

Genentech

IN BUSINESS FOR LIFE

DEPARTMENT OF REGULATORY AFFAIRS

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May 17, 2004

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

Subject: Docket No. 2004D-0118, Federal Register: March 30, 2004 (Volume 69, Number 61, Pages 16580-16581)

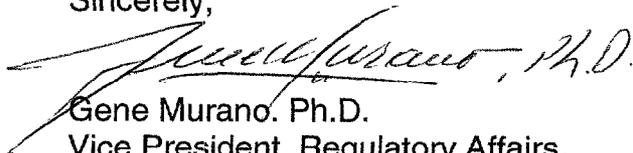
Genentech, Inc. appreciates the opportunity to comment on the Food and Drug Administration's (FDA's) draft Guidance for Industry: *ICH: Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process*. Genentech, Inc. is a biotechnology company that has headquarters in South San Francisco, California.

Genentech, Inc. is very pleased with the work done to date on the draft guidance and believes that it will serve as a valuable resource for industry once implemented.

In the way of further enhancing the utility of the document, Genentech, Inc. offers the following commentary. For clarity, the comments and questions have been compiled into a single comment matrix (attachment).

If you have any questions regarding our comments, please contact Robert Mills, Regulatory Affairs Manager, at (650) 225-3384.

Sincerely,


Gene Murano, Ph.D.
Vice President, Regulatory Affairs,
Genentech, Inc.

2004D-0118

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Comment Matrix
*ICH: Q5E Comparability of Biotechnological/Biological Products Subject to
 Changes in Their Manufacturing Process*
Draft Guidance – May 2004

Line No.	Proposed Change/Clarification Request	Justification/Clarification Question
Lines 140-143	<p>Please respond to the question (see right) regarding the following statement:</p> <p>“Critical control points in the manufacturing process that affect product characteristics, e.g., the ability of downstream steps to accommodate material from a changed cell culture process, as well as the impact of the process change on the quality of downstream product;”</p>	<p>Please define the term “critical control point” and provide examples.</p> <p>The example in this section refers to all of recovery, which doesn’t coincide with a singular critical control point.</p>
Lines 144-147	<p>Please respond to the question (see right) regarding the following statement:</p> <p>“Adequacy of the in-process controls including critical control points and in-process testing: In-process controls for the post-change process should be confirmed, modified, or created, as appropriate, to maintain the quality of the product;”</p>	<p>Does the term “critical control point” have the same meaning in lines 144 – 147 as in lines 140-143?</p>
Lines 173-174	<p>Please replace the word ‘valid’ with the word “appropriate” or “suitable” (or other fitting term) in the following sentence.</p> <p>“Whether or not existing tests remain valid suitable for their intended use or should be modified.”</p>	<p>To ensure that “valid” is not confused with, or incorrectly interchanged with “validated”.</p>

Comment Matrix
*ICH: Q5E Comparability of Biotechnological/Biological Products Subject to
 Changes in Their Manufacturing Process*
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Line No.	Proposed Change/Clarification Request	Justification/Clarification Question
Lines 236-237	<p>Please make the following modifications to the following statement:</p> <p>“Where one or more of the multiple activities are not completely show a change and the activities are not correlated with clinical safety or efficacy...”</p>	For clarification
Lines 268-269	<p>Please remove or modify the following statement:</p> <p>“However, a widening of the acceptance criteria is generally not considered appropriate and should be justified”</p>	<p>Acceptance criteria established in the BLA are usually tightened based on the manufacturing experience. When a new manufacturing process is implemented it would be reasonable to widen the acceptance criteria to the ranges established in the BLA , provided that they will eventually be tightened once there is sufficient manufacturing experience with the change. Perhaps a statement can be added to allow acceptance criteria to be reset to the ranges established in the BLA with the understanding that the ranges will be tightened based on the manufacturing history incorporating the change.</p>
Lines 315-317	<p>Please respond to the question (see right) regarding the following statement:</p> <p>“For example, analysis of process intermediates might suggest potential differences that should be evaluated to determine the suitability of existing tests to detect these differences in the product.”</p>	Please define the term “process intermediates” and provide examples.