

Genentech

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DEPARTMENT OF REGULATORY AFFAIRS

1 DNA Way MS#242
South San Francisco, CA 94080-4990
(650) 225-1558
FAX: (650) 467-3198

December 3, 2004

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

Subject: **Docket No. 2004D 0443, OC 2004115**
Comments on Quality System Approach to Pharmaceutical
Current Good Manufacturing Practice Regulations (DRAFT GUIDANCE)

Dear Dockets Management Branch:

Enclosed are comments, provided by Genentech, for the *Draft Guidance for Industry Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations*.

We welcome the FDA's efforts to update and harmonize cGMP regulations to the current understanding of quality systems for the manufacturing of human and veterinary drugs, including biologics.

Thank you for providing us the opportunity to comment on this Draft Guidance.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

If you have any questions regarding this document, please contact Amparo Salgado, Associate, Regulatory Affairs at (650) 225-2214.

Sincerely,

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

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Draft Guidance for Review and Comment

**Draft Guidance for Industry
Quality Systems Approach to Pharmaceutical
Current Good Manufacturing Practice Regulations**

**Docket No. 2004D-0443
CDER 2004115**

**Issued for Comment September 2004
Comments due December 3, 2004**

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

GENERAL COMMENTS

The following comments are provided by Genentech, Inc. We welcome FDA's efforts to update and harmonize CGMP regulations to the current understanding of quality systems. In general, this draft guidance provides clarity on the quality system model. Our comments are outlined in the following table.

Table1-1
Specific Comments for Draft Guidance
“Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations”

Section	Line Reference	FDA Guidance	Genentech Comment
IV.A.3.	362	The standard of quality that will be used.	Clarification: It would be helpful for FDA to clarify “standard of quality” definition in reference to documenting a quality system. An example would be helpful.
IV.A.5.	418-420	When developing and implementing new quality systems, reviews should take place more frequently than when the system has matured. Outside of scheduled reviews, the quality system is typically included as a standing agenda item in general management meetings.	Recommend deleting lines 418-420. This topic is covered on lines 402-407
	462	Management is also expected to develop cross-cutting groups...	Replace “cross-cutting” with “cross-functional”
IV.C.2.	569	Packaging and labeling controls, critical stages in the pharmaceutical manufacturing process, are not specifically addressed in quality systems models.	Contradictory to statement on line 94, which states that “ it is important to harmonize the CGMPs to the extent possible with other widely used quality management systems including ISO 9000, non-U.S. pharmaceutical quality management requirements.....” , since 21 CFR 820 does address Labeling and Packaging Control.
IV.C.4.	644–648	In a modern quality system, a design concept established during product development typically matures into a commercial design after process experimentation and progressive modification. Areas of process weakness should be identified, and factors that are influential on critical quality attributes should receive increased scrutiny.	Clarification is recommended for how Design Control aligns with the Pharmaceutical Development Process.

Table1-1 (cont'd)
Specific Comments for Draft Guidance
“Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations”

Section	Line Reference	FDA Guidance	Genentech Comment
IV.C.4.	677	Process steps should be verified using a validated computer system or a second person.	Add to clarify: At a minimum, critical process steps should be verified using a validated computer system or a second person. Non-critical steps should not require verification. Clarification will be consistent with line 674, “critical process parameters”, ICH Q7A guidelines, and 211.110.
IV.C.5.	750	(e.g., specific control parameters strength)	Rewording of this example would be helpful.
IV.C.5.	751	Discrepancy may be detected during any stage of the process by an employee or during quality control activities.	Recommend to broaden the scope of detecting discrepancies to include other quality systems, i.e., automation. Add to clarify: Discrepancy may be detected during any stage of the process by an employee, automation systems , or during quality control activities.”
Glossary			Overall comment to the glossary terms: the terms defined in this section are too broad and do not specifically relate to how they are referenced within this guidance. Recommendations to terms are listed.
Glossary	1013	Continuous Improvement—ongoing activities to evaluate and positively change products, processes, and the quality system to increase effectiveness.	Recommend: ongoing activities to evaluate and positively improve product quality, processes reliability and robustness, and/or quality system effectiveness.
	1039	Pre-production—drug development phase prior to pilot production.	It is our comment that some companies consider pilot production as a GMP process and other companies consider it to be prior to GMP production. A clarification of the term “pilot production” will be helpful.
	1041	Preventive Action—Action taken to eliminate the cause of a potential non-conformity, defect, or other undesirable situation to prevent occurrence.	Add: action taken to eliminate the cause of a potential nonconformity, discrepancy , defect, or other undesirable situation to prevent occurrence

Table1-1 (cont'd)
Specific Comments for Draft Guidance
"Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations"

Section	Line Reference	FDA Guidance	Genentech Comment
	1050	Quality Assurance—proactive and retrospective activities that provide confidence that requirements are fulfilled.	Add: proactive and retrospective activities that provide confidence that requirements are fulfilled and the organization with responsibility for such activities.
	1053	Quality Control—the steps taken during the generation of a product or service to ensure that it meets requirements and that the product or service is reproducible.	Add: the steps during the generation of a product or service to ensure that it meets requirements and that the product or service is reproducible and the organization with responsibility for such activities.
	1056	Quality Management—accountability for the successful implementation of the quality system.	Recommend: personnel who are accountable for the successful implementation of the quality system.
	1073	Quality System—... In the CGMP regulatory context, the quality system establishes the foundation to promote the effective functioning of the five other major systems.	Recommend deleting "in the CGMP regulatory context" Quality systems establishes the foundation to promote the effective functioning of the major systems.
	1083	Senior Management—top management officials in a firm who have the authority and responsibility to mobilize resources.	Recommend: executive level personnel in firm who have the authority and responsibility to ensure operations and system compliance with CGMP.