

# Genentech

IN BUSINESS FOR LIFE

DEPARTMENT OF REGULATORY AFFAIRS

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March 2, 2007

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

Subject: **Docket No. 2006N-0525**  
Supplements and Other Changes to an Approved Application  
(PUBLIC MEETING)

Dear Dockets Management Branch:

Enclosed are comments, provided by Genentech, for the *Public Meeting* Supplements and Other Changes to an Approved Application.

Thank you for providing us the opportunity to comment on the Public Meeting. We hope that you will find our comments useful and constructive.

Sincerely,



Robert L. Garnick, Ph.D.  
Sr. Vice President  
Regulatory Affairs, Quality, and Compliance

**Docket for Review and Comment**

**Supplements and Other Changes to an Approved Application; Public Meeting**

**Docket No. 2006N-0525**

**Notice Issued January 5, 2007  
Comments due March 7, 2007**

Genentech, Inc.  
1 DNA Way  
South San Francisco, CA 94080-4990

**Genentech, Inc.**

1/Response to Docket on Supplements and Other Changes to an Approved Application; Public Meeting

Genentech supports the Agency's effort to seek stakeholder input on issues to consider when developing revisions to its regulations regarding CMC supplements and other changes to approved marketing applications for human drugs. We believe that providing increased regulatory flexibility based on use of risk-based approaches to reduce the reporting burden for certain changes is a positive step forward in implementing the Agency's 21st Century CGMP initiative and embracing pharmaceutical quality by design and risk management practices defined in ICH Q8, 9, and 10. We also believe that implementing risk based approaches based on manufacturing process understanding, prior knowledge, and internal change control procedures in the context of a company's demonstrated quality systems will facilitate product innovation and improvements and allow for more rapid and predictable release of life saving medicines for our patients. However, we have the following comments and concerns for the Agency's consideration.

- The background section of the FR notice specifically addresses FDA's thinking on possible revisions to 314.70, which prescribes the requirements for reporting changes to approved drug products and abbreviated drug products regulated under the FD&C Act. However, the FR notice is silent with regard to its intent to revise 601.12 which prescribes the requirements for reporting changes to approved biological drug products regulated under the PHS Act. Many natural and recombinant DNA-derived protein products are regulated as drugs under the FD&C Act. There is no scientific and technical reason that biotechnology and other protein products regulated under 601.12 should be treated differently. The increased regulatory flexibility, afforded by the use of risk based approaches to facilitate innovation and improvements in manufacturing processes to reliably produce pharmaceuticals of high quality, can and should apply to manufacturers of protein drugs and specified biotechnology products. Therefore, to ensure consistency in handling manufacturing changes for this class of products, any revisions proposed to 314.70 should also be applicable to 601.12, and the specified biotechnology products. This would be particularly beneficial to sponsors who manufacture biotech products in both categories. We note that when the Agency last revised its regulations governing changes to approved marketing applications to implement Section 116 of the Food and Drug Administration Modernization Act, it revised both 314.70 and 601.12. It seems logical and scientifically appropriate then, that FDA should revise both 314.70 and 601.12 to allow for use of an enhanced risk-based approach to the CMC regulatory process for all specified biotechnology products in order to reduce the number of supplements.

**Genentech, Inc.**

2/Response to Docket on Supplements and Other Changes to an Approved Application; Public Meeting

- We believe it is critical to the success of this approach that Field Investigators and Center reviewers work as a team to assure clear communication, uniform expectations and a shared understanding of a manufacturer's design space and regulatory agreements which support a reduced reporting requirement for manufacturing changes.
- We encourage the FDA to work closely with other international regulatory agencies to harmonize respective variation regulations with any revisions made by the Agency to 314.70 and 601.12 so that innovations and improvements in manufacturing processes can be implemented globally without disparate supplement submission.

**Genentech, Inc.**

3/Response to Docket on Supplements and Other Changes to an Approved Application; Public Meeting