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Wyeth

August 25, 2003

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

RE: Comment on Docket No. 2003D-0231
Providing Regulatory Submissions in Electronic Format – Postmarketing Periodic Adverse Drug Experience Reports

Dear Sirs:

Wyeth Pharmaceuticals (Wyeth) hereby submits comments to Docket No. 2003D-0231 pertaining to the draft guidance, **Providing Regulatory Submissions in Electronic Format – Postmarketing Periodic Adverse Drug Experience Reports,** published in the *Federal Register,* Volume 68, Number 121, pages 37504-37505 (June 24, 2003).

Wyeth is one of the world's largest research-based pharmaceutical and healthcare products companies, and is a leading developer, manufacturer and marketer of prescription drugs, vaccines and over-the-counter medications.

We fully support the Agency's efforts in developing guidance for the electronic submission of post-marketed periodic safety reports. Specific comments on FDA's draft guidance are attached. In addition to these specific comments, Wyeth has four general comments on the proposed guidance:

- Wyeth requests that FDA clarify how this draft guidance fits with FDA's March 14, 2003 proposed rule, Safety Reporting Requirements for Human Drug and Biological Products (the "proposed rule"). 68 FR 12406. That is, if finalized with substantially the same requirements as drafted, the proposed rule would result in substantial changes to the current periodic reporting requirement by requiring periodic safety update reports (PSURs). Wyeth questions whether industry should spend time and resources developing systems and practices to conform with the current proposed guidance when the requirements for periodic reporting might

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change – this is particularly true since the Agency has indicated in the draft guidance that it will suggest a different method for electronic submission of PSURs than periodic reports. Wyeth recommends that any final guidance developed by FDA be handled in conjunction with the implementation of the final rule on safety reporting, with whatever final periodic reporting requirements are contained therein.

- Wyeth suggests that FDA consider revising the guidance to permit all electronic submissions through FDA's Electronic Data Interchange (EDI). The current proposed guidance anticipates a process whereby individual case safety reports, attachments, and descriptive information are sent using different electronic methods. This proposal appears inefficient and would require industry to maintain separate tracking mechanisms for each of the various components of a periodic submission.

- FDA has issued various draft guidances on electronic submissions from 1999 to the current draft. Given the Agency's thinking about electronic submissions has changes over time; the guidances do not all suggest the same methods of compliance. To avoid confusion, Wyeth suggests that the Agency incorporate all of their thoughts on electronic submission in one final guidance document. The Agency can then revise that one guidance going forward. This approach would ease the compliance burden on the industry and simplify FDA's updating of the guidance document.

- Wyeth suggests that FDA allow for a period of time during which industry could test transmission of electronic periodic reports to FDA.

- We request that FDA clarify the relationship between the draft guidance and the evolving guidance for the electronic Common Technical Document (eCTD).

This letter with its attachment is submitted in duplicate. Wyeth appreciates the opportunity to provide this constructive input to the rulemaking process. Please contact the undersigned at 484-865-3794 if there are any questions regarding the submitted comments.

Sincerely,

Roy J. Baranello, Jr.
Assistant Vice-President
Worldwide Regulatory Affairs
Attachment.

Wyeth Comments on Guidance for Industry Providing Regulatory Submissions in Electronic Format – Postmarketing Periodic Adverse Drug Experience Reports

Line	Comment
Line 63-64	Although FDA states that the proposals in the guidance should be viewed as recommendations only, FDA also counsels industry to contact the Agency if they wish to submit reports in a manner other than described in the guidance. Please clarify that the Agency is not imposing a substantive requirement that companies submit periodic reports electronically or in the manner described in the draft guidance.
Lines 143, 149, 153	FDA requests that the "protected physical media…be attached securely to a jacket." Please clarify what FDA considers an acceptable jacket and whether clearly labeling CDs containing submission data would be sufficient.
Lines 185-197, 194-201	FDA states that they anticipate that it will take 24 hours to receive ICSR submission acknowledgements. Wyeth suggests that this turn around time is too long and may result in late reports if any issues with transmissions are not picked up quickly enough. Although FDA has stated that it will work with applicants to avoid late reports, a quicker acknowledgement time would reduce the amount of negotiation needed between FDA and industry. FDA also states that the date of the acknowledgement will serve as the official FDA receipt date. Wyeth suggests that FDA harmonize with the EMEA whose first acknowledgement (and the official submissions date) is marked at the Gateway Received point.
Lines 203-207	FDA has requested that companies not re-send submissions electronically if the gateway or AERS is non-functional; rather, companies should submit paper copies to meet their regulatory reporting time-frames. Wyeth requests clarification on FDA's flexibility on this point.
Lines 232-234	FDA states that the receipt date of a report is the date it arrives at the Agency. Please clarify that the submission date (the date by which compliance to reporting time frames has been measured by the Agency in the past) remains the day a report is submitted by the applicant.
Lines 249-262	FDA anticipates different sections of the periodic report may be submitted to the Agency on different days and notes that applicants must plan submissions accordingly to ensure timely reporting. Wyeth requests clarification on the date applicants should use as the official submission date for the periodic report.
Lines 277-288	FDA suggests that applicants use the preferred term from MedDRA that most closely corresponds to the term

Line	Comment
	used for the event by the original reporter. Wyeth requests clarification of FDA's expectation regarding timing of applicants using MedDRA upgrades.
Lines 319-329	FDA provides a different suggestion for including follow-up information in the narrative of an electronically submitted ICSR than was suggested for paper submissions of ICSRs in the March 2001 draft guidance Postmarketing Safety Reporting for Human Drugs and Biological Products Including Vaccines. Wyeth suggests that FDA adopt one suggested standard for narratives and that this suggestion be part of any implementation of FDA's proposed safety rule. The issuing of various draft guidance documents with conflicting suggestions is confusing and unnecessarily burdensome on industry.
Lines 356-358	Please provide additional guidance regarding bookmarks for each PDF for descriptive information.