STATEMENT OF DR. RONALD E. CAPE
CHAIRMAN AND CHIEF EXECUTIVE OFFICER
CETUS CORPORATION
BEFORE THE
SUBCOMMITTEE ON COURTS, CIVIL LIBERTIES AND THE
ADMINISTRATION OF JUSTICE
OF THE
COMMITTEE ON THE JUDICIARY
U.S. HOUSE OF REPRESENTATIVES
HEARINGS ON H.R. 3605
JUNE 27, 1984

Mr. Chairman and Members of the Subcommittee:

My name is Ronald E. Cape. I am the Chairman and Chief Executive Officer of Cetus Corporation. Accompanying me is Harold C. Wegner of Wegner & Bretschneider, an attorney for Cetus and an adjunct Professor of Law at Georgetown University.

Since 1971, Cetus has pioneered the commercial application of biotechnology in the development of new or improved products and processes for human and animal healthcare and for the production of food, energy and chemicals. Cetus-modified microorganisms are currently used in the commercial production of antibiotics, vitamin B_{12}, and an animal vaccine containing components developed by Cetus through recombinant DNA technology.

Cetus has produced two potential therapeutic products through recombinant DNA that are now in human clinical trials. Preclinical data has indicated that these two products, beta-interferon and interleukin-2, may have significant value in the treatment of certain cancers and infectious diseases, including AIDS.

At Cetus Corporation we are proud that our pioneering efforts over the past decade have contributed to the development of the

biotechnology industry. We are now in a position to demonstrate the promise of this industry by making new therapeutics and diagnostics available to the American consumer. However, continued success in meeting this goal depends upon whether our substantial investment of time and resources can be protected on an exclusive basis for a reasonable period.

Stimulation of biotechnology is important and not at all inconsistent with the objectives of H.R. 3605. We are in complete agreement with the goals of H.R. 3605 to foster availability of drugs through the generic drug industry and to foster a return on the investment made to develop new pioneer drugs. Our concern is that the present form of the bill, as it relates to biotechnology companies, requires revision before those goals can be reached in a fair and reasonable manner.

Cetus has not been included in the discussions of the past months between the generic and research-based pharmaceutical companies, which have resulted in this Bill. We were not invited to these lengthy negotiations, nor did there appear to be any reason to become involved in a process that would reach the laudable goal of providing inexpensive, off-patent drugs to the public. After all, our potentially most significant products, such as the potential cancer therapeutics, are still in clinical trials or in our research laboratories. The patents covering these products will not expire until the turn of the century.

We understand the desire to "balance" the benefits gained by the established pharmaceutical companies through extension of the patents on their marketed drugs with the ANDA process of Title I of the bill. We make no comment on whether this is the appropriate balance in the context of the varying interests of the established pharmaceutical companies and the generic drug industry. However, this compromise does have an inadvertent but

substantial negative impact on companies such as ours. Title I will severely hamper our efforts to bring new products to the market, and yet no immediate counterbalancing benefit will be provided to us under Title II.

Congress, more than any other institution in America, recognizes the importance of incentives to domestic industry, including biotechnology. Congress also fully recognizes the important role that biotechnology is playing in the development of new drugs, including the search for products to detect and treat cancer. We read H.R. 3605 to possibly provide a disincentive to this vital research, albeit unintentional.

An amendment is needed to avoid the new biotechnology research disincentives for development of our vitally important industry, without therewith removing a single pharmaceutical product now in the marketplace from eligibility for an Abbreviated New Drug Application (ANDA).

Biotechnology, including its most modern tools of recombinant DNA and monoclonal antibody research, holds the promise of unlocking the secrets of the diseases that the established pharmaceutical industry has failed to unlock through usual chemical means. Thus, we are close to the early detection and treatment of cancer and highly infectious diseases such as AIDS.

We fully agree with the general principle that after the expiration of a patent, generic competition should be permitted, and indeed encouraged. Unfortunately, the present bill achieves this objective in a manner which creates several disincentives to future biotechnology research and could result in the delay of important new biotechnology products and reduce the number of drugs that will become available to the generic industry.

We support the concept that inexpensive drugs should be available after the pioneer has had a reasonable period for an exclusive position. Legislation meeting that objective could be passed, without affecting the biotechnology industry in an inequitable fashion.

I. CANCER DETECTION AND TREATMENT, THE PROMISE OF BIOTECHNOLOGY

We take particular pride in what the American biotechnology community has accomplished in just a few years, and, more importantly, in what can be done in the next decade in the important areas of cancer detection and treatment. There will not be a single "cure" for cancer. But many specific types of cancer will be "fingerprinted" for early detection. Above all, ongoing research efforts hold the promise of actual cures for specific cancers.

II. THE RIGHT CLIMATE FOR BIOTECHNOLOGY RESEARCH - THE BIG RISKS

Millions of dollars are required for research and regulatory approval of the breakthrough drugs being pioneered by the emerging biotechnology companies. Such an investment is undertaken in the hope that a particular recombinant DNA or monoclonal antibody invention can be developed in a safe and effective drug. In cancer treatment, a particular success may help only a small fraction of the population that has or will get cancer; with each success further research is needed for the next type of cancer.

Biotechnology companies in the United States can survive, and even flourish, in the expensive and risky world of cancer research with the current protections of the FDA and the patent system:

- Under FDA regulations, third parties are restricted from copying the exact approved formulation (but are totally free to either reduplicate the regulatory work or to make a different, competitive product).

- The patent rights in biotechnology under the present scheme are quiet rights, by and large free from short range litigation.

III. WHILE JAPAN PROVIDES GOVERNMENTAL STIMULATION TO BIOTECHNOLOGY RESEARCH, CONGRESS SHOULD NOT PROVIDE A DISINCENTIVE TO DOMESTIC-BASED BIOTECHNOLOGY RESEARCH

The limited period of exclusivity that is today fairly certain provides the necessary incentive for future and continued cancer research. Both the United States and Japan presently provide this climate.

Just in the past ten years, Japan has made many statutory and regulatory changes to benefit pharmaceutical and biotechnological research. The patent law was greatly strengthened for pharmaceutical product protection; pricing policies for pharmaceuticals have put a premium on pioneer research; high technology drugs are given a period of up to six years exclusivity for marketing independent of the patent right.

Congress is keenly aware of the threat of international competition in biotechnology. Just this year the Office of Technology Assessment (OTA) has published a report manifesting the urgent need for progressive legislation. Commercial Biotechnology: An International Analysis (Washington, D.C.: U.S. Congress, Office of Technology Assessment, OTA-BA-281, January 1984) ("OTA Report"). The report summarizes that:

> Although the United States is currently the world leader in both basic science and commercial development of new biotechnology, continuation of the initial preeminence of American companies in the commercialization of new biotechnology is not assured. Japan and other countries have identified new biotechnology as a promising areas for economic growth and have therefore invested quite heavily in R&D in this field.
> [OTA Report, page 3.]

IV. AMERICAN-BASED BIOTECHNOLOGY RESEARCH

With the present wording of H.R. 3605, the biotechnology industry is trapped in ways obviously unintended and undoubtedly unforeseen which hit directly at the heart of the two present regulatory safeguards, freedom from ANDA competition and quiet patent title.

A. ANDA Freedom for a Reasonable Period

Exclusivity for a reasonable period of time is now a guarantee under the present law, as there is no ANDA possibility. Biotechnology needs a certain period of exclusivity free from ANDA competition for future drugs, as patent litigation would seriously dilute our clinical and research efforts. A number of finally litigated patent infringement test cases in modern biotechnology are necessary before conservative reliance can be placed exclusively on the patent system. In the modern biotechnology areas of both recombinant DNA and hybridomas, the total number of such finally litigated test cases is zero. Particularly throughout this decade when biotechnology patent case law has not been crystallized, we need freedom from ANDA's. Otherwise, it becomes virtually impossible to justify the investment in the sophisticated level of research necessary to enter the biotechnology marketplace.

To optimize present investment in biotechnology research, there simply must be a promise independent of the patent system that,

after spending the tens of millions of dollars for research and regulatory review, a marketing position can be secured against "me too" competitors unwilling to incur these substantial costs and risks. Provision for an Abbreviated New Drug Application (ANDA) immediately is unthinkable. Such competitors will discourage companies such as ours from making these investments.

Japan and the major European countries all give the pioneer a reasonable period of exclusivity for pharmaceuticals independent of the patent right.

It would be ironic when Japan provides an exclusive period for marketing of up to six years for new drugs under its Health Ministry regulations, for America to turn the opposite way and eliminate ANDA freedom altogether, except for the limited circumstances of the bill.

B. The Litigation Incentives

The two titles of the bill taken together provide a strong incentive to litigate patents at the earliest stage. Whatever merit this may or may not have for more traditional areas of "big drug" research, this is the last thing needed for the relatively small and young biotechnology drug companies. At present, there is zero precedential law directly on point for biotechnology patent infringement in recombinant DNA and monoclonal technologies. A carte blanche to foster early litigation will force the new American biotechnology industry to allocate a larger share of its resources for litigation of its patents, as opposed to investments in cancer research itself.

Cetus has had substantial funding and has a first class patent department. We expect the company to do quite well. Others may not be so fortunate.

C. The Cash Flow of Biotechnology is Unique

Biotechnology companies are unique in the pharmaceutical field not only in terms of the patent situation, but more importantly from the viewpoint of their infant position in a major industry. Development of these products requires large investment of risk capital over a long period of time before substantial return can be realized.

Unlike the rich and established pharmaceutical companies, the vitality of the biotechnology industry is dependent upon careful conservation of cash. The major drug companies may invest money in patent litigation or the uncertainties of exclusivity. We do not believe this is an appropriate basis for the independent biotechnology companies. Yet, the promise of cancer detection and therapy is being met by the smaller, independent biotechnology companies that have shown the initiatives of the past few short years.

V. PATENT TERM RESTORATION

A. Cetus Supports (but Can Live Without) Patent Extension

Cetus supports patent term "extension" or "restoration", and perhaps that is a necessary goal for the traditional established drug companies. But, in the context of the 1980's, with Cetus' patent position on any new drugs expected to run to the year 2000, whether the patent expires in the year 2006 instead of the year 2001 is hardly a major factor in today's biotechnology investment decisions.

B. Section 202 and Pre-Expiration Testing

Recombinant DNA technology will not go off patent on any major scale until after the year 2000. Whether a third party starts his clinical trials after a patent expires in 2001 or gets an early jump in the year 1999, is not just vitally important to our industry at this time. What is critical is that we provide Americans with new biotechnology drugs and methods of disease detection during the next ten years to create a new industry for future generations.

VI. AMENDMENTS TO TITLE I TO KEEP FUTURE BIOTECHNOLOGY RESEARCH OPEN

Cetus and the other biotechnology independents must be given relief from the inequitable and unintended effects of Title I. Whatever happens in Title II may have long range importance, but is clearly not of immediate benefit to such independents.

Cetus is sympathetic to the goal of post-patent expiration drug competition. We wish to cooperate with Congress in achieving the goal of price competition, while providing a safe harbor for biotechnology research to continue and grow in California and elsewhere in the United States. We believe that this goal most sensibly would be achieved by providing a prospective exemption to new drugs from biotechnology research (recombinant DNA and hybridomas). Let the generic industry have all existing drugs now on the market, if that is the will of the traditional drug industry and the generics.

A. Cancer Research, Not Painkillers and Antidepressants

A biotechnology company is not fungible with any of the old line pharmaceutical companies. What is good for the majors is not necessarily good for our developing industry. Cetus speaks for its own very real concern that its research in high technology areas such as cancer will suffer in the absence of special Congressional recognition of the unique problems caused by ANDA competition for biotechnology products.

Biotechnology research should be left out of the bill, or be given a more equitable treatment. Otherwise Cetus and the other biotechnology companies will be unable to address some of the more important life-saving areas such as cancer detection and treatment in their fullest capacities.

The more general non-biotechnology pharmaceutical industry is not the concern of the biotechnology companies. We are not impacted directly by whether the generic industry should or should not use traditional chemical synthetic routes to make a slightly different proprietary product with the same indication as the old product. We are thus not in the business of determining whether there should be a slightly better painkiller, a more precisely acting antidepressant, or a different sleeping pill. These are the primary concerns of the established pharmaceuticals companies.

B. Prospective Relief is All Cetus Asks

Cetus has no interest in taking away any existing drug from the marketplace. We only seek the incentives for future research gained through an exception to H.R. 3605 for biotechnology.

This is far more in the public interest than the present wording of H.R. 3605, which even gives equitable relief in the case of some already approved drugs. Certain drugs already approved (but only since January 1, 1982) would be taken away from the supply of drugs to the generics under proposed 21 USC §505(j)(4)(D)(i). Biotechnology needs at least the same freedom.

VII. SECTION 202 ENCOURAGES LITIGATION

Cetus is deeply troubled by Section 202 and particularly the invitation to litigate that is built into 35 USC §271(e)(2) and §271(e)(4).

If the relief sought in Title I is not forthcoming, biotechnology companies will indeed have to beef up their litigation budget and cut down on their future plans for at least domestic R&D expansion. The fuel of Section 202 added to the fire of a broad Title I is unacceptable.

With an exemption from ANDA's proposed under Title I, then the effects of Section 202 on biotechnology would be greatly reduced.

VIII. EVERYONE BENEFITS FROM STRONG AMERICAN BIOTECHNOLOGY

All benefit from a strong domestic biotechnology industry:

A. The Public...

The majority of cancer victims today die, despite some significant progress in chemotherapy. All suffer a significant impaired quality of life due to the side effects of this chemotherapy. Many physicians resist such treatment until there is no other recourse. Biotechnology products offer not only the promise of improved therapy, but the avoidance of these terrible

effects. These products will be used much earlier in the course of therapy with much better results. The keys to a virtual revolution in chemotherapy are available from modern biotechnology of the 1980's. If biotechnology is given the climate to grow, some cancers are sure to be successfully detected and attacked in the 1980's, more in the 1990's, and then at some point in the next century cancer may become a disease of the past.

Whether we reach the promise of the 1990's already in this decade or perhaps only in the next century will be governed largely by the regulatory climate: Will money be put into cancer research or will better aspirin substitutes, Valium's and the like be where America puts its money?

B. American Industry ...

The United States and Japan are struggling for preeminence in biotechnology. We welcome this open competition, and everyone in both countries and indeed the world will benefit. But as Japan improves its regulatory climate and incentives for biotechnology, America should not move backward to cripple our competitive efforts.

C. The Generic Industry ...

The generic industry has shown no interest in moving into complex biotechnology. Virtually no products are available for an ANDA even without any restrictions, and the technology is far different and more sophisticated than conventional pharmaceuticals.

For the future, if the generic industry of the 1990's wants to move into biotechnology, a strong patent and regulatory climate now will lead to a large number of products which then may be

available for such expansion. Without a strong system now, there may be no market to enter.

We hope that we may have the opportunity to aid the committee in recognizing the effect of this bill on our industry, and the need for careful consideration of the issues raised today. We hope to achieve an early resolution of these matters so that the objectives of the bill can be met in the fairest and most reasonable way.

Thank you, Mr. Chairman.

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