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May 11, 2001

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

Subject: **Docket No. 01D-0056**
Guidance for Industry on Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines (March 2001)

The purpose of this document is to provide comment on the Food and Drug Administration's Draft Guidance for Industry "Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines" (March 2001).

Genentech, Inc. appreciates FDA's efforts to clarify and revise its regulations regarding pre- and postmarketing safety reporting requirements for human drug and biological products. This postmarking safety reporting guidance is a step in the right direction and incorporates final ICH guidance into applicable US safety reporting regulations. We encourage the FDA to finalize this guidance and incorporate it into applicable regulations as soon as possible (e.g., 21 CFR 314.80 & 600.80).

Genentech's primary comment regarding the FDA's postmarketing safety reporting guidance (PSRG) relates to term definitions used within the guidance document and their consistency across other FDA regulations and guidance documents. The other FDA draft guidance document that is most relevant to this discussion is the FDA's *Guidance for Industry: Content and Format of the Adverse Reactions Section of Labeling for Human Prescription Drugs and Biologics*, which was issued in May 2000. *Adverse Reactions* has been underlined because nowhere in the PSRG is this term defined or used.

In the FDA's PSRG, the term "adverse experience" is used. The FDA defines an *adverse experience* as "any undesirable event that is associated with the use of a drug or biological product in humans whether or not considered product related by the applicant." This could be interpreted as a somewhat contradictory definition because in the IND safety report regulation (i.e., 21 CFR 312.32), the FDA has defined *associated with the use of the drug* to mean "There is a reasonable possibility that the experience may have been caused by the drug."

Docket-016 misc ss

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These term inconsistencies become more evident and problematic when one compares the PSRG and labeling guidance documents. The labeling guidance document states: "In general, the ADVERSE REACTIONS section (of a US package insert) should include only information that would be useful to clinicians when making treatment decisions and in monitoring and advising patients. Long and exhaustive lists of every reported adverse event, including those that are infrequent and minor, commonly observed in the absence of drug therapy, or not plausibly related to drug therapy, should be avoided." All throughout the labeling guidance document the term *adverse reaction* is used.

In contrast, the PSRG defines an *expected adverse experience* as an "Adverse experience listed in the current FDA-approved labeling for the drug or licensed biological product. This would include any section of the labeling that refers to adverse experience information." Since the FDA's definition of an *adverse experience* is inclusive of undesirable events not considered product related by the applicant, this appears to represent a philosophical inconsistency in guidance documents. According to the FDA's draft labeling guidance, only *adverse reactions* (i.e., possibly related) are suppose to find their way into FDA-approved labeling.

RECOMMENDATIONS

1. Incorporate the exact ICH definitions of an **adverse event** (not adverse experience) and an **adverse drug reaction** (synonymous with adverse reaction) into the PSRG and applicable regulations.
2. Make explicit in the PRSG that all spontaneous reports are to be classified (by the applicant) as adverse reactions for regulatory reporting purposes, but not necessarily for future labeling purposes.
3. Make the glossaries in the PSRG and labeling guidance documents consistent.

We appreciate the opportunity to provide comment on this draft guidance document and

If you have any questions regarding this submission please contact Cheryl A. Madsen, Manager, Regulatory Affairs at (650) 225-3187.

Sincerely,

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