

Genentech

IN BUSINESS FOR LIFE

DEPARTMENT OF REGULATORY AFFAIRS

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April 11, 2005

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

Subject: **Docket No. 2005D-0021**
Comments on ICH Q8 Pharmaceutical Development (DRAFT GUIDANCE)

Dear Dockets Management Branch:

Enclosed are comments, provided by Genentech, for the *Draft Guidance* ICH Q8:
Pharmaceutical Development.

Thank you for providing us the opportunity to comment on this Draft Guidance.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 Michelle Tallin,
Associate Director, Regulatory Affairs at (650) 225-6098.

Sincerely,



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

2005D-0021

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Draft Guidance for Review and Comment

**Draft Guidance for Industry
Q8 Pharmaceutical Development**

Docket No. 2005D-0021

**Issued for Comment November 18th, 2004
Comments due April 11th, 2005**

Genentech, Inc.
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GENERAL COMMENTS

The following comments are provided by Genentech, Inc. We welcome FDA's efforts to update and harmonize the 3.2.P.2 Pharmaceutical Development section of a regulatory submission in the ICH M4 Common Technical Document (CTD) format.

In general, this draft guidance provides clarity on the development of a product and its manufacturing process. It is our general opinion however that it is unclear whether this document is intended to relate to both small molecules (synthetic drug products or chemical substances) and biotech products. If intended to cover both, separation of examples in to those applicable to small molecules (synthetic drug products or chemical substances) and those applicable to biotech products would make the document easier to interpret. The format used in ICH Guidance for Industry: M4Q is a good example.

Specific comments on the Guidance are included in the following table.

Table1-1

**Specific Comments for Draft Guidance
“Q8 Pharmaceutical Development”**

Section	Line Reference	ICH Guidance	Genentech Comment
2.0	43	The aim of pharmaceutical development is to design a quality product and the manufacturing process to deliver the product in a reproducible manner.	For clarification on this add drug product : The aim of pharmaceutical development is to design a quality product and the drug product manufacturing process to deliver the product in a reproducible manner.
2.0	66		Insert at end of paragraph: Cross reference may be made to justification of specifications 3.2.S.4.5 and/or 3.2.P.5.5
2.1	97-104	The physicochemical and biological properties of the drug substance that can influence the performance of the drug product and its manufacturability, or were specifically designed into the drug substance (e.g., crystal engineering), should be identified and discussed. Examples of physicochemical and biological properties that might need to be examined include solubility, water content, particle size, crystal properties, biological activity, and permeability. These properties could be inter-related and might need to be considered in combination. Some of these properties can change with time and might be supplier dependent.	It may be advisable to split paragraph in to properties applicable to small molecules in one instance and biologicals in another instance. Examples of physicochemical and biological properties that might need to be examined for biological molecules in addition to those named are aggregation; deamidation and glycosylation.
2.1	100	Examples of physicochemical and biological properties that might need to be examined include	Change to: Examples of physicochemical and biological properties that might need to be examined include but are not limited to

Section	Line Reference	ICH Guidance	Genentech Comment
2.1.1	95		This section may not be applicable to Biotech products
2.1.1	107-111	For example, the ICH Q6A <i>Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances</i> describes some of the circumstances in which drug product studies are recommended (e.g., Decision Tree #3 and #4 (Part 2)).	Reference also Q6B: Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
2.2.1	171-173	Any special design features of the drug product (e.g., tablet score line, overfill, anti-counterfeiting measure) should be identified and a rationale provided for their use. Information to support the appropriateness of such features should be provided.	To exclude counterfeiting measures related to the primary and secondary packaging of the product, change to: anti-counterfeiting measure as it affects the drug product
2.1.2	128		Insert at end of paragraph: Cross reference may be made to drug product stability 3.2.P.8
2.2.2	179-186	An overage is a fixed amount of the drug substance added to the formulation in excess of the label claim. Any overages in the manufacture of the drug product, whether they appear in the final formulated product or not, should be justified considering the safety and efficacy of the product. Information should be provided on the 1) amount of overage, 2) reason for the overage, (e.g., to compensate for expected and documented manufacturing losses), and 3) justification for the amount of overage. The overage should be included in the amount of drug substance listed in the representative batch formula (3.2.P.3.2).	This is a definition and should appear in the glossary and not in the text.
2.2.3	199-200	A summary of the development studies that were carried out to investigate the potential impacts of the physicochemical...	Change to: A summary of the development studies that identified aspects that impact the physicochemical...
2.2.3	202, 206		Biotech product examples would help clarify

Section	Line Reference	ICH Guidance	Genentech Comment
2.2.3	210-212	See also ICH Q6A <i>Specifications: Test Procedures And Acceptance Criteria For New Drug Substances And New Drug Products: Chemical Substances</i> ; Decision Tree #4 (Part 3) and Decision Tree #7 (Part 1).	Reference also Q6B: Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
2.3	223	Process development studies should provide the basis for process optimisation, process validation and process control requirements.	Change to: Process development studies should provide the basis for process optimisation, equipment selection , process validation and process control requirements.
2.3	230	should be provided	Change to: may be provided to allow for future process development
2.3	248		Insert at end of paragraph: Cross reference may be made to drug substance development section 3.2.S.2.6 as appropriate.
2.5	290-293	The rationale for performing or not performing microbial limits testing for nonsterile drug products, (e.g., Decision Tree #8 in ICH Q6A <i>Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances</i>)	Reference also Q6B: Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
3.0	318	Overage and Overfill	Add definition for Overage vs. Overfill "An overage is a fixed amount of the drug substance in the dosage form that is added in excess of the label claim" (From http://www.fda.gov/cder/guidance/1215dft.pdf Line 531-532) "Overfill is the volume or weight of the formulation filled in each container in slight excess of the labeled content" ((http://www.fda.gov/cder/guidance/1215dft.pdf Line 515-516)