ASSOCIATION OF AMERICAN UNIVERSITIES

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New York University
Northwestern University
The Ohio State University
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Princeton University
Purdue University
Rice University
Rutgers, The State University of New Jersey
Stanford University
Stony Brook University – State University of New York
Syracuse University
Texas A&M University
Tulane University
University at Buffalo – State University of New York
The University of Arizona
University of California, Berkeley
University of California, Davis
University of California, Irvine
University of California, Los Angeles
University of California, San Diego
University of California, Santa Barbara
University of Chicago
University of Colorado, Boulder
University of Florida
University of Illinois, Urbana-Champaign
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University of Maryland, College Park
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University of Missouri, Columbia
University of Nebraska - Lincoln
University of North Carolina at Chapel Hill
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University of Wisconsin - Madison
Vanderbilt University
Washington University in St. Louis
Yale University

May 2, 2008

The Honorable Frank Pallone, Jr.
Chairman
House Subcommittee on Health
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Nathan Deal
Ranking Member
House Subcommittee on Health
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Pallone and Ranking Member Deal:

This letter is in response to your April 3, 2008 letter inviting the Association of American Universities, an organization of 62 leading public and private research universities, to answer a set of thoughtful questions concerning issues to be resolved in developing legislation to create a pathway for the approval of generic biologic products.

We are especially grateful for the opportunity to offer a university perspective as you develop biosimilars legislation because we share the same goal: to strike the optimal balance between access to safe, effective and affordable biologic treatments while continuing to promote innovation in the life sciences.

In our attached comments, we have chosen not to address issues on which we do not have standing and, accordingly, have limited our comments to questions from the sections on Patents, Incentives/Exclusivity/Investment, and Economic Impact. Moreover, we thought it most helpful provide the university perspective on the general thrust of the questions rather than answering each of the specific questions.

We believe that the process you have undertaken to seek stakeholder input on key issues will provide extremely valuable information to inform the development of effective biosimilars legislation. However, if some critical issues remain unresolved, you might consider asking the National Academies of Science to convene a panel to address those issues.

Thank you again for the opportunity to comment on this important health policy issue. We look forward to continued engagement with you as the process moves forward.

With best regards,

Robert Berdahl
President

Patents

The patent provisions in the proposed biosimilars legislation are of vital importance to universities and the public. Many of the biologic therapies available today are the fruits of pioneering academic research at universities, hospitals, and other research institutions throughout the United States. Because universities are able to protect the intellectual property associated with their research through the patent system, their innovations can be patented and licensed to the private sector for development and commercialization. Examples of approved biologics include Enbrel® for rheumatoid arthritis (Massachusetts General Hospital); Remicade® for autoimmune disorders (New York University); Fabrazyme® for Fabry disease (Mt. Sinai School of Medicine); Somavert® (Ohio University); and many other therapeutics produced by recombinant DNA or monoclonal antibody technology. Indeed, the pathbreaking research that made recombinant DNA technology feasible was conducted at leading U.S. universities, including Stanford, the University of California, and Columbia. It is no exaggeration to say that today's biotechnology revolution would not have occurred without university research and technology transfer.

In finding the right balance between access to safe, effective and affordable biologic therapies and continued encouragement of innovation in the life sciences, Congress should carefully evaluate the effect of any proposed legislation on university technology transfer. There are several areas of concern we hope will receive careful consideration by the Subcommittee on Health.

First, the proposed legislation should avoid the unintended consequence of encouraging patent challenges that unnecessarily involve our researchers in patent litigation, diverting institutional resources away from scientific research. We recognize that any biosimilars legislation, such as Hatch-Waxman, will include a mechanism for early resolution of patent disputes, in advance of product launch. We support this model, which benefits both innovators and generic manufacturers by providing certainty and permitting rational product planning. But the institution of these procedures will almost certainly involve universities in new biotech patent litigation they did not anticipate when licensing their patents. Indeed, studies have shown that in recent years Hatch-Waxman patent challenges directed to patents on small molecule drugs have skyrocketed, with the number of paragraph IV certifications increasing four-fold from 2001 to 2007. Any steps that can be taken to minimize litigation will not only help universities and their researchers, but will help the system overall.

It is important to understand that litigation directed to patents covering biologics would not be confined to the companies that hold BLAs. If the patent challenge relates to one or more patents that are owned by a university and licensed to the BLA holder, the litigation will almost certainly require participation of the university as a co-plaintiff due to standing requirements applicable in patent cases.

Universities do not seek to avoid their responsibilities as patent owners. As further discussed below, however, the extent of patent litigation resulting from biosimilars

legislation will depend to a significant degree on the length of the data exclusivity period provided the the innovator. The longer the data exclusivity period, the more likely it is that a university's patent will expire before FDA approval of the biosimilar, and thus the less reason for an FOB applicant to challenge the university's licensed patents.

A related concern is that legislation encouraging frequent and possibly repetitive challenges to university-owned patents in the biotechnology field may weaken the value of those patents and impede out-licensing programs at universities. Most university and hospital licenses are entered into with start-ups and small business entities, not with large pharmaceutical or biotechnology companies. These licensees typically depend on venture capital funding to support their research and clinical development activities. The ability of universities to transfer fundamental discoveries into the commercial sector for development will be impaired if the legislation diminishes the expectations of licensees and their investors that the licensed patents will provide them a relatively certain period of exclusivity sufficient to support a reasonable return on investment.

These concerns are heightened by the fact that the proposed biosimilars legislation will create new incentives to *design around* patents covering the approved biologic, a further reason why the period of data exclusivity is so important. Unlike Hatch-Waxman, which requires that a generic small molecule drug have the "same" active ingredient as the approved drug, the proposed biosimilars legislation will authorize the marketing of biologics that are "similar" rather than identical to the approved biologic. The result will be that a generic manufacturer will be encouraged to develop a commercial product that is similar enough to the reference product from a clinical perspective to satisfy the FDA's standards for biosimilars, but different enough to avoid the relevant patents.

Therefore, we believe that any biosimilars legislation should complement its patent provisions with strong data exclusivity protection for the innovator, so that the patents are not the principal protection for the innovator. A short period of data exclusivity, such as the five years provided in Hatch-Waxman, would create strong incentives for FOB applicants to challenge a university's patent protecting an innovator's product, just as it has encouraged ANDA litigation directed at small molecule patents. A lengthier period, by contrast, such as the 12-year period proposed in S. 1695 (Kennedy, Enzi, Clinton, Hatch) and H.R. 5629 (Eshoo, Barton) will reduce the extent of patent litigation and its attendant cost and diversion of resources, because the data exclusivity period and the patent term will significantly overlap.

A further patent-related concern relates to the procedures that will govern any newly authorized patent challenges. As noted above, standing requirements applicable to patent infringement cases generally mean that the university must be a co-plaintiff in patent enforcement actions. To ensure a fair and expeditious process for patent resolution, any legislation should provide fair notice and opportunity for third party patent owners such as universities to participate in the process of identifying and enforcing relevant patents. In addition, the university and its inventors should be given confidential access to technical information about the proposed biosimilar product and its method of production, since without this information the university will be unable to make an

informed determination as to whether its patents are infringed, given that the approval pathway does not require the product to be the same as the licensee's approved product.

We are grateful that the recently introduced Eshoo/Barton bill includes provisions expressly designed to protect the rights of university patent owners and other third parties. This proposal has gone a long way to ameliorate concerns we raised earlier with respect to S. 1695.[1]

Incentives/Exclusivity/Investment

Separate from its treatment of patents, any biosimilars legislation must provide a period of data exclusivity sufficient to sustain the extraordinary private sector investments necessary to move promising basic research into product development. Early-stage research is basic research that carries no guarantee of success in terms of leading to marketable products. Investment in early-stage research by private sector companies is a high-risk undertaking. If legislation does not provide a period of exclusivity commensurate with the attendant financial risk, such investments will become a bad business decision. The small businesses that invest in early-stage university research, and the investors that fund those companies, no longer will do so, and the result will be sharply reduced transfer of basic research discoveries from universities and other research institutions into product development.

Our experience with technology transfer over the past three decades has given us an appreciation of the private sector's need for an adequate period of exclusivity in order to justify the risk and expense associated with taking early-stage academic research all the way through clinical trials and FDA approval before the first sale is made. Prior to the Bayh-Dole Act in 1980, universities could not own their patented inventions if the federal government funded any part of the research that led to the patentable discovery. As a result, universities could not offer private companies exclusive licenses, and companies refused to invest in academic research.

The passage of Bayh-Dole had a dramatic effect on technology transfer from academia to the private sector. By 2006, more than 3,000 U.S. patents were issued to universities and hospitals, and nearly 5,000 new patent license agreements were executed. The benefits to society and the public health are immeasurable. No longer do promising new medical technologies sit on the shelf in academic laboratories.

Our point is this: in the pathway from fundamental discovery to biologic products, the role that patents play in other technology transfer areas must be played by both patents and data exclusivity. If the data exclusivity period provided in any new biosimilars legislation is inadequate, and if we rely primarily on patents to protect biotech innovation at the same time that we encourage patent avoidance by authorizing an abbreviated

[1] http://www.aau.edu/intellect/Ltr_White_Biologics_Kenn-Enzi_6-26-07.pdf
http://www.aau.edu/intellect/Cmts_AAU_Biologics_6-26-07.pdf
http://www.aau.edu/intellect/Ltr_Berdahl_Kennedy_Biologics_61807.pdf

regulatory pathway for approving "similar" biologics, we could find ourselves in the field of biologics in the same position as before Bayh-Dole in other technologies.

Whatever exclusivity period is chosen, the key point is that it be of sufficient length to assure a reasonable and predictable economic return on the substantial investments necessary for the private sector to pursue the high-cost, high-risk process of moving basic research into clinical development and regulatory approval. As universities, we do not presume to specify what the period of exclusivity should be. We do note, however, that the public policy debate on small molecule drugs concluded that a patent term restoration period of up to 14 years – under circumstances where the generic product had to be the "same" as the reference product and patent infringement therefore was assumed -- strikes an appropriate balance between the need for substantial up-front investment and downstream access to affordable follow-on products. In discussions with the Senate, AAU also expressed appreciation for the 12-year period that was added during negotiations, and we are pleased to see that the Eshoo/Barton bill similarly recognizes the importance of a reasonable data exclusivity period.

Economic Impact

American universities contribute $40 billion annually to the U.S. economy Technology transfer from universities to the private sector has produced thousands of new products and companies, contributing to the creation of 260,000 new jobs since the passage of Bayh-Dole in 1980. While we do not have data to show the specific contribution our universities have made to the growth of biotechnology, we believe that it represents a substantial and growing part of our annual technology transfer to the private sector. To maintain this highly successful enterprise, legislation to provide an abbreviated pathway for regulatory approval of biosimilars must include economic incentives that will effectively support and encourage innovation. Otherwise, fewer potential therapies for rare or unmet medical needs will be licensed for clinical development, especially early-stage research, the stage at which scientists most need support and the most fundamental breakthrough discoveries in biotechnology often occur. If investment in biotechnology is perceived as higher risk, because the biosimilars pathway makes it too easy for generic competition to enter the market before the innovator has an opportunity to recoup its R&D costs, then investment will move toward later stage improvements to proven therapies rather than research aimed at fundamental new discoveries that can prevent and cure the most confounding diseases.

Lastly, if we fail in this endeavor, there is a risk that we will drive investment in biotechnology research and development outside the U.S. to countries viewed as more hospitable to innovation. Certainly any legislation should ensure that the economic incentives available to researchers in the U.S. are no less favorable than those available in Europe, Canada, and Asia.

Conclusion

Today, research being conducted in university laboratories offers the hope of new biological therapies to treat crippling diseases. However, there is a misconception that when a potential new therapeutic pathway is being explored in a university lab, there is a vibrant private market ready to take that research and develop it. Increasingly, this is not the case. Private investors and industry are now starting to avoid the earliest-stage academic research in favor of research having a more mature proof of concept and a more favorable risk profile. Universities often have great difficulty in finding a partner to bring early-stage research to next-phase development, yet it may be that precise, early-stage discovery that leads to the next dramatic breakthrough. We are concerned that additional uncertainty caused by the lack of a sufficient period of data exclusivity and the prospect of increased patent litigation will make it even more difficult for universities to transfer new innovations in biotechnology to the private sector for development into therapies that can benefit public health and safety and ameliorate human suffering.