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

Subject: **Docket No. 98D-0813**
Guidance for Industry on Fast Track Drug Development Programs:
Designation, Development, and Application Review;
(Federal Register: November 18, 1998 [Volume 63, (63 FR 64093)])

Genentech Inc. commends the agency in drafting this well thought-out guidance document. This guidance will be very helpful to both agency and industry representatives in interpreting and seeking Fast Tract Designation (FTD).

We have specific comments for the FTD guidance document, but we would like to make the following general recommendations:

- For a clearer understanding of terminology used within the guidance, a consolidated glossary of terms should be provided. For example, definitions of what is meant by Fast Track Designation, Priority Review and Accelerated Approval and how they are different would ensure that the reader and author have the same point of reference. The convenience of a glossary would eliminate the need to have to go through each of the guidance attachments to find the definition of a term.
- We recommend that the agency reassess the strong focus of the guidance on Phase I given that only 25% of products that enter Phase I succeed to Phase III. It would seem unrealistic and burdensome to the Agency to load up the Fast Track queue with "potential" products when 75% of the products will not make it to Phase III. It is also unrealistic to expect a Sponsor to predict, with a high degree of assurance, the efficacy of a drug in Phase I development. We all believe in and have high expectations of our new drug products until proven otherwise. Therefore, we recommend that the Agency define very clear criteria for the demonstration of "potential" that sets a higher

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bar for products very early in development than those that have demonstrated efficacy in Phase II trials and lower still for those at the pre-NDA or -BLA stage.

- We recommend that the Flow Chart/decision tree in Figure 1 be modified to relate FTD, Priority Review, Accelerated Approvals and Treatment Investigational New Drugs (TINDs) to the drug development process. This would provide a quick reference to the Sponsor of options available and clarify when the Sponsor should approach the FDA.

SPECIFIC COMMENTS BY SECTION OF THE GUIDANCE:

SECTION I: INTRODUCTION

- This section was confusing to several of our reviewers. We recommend moving the first two paragraphs in Section IV to the beginning of this section. These paragraphs explain Fast Track Designation clearly.
- We recommend that the guidance decouple the concept of Fast Track from Treatments INDs. The explanation is confusing rather than elucidating. We recommend that the discussion of TINDs be moved to Section IV. Another possibility would be to add TIND to the logic tree schematic (Figure 1) as an option.

SECTION II: CRITERIA FOR QUALIFICATION AS A FAST TRACK DRUG DEVELOPMENT PROGRAM

II B. Demonstrating the Potential to Address Unmet Medical Needs

- We restate that we would like the Agency to re-evaluate the weight given to "demonstration of potential" for Phase I products vs. Phase III. We think that the criteria to demonstrate "potential" should be stricter for a Phase I product vs. Phase III.
- We would also like further clarification of what information the sponsor would need to provide to demonstrate the "potential" of a Phase I product. Could animal studies be used?

SECTION III: PROCESS FOR THE DESIGNATION OF A DRUG AS A PRODUCT IN A FAST TRACK DRUG DEVELOPMENT PROGRAM

This section is very clear on what and where to send the FTD submission what seems to be missing is guidance on format. Can the FTD submission be sent as an electronic submission?

SECTION IIIE: Continued Designation as a Fast Track Drug Development Program

- The statement "The Agency may choose to send a letter notifying the sponsor that the program is no longer designated as a FTD development program" raises some concerns. We would like consideration of the following recommendation:

If FDA believes that FTD status is no longer supported, the sponsor would be given written advance notice with a letter delineating the Agency's position and rationale for the planned withdrawal of the FTD status. In the letter to the Sponsor the Agency should request that the sponsor respond in writing to either concur (so that FTD status can be terminated) or provide for an appeal by refuting the basis for the determination within 60-day time period.

SECTION IV: PROGRAMS FOR EXPEDITING DEVELOPMENT AND REVIEW

A. Meetings

We recommend that the discussion of "Structure and content of an electronic submission" take place earlier in the process than at the pre-BLA meeting as suggested in the Guidance. There is a potential of delaying the submission considerably if there is a difference in what the Sponsor has prepared and what the FDA is expecting. Since the electronic portion of the submission is ideally created during the drug development process (examples: CRF images, datasets, etc.). It would be to the Sponsor's and FDA reviewers' advantage to agree upon the general format of the electronic submission early to make it more useful to the reviewer.

B. Written Correspondence

In the first bullet point "timely" maybe too open-ended. We would like a more specific definition of the Agency's expectation for "timely," e.g., 30 days.

C. Review Programs (d) Commencement of review

Recommend that wording be added that the Agency would communicate information during meetings to the Sponsor regarding whether or not early review was possible. This would assure both FDA and Sponsor have the same expectations.

Figure 1: Scheme for Determining Fast Track

To be a more useful and complete decision tree schematic, we recommend that the eligibility for accelerated approval and priority review be added.

If you have any questions regarding this information, please contact Taylor Burtis, Genentech Regulatory Affairs – Policy at (650) 225-7729.

Sincerely,

A handwritten signature in black ink, appearing to read "Robert L. Garnick for RLB". The signature is written in a cursive, flowing style.

Robert L. Garnick, Ph.D.

Vice President

Regulatory Affairs

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