BIO

BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

June 16, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20857

Re: Docket No. 2004P-0171
BIO Comments

Dear Sir or Madam:

The Biotechnology Industry Organization ("BIO") submits the following comments in support of arguments made in a citizen petition filed by Genentech, Inc., referenced above (hereafter "Genentech Petition"). BIO is the largest trade organization serving and representing the biotechnology industry. With more than 1,000 worldwide members, BIO is committed to representing the interests of large and small biotechnology companies, academic institutions, and research institutions that develop biotechnology products. As a leading voice in the biotechnology industry, BIO has taken a strong and consistent interest in FDA's possible actions concerning follow-on biological products.[1]

Genentech's petition raises a serious public policy concern: the manner in which FDA uses and controls the highly valuable data and information that BIO members regularly submit to the agency for one limited purpose – so that FDA may review and approve a specific biotechnology product. Before FDA publishes a draft guidance or approves a follow-on biotechnology product, it must assure the biotechnology industry that the agency has taken steps to protect innovators' legal rights in their own data and information.

---

1 Genentech identifies as a "generic biologic" a product that purports to be the same or similar enough to an innovator's biotechnology-derived product that it may be approved for use in humans based in part on a non-clinical and clinical data developed by an innovator company for an original, or reference, product. *See* Genentech Petition at 2. BIO uses the term "follow-on" to refer to products that purport to be similar enough to the innovator's product that the follow-on manufacturer may rely on data and information developed by the innovator for approval.

1225 EYE STREET, N.W., SUITE 400
WASHINGTON, D.C. 20005-5958

202-962-9200
FAX 202-962-9201
http://www.bio.org

2004P-0171

C1

BIO agrees that FDA should refrain from approving a "follow-on" biological product under section 505(b)(2) of the Food, Drug, and Cosmetic Act ("FDCA"), 21 USC 355(b)(2) (hereafter section 505(b)(2)) with respect to a biotechnology-derived product the review of which relies on an innovator's trade secret and confidential commercial data and information.[2]

Nor can FDA rely on such data to draft or issue a guidance document concerning the scientific principles underlying follow-on products. Although FDA occasionally drafts guidance documents without the benefit of public comment, those guidances generally do not affect or change long-standing policy positions ; draft guidance documents are no substitute for the public's right to participate in agency policy-making.[3] BIO does not believe that a draft guidance on approval of follow-on biotechnology products should be the vehicle to change FDA policy on such an important matter. The agency should make such a change only after engaging in a public participatory process designed to fully vet the myriad issues presented by this complex subject.

BIO filed its own citizen petition in April 2003 requesting that FDA use a public process in designing and implementing a follow-on biologics policy and that the agency refrain from using data gathered in clinical studies of one biotechnology product when approving a different product under section 505(b)(2). *See* FDA Docket No. 2003P-0176 ("BIO Petition"). FDA partially denied our petition on October 14, 2003,[4] and continues to move forward without public participation in its efforts to devise and implement a follow-on policy.

For example, BIO has learned that the agency has formed a follow-on biologics "working group" that is developing a draft guidance document describing scientific methods for determining the "sameness" or "similarity" of two biotechnology products made through different manufacturing

---

[2] These concerns were also expressed by Pfizer, Inc., in a citizen petition it filed concerning follow-on biologics on May 13, 2004. See FDA Docket No. 2004P-0231 (May 13, 2004). BIO supports Pfizer's arguments against the use of an innovator's confidential or trade secret data in the approval of a 505 (b)(2) product.

[3] Agencies may not change long-standing interpretations or positions without notice and comment rulemaking. *Syncor Internat'l Corp. v. FDA*, 127 F.3d 90 (D.C. Cir. 1997).

[4] *See* October 14, 2003 letter from J. Woodcock, FDA, to Ms. Sanzo and Messrs. Chasnow, Lawton, and Rakoczy, regarding FDA Dockets No. 2001P-0323/CP1 & C5, 2002P-0447/CP1, and 2003P-0408/CP1 ("Petition Response").

processes. FDA has also acknowledged that the working group is basing the draft guidance, in part, on knowledge the agency has gained through its review of innovator comparability data. As Genentech correctly points out, the agency cannot use innovators' trade secret and confidential commercial data and information, such as comparability data, to draft a guidance document because FDA does not have the authority to control the use of that data and information. Moreover, BIO agrees with Genentech that FDA should not use the chemistry, manufacturing and controls ("CMC") data from the innovator. That would constitute an improper and illegal use of BIO members' trade secret and confidential commercial data and information.

A senior agency official recently acknowledged that FDA does not have the legal authority to reference information in an innovator's biologics license application ("BLA") and stated that FDA plans to hold public workshops as part of the comment process on the draft guidance.[5] We commend the agency for these positions. However, FDA has yet to open its internal deliberations about the standards that should apply to follow-on products to interested parties. For this reason and because several substantive legal issues concerning follow-on biologics remain unresolved, we are compelled to comment.

Comment One: FDA Should Engage in a Public Process and Only Then Develop a Scientific Draft Guidance Document

In developing any follow-on biologics initiative, FDA should take steps to assure that all interested parties – whether innovators, potential follow-on manufacturers, patient advocates, and other governmental agencies – have the opportunity to participate *before* FDA takes action. In its Petition, BIO suggested that FDA publish in the Federal Register a list of issues under consideration at the agency, hold a series of public meetings at which it would receive information from interested persons about the identified issues, and publicly respond to the comments received. BIO Petition, Summary of Petition.

Although FDA initially denied BIO's request, it is now, apparently, considering holding a public meeting – but not until *after* it publishes a draft scientific guidance.[6] BIO does not believe that any process in which a draft

---

[5] *See* FDA Follow-On Biologics Guidance: A Preview (remarks by Dr. Steven Galson), *The Pink Sheet*, Vol. 66, No. 19, p. 4 (May 10, 2004) ("May 5 FDA Statement).

[6] "Follow-On" Biologics Guidance Will Limit Use of Data to "Public Domain", *The Pink Sheet*, Vol. 66, No. 19, p. 3 (May 10, 2004).

scientific guidance is developed without the benefit of early input from expert stakeholders will satisfy the agency's obligations.[7] Rather than publishing a draft guidance and then holding public meetings, BIO proposes that FDA reverse the order of these events. Were it to do so, FDA could easily satisfy two pending requests from the innovator biotechnology industry.

First, a public meeting process could help alleviate the concerns raised by Genentech concerning inappropriate agency use of innovator proprietary data. At the public meetings, the agency could solicit public scientific data and information about product comparability and use that information as the basis for its draft guidance. This would provide some assurance to biotechnology innovators that FDA was not drafting a follow-on biologics policy based on proprietary data and information submitted to FDA as part of a CMC section of an approval application. *See generally* Genentech Petition.

Second, such meetings would allow FDA to address BIO's request that FDA take concrete and public steps to resolve several difficult issues surrounding follow-on biologics before it formulates a follow-on approval policy. For example, FDA has historically taken the position that the manufacturing processes used to create a biotechnology product are inexorably linked to the unique characteristics of the resulting protein molecule. Only in very specific circumstances (when intracompany manufacturing changes are made or when a different manufacturer has access to detailed trade secret manufacturing data about how the molecule is created) will the agency allow any safety and effectiveness data derived from clinical studies on one protein product to be applied to a product resulting from even a slightly different manufacturing process. *See FDA Guidance Concerning Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-Derived Products* (April 1996); *Berlex Laboratories, Inc. v. FDA*, 942 F. Supp. 19 (D.D.C. 1996). The agency should only consider changing this position if it receives detailed, relevant scientific information from experienced experts in a public setting about workable and scientifically valid alternatives that would support such a change.

Third, FDA should discuss its legislative authority as part of a public meeting process. FDA's recent decision to expand its interpretation of section 505(b)(2) to include recombinant active ingredients was made without public participation. Because the case has been stayed, it is unlikely that litigation

---

[7] Our concerns are especially acute given that FDA has often implemented draft guidance documents immediately after their publication in draft form. *See* Civil Action No. 03-2346 (RCL) (D.D.C.) (complaining that FDA's approval of generic amlodipine was arbitrary and capricious).

concerning FDA's approval of generic amlodipine will resolve in the near future the legal issues raised by FDA's expanded interpretation of section 505(b)(2) before that interpretation is applied to a biotechnology product. *See* Civil Action No. 03-2346 (RCL)(D.D.C.).

However, FDA's recent comments indicate that the agency continues to review biotechnology products under section 505(b)(2) even though issues surrounding FDA's legal authority remain unresolved. *See* May 5 FDA Statement. FDA should act now to assure that these legal issues are fully resolved through public notice and comment rulemaking before any biotechnology approvals take place.

Comment Two: Important Legal Concerns About FDA's Approach to Follow-On Approvals under Section 505(b)(2) Remain Unresolved

Both BIO's and Genentech's citizen petitions raised substantive legal concerns about FDA's recent interpretation of section 505(b)(2) as allowing approval of drugs with recombinant active ingredients.[8] Specifically, BIO shares Genentech's concern that FDA's reviews of follow-on biological products under 505(b)(2) cannot rely on the detailed non-public data and information included in the innovator's application concerning its manufacturing processes as well as safety and effectiveness data and information about the behavior of a different product in humans. Nothing in section 505(b)(2) allows FDA to review, reference, or rely on any non-public data or information contained in an innovator's NDA to approve a competitor's product. Further, the law does not allow FDA to rely on trade secret or other proprietary data when drafting and issuing a draft or final guidance.

---

[8] *See Draft Guidance for Industry: Applications Covered by Section 505(b)(2)*, (October 1999); Petition Response at 13.

Conclusion

BIO supports Genentech's request that FDA refrain from publishing a draft guidance document or approving a biotechnology product that relies in whole or in part on trade secret and confidential commercial data and information submitted by innovator biotechnology companies. And, we reiterate our request that FDA move forward in developing a follow-on biologics policy only through an inclusive public process.

Sincerely,

Stephan E. Lawton
Vice President & General Counsel

SEL:fz

cc: Lester M. Crawford, D.V.M., Ph.D.
Acting Commissioner
Food and Drug Administration
HF-1, 5600 Fishers Lane
Rockville, MD 20857

Alex Azar, Esquire
General Counsel
Department of Health and Human Services
200 Independence Ave., Southwest
Washington, DC 20201

Daniel E. Troy, Esquire
Chief Counsel
Food and Drug Administration
GCF-1, 5600 Fishers Lane
Rockville, MD 20857

Janet Woodcock, M.D.
Deputy Commissioner for Operations
HF-2, 5600 Fishers Lane
Rockville, MD 20857