminary third-party confirmation of Dr. Prudden's clinical results, i.e., in vitro and in vivo testing of Catrix and its fractions.

It is tempting to promise more than this. At best, for example, an IND for cancer or for some other disease such as psoriasis might be achieved and clinical testing begun. A license might well be executed. Plans for near-term marketing of Catrix in a topical application may have been developed. The attitude of the Reagan administration toward inefficiencies of regulatory processes may have shortened the regulatory cycle in the United States.

It seems unwise to be overly optimistic, in spite of the human need for Catrix and its fractions. For better or for worse, corporate and governmental organizations have developed methods and procedures that have come to have a life of their own. Budgets and capital estimates have to be based on the world as it is. On the other hand, third-party confirmations of Dr. Prudden's results, as well as publication of papers by Dr. Prudden himself, could well accelerate the regulatory process.

Section XIII. Positive and Negative Considerations

The Company is well aware of major and minor considerations that argue both for and against its success. If success is defined as the ultimate sale of Catrix or its derivatives, success could be frustrated if:

1. Dr. Prudden's results cannot be sufficiently confirmed by third parties to establish the necessary credibility for FDA approvals, licensing agreements, or additional capital.
2. Capital requirements become so large that sufficient additional financing cannot be achieved.
3. Other immunomodulators are found to be more effective than Catrix.
4. Patents are found to be insufficient to protect the Company or cannot be enforced without excessively large expenditures.
5. Appropriate management experience and talent cannot be acquired and effectively put to use early enough to assure success.
6. Catrix powder cannot be produced in sufficient amounts or at low enough costs.
7. Catrix, as a natural product and therefore a medication whose biological activity cannot be consistently assured, proves to be unacceptable to licensees and regulatory authorities.
8. The cost of production of Catrix fractions proves to

be too high to provide a reasonable return on investment.

The Company presently believes that all of these negative factors, while relevant to the Company's success, can either be overcome or avoided. Considerations that augur well for success are as follows:

1. Dr. Prudden's remarkable results with his own patients over a period of fifteen years.
2. The unique non-toxicity of Catrix in all dosage forms.
3. Results already achieved in animal pharmacology and in fractionation.
4. The probable need for more than one medication for the treatment of the many diseases treated by Catrix.
5. The relative inadequacy of medications presently used for the treatment of those diseases.
6. An extensive American patent position.

THE JOURNEY

JOHN F. PRUDDEN, M.D., MED.SC.D.

This is the story of a still unfinished journey. More than twenty years ago, an article caught my eye, and the ideas it inspired became and have remained the center of my life's work.

It tells of the unusual serendipities which have marked my journey, with each such good fortune demonstrating a different and unexpectedly powerful biological effect of bovine cartilage preparations and their processed fractions. It also tabulates the specific clinical results which have been achieved thus far utilizing our present dosage forms.

The journey will be completed with help from many other scientists who now have begun to work on this promising research. Our destination is the isolation, and probable synthesis, of the active biochemically distinct components of the present material, and the markedly increased potency which this will make possible.

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PART I

CHRONOLOGICAL HISTORY OF THE DEVELOPMENT OF CATRIX

THE JOURNEY

In 1954 I returned from my tour of duty in the Army Medical Corps to assume an instructorship in surgery at the College of Physicians and Surgeons of Columbia-Presbyterian Medical Center in New York. I did so with the sense that I was coming into a splendid and assured future in the medical establishment.

I had graduated from both Harvard College and Harvard Medical School and had had my internship, fellowships and residencies in such diverse and distinguished places as Bellevue, Presbyterian, Roosevelt, Pondville Cancer Hospital, and the Peter Bent Brigham Hospital. I had also been one of the initial members of the Army Surgical Research Unit and Burn Facility at Brooke Army Medical Center in Texas, where I had been Chief of the Laboratory Division and received a Certificate of Merit for my work.

At Columbia I had a large laboratory and considerable funds at my discretion due to the then remarkable largesse of the National Institutes of Health Grants Program. In those days we lucky few at Columbia were filled with a delicious feeling that we were where we ought to be. Only the Harvard institutions were felt to be our equal; but it seemed inevitable that this parity would not persist for long. Little did I suspect that I would forego this predictable and tranquil future in favor of a less traveled road, and all because my wretched intellectual curiosity prompted me to investigate a lead provided by my own treacherous colleagues.

This lead involved an unusual finding by a Professor of Pathology, a Professor of Biochemistry, and a Professor of Medicine. They were

investigating the disastrous news that cortisone in its various forms did not provide a surgical millenium when given intra- and postoperatively. It had been hoped that cortisone, the presumptive wonder drug, would significantly reduce the painful inflammation that follows surgery. Instead, a nightmare of leaking anastomoses, occult infections, debilitating metabolic disturbances, disrupted abdominal wounds, and nonhealing ulcers ensued.

In order to study the cortisone-induced inhibition of wound healing, my colleagues loaded rats with steroids and then, in successive experiments, placed different materials in a small micropore chamber in the subcutaneous tissue of the rat's back. If these caused a reversal of the wound-healing inhibition it would be evident in histologic studies of the tissue surrounding the chamber.

This formidable trio had tried (unsuccessfully) every substance that had even been rumored to have a positive effect on wound healing. To make matters worse, their concentration had been disturbed by the presence of a pesky Canadian pathology fellow who kept insisting that what was needed to reverse the cortisone-induced inhibition of wound healing was, simply, cartilage chips. The professors regarded this suggestion with the contempt that it deserved, but their attitude did not deter the young Canadian in the least.

Eventually, they decided to humor him. They made small cartilage chips from the knee joint of an amputated leg which had come their way from the operating room, and put them in the micropore chamber. As he had predicted, there was a complete reversal of the inhibition of fibroplasia (wound healing) in the vicinity of the micropore chamber. But sad to say, by the time the rats were sacrificed to tell their story, the young Canadian had gone

back north -- never to be heard from again.*

At that time I was more or less of a classical "cuttin'" surgeon, and certainly almost never sat down to read the latest pathology journals, very few of which I considered to have much significance to the success of treatment, good surgical judgment being (so I thought) the critical variable. And so it seems a semimiraculous event that I happened to come upon the article published by the three professors and the pesky Canadian which reported the findings I have just summarized.

I was immediately fascinated by these findings. Wound healing had always been regarded as something that was inbuilt in some unknown way into the organism; in every species under any given biological circumstance it was thought to be a biological maximum that could not be improved upon. Their findings seemed to indicate, however, that wound healing could be accelerated if the proper building blocks of tissue could be furnished. I was convinced that I had just read about the first step in the discovery of a new biological principle. (And since much of the morbidity and mortality in surgery still is related to wound healing failures, the development seemed promising for the improvement of surgical care as well.)

Simply to satisfy my curiosity about what they were going to do next, I sought out the three professors, who were my personal friends. To my amazement, I learned that they weren't going to do anything! They regarded

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* This is strange, because he was due back at his hospital to recommence his surgical residency. Repeated later efforts to locate him were unsuccessful. My personal conviction, in light of subsequent developments, is that he was a messenger from a region higher even than Canada.

their findings as a kind of curio shop item, akin to but less spectacular than Dr. Lewis Thomas's famous demonstration that erect rabbit ears plop down dejectedly when injected with papain. I told them that I was surprised to learn that they were not planning to proceed with follow-up studies, but since they were not -- I would.

The first step was to see if the remarkable wound-healing characteristics so evident when cartilage chips were placed in the steroid-loaded rats also applied when cartilage was used in endocrinologically and nutritionally normal rats.

The experiment began with a special enzymatic deproteinizing of the cartilage rings of cow trachea, which we obtained in fresh state at a slaughterhouse. We then ball-milled the material with dry ice to an average particle size of about 20 microns. The product was atomized lightly onto the wound edges of standardized midline incisions in rat abdomens. After the incisions had healed for the desired period of time (usually seven days), the sutures were removed, and the wounds tested for their bursting strength by a special technique.*

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* I devised this technique of wound tensiometry in order to have a method which, due to its simplicity and rapidity of application, would permit us to test large numbers of rats in one day. Basically it consisted of the insertion of a latex balloon into the peritoneal cavity of the freshly killed rat through the vaginal apex in females or through the rectum in those relatively few males we utilized. The balloon was connected through tubing and a Y-tube to a positive setscrew pressure pump and to a mercury column which were used respectively to raise the pressure in the balloon at a steady rate and to read the pressure on the mercury column.

The results justified my early enthusiasm. This specially prepared cartilage material, which we named Catrix® from the second part of cicatrix, the technical term for a healed wound, was a true accelerant of wound healing -- the first ever to be demonstrated.

This remarkable healing capacity of Catrix powder was demonstrated most convincingly in a completely controlled study of human wound healing published in the Journal of the American Medical Association.[1] In this work, two exactly corresponding incisions were made on opposite sides of the subject's body and deepened to the muscle level. One of the paired incisions was treated with topical Catrix powder and one was not. Otherwise they were closed in an identical way. Later the incisions were themselves excised and taken to the laboratory for tensiometric analysis. The striking result was that

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When the pressure was greater than the tensile strength of the wound, the balloon would extrude itself through the wound's entire length, a flap valve would hold the mercury column at the level which produced the disruption, and the reading would be taken at leisure.

It turned out that an admirable and cheap balloon for this test was a standard condom. After a time, they developed fatigue and broke, whereupon we tied a new one onto the tubing and proceeded as before. One day, I had performed only a few of these determinations when the balloon burst. I was in a hurry because I had patients waiting, and therefore I was annoyed when my loyal and efficient laboratory assistant told me that she had forgotten to get more condoms. She was a person of considerable dignity. To avoid embarrassment, I had made arrangements with the hospital drugstore so that all she had to do was enter, state that she wanted some of Dr. Prudden's "supplies," and retire discreetly with enough Trojans for a battalion.

This time, however, spurred on by my annoyance, she burst into the drugstore (where some of my startled friends were shopping) and cried out in a loud voice, "Quick! Dr. Prudden needs more condoms!" And so it was that I achieved an entirely undeserved reputation in and around the Medical Center for a time.

the Catrix-treated incisions were 42% stronger. The JAMA, in an editorial in the same issue, called for the pharmaceutical development of Catrix, emphasizing that wound-healing failures are an important factor in the morbidity and mortality of surgery.[2]

Unhappily, this clarion call went unheeded, largely because of the difficulty of complying with what was then a new and unyielding fascination with double-blind studies. In the area of nonhealing clinical wounds, these require an experimental condition virtually impossible to fulfill, since complete compliance means wounds of identical size and longevity, in individuals of identical age and medical history. While this is perhaps somewhat overstated, it is astonishing that it is not more so. It is one example of the overly rigid application of basically good concepts (such as double-blind studies) during the recent efflorescence of legislatively mandated control of medical research.

It was clear that we must try to isolate the specific molecular entities responsible for the remarkable wound-healing capacity of Catrix. One day an opportunity presented itself. I was experimenting with three saline extracts of Catrix to determine if they would accelerate healing in anatomically distant wounds when injected subcutaneously in the backs of our experimental animals. All were effective, but each extract was of distinctly different potency. This was annoying, but it occurred to us that we should attempt to capitalize on the situation by means of an analysis to see if any specific chemical accounted for the differential efficacy.

When we performed amino acid chromatography, a distinct gradation in the level of a single constituent appeared. This was glucosamine, which was

of the highest concentration in the most effective extracts. There followed a number of experiments with various chemical forms and combinations of glucosamine. These experiments established that the utilization of another entity, polymeric-N-acetyl glucosamine, which we named Poly-NAG®, stimulated surgical wound healing to a much greater extent than Catrix.* This material had been thoroughly studied in the polymer industry. The techniques are available for use of Poly-NAG in sutures, sponges, nonwoven mats, and prosthetic devices. A low molecular weight polymer of the material can be used intravenously.

At this time we labored under the impression that we had completed our objective of discovering a powerful wound-healing accelerant and then identifying the organic molecular configuration of the active component -- polymeric-N-acetyl glucosamine, Poly-NAG. We were soon disabused of our complacency by a startling observation: when Poly-NAG powder was placed on chronic nonhealing wounds (which are always infected), it didn't do much good at all! Suspecting that we had lost something in the transition from Catrix to Poly-NAG, we applied whole Catrix powder to the same wounds. Clean healthy granulation tissue rapidly developed, followed by speedy epithelization. Since the dominant variable in these chronically infected wounds is inflammation, we could only conclude that Catrix possessed powerful anti-inflammatory capacities which Poly-NAG did not.

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* For example, we demonstrated that the use of Poly-NAG sutures would result in about a 50% increase in wound strength at seventh postoperative day. Also, we lay strips of Poly-NAG nonwoven mats on the wound edges prior to closure and increased the tensile strength 120% at the seventh day. And so forth.

The recognition that Catrix possessed both the stimulatory capacity necessary to accelerate wound healing and the inhibitory capacity required to reduce inflammation led us to realize that we were dealing with a substance of almost daVincian potential. It caused us to return to the investigation of Catrix when otherwise we might have stopped after the identification of Poly-NAG. As has been true of this journey from the start, when we needed to test new perceptions, clinical opportunities soon presented themselves.

The first of these were the cases of two gentlemen who were suffering from a classic chronic inflammatory condition: pruritus ani, a humbling malady where one scratches his anus all the day. (It is never fatal, although many have prayed for deliverance!) Both of these patients had had the disease for a long time, one for ten and one for fifteen years, causing severe problems in their lives and marriages.

I treated their excoriated, red perianal tissues with a 5% Catrix cream. Both were free of symptoms in only two days; and after a week treatment was terminated. The patients remained free of symptoms, and indeed of any physical evidence of the disease, for two and three months respectively, at which time the symptoms recurred and the treatment was repeated. The intervals between exacerbations of the disease lengthened; whenever it did return, the treatment was again 100% effective.

Our success with pruritus ani prompted us to go on to the treatment of other chronic inflammatory states.* For instance, because many of our

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* We followed a general policy of treating at least fifty cases of each condition and then compiling the results, which can be found in Part II of this paper.

pruritis ani sufferers also had hemorrhoids and fissures-in-ano, we decided to experiment with these conditions. Two double-blind studies were performed using Catrix in a suppository form to treat hemorrhoids, both with highly significant positive results (see page 26).

I discovered close to home that plant allergies also respond to application of a Catrix cream. One fall day a member of my family was gathering beautiful red leaves to decorate the house. Unhappily, she did not realize that she was carrying an armful of poison oak. She returned from her walk metamorphosed into a pumpkin, already markedly edematous with an acute antigen-antibody skin reaction. I applied large amounts of topical corticosteroids with no effect whatsoever. It became clear that, in order to prevent her from scratching the lesions and causing infection, it would be necessary to admit her to the hospital for sedation. Prior to this distasteful solution, I applied Catrix cream over all the weeping lesions. The unbearable itching disappeared completely for 1½ to 2 hours. Each time the itching returned, I reapplied the Catrix cream with the same happy effect, until the allergic reaction had passed.*

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* An interesting experiment involving plant allergies is the one I conducted on my colleague and partner in this journey, Dr. Leslie Balassa. He had the good fortune to possess a large patch of poison ivy in his front yard. In the name of science, I convinced him to allow me to test the prophylactic effect of Catrix on plant-induced skin allergies. I covered his left arm with the cream and then requested that he plunge both arms into the malevolent weed. A few hours later his right arm was covered with a typical poison ivy rash (which I then successfully treated with Catrix cream). The prior treated (with Catrix) arm remained free of any allergic reaction whatever.

At about the same time, a dentist in Illinois wrote to inquire about possible uses of Catrix in dentistry after having read some of my wound-healing papers. I thought that Catrix might be effective in treating the condition known as dry socket (alveolitis), which occurs in approximately 7-18% of tooth extractions. This is a localized inflammation of the jawbone which causes extreme pain at the site of the extraction. I suggested the treatment of this particular condition because the pain is so dramatic that efficacy of treatment is easy to assess.

We made a paste of Catrix with saline solution and gently packed it into the socket. Once begun, dry socket normally lasts ten to fourteen days. My hope was that, because Catrix had proven to be such an effective wound healer, it would heal the gum over the top of the painfully exposed bone and nerve endings within five days, thereby decreasing the duration of the agony by half. I was understandably surprised and delighted when the pain totally disappeared in twenty minutes and never returned.

This was most astounding because our previous work had never indicated that Catrix was in any way an analgesic or an anesthetic. And obviously, it had not healed the wound in twenty minutes. I consulted the inflammatory savants at Columbia. They agreed with my conclusion that only a substance with profoundly anti-inflammatory properties could have achieved such immediate relief. (See p. 22 for the identical results achieved in our subsequent pilot cases.)

While we were still testing Catrix in these topical applications, a patient appeared with particularly severe ulcers (cold sores) around the mouth. Although I knew the herpes simplex virus to be the cause of the ulcers, I thought Catrix might be an effective treatment from a wound-healing point of view. When I applied the medication, the painful lesions healed with extraordinary rapidity; in about four days they were entirely dry. Even given an optimum local wound-healing effect, this far exceeded my expectations and led me to think that Catrix might have some specificity in this regard. We learned shortly thereafter, as a result of *in vitro* testing, that Catrix indeed has a direct Herpes virucidal effect. We have since treated a large number of cases of herpes simplex, and of herpes zoster (shingles), with almost 100% effectiveness (see p. 28)*

* There is also reason to believe that Catrix is effective treatment for a variant of herpes called the Epstein Barr virus, responsible for infectious mononucleosis.

After the initial results in these studies of simple chronic inflammatory conditions, we moved to more serious systemic inflammatory diseases: osteoarthritis and the rheumatoid diseases such as rheumatoid arthritis, dermatomyositis, lupus erythematosus, ulcerative colitis, and regional enteritis.*

Unlike the rheumatoid diseases, which are characterized by dramatic flareups and remissions, osteoarthritis is an ideal disease to study because of its slow progress and relative stability. Shifting baselines are not an interpretive problem even when patients are carried for long periods of time in double-blind studies.

The joint pain characteristic of osteoarthritis is caused by the body's inappropriately vigorous inflammatory response to bone spurs and bumps in the vicinity of the joints. The administration of Catrix to over 700 osteoarthritis patients, either by subcutaneous injection or by ingestion, has shown that it markedly reduces this inflammation and the resulting pain and disability (see p. 32).

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* I originally treated those diseases by subcutaneous depot injections of a solution of the Catrix powder, referred to as Catrix-S. But while treating ulcerative colitis and regional enteritis, I discovered a fact with broad significance. It occurred to me that in these diseases of the intestinal tract, rather than giving large-volume subcutaneous injections, I could effectively administer the drug "topically" by giving it to the patient in an ingestible form and thereby bringing it into direct contact with the diseased intestinal tract. Many of these patients also suffered from osteoarthritis. When their arthritis began to improve, I realized that the drug might be effective by the oral route, a feature I had not expected with so complex a biological mixture. Subsequent clinical observation and laboratory tests have led me to believe that it is almost as effective when administered orally as when injected under the skin.

Psoriasis was one of many diseases we considered treating next because at the time we naively thought that it was simply a massive inflammation. The first case of psoriasis, however, was treated inadvertently. A huge ulcer due to varicose veins had occurred in a leg which incidentally was covered with psoriasis. We hoped to heal the ulcer by covering the wound with Catrix powder, after cleansing. The ulcer was so chronic and infected that it oozed sufficient serum to dissolve all of the Catrix, which then saturated the fluffed dressing I had applied to the leg. When I removed the bandage, after two days, the psoriasis was completely gone. The subsequent pilot work on the treatment of total-body psoriasis with injections of Catrix-S and with oral Catrix was highly successful (see p. 29).

We now know that psoriasis is one of the autoimmune or self-sensitivity diseases (as are the rheumatoid diseases). It is a special kind of inflammation resulting from the body's rejection of the basal layer of the epidermis, which fights back by rapid cell division in order to preserve itself from the attempted rejection. As our perception of psoriasis became more sophisticated, we began to see the effectiveness of Catrix in treating psoriasis primarily as an indication of its ability to inhibit mitosis, i.e., cell division.

Because the rates of mitosis in psoriasis are as rapid as those prevalent in some cancers, the disease once enjoyed a reputation as a good cancer model. I no longer subscribe to this concept, but fortunately I still did when, prompted by our success with psoriasis, I decided to try Catrix in the case I will now describe.

A woman came to me with an enormous breast cancer that had ulcerated her entire right chest wall. She had allowed herself to reach this pitiable condition because her mother had had a stroke, and she would not desert her mother's side. In any case, radiation, palliative surgery, hormone therapy, and chemotherapy were all tried, and each had failed in turn.

This left her at the conclusion of conventional therapy with as big an ulceration as ever, and a partially paralyzed left arm due to a huge supraclavicular mound of metastases which had invaded the brachial plexus and surrounded the vascular supply to the arm.

There being no other hope, we began to treat the cancer with Catrix-S injections. As noted above, this was based on the then popular concept of psoriasis as a reasonable cancer model, and upon our excellent success in the treatment of psoriasis with Catrix-S injections.

Although we now consider that we did it for the wrong reasons, it was soon apparent that it had been, for whatever reason, the right thing to do. She began to improve immediately, and her cancer-ulcer of the chest wall healed completely. She has now been cancer-free by biopsy for more than six years. The specifics of her clinical history are of course more complex, but this is the essence of it.

As indicated in the table on page 43, many cases of various kinds of cancer have been treated since this first one, with encouraging results. Advances in diagnostic immunochemistry have enabled us to identify specific components of the immune system, and measure the effect of Catrix on their production. These measurements, and our clinical successes, have strengthened our conviction that Catrix is a powerful immunostimulant, whether administered by mouth or by injection.

Catrix increases total complement and Complement C-3. An increased production of immunoglobulin A occurs at much the same time. When these two immunologic components fall, after peaking at about twice their normal level, immunoglobulin M begins to rise. This trend then continues until the patient's cancer is gone, or until death ensues.

We also know that Catrix causes a rise in Cyclic Adenosine Monophosphate of about 700% and a marked increase (~600%) in the lymphoblast count (as measured by the uptake of labeled thymidine in cell culture). In addition, there is an even greater lymphoblastic response to the presence of such mitogens as phytohemagglutinin, conconavalin A, or pokeweed mitogen. All this is the result of the presence of a stimulatory component in Catrix.

On the other hand, there is evidence that Catrix contains an inhibitor of mitosis which exerts a powerful effect on both inflammatory and cancer cells. This accounts for the anti-inflammatory effect of the medicine, and for its assistance in the specific immunological rejection of cancers which the stimulatory component causes through the enhanced activities noted above.

We believe the "natural" entities which are responsible for the activity of Catrix represent an important therapeutic shift away from the harshly artificial and toxic substances (used in traditional chemotherapy) to agents which influence the "balance" of things, yet destroy nothing and replace nothing of the normal physiological biochemistry.

* * * * * * * * *

A combination of intuition, wisdom, and Providence has characterized this journey, as it no doubt does the course of all discovery. Our original perception of Catrix (and then of Poly-NAG*) was of a wound-healing accelerant, i.e., a stimulant of cell growth. When Catrix then healed chronic inflammation, we were faced with the apparent contradiction that it possessed anti-inflammatory, and therefore inhibitory properties as well. To explain the contradiction, I hypothesized that the complex biologic mixture comprising Catrix must contain at least two active components. We now know this to be the case. We also know that in treatment of so-called inflammatory diseases and the neoplastic diseases, both components are not only useful, but necessary. Work that began with rather simple qualitative analyses in the laboratory, and expanded into observation and treatment in the clinic, has progressed to use of the most sophisticated techniques for fractionation, isolation, and possible synthesis of the components of Catrix responsible for its broad spectrum of activity. The journey must now continue with the laboratory and clinical testing necessary to fulfill the great potential of Catrix for the alleviation of suffering.

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* Poly-NAG remains a highly significant and self-contained element of our work. Each of the various Poly-NAG products appears to possess a significant advantage over the corresponding surgical adjunct in current use.

PART II

GENERAL DESCRIPTION OF CATRIX, SUMMARY OF DOSAGE FORMS, AND THE RESULTS OF CATRIX THERAPY

SUMMARY OF DOSAGE FORMS

I. General Description

Catrix is a highly processed preparation of bovine tracheal cartilage which is available as a micronized powder averaging twenty (20) microns in diameter. It is a biological mixture which contains mucopolysaccharides, glycopeptides, glycoproteins, and collagen. Catrix has an extraordinary range of pharmacologic activity that is achieved without toxicity (see Section III below). Fractionation is proceeding well, and we have already adduced information which suggests that considerable potentiation of the clinical efficacy of Catrix will soon be possible.

Catrix powder is formulated into the dosage forms outlined below.

II. Dosage Forms

A. Catrix Powder

This is the basic Catrix material described above. Its use, as is the case with other dosage forms, will be discussed under THE RESULTS OF CATRIX THERAPY section which follows.

B. Catrix Paste

This dosage form is made by mixing the powder with isotonic saline into a smooth paste of appropriate viscosity.

C. Catrix Cream

This dosage form is available in two percent, five percent and ten percent concentrations of Catrix. Catrix cream is a water soluble

formulation which is designed for use in topical therapy of macerated, "weeping" inflammations. In this situation, the Catrix within the cream is solubilized by the exudates characteristic of such inflammation.

D. Catrix Ointment

This is also available in two percent, five percent, and ten percent concentrations. This dosage form differs from Catrix cream principally in the presence of wax and oils which aid in penetration of the Catrix into dry lesions. These lack the exudate with which "wet" lesions (see C above) solubilize the Catrix.

E. Catrix Suppositories

This dosage form, available in two percent, five percent, and ten percent strengths, utilizes Catrix powder in a suitable vegetable oil with an appropriate melting point for topical absorption in the anus.

F. "Chap Stick-Like Preparation"

This topical dosage is available in two percent, five percent, and ten percent strengths. It also is made up in a vegetable oil base with a melting point appropriate to application on the lips.

G. Catrix Capsules

This is the oral dosage form. Each No. 1 gelatin capsule contains 375 mg of the basic Catrix powder as described above.

H. Catrix-S

This is the injectable dosage form of Catrix. It consists of five percent weight per volume of Catrix. This solution has been cleared of most of the collagen contained in Catrix powder by special processing. This results in a brown solution with a slightly acidic pH. Benzyl

alcohol in a concentration of .9 percent acts as the preservative, and also has the happy property of being an anesthetic agent. Catrix-S is usually given in 25 cc subcutaneous depots in two sites per visit, on a schedule of two visits per week. If circumstances dictate, the dosage may be increased to 50 cc in two subcutaneous depots per visit, and the frequency has on occasion been advanced to three times per week.

This dosage form is employed when there is a contraindication to the oral route for whatever reason, from psychic inability to take the capsules to lesions of the gastrointestinal tract which prevent it. It may be coupled with hospitalization for total intravenous parenteral nutrition (TPN) or NG tube feedings.

III. Toxicity

Individual patients have received up to 5,000 cc of Catrix-S without any immediate or long-term toxicity of any kind. This is quite in keeping with complete FDA-mandated toxicity studies which have shown no acute or chronic toxicity, and no teratogenicity or carcinogenicity in studies up to two years in length. The other dosage forms (oral and topical) have also been administered without resultant toxicity of any kind.

THE RESULTS OF CATRIX THERAPY

-- BY DISEASE --

1. Nonhealing Wounds

As noted in Part I, this was the original area in which the biological activity of Catrix was recognized. In general, this category of disease includes such chronic conditions as varicose ulcers, post-phlebetic ulcers, nonhealing perineal wounds following abdomino-perineal resections of the rectum, chronic fistulas, and sinus tracts.

The technique of treatment is to clean the surface of the lesion with three percent hydrogen peroxide, and then with 70 percent alcohol providing this can be tolerated (otherwise, aqueous zephiran may be used). Débridement (removal of nonviable tissue) is then done to create a surface which bleeds minimally. This ensures that the Catrix applied will be in contact with capillaries, since this is a necessary condition for inception of its wound healing acceleratory action. The lesion is then patted dry and Catrix powder is applied topically as a moderate "frosting."

The dressing usually consists of a xeroform sheet under fluffed gauze. In highly infected lesions, the dressing is changed three times a week (dressing frequencies decrease as clean granulations and epithelization proceed). The extraordinary efficacy of Catrix in all manner of nonhealing wounds (see Table I) includes many lesions which had been unhealed under standard treatment for years.

Table I

Topical Therapy of Nonhealing Wounds with Catrix Powder

Type of Lesion	No. of Cases	Percent Successful Closure	Percent Relapse
Varicose Ulcers	64	100%	0%+
Post-Phlebetic Ulcers	20	100%	0%++
Perineal Defects following Surgery for Ulcerative Colitis	15	100%*	0%
Chronically Unhealed Pyoderma Gangrenosum	16	100%	20%
Rheumatoid Ulcers	12	100%	0%
Lupus Erythematosus	1	100%	0%
Sinuses and Fistulas	10	65%**	0%

* Although all such lesions healed at what appeared to be a markedly accelerated rate, some still took many months. This problem is the result of, and is characteristic of, the basic immunological pathology in ulcerative colitis.

** The success rate in fistulas is dependent somewhat upon the anatomic situation in that some fistulas are "obligatory," there being no other tract for the exit of the contents. Nevertheless, those which healed had shown no evidence of doing so for protracted periods.

\+ This 0% recurrence rate does presume proper surgical care of the venous insufficiency, as was carried out in each of these cases.

++ This also presumes proper care of the venous insufficiency.

2. Dry Sockets (Alveolitis)

This condition is a complication of tooth extraction which has an incidence of approximately seven to eighteen percent. Incidence is dependent upon such variables as the site of the extraction, oral hygeine, general nutrition, and dental skill. The lower jaw is the most common site of incidence. Basically, dry socket is a highly localized, self-limited, but extremely painful, inflammation of the jawbone. In its early stages, it is characterized by a lack of blood clot in the socket. The cause of this absence is unknown, but its effect is to delay gum closure, resulting in severe discomfort for up to fourteen days.

The technique of Catrix application is to produce a paste of appropriate consistency on the dental tray by mixing Catrix powder with isotonic saline, and then very gently packing the paste in the involved socket without any other manipulation (none could be tolerated). Relief occurs in approximately thirty minutes without recurrence, unless the paste is washed out by saliva. This seldom occurs. If it does, pain may return to an extent, but is completely relieved by an identical procedure.

Table II

The Treatment of Dry Socket with Catrix Paste

No. of Cases	Percent Immediate Relief*	Percent Relapse	Percent Successful Treatment of Relapse
55	100%	4%	100%

* Within thirty minutes

3. Pruritus Ani

This chronic condition is characterized by a macerated, red and intensely painful and pruritic area immediately surrounding the anus. It usually, but not invariably, occurs in individuals who have large buttocks, and therefore a deep intergluteal fold. This anatomic circumstance predisposes to the proliferation of a rich growth of organisms which thrive in moist, warm, relatively unaerated locales. The fact that other variables may be at play is exemplified by the occasional appearance of the malady in a small, flat-buttocked woman.

The technique of therapy is to bathe the affected area, pat it dry, and then apply the Catrix cream by massaging it into the affected skin. The etiology of the condition, however, has no influence on the uniform success of Catrix cream therapy.

Table III
Treatment of Pruritus Ani with Catrix Cream

No. of Cases	Initial Success Rate	Mean Time to Remission	Length of Therapy	Mean Time to Relapse	Successful Treatment of Relapse
51	100%	3 days	3 weeks	3 months	100%

4. Chemical and Plant Allergies

Here the Catrix dosage form chosen by the physician will depend upon the location and character of the allergic reaction. In general, dry lesions require an ointment base, while exudative (weeping) lesions are best treated with a cream.

Despite the difference in choice of dosage form dictated by the nature of the allergy (e.g., cream for poison ivy and poison oak, ointment for detergent rash, insecticide reactions, etc.), the technique of therapy is the same: the lesion is cleansed to the extent possible, patted dry, and the Catrix topical massaged in firmly to achieve penetration.

The total number of patients treated for chemical and plant allergies was less than our usual criterion (50) for decision as to efficacy. Qualitatively, however, the treatment was uniformly successful. Two rather dramatic, historically controlled cases are discussed in Part I.

5. Hemorrhoids and Fissures-in-Ano

This combination is one of the most frequent and familiar of human miseries, for which a large number of relatively ineffectual but heavily advertised preparations are urged upon the sufferers. "Cross-over" studies, in which patients were started on Catrix suppositories and then shifted to the most common extant formulations, demonstrate that Catrix suppositories are markedly superior. In all of the twenty "crossed-cases," except one, the subjects requested a return to the original Catrix suppositories.

We have done two double-blind studies on the efficacy of Catrix suppositories. One was a two-variable and the other a four-variable study. For the sake of simplicity, the results of the two-variable study are given in Table IV below.

The recommended therapy is to rub the external anal skin briefly with the suppository, and then insert the suppository into the rectum. This is invariably done after each bowel movement, and whenever the condition produces discomfort. In general, a suppository is inserted at least twice per day.

It should be noted that our studies have demonstrated no difference between the efficacies of the two percent and the five percent suppositories. The ten percent suppositories, on the other hand, have been shown to be markedly more effective in the more serious ano-rectal problems such as proctitis and painful postoperative states.

Table IV

The Treatment of Hemorrhoids and Fissures-in-Ano with Catrix Suppositories

A. Pilot Studies

No. of Cases	Percent with Symptomatic Relief	Percent with Relapse Within Three Weeks*	Percent with Successful Treatment of Relapse
115	91%	8%	100%

* This figure presumes proper general measures to prevent constipation, and pointless "straining at the stool."

B. Double-Blind Study

	No. of Cases	Good or Excellent Results	Fair Results	Poor or Ineffective Results
Controls - Vegetable Oil Suppository with no Catrix	18	0%	5%	95%
Test - Vegetable Oil Suppository with 2% Catrix	40	75%	12%	13%

6. Herpes Simplex and Zoster

In the case of Herpes simplex, Type I (cold sores), a chap stick-like preparation was utilized on the original presumption that it would be anti-inflammatory, and therefore palliative. The great rapidity with which these lesions respond to the regular (at least four times per day) application of this two percent Catrix dosage indicated a specific virucidal activity. This was later confirmed by *in vitro* work. When the preparation is applied with the frequency noted above, the cold sore becomes dry and inactive promptly, and is usually gone in four days. Individuals prone to cold sores can completely prevent an incipient lesion (which they almost invariably can recognize prior to its appearance) by the same frequency of treatment in the area of the developing lesion.

The results of our pilot studies are in Table V.

We do not have a sufficient number of cases of Herpes zoster (shingles) to quantify our results statistically; but the experience has been so remarkably successful in the small number of cases treated that a comment is in order. For example, we have had two instances of shingles involving the ophthalmic division of the trigeminal nerve with a severe threat to the eye. In both instances, the herpetic lesions of the head and the eye became markedly better in twenty-four hours, and were essentially gone (except for residual crusting) in four days. In such widespread and threatening cases of shingles, we have employed both systemic (oral or injectable) and topical therapy. In those cases with ophthalmic involvement, the eye has been treated with two drops of Catrix-S liquid directly into the conjunctival sac every four hours. These

results in sixteen cases are so impressive that much further study is warranted and indicated.

We are currently investigating the efficacy of systemic Catrix therapy in venereal Herpes.

Table V

The Treatment of Herpes Simplex (Type I)
by 2% Chap Stick-Like Preparation

No. of Cases	Percent Successful Result	Percent Relapse Within One Week	Percent Relapse Within Three Months
62	100%	0%	*

* We are not yet in possession of sufficient data to make a statement regarding the effect of repeated topical treatment on recurrence rate.

7. Psoriasis

This disease was one of the first to be subjected to systemic therapy with Catrix. The initial mode of treatment was by injection with Catrix-S. The complete details of the technique employed are described in The Biological Activity of Bovine Cartilage Preparations (see page 45).

The results in total body psoriasis can be summarized in tabular form:

Table VI

The Treatment of Total Body Psoriasis with Catrix-S

No. of Cases	Average Duration of Disease	Results of Previous Treatment	Dosage and Total Average Dosage	Excellent Results	Good Results	Poor Results
38	17 years	Uniformly poor with corticosteroids, tar, and occasional ultraviolet light, methotrexate, and X-ray.	50cc Catrix-S in two subcutaneous depots twice a week 543 cc	58%*	40%**	2%***

* Excellent results were those in which total clearing of the skin occurred for periods of at least six weeks and up to one year.

** Good results were those in which only a few minor lesions remained which were easily controlled with standard topical corticosteroids when these same agents had previously been totally ineffective.

*** Poor results were those in which there was no discernible effect.

We next investigated the efficacy of the oral route, utilizing 375 mg Catrix capsules in a dosage of 9 gm/day. It became apparent that the oral route was not so effective as were injections; and yet it was a much more convenient technique. This led to the preferred use of the oral dosage form.

Fortunately, at this time a singular synergistic response with one of the standard drugs on the market was noted. The marked increase in efficacy of Catrix which it produces is reported below. It is important to state that this material by itself has no effect under the conditions of treatment.

Table VII

The Treatment of Psoriasis with Catrix and with Catrix in Conjunction with a Synergistic Agent

Form of Treatment	No. of Cases	Average Duration of Disease	Excellent Results*	Good Results*	Poor Results*
Oral Catrix (9 gm/day)	16	12 years	31%	31%	38%
Oral Catrix (9 gm/day) plus synergistic material in standard dosage	8	14 years	63%	25%	12%

* These results are defined exactly as in Table VI above.

The concomitant use of the synergistic material is seen to raise the efficacy of the oral route to about the same level as that achieved with Catrix-S. The duration of treatment necessary to achieve this result with both methods was about eight weeks; however, the discomfort of injection is avoided and the necessity of frequent visits to the physician is diminished. We conclude that this is the preferred method, and that it will become more so as fractionation of the active principle(s) permits a progressive diminution in the size of oral dosage.

It should be noted that these results are distinctly superior to all existing therapy, including corticosteroids and PUVA (high-intensity ultraviolet light with psoralens).

8. Osteoarthritis

Although osteoarthritis is characterized by slow progression, it is the cause of great suffering, both because of the profound disability produced by its end stages, and because of the very large numbers of the afflicted. The excellent results of therapy with both Catrix-S and Catrix capsules are presented in Tables VIII and IX.

Table VIII

The Treatment of Osteoarthritis with Catrix-S

No. of Cases	Average Age	Dosage and Total Average Dosage	Excellent Results	Good Results	Fair Results	Poor Results
28	66	50 cc Catrix-S in two subcutaneous depots twice a week 524 cc	68%*	21%**	7%***	4%****

* Excellent results are those in which virtually all pain and disability have disappeared.

** Good results are those in which there is marked decrease in pain and increase in mobility with some residual discomfort and disability.

*** Fair results are those in which there are good to excellent initial results with return of pain and disability after about two months.

**** Poor results are those in which there is no discernible improvement.

As the oral dosage form became available, it was utilized increasingly in osteoarthritis. Large numbers of osteoarthritics have been treated by the oral route, and its effectiveness is indubitable.

In a recent series of observations, the utilization of a standard drug has been found to enhance the efficacy of the Catrix oral dosage form to a level considerably greater than that of the injection route alone, thus making this "synergistic oral route" the therapy of choice (see Table IX).

Table IX

The Treatment of Osteoarthritis by Oral Catrix in a Dosage Form of 9 Grams Per Day Without and With a Synergistic Agent

Therapeutic Regime	Dosage	No. of Cases	Excellent Results*	Good Results*	Fair Results*	Poor Results*
Oral Catrix	9 gm/day	700	59%	26%	8%	7%
Oral Catrix with "Synergizer"	9 gm/day plus one pill per day of "Synergizer"	27	81%	19%	0%	0%

* These categories of results are defined exactly as in Table VIII.

My personal observations in historically-controlled cases previously treated with such standard anti-inflammatory agents as Motrin®, Clinoril®, Naprosyn®, and Indocin®, have shown Catrix therapy to be superior. Furthermore, Catrix treatment is distinguished by a unique lack of side effects, many of which plague the users of these standard agents. It should be noted that the remissions from discomfort achieved with Catrix-S last many months (an average of about seven), while the improvement from the oral dosage lasts

about six to eight weeks. This is a reflection of the large reservoir of active glycopeptides which it is possible to accumulate during a course of Catrix-S injections. However, oral Catrix seems preferable since the use of the "synergizer" with oral Catrix enables the physician to obtain distinctly better results than those achievable with Catrix-S. We have not yet utilized the presumably ideal combination of Catrix-S and "synergizer."

As separation of the active principles contained in Catrix proceeds, we believe that even better results in osteoarthritis will be achieved at markedly lower oral dosage levels.

9. Rheumatoid Arthritis and Other Autoimmune Diseases such as Scleroderma, Dermatomyositis, Ulcerative Colitis, and Regional Enteritis.

The results in the treatment of this group of diseases are very encouraging (see Table X). However, the experience is not so large as in the other categories previously discussed. Nevertheless, the unusual results require further scientific investigation, and warrant formal clinical evaluation.

Rheumatoid arthritis is known to be a more complex disease than osteoarthritis. This is because it has numerous biological feedback mechanisms which may defeat therapy, whereas osteoarthritis doesn't "fight back" in so destructive a way.

Table X

The Treatment of Rheumatoid Arthritis with Catrix-S

No. of Cases	Average Age	Percent Female	Distribution of Disease	Severity	Excellent Results*	Good Results*	Poor Results*
12	53	67%	Classical	Marked	25%	50%	25%

* For definition of efficacy, see Osteoarthritis (Section 8) above.

As was the case with osteoarthritis, the treatment of rheumatoid arthritis with Catrix capsules was evaluated with and without the addition of the drug which has been discovered to act synergistically with Catrix. The results follow:

Table XI

The Treatment of Rheumatoid Arthritis with Catrix Capsules by Mouth

No. of Cases	Average Age	Percent Female	Distribution of Lesions	Severity	Excellent Results*	Good Results*	Poor Results*
18	58	56%	Classical	Marked	22%	44%	34%

* For definition of efficacy, see Osteoarthritis (Section 8) above.

Table XII

The Treatment of Rheumatoid Arthritis with Catrix Capsules Plus One Tablet of "Synergizer"

No. of Cases	Average Age	Percent Female	Distribution of Lesions	Severity	Excellent Results*	Good Results*	Poor Results*
9	55	78%	Classical	Marked	67%	22%	11%

* For definition of efficacy, see Osteoarthritis (Section 8) above.

Although we need more pilot cases, the usefulness of Catrix per se and the enhanced efficacy resulting from concomitant use of the "synergizer" with Catrix is evident. This disease category also is now suitable for formal clinical evaluation.

Insufficient data have been accumulated in ulcerative colitis and regional enteritis to enable us to tabulate the results. Nevertheless, it is interesting that virtually all cases of ulcerative colitis referred to the author had to undergo total colectomy prior to the use of Catrix, while only two such cases required operation in the seven-year interval since Catrix treatment was begun. Twelve such cases have been treated; six by Catrix-S and six by Catrix capsules. (One colectomy was necessary in each group.)

While no case has become totally asymptomatic, only two have required surgery and the remainder are doing fairly well with marked diminution of bowel movements and cramping. Clearly this is good; but whether it is excellent is not something that can be decided without the recounting of much more detail than a summary permits. There has been no attempt to assess the use of the "synergistic" drug with Catrix in ulcerative colitis. This is planned for the near future.

A total of four cases of regional enteritis were treated with Catrix-S with excellent responses in three and a good response in one. All of these had had the disease for many years (average 16) and were therefore advanced. Each had had a previous ileocolectomy and extensive steroid therapy. All have gained weight and strength, have less cramps, and have had their steroid intake reduced or eliminated.

All three cases given Catrix capsules have done well, and one has gone from widespread fistulization (into the vagina, abdominal wall, and between loops of bowel) to absence of radiographic and histologic evidence of disease (the latter was obtained incidentally at operation for a different reason).

Scleroderma and other rare autoimmune diseases - A total of three cases have been treated, and the unusual results warrant comment. When Catrix-S is injected into an area of scleroderma, there is a very prompt softening of the leathery skin to a texture closely resembling normalcy. The rapidity of this change is truly startling. Since there is no present effective therapy, scleroderma seems ideally suited for a formal study by a university group interested in the entity. A case history is presented in The Biological Activity of Bovine Cartilage Preparations (see page 45).

At present, there is insufficient documentation of efficacy in dermatomyositis or lupus erythematosus to categorize the results. We have, however, healed a total of four of the typical skin ulcers which characterize both diseases, and one case of discoid lupus vanished promptly following brief treatment with topical 5% Catrix cream. While discoid lupus is not the same as the disseminated variety, the promptness of the change nevertheless suggests a wider efficacy, which warrants further investigation.

10. Cancer

We recognize that it is superficially paradoxical for the same preparation to be effective against inflammatory diseases and neoplasia. However, there is now evidence that Catrix harbors two components, one of which is stimulatory to a variety of cell clones, and one of which is inhibitory. Our fractionation effort has identified them and their approximate molecular weights. The components are being separated progressively, and produced in laboratory quantities.

We have also documented the fact that Catrix produces a large (averaging 700%) increase in Cyclic Adenosine Monophosphate (Cyclic AMP), the substance which has been demonstrated to produce a sensitization of the cells to their hormonal "messages." Moreover, under Catrix therapy, the lymphocytes are converted into lymphoblasts (as measured by the uptake of labeled thymidine in cell culture), both with or without the presence of mitogens such as Conconavalin A (Con A), Phytohemagglutinin (PHA), or Pokeweed Mitogen (PWM). In addition, a remarkable initial rise in a widely used cancer marker (CEA, or carcino-embryonic antigen) occurs as Catrix treatment proceeds. This bespeaks, not an increased cancer volume, but a change back toward normal cell differentiation for the malignant cells. After peaking, these values can be utilized as a clear index of remaining cancer mass. Finally, Catrix induces an initial rise in total complement, C-3, and IG-A. Once these begin to fall, IG-M rises progressively until the patient's cancer diminishes, or death ensues.

One particularly striking evidence of our success in the treatment of clinical cancer is the demonstration that the average size of the cell and

nucleus decreases markedly under Catrix treatment when sequential biopsies are analyzed with a computerized area-scanner (the "Quantiment") programmed to measure these features. Not only do these cellular characteristics decrease, but the distribution curve becomes essentially "normalized." Examples of this remarkable effect are evident in Figures 1 and 2.

Our results in fifty-one cancer cases in which standard treatment modalities (surgery, radiation and chemotherapy) have failed have been compiled into a three-volume report which has been filed with the National Cancer Institute and the FDA as part of an IND application. These volumes detail every event in the medical care these individuals received. The results of the treatment of cancer with Catrix in these cases are summarized in Table XIII.

Approximately forty more cases have been treated subsequent to this compilation. All treated cases will be reported in a paper to be published.

The dosage of Catrix capsules is 9 gm/day. This is kept up for at least a year and a half after all evidence of cancer is gone, and then slowly decreased to zero over an additional three-year period. All patients are followed closely, since we have noted two examples of cancer recurrence when the dosage was decreased too rapidly. These recurrences were controlled when full dosage was reinstituted. These cases illustrate the delicacy of the immunological balance which is established.

Our presumption is that the use of Catrix will rise progressively as its efficacy becomes increasingly apparent. It is more effective than chemotherapy in the great solid tumor cancers such as breast, colon, prostate, stomach, ovary, cervix, pancreas, lung, etc. As yet, we can make no statement on the efficacy of Catrix in the lymphomas or leukemias, since

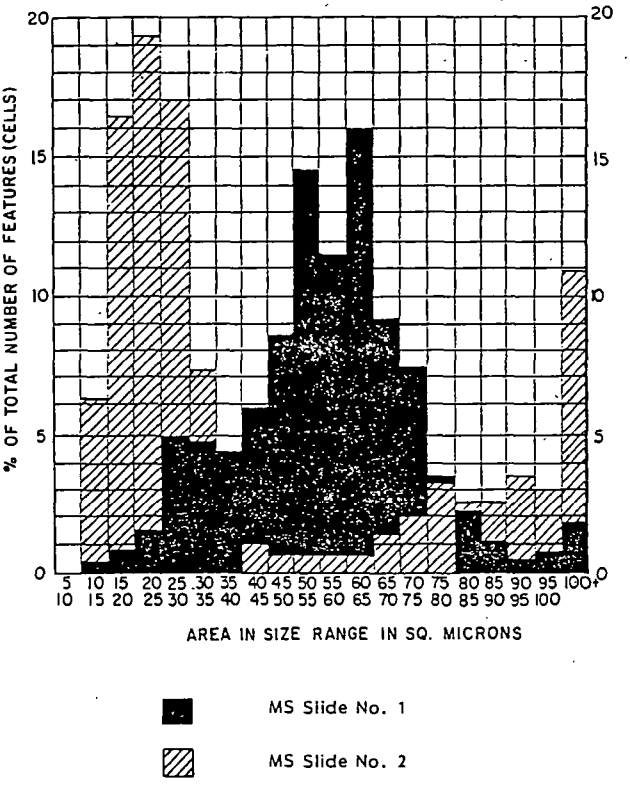

Figure 1

The Change in Cell Size Induced by Catrix Therapy in Patient MS.

Note - The time interval between biopsies was 8 weeks.

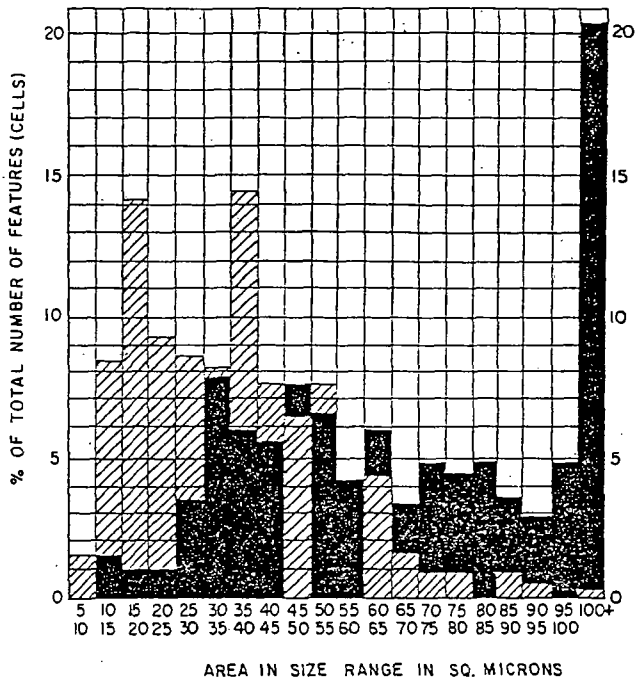

Figure 2
The Change in Cell Size Induced by Catrix Therapy in Patient MB.

Note - The time interval between biopsies was 6 weeks.

Table XIII

Treatment of Fifty-One Cancer Cases with Catrix

Origin of Malignancy	No. of Cases	Not[1] Effective	Partially[2] Effective	Probably[3] Effective	Effective[4]
Breast	9	2	1	1	5
Colon	9	4	1	2	2
Prostate	7	-	-	1	6
Lung	5	-	-	3	2
Ovary	3	1	-	-	2
Pancreas	3	-	-	1	2
Stomach	3	-	-	2	1
Melanoma	3	1	2	-	-
Basal Cell Carcinoma	2	-	-	1	1
Glioblastoma Multiforme	1	-	-	-	1
Embryonal Cell Carcinoma of the Testicle	1	-	-	-	1
Osteogenic Sarcoma	1	-	1	-	-
Embryonic Cell Carcinoma of the Kidney	1	-	-	-	1
Hodgkin's Disease	1	-	-	1	-
Lymphosarcoma	1	-	1	-	-
Cervix	1	-	-	-	1
Total Cases	51	8	6	12	25
Categories of Effectiveness In Percent		15.7	11.8	23.5	49.0

1. Not Effective - Slight or no evidence of decrease in tumor mass.

2. Partially Effective - Definite temporary shrinkage in tumor mass accompanied by a period without evidence of metastatic growth, but followed by resumption of growth and metastasis leading to death.

3. Probably Effective - Definite and continuing shrinkage in tumor mass with the ultimate outcome still considered uncertain because of a treatment period of less than a year; or the maintenance of well-being for a prolonged period (greater than a year) with the cancer remaining approximately the same size by the applicable measurements.

4. Effective - Definite and continuing decrease in tumor mass over so long a period (greater than a year) that its total obliteration seems virtually certain; or already documented complete disappearance of the malignancy; or virtual absence of the cancer at autopsy after death presumably produced by too rapid a necrosis of a large tumor load.

standard chemotherapy is much more successful there than in epithelial tumors. This fact has quite properly inhibited our investigation of these diseases; however, we have had two successful examples of Catrix therapy in chronic lymphatic leukemia.

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5. Prudden, J.F. and Balassa, L.L.: THE BIOLOGICAL ACTIVITY OF BOVINE CARTILAGE PREPARATIONS, Seminars in Arthritis and Rheumatism, 1974, 3:287.

6. Prudden, J.F.: THE TREATMENT OF CARCINOMA WITH ORAL AND INJECTED PROCESSED CARTILAGE PREPARATIONS ("CATRIX"), to be published.

The published papers are available on request.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

August 24, 1981

35-NF-245

Ms. Marge Portoro
Airco, Incorporated
85 Chestnut Ridge Road
Montvale, New Jersey 07645

Dear Ms. Portoro:

This replies to your July 29, 1981 letter asking (a) how many drugs were approved in the years 1962 through 1980, (b) the length of time for approvals, and (c) the number of new chemical entities verses other drugs approved.

Graph II-2 answers parts (a) and (c) of your request. Graphs III-1 thru III-7 related to part (b) of your request for the years 1974 thru 1980.

Additional information concerning the New Drug Evaluation Project is available from:

National Technical Information Service
Department of Commerce
5285 Port Royal Road
Springfield, Virginia 22151

When ordering specify -
New Drug Evaluation Briefing Book
Order Number - PB81-181000

Cost is $11.00.

I trust this is helpful.

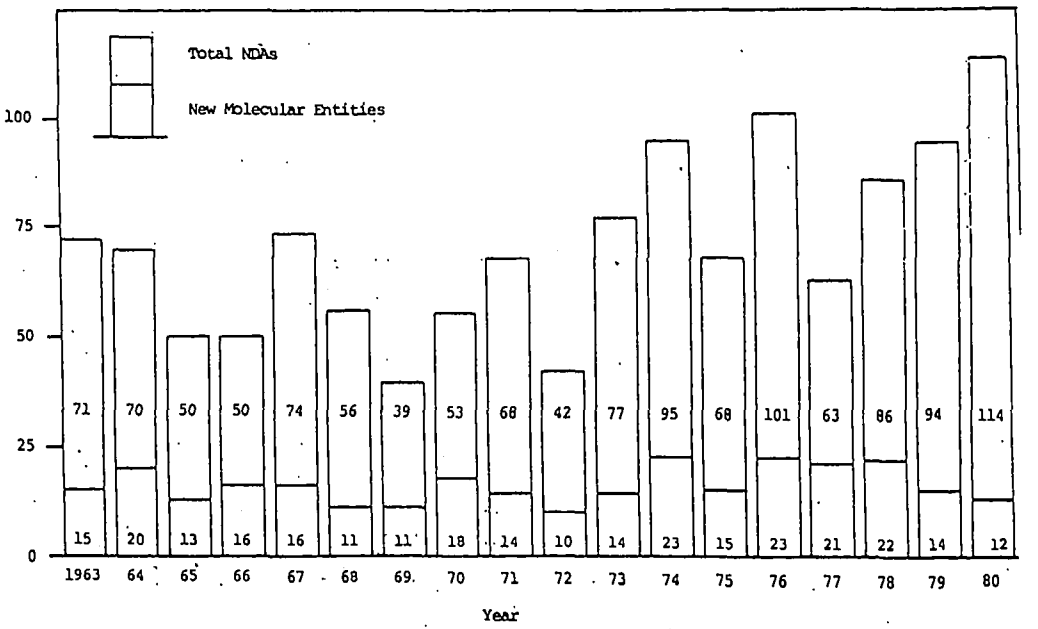
Sincerely yours,

Stanley A. Stringer
Chief, Product Coordination Staff
New Drug Evaluation
Bureau of Drugs

Enclosures

GRAPH II - 2

Graph showing the Number
of NDAs and New Molecular Entities
Approved by Year



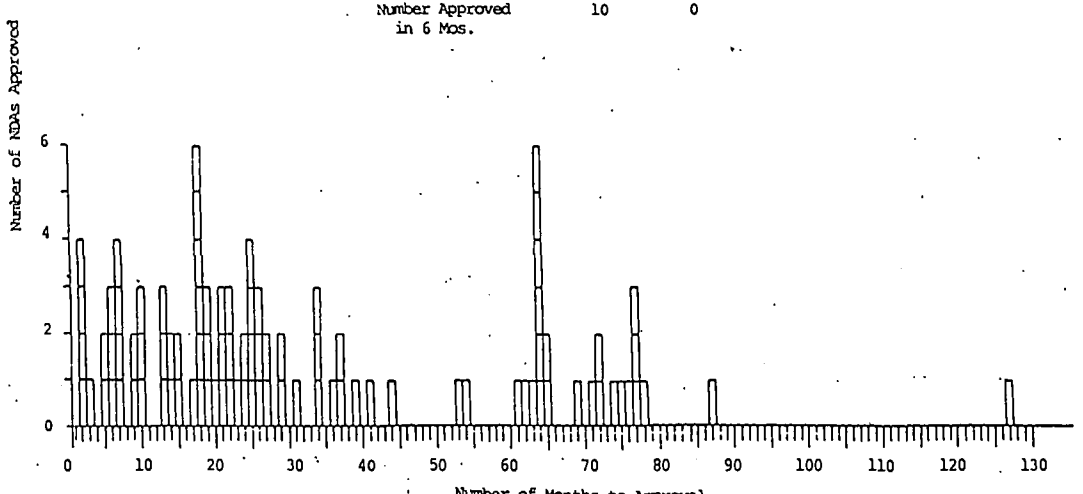
GRAPH III - 7

Data from Calendar 1980 Approvals
All NDAs
NMEs
Sample Size 114 12
Maximum 85.1 85.1
Minimum 2.4 11.8
Range 82.7 73.3
Mean 21.3 34.5
Variance 290.4 407.3
Standard Deviation 17.0 20.2
Median 16.1 32.5
Mode 9 None
Number Approved in 6 Mos. 15 0
Number of NDAs Approved
0
2
4
6
8
10
0
10
20
30
40
50
60
70
Number of Months to Approval

G R A P H III - 6

Data from Calendar 1979 Approvals

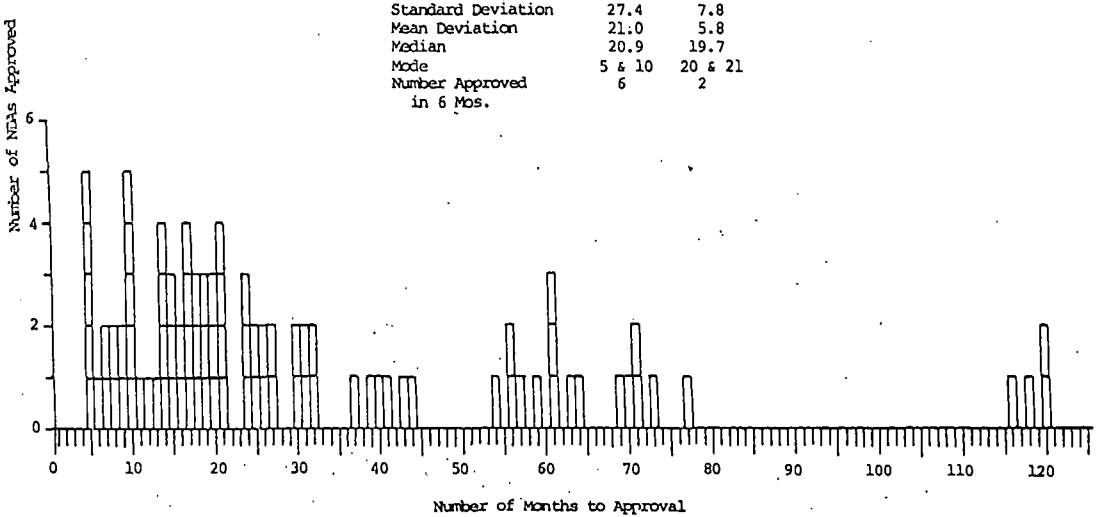
	All NDAs	NMEs
Sample Size	94	14
Maximum	131.8	131.8
Minimum	2.3	7.4
Range	129.5	124.4
Mean	33.6	37.5
Standard Deviation	26.1	32.3
Median	25.0	25.8
Mode	18 & 64	65
Number Approved in 6 Mos.	10	0



GRAPH III - 5

Data from Calendar 1978 Approvals

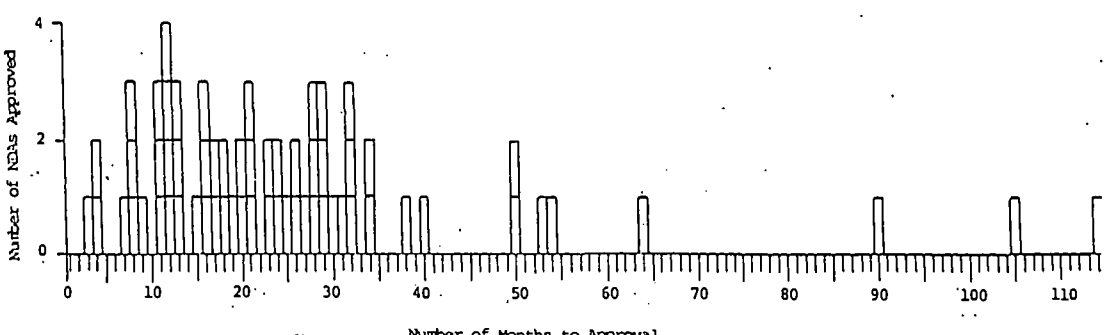
	All NDAs	NMEs
Sample Size	86	22
Maximum	119.8	37.0
Minimum	4.6	5.2
Range	115.2	31.8
Mean	32.2	20.3
Variance	753.5	60.8
Standard Deviation	27.4	7.8
Mean Deviation	21.0	5.8
Median	20.9	19.7
Mode	5 & 10	20 & 21
Number Approved in 6 Mos.	6	2



G R A P H III - 4

Data from Calendar 1977 Approvals

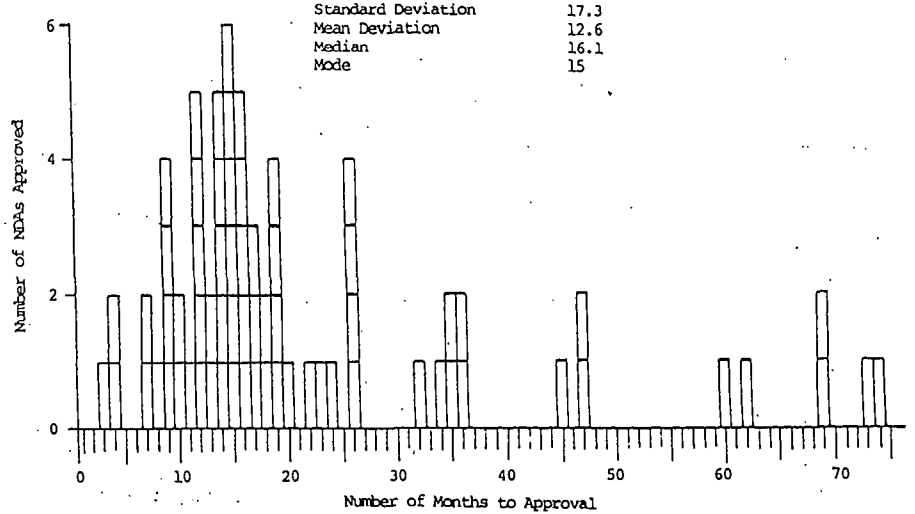
Sample Size	63
Maximum	113.9
Minimum	3.3
Range	110.6
Mean	26.6
Variance	470.3
Standard Deviation	21.7
Mean Deviation	14.1
Median	21.1
Mode	12



G R A P H III - 2

Data from Calendar 1975 Approvals

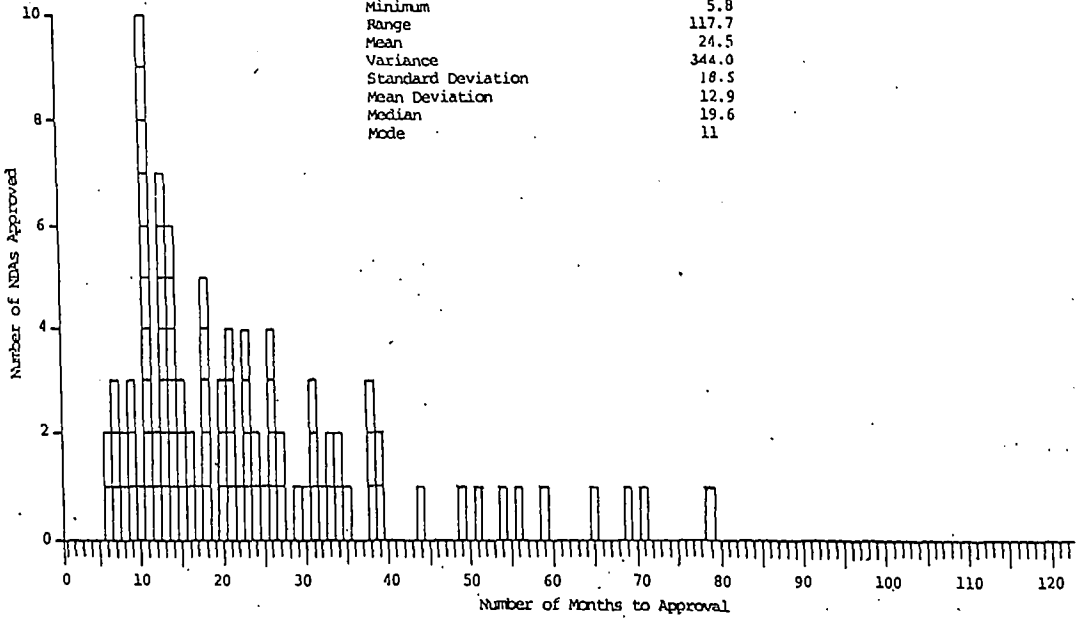
Sample Size	68
Maximum	74.1
Minimum	3.4
Range	70.7
Mean	22.5
Variance	298.1
Standard Deviation	17.3
Mean Deviation	12.6
Median	16.1
Mode	15



G R A P H III - 1

Data from Calendar 1974 Approvals

Sample Size	95
Maximum	123.5
Minimum	5.8
Range	117.7
Mean	24.5
Variance	344.0
Standard Deviation	18.5
Mean Deviation	12.9
Median	19.6
Mode	11



GRAPH III - 3

Data from Calendar 1976 Approvals