BIOTECHNOLOGY INDUSTRY ORGANIZATION

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Testimony of Jonca Bull, MD, Genentech, Inc.
On Behalf of the Biotechnology Industry Organization (BIO)
To
The Institute of Medicine Committee on Conflict of Interest in Medical Research, Education and Practice
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Good morning. My name is Dr. Jonca Bull. I am Director, Clinical Regulatory Policy and Liaison for Genentech, Inc. a biotechnology company headquartered in South San Francisco, CA. I am testifying on behalf of the Biotechnology Industry Organization (BIO).

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

BIO welcomes the Institute of Medicine's inquiry into the issues surrounding conflicts of interest. We appreciate the opportunity to share with you our views on these matters which are critical to our members.

BIO has long standing views on issues relating to conflict of interest in research, particularly in the context of Food and Drug Administration (FDA) product review and potential conflicts on FDA Advisory Committees.

In sum, BIO believes that potential conflicts of interest in research should be identified and appropriately managed. Conflict of interest guidelines and policies should emphasize disclosure of financial interests, rather than prohibition of certain relationships. Moreover, FDA should continue to have the authority to grant conflict of interest waivers to ensure that qualified experts are able to serve on agency Advisory Committees.

In General

Health system developments have made conflict of interest issues more salient over the past several years. The complexity of relationships in biomedical research among physicians, institutions, industry and other actors can lead to potential conflicts. They could arise from the research itself, the relationships between a company-sponsor and the physicians/researchers who act as investigators, the relationship between the company-sponsor and the trial participants, the relationship between researchers and their institutions, or between researchers and patients.

None of these relationships are prohibited by law, but successfully managing potential conflicts is essential. The stakes are high for BIO member companies. The ramifications of ignoring these issues can be severe. A conflict of interest – or the perception of a conflict – may cause FDA to question the reliability of a company's data or be the subject of unflattering articles in the media. Both could affect a company's ability to attract investment or move a product through the approval process. It also might make it impossible to collaborate with the physician or institution of a company's choice.

Some observers have argued that financial relationships with industry inherently create a bias. They say that the presence of private money in the health care setting creates conflicts of interest in researchers that may affect results and/or the quality of care provided to research participants.

The perception that certain financial relationships with industry lead to bias, no matter how false, has the potential to diminish the public's trust in biomedical research. This trust is vital for companies looking to continue their work. Therefore, as sponsors of research, BIO members know all stakeholders must take steps to maintain public confidence. That's why BIO supports this committee's work as an important step forward and will be pleased to collaborate with you in the days and months ahead to develop appropriate policies and guidelines.

As you consider the issues surrounding conflicts of interest, BIO urges you to remember that the tremendous investment by the private sector over the past two decades has led to remarkable medical breakthroughs. Government policy to encourage private investment has been a major factor in the development of a biotechnology industry in the United States that is the envy of the world. It has led to the approval of hundreds of drugs and vaccines that have helped hundreds of millions of people worldwide.

Developing policy pertaining to conflicts of interest involves balancing two objectives – supporting necessary industry-academic collaboration, while maintaining the integrity of medical research so as to inspire public confidence. Policy makers must recognize that these are mutually obtainable goals if our nation is to continue to develop breakthrough products for patients.

BIO believes the best way to protect the integrity of research while allowing that work to advance is to ensure that research protocols are independently reviewed and that financial

interests are disclosed. Policies governing conflict of interest should require disclosure of financial relationships between and among researchers, investigators, sponsors, and Institutional Review Boards (IRBs). They should not prohibit nor otherwise impose rigid restrictions on the existence of such relationships.

Specifically, BIO policy says that:

- Investigators and sponsors of a clinical trial should be responsive and cooperative with institutions' efforts to identify financial or other interests that may create a conflict of interest, or the appearance of a conflict in reviewing research risks.
- Investigators should disclose to a reviewing IRB or other institutional oversight committee any financial or other interest in the research protocol that could have professional, personal, or material financial implications.
- Sponsors of a clinical trial should be forthright in responding to requests for information about financial or other interests of investigators that may create a conflict or appearance of a conflict in conducting research.
- Investigators should disclose to participants that they are compensated for conducting clinical trials. Payments to investigators and research institutions should not be contingent on the research outcome.
- Investigators and sponsors should support a reviewing IRB's determination that an interest of an investigator or research institution presents a conflict of interest, and its recommendation for dealing with the conflict, whether the interest is
    - Disqualifying,
    - Is one of the risks that should be disclosed to research participants during the informed consent process, or
    - Is an interest that can be managed by the IRB through research process and oversight.

The emphasis on disclosure rather than prohibition of financial interests that forms the crux of BIO's position is consistent with the position expressed by former President Clinton's National Bioethics Advisory Commission[1]. FASEB (Federation of American Societies for Experimental Biology)[2], the ICMJE (International Community of Medical Journal Editors),[3] and other stakeholder groups have also tried to strike the right balance by emphasizing disclosure of financial interests, rather than prohibiting certain relationships.

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[1] "Ethical and Policy Issues in Research Involving Human Participants", National Bioethics Advisory Commission, August, 2001.

[2] In its Conflict of Interest "Toolkit", FASEB notes that academic-industry collaborations "are a fundamental and beneficial part of modern biomedical science", that "benefit society by leading to the development of new medical treatments, diagnostic tools, and other practical ramifications of research." Rather than urging a ban on relationships with industry, FASEB goes on to say that investigators must be aware of how their actions are perceived to maintain credibility.

[3] The ICMJE's Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (2007).

In addition, some groups have appropriately recognized that financial gain is not the only interest that could create bias. For example, professional recognition and relationships with peers could also be potential conflicts. To that end, the ICMJE requires disclosure of all relationships that could be viewed as presenting a possible conflict of interest.[4]

Possible Conflicts of Interest during FDA Product Review

Biotechnology companies must comply with FDA regulations to get approval to market their products in the United States. FDA rules govern all aspects of clinical trials including protocol submissions, informed consent, and conflicts of interest.

Generally speaking, federal law only applies to those potential conflicts that could affect the reliability of the data in a marketing application submitted to FDA. Federal law does not prohibit – nor even define – a conflict of interest. Rather, FDA regulations address issues surrounding financial disclosure by investigators. They focus on the bias that could arise from an investigator's financial interest in the outcome of a study because of the way payment is arranged, because the investigator has a proprietary interest in the product or because the researcher has an equity interest in the company-sponsor of the study.[5]

These regulations require disclosure by the sponsor of financial arrangements between the sponsor and clinical investigators and certain interests of the clinical investigators in the product under study or in the sponsor of the covered study. Companies must disclose or certify "information concerning the financial interests" of a clinical investigator. Specifically, the company must disclose:

- Any financial arrangement with an investigator performing the trial if the value of the compensation could be influenced by the outcome of the study;
- Any significant payments of other sorts from the sponsor such as grants to fund ongoing research, a retainer for ongoing consultation, honoraria, or compensation in the form of equipment;
- Any proprietary interest in the tested product held by a clinical investigator involved in a study;
- Any significant equity interest in the sponsor held by any clinical investigator involved in the study; and
- Any steps taken to minimize the potential for bias resulting from any of these arrangements, interests or payments.[6]

FDA will use this information as part of its assessment of the reliability of the clinical data presented.[7]

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[4] ICJME *supra.*
[5] 21 CFR 54.1
[6] 21 CFR 54.4
[7] 21 CFR part 54

Thus, BIO's views on potential conflicts of interest mirror federal regulations. FDA rules require identification of possible conflicts and disclosure as the means of managing them. This regulatory framework has been in place for many years and has successfully protected the integrity of drug discovery research while allowing innovation to advance.

FDA Advisory Committees

Another context in which potential conflicts of interest have been discussed has been regarding the makeup of FDA Advisory Committees. Some agency and industry critics have charged that these committees are comprised of individuals with significant interests – usually financial interests – in the outcome of the committee's deliberations about particular products. They have called for strict limits on FDA's ability to grant conflict of interest waivers for certain individuals.

Consistent with BIO's general view in opposition to rigid prohibitions and in support of case-by-case identification and management of potential conflicts, BIO has opposed that position. FDA Advisory Committees have historically used the most knowledgeable and highly qualified individuals to obtain the best available information. FDA should continue to have significant discretion to grant waivers regarding financial conflicts of interest for potential advisory committee members whose expertise is essential.

This authority is critical for reviews of the cutting-edge science and next generation innovation that is the bailiwick of biotechnology companies. In many cases, only a handful of qualified experts may exist to provide the agency with appropriate review of complex and technical issues surrounding new products. For example, for certain rare diseases areas or product categories, the universe of highly knowledgeable and qualified individuals may be quite small. In some circumstances, virtually the only experts in an area are individuals who are involved as advisors or participants in the research and development leading to the innovation being reviewed by FDA.

These individuals, who may have financial interest and thus a potential conflict, can be essential to a meaningful discussion of the issues surrounding review of a new product. Disqualifying them, or limiting their ability to meaningfully participate, could adversely impact the ability of an advisory committee to comprehensively evaluate a particular issue. Allowing such individuals to participate in an FDA advisory committee is vitally important because making decisions based on the best and most relevant science depends on the Agency's ability to seek and use the advice of these experts. Flexibility in the issuance of waivers is crucial to achieving this goal.

As with efforts to reduce private financing of research, policies that prohibit participation on advisory committees or impose other rigid standards contain a flawed, underlying assumption – that certain experts are necessarily biased simply because they work with industry. Basing national policy on that assumption undervalues the expertise and professional integrity of many of the scientists and researchers who participate in FDA deliberations.

It should be pointed out that FDA commissioned a study by the Eastern Research Group to assess the expertise and financial conflicts of interest of FDA Advisory Committee members.

The study, published last year, found that advisory committee members with higher levels of expertise were more likely than other standing advisory committee members to have been granted waivers for financial conflicts of interest. Moreover, study authors found that although potential alternative experts can be initially identified, some of these individuals may not otherwise be appropriate or available to serve as advisory committee members. They concluded that "we judge the ability to create alternative conflict-free advisory panels to be speculative" and that "FDA might not always be able to match the specialized expertise of some existing advisory committees."[8]

Congress endorsed this view and included provisions in the recently enacted FDA Amendments Act that provide the agency with the authority to grant conflict of interest waivers for potential members of advisory committees.

We urge the committee to support federal policies providing FDA the discretion to provide these waivers on a case-by-case basis.

Conclusion

Conflicts of interest have the potential to diminish public trust in medical research. All stakeholders must work together to develop policies and guidelines to ensure public confidence. At the same time, policies must allow critical biomedical research to advance.

BIO believes the best way to achieve the twin goals of maintaining research integrity while promoting innovation is to enact policies that ensure maximum disclosure of possible conflicts as well as provide regulators or other oversight bodies the discretion to make case-by-case decisions. This has been the federal regulatory framework that has led to the discovery and development of hundreds of biotechnology products over the years.

BIO stands ready to work with this committee as well as other stakeholders as they investigate these issues further.

Thank you. I'd be happy to answer any questions.

[8] "Measuring Conflict of Interest and Expertise on FDA Advisory Committees", Eastern Research Group, submitted to the FDA October, 2007