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MILLENNIUM

15 July 2003

Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane
Rm. 1061 HFA-305
Rockville, MD 20852

Re: Draft Guidance for Industry – Continuous Marketing Applications: Pilot 1 – Reviewable Units for Fast Track Products Under PDUFA [Docket No. 2003D–0228, 68 *Federal Register*, 35903, 17 June, 2003]

Dear Sir or Madam,

Millennium Pharmaceuticals, Inc. ("Millennium") is a global research-based biopharmaceutical company and leader in genomic drug discovery based in Cambridge, Massachusetts with a European affiliate in London, UK. Millennium's research, development and commercialization activities are focused on genomic approaches to the innovation of breakthrough products to treat cancer and endocrine, metabolic, cardiovascular and inflammatory diseases. Millennium is grateful for the opportunity to provide comments for consideration on this important draft guidance.

Although the draft Guidance is generally practical and easy to understand, there seem to be some issues upon which greater detail would be helpful to industry sponsors.

1. We suggest that the language regarding eligibility for Pilot 1 be clarified. Since all Fast-Track designated products would be considered eligible for this Pilot program, what additional criteria will be used on deciding whether to accept an NDA or BLA into Pilot 1? Will this be based on resources or is it generally likely that most Fast-Track designated products would be included in Pilot 1 by mutual agreement of FDA and the company? Also, it should be mentioned, that non-acceptance into Pilot 1 does not affect the rights under Fast-Track designation to

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submit RUs of the NDA or BLA as part of a "rolling submission".

2. Is there a practical limit on the numbers of applications that can be accepted into Pilot 1 at the same time? Will all requests from equally qualified sponsors be accepted?

3. Under the recommendations for subsections to be considered for potential submission, please clarify that RUs pertaining to the drug product "alone" are not encouraged.

4. We believe that submissions of a CMC subsection RU on drug substance only would be inefficient in practice. For example, to extract the Drug Substance information from the Pharmaceutical Development Report (PDR) (Section P2 of the Common Technical Document (CTD)), and submit it separately, would provide very little context from which the reviewer would be able to comment. Specifically, the Drug Substance information in the PDR is written to support the development of the formulation.

5. Under Section B.6 Statistical Section, it should be clarified that statistical data and analyses are to be provided in each of the RUs as appropriate in support of the conclusions made.

6. Section C.1 describes the need for specified timelines and provides that failure of the applicant to meet projected timelines might result in removal from the pilot. What level of granularity is FDA expecting for timelines, e.g., to the day, week, month or quarter? Also, if a sponsor anticipates not meeting a specified timeline, will they have the option to negotiate an extension without risking removal from the pilot?

7. Under Section C.1 Process for Reviewable Units, it is unclear how RU subsections are prioritized. If a subsection undergoes review, does this preclude review of another subsection within this technical section?

8. It would be useful to have periodic reports on the status of Pilot 1, such as the number of Fast-Track products in the Pilot and the number and type of "subsections" being evaluated by each Division in the Pilot.

We thank you for the opportunity to comment and look forward to seeing clarifications of these questions in the next version of the guidance.

Sincerely,

Robert G. Pietrusko, Pharm.D.
Vice-President,
Worldwide Regulatory Affairs and Pharmacovigilance
Millennium Pharmaceuticals, Inc