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US Food and Drug Administration
Division of Dockets Management (HFA-305) 41 '03 OCT -1 A9:36
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: Docket No. 2003N-0268
Federal Register: June 30, 2003 (Volume 68, Number 125)
Agency Information Collection Activities; Proposed Collection; Comment Request, Biological Products: Reporting of Biological Products Deviations in Manufacturing

Dear Sir/Madam:

PDA appreciates the opportunity to comment on the questions presented in the Federal Register notice referenced above. PDA is an international professional organization representing over 10,500 scientists and experts involved in the manufacturing and quality aspects of medicinal products. PDA has a tradition of constructive consultation with the regulatory authorities with the goal of GMP guidance that is clear, appropriate and consistent with current industrial practice. Our comments are listed below in order of the 4 topics for comment listed in the notice. These comments reflect the perspectives of the PDA and its members, including representatives from the traditional biologics industry, the biotechnology industry and the pharmaceutical industry.

(1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility

As per PDA's comments of December 22, 1997 (proposed changes to 21 CFR 601.14), PDA remains confident that the intent of the 21 CFR 600.14 regulation is covered by the 21CFR314.81(b)(1), NDA Field Alerts Reports (which already cover "biologics" that are filed as NDAs). The adoption of the NDA field alert regulations for all biologics would streamline compliance activities for both the FDA and the industry and would facilitate and align the recent transfer of biotech products from CBER to CDER. In this regard, it is important to consider that specified biologics, vaccines and other traditional biologics are governed by the same CGMP requirements as the majority of products regulated by CDER. The compliance expectations for the identification, investigation and resolution of manufacturing deviations are the same. The existing NDA Field Alert regulations have historically provided adequate surveillance and notification for distributed drug products.

Additionally, PDA feels that in keeping with the spirit of the current "GMPs for the 21st Century" initiatives, revocation of the existing 21 CFR 600.14 would lessen the reporting burden while continuing to support the industry in

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making good, risk based quality decisions. PDA still believes that harmonization with 21 CFR 314.81(b)(1) would reduce the burden of unnecessary regulation without diminishing public health protection.

Finally, PDA feels it is difficult at this time to fully assess the utility of the current reporting system as the manner in which the collected information is actually used at the FDA is not clear from the FR Notice, nor any other official FDA publication.

2) The accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used

Similar to PDA's comments on FDA's estimates of the burden of GMP regulations (February 22, 1999, Docket No. 98N-1110), PDA feels the current estimate of 2 hrs per report grossly underestimates the time needed to draft, review and verify the report information, circulate and file the report within the firm, publish the information and/or load the information onto FDA's web site.

PDA is not clear as to the methodology and assumptions employed by FDA to determine the 2 hours annually figure described in the FR Notice dated November 7, 2000. PDA assumes that FDA's estimate merely covers the average time necessary to simply fill out the electronic form and submit the form electronically, which is an unfair estimation of the true burden on the sponsor for complying with this reporting requirement. As reported by a number of PDA's member companies, a conservative estimate of the associated activities is approximately 20 person hours (ten times the FDA's estimate) per report.

In addition to the estimated 20 hrs per report, additional time is required to update SOPs associated with this regulation and to perform ongoing training of staff on SOPs associated with this regulation. The burden of this activity would largely be dependent on the number of staff receiving ongoing training on this regulation and the associated SOPs.

(3) Ways to enhance the quality, utility, and clarity of the information to be collected

As it is not clear to PDA how this information is used by the FDA, it is difficult to respond to this particular question, especially the utility of the information. Furthermore, PDA remains confident in its position that harmonization with NDA field alert regulations (21 CFR 314.81(b)(1) adequately covers all biologics and would serve to enhance the quality, utility and clarity of information to be collected, therefore the existing 21 CFR 600.14 regulation is not necessary.

Several recommendations for enhancement of the quality and clarity of the information to be reported as well as the mechanisms available for reporting under 21 CFR 600.14 have been articulated by PDA in our comments of November 12, 2001 regarding the *Draft Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components* (Docket No.: 01D-0221).

(4) Ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

While PDA continues to believe that 21 CFR 600.14 is not a necessary regulation and therefore, comment on this question is not particularly relevant to PDA's position; clarity regarding the utility of the information collected would be of interest. PDA does feel it is important to note several points in this regard.

The FDA FY01 Annual Summary of Biological Product Deviation Reports identifies 1153 (4.5%) of reports submitted that did not meet the threshold for reporting. No numbers were reported in the FY02 Annual Summary. PDA requests that FDA share the criteria by which reports are deemed "not meeting the threshold for reporting". If this regulation remains or during an interim period prior to revocation, PDA feels that firms should be alerted when reports are submitted that do not meet the threshold so as to further reduce the burden of the collection of information for these reports.

It is also very important to note that many firms are uncomfortable with electronic submissions of these reports as it is felt that there are inadequate safeguards to assure the reports are in fact coming from the firm identified in the report and are not false reports.

PDA appreciates this opportunity to provide comments and looks forward to the outcomes of this request for comment and any opportunity for further dialogue on this important topic. Please contact me if you have any questions.

Sincerely,

William Stoedter, RAC
Director of Regulatory Affairs
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