

Aventis Pharmaceuticals

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August 12, 2002

Via Fax and UPS

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

Re: Docket No. 00N-1652

Proposed rule – Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format; 67 FR 22367 (May 3, 2002)

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. is pleased to provide the following comments on the above-referenced proposed rule entitled, "Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format". The FDA is proposing to amend its regulations governing the format in which certain labeling is required to be submitted for review with new drug applications (NDAs), certain biological license applications (BLAs), abbreviated new drug applications (ANDAs), supplements, and annual reports. The proposal would require that certain labeling content be submitted electronically, preferably in portable document format (PDF). The proposal would result in revisions to Title 21 of the Code of Federal Regulations, sections 314.50, 314.81, 314.94 and 601.14 to encompass submission of electronic labeling.

Page 22369, Section III: Description of the Proposed Rule:

This proposed regulation is in addition to 21CFR314.50(e)(2)(ii) requirement that copies of labeling be submitted. This should be clarified, especially in view of the *Guidance for Industry - Providing Regulatory Submissions in Electronic Format-NDAs* (64 FR 4432, January 28, 1999) and the *Guidance for Industry: Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format* (64 FR 61647, November 12, 1999) to determine if it will be necessary to provide additional labeling copy above that already provided electronically as PDF files when submitting labeling electronically as part of an NDA, sNDA, BLA or sBLA.

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Recommendation/Comments: Clarify within the proposed *Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format* if additional electronic files should be provided to meet this requirement when providing entire regulatory submissions in electronic format. If additional labeling will be required to satisfy this proposal, also amend the *Guidance for Industry - Providing Regulatory Submissions in Electronic Format - NDAs* and *Guidance for Industry: Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format* to include this electronic labeling as an additional review aid over the word-processed review aid already required.

Pages 22371, 22372, Section VI: Paperwork Reduction Act

For new NDAs, ANDAs and BLAs the agency is estimating that the additional time required for submission of the content of labeling in electronic format for these applications will be less than 15 minutes. For labeling not already in electronic format the time required to put labeling content into an electronic format and convert it to a PDF file will be approximately eight hours.

Recommendation/Comments: While Aventis agrees that it would generally take less than 15 minutes to create a PDF file from an electronic word-processed document, this does not take into account the time required to proofread and, if necessary, correct the PDF document compared to the word-processed version. Conversion of word-processed documents to PDF versions may distort or change text format or symbols if fonts have not been embedded as required using software such as ADOBE ACROBAT to create PDF files. Based on the average size of current US prescribing information it may take on average an additional four hours to complete proofreading of these documents.

Additionally, based on the average size and content of current prescribing information, creation of a new file in electronic format would take considerably longer than eight hours if the time spent for proofreading of both the word-processed and PDF versions are considered. We estimate that the process would take on average between 16 and 20 hours per package insert.

Pages 22374, 22375: Part 314 – Applications for FDA Approval to Market a New Drug and Part 601 – Licensing

These sections of the proposed revised regulations apply to filing of a new drug or biologic product and to the submission of labeling for post marketing reports. There is no mention of submission of labeling supplements to the NDA or BLA as described in 314.70 and 601.12.

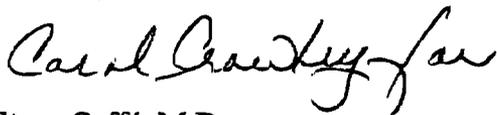
Recommendation/Comments: In addition to the citations already mentioned within the proposed regulations, describe the requirements for electronic submission of labeling in PDF format for labeling submitted as either draft for approval or changes being effected under 21 CFR 314.70 and 601.12.

Labeling Negotiations and Review: While not specifically mentioned within the proposed regulations, use of electronic documents could also enhance the labeling review and approval between the sponsor and the FDA.

Recommendation/Comments: In addition to the use of these documents by FDA as an electronic method of comparison between new and past labeling, consideration should be given to using these documents and/or the word-processed versions (e.g., original labeling prepared using Microsoft WORD) in a secure electronic mail exchange system between sponsors and the agency during labeling negotiations. The proposed regulations could be further expanded to request word-processed versions of labeling in addition to the PDF versions. This could enhance the preparation and review of initial and interim labeling submissions during labeling negotiations prior to final agency or sponsor action regarding labeling approval.

On behalf of Aventis Pharmaceuticals Inc., we appreciate the opportunity to comment on the proposed rule on "Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format" and thank you for your consideration.

Sincerely,



Steve Caffé, M.D.

Vice President, Head US Regulatory Affairs



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FAX

Date: August 13, 2002

Number of pages including cover sheet: 4

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REMARKS: Urgent For your review Reply ASAP Please comment

Dear Sir/Madam:

Attached please find comments regarding Proposed Rule – Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format; 67 FR 22367 (May 3, 2002).

Should you have any questions, please call me at your convenience.

Regards,

Jackie Knoble