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Assistant General Counsel



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By Messenger

February 14, 2000

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

RE: FDA's Proposed Rule on Postmarketing Studies for Human Drugs and Licensed Biological Products; Docket No. 99N-1852

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, happier, healthier and more productive lives. Investing over \$24 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures. PhRMA is pleased to submit these comments on FDA's Proposed Rule on Postmarketing Studies for Human Drugs and Licensed Biological Products.

As noted in the attached comments, some aspects of the proposed rule implement section 130 of the FDA Modernization Act of 1997 (FDAMA) in a straightforward manner but other aspects would impose significant new reporting and public disclosure requirements on pharmaceutical manufacturers. PhRMA proposes some specific changes in the proposed rule to modify the aspects of the proposed rule that exceed the requirements of FDAMA section 130. PhRMA urges FDA to accept these recommendations and limit the potential for duplicative reporting and the inappropriate disclosure of confidential commercial information.

Sincerely,

A handwritten signature in black ink that reads 'Marjorie E. Powell'.

Marjorie E. Powell

Enclosure

Comments Of The Pharmaceutical Research And Manufacturers Of America On
Proposed Rule On Reporting Postmarketing Studies

99N-1852

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Pharmaceutical Research and Manufacturers of America

February 14, 2000

**COMMENTS OF THE PHARMACEUTICAL RESEARCH AND
MANUFACTURERS OF AMERICA**

On

PROPOSED RULE ON REPORTING POSTMARKETING STUDIES

DOCKET NO. 99N-1852

**SUBMITTED TO THE DOCKETS MANAGEMENT BRANCH (HFA-305),
FOOD AND DRUG ADMINISTRATION**

The Pharmaceutical Research and Manufacturers of America (“PhRMA”) submits these comments on the proposed rule FDA published to implement section 130 of the FDA Modernization Act of 1997 (“FDAMA”)¹ and to establish revised reporting requirements for certain postmarketing studies on human drugs and biologics.² PhRMA represents the country’s leading research-based pharmaceutical and biotechnology companies. PhRMA companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. Investing over \$24 billion a year in discovering and developing new treatments, PhRMA companies are leading the ways in the search for cures.

As pioneers in the discovery and development of new medicines, PhRMA companies are directly affected by FDA’s postmarketing reporting requirements and the new proposed rule. Certain aspects of the proposed rule implement section 130 of FDAMA in a straightforward manner that integrates the new statute with FDA’s existing regulations.

¹ Codified as Section 506B of the Federal Food, Drug, and Cosmetic Act (“FDCA”) (21 U.S.C. § 356b).

² See 64 Fed. Reg. 67207 (Dec. 1, 1999).

However, other parts of the proposed rule would impose significant new reporting and public disclosure requirements. These expanded reporting and disclosure requirements exceed the scope of FDAMA and FDA's current regulations, and are without justification. Accordingly, substantial revisions should be made to the proposed rule.

Specific comments on the objectionable aspects of the proposed rule follow.

1. CONTENT OF STATUS REPORTS

Section 130 of FDAMA is quite straightforward in the information it requires sponsors to submit in their status reports to FDA on postmarketing study commitments. The statute states in plain terms that sponsors shall submit "a report on the progress of the study or the reasons for the failure of the sponsor to conduct the study." FDCA § 506B(a)(1); 21 U.S.C. § 356b(a)(1). The statute further provides that FDA shall establish the form for such reports by regulation, but the content of the reports is clear from the statute itself. Only limited basic information is to be provided on the status of a covered postmarketing study commitment.

FDA's proposed rule turns the simple reporting requirement contemplated by FDAMA into a potentially complicated and burdensome exercise. For example, sponsors must provide detailed information on the postmarketing study commitment related to the study purpose, patient population, indications and dosages. See Proposed 21 C.F.R. § 314.81(b)(2)(vii)(a) & (viii). Sponsors must further report on patient accrual, initiation dates for different study phases, and projected completion dates, and explain the study's status (which would be categorized separately). Id. This information well exceeds that necessary to determine "the progress of the study or the reasons for the failure of the sponsor to conduct the study."

There is no reason to expand the postmarketing reporting obligations imposed on a sponsor in this manner. The essential information on the status of the study is already captured in the standardized categories FDA has identified in the proposed rule (pending, ongoing, delayed, terminated, submitted). This use of standardized descriptions accords with the approach set forth for tracking and reviewing Phase IV commitments in FDA's existing Manual of Policies and Procedures (MAPP 6010.2). Section 130 of FDAMA does not call for any additional information. The only instance in which any further explanation is required is when a sponsor must set forth the reasons for its failure to conduct a study. FDA's current regulations also do not call for any further information, since those regulations set forth no particular requirements for the content of status reports.

The proposed rule thus represents a significant and unwarranted departure from current practice and the plain provisions of FDAMA. PhRMA recommends that the proposed rule be revised to require sponsors simply to identify a pertinent postmarketing study commitment and report on its status using a standardized description. If individual sponsors wish to include additional details, that should be left to their discretion.

2. PUBLIC DISCLOSURE OF INFORMATION

Perhaps the most serious issue raised by the proposed rule is its potential to disclose confidential and highly sensitive commercial information to the public. These public disclosure provisions of the proposed rule are based on a misreading of FDAMA and are contrary to established law under the Freedom of Information Act ("FOIA").

Section 130 of FDAMA is very clear in its specification of what information is to be considered public. The only information deemed public is that information that “is necessary (1) to identify the sponsor; and (2) to establish the status of a study described in subsection (a) and the reasons, if any, for any failure to carry out the study.” FDCA § 506B(b); 21 U.S.C. § 356b(b). The statute on its face indicates a clear intent to limit public disclosure to certain core information necessary to identify the sponsor and the status of a study, or the reasons for any failure to carry out a study commitment. The only information that falls within these narrow parameters is the standardized information that a sponsor reports on the status of a study (pending, ongoing, delayed, terminated, submitted), or, if applicable, a brief statement of why a study was not carried out.

FDA’s proposed rule directly violates the limits set by FDAMA when it calls for the disclosure of the study protocol, patient accrual rates, reports of unexpected suspected adverse drug reactions, and study results. See Proposed 21 C.F.R. § 314.81(b)(2)(vii)(b). The preamble to the proposed rule is simply wrong when it asserts (64 Fed. Reg. at 67211) that this additional information is “necessary to identify the sponsor and to establish the status of a study.” The proposed rule calls for disclosure well beyond such necessary information, and thus violates the limits established by FDAMA.

The proposed rule is also flatly contrary to FOIA and the Trade Secrets Act. FOIA specifically exempts confidential commercial information from public disclosure. 5 U.S.C. § 552(b)(4) (so-called “FOIA Exemption 4”). And the Trade Secrets Act makes it a crime for a federal employee to disclose any information within the scope of FOIA Exemption 4,

including confidential commercial information. 18 U.S.C. § 1905; see also FDCA § 301(j); 21 U.S.C. § 331(j).³ Section 130 of FDAMA was enacted against the well-established statutory backdrop and the FOIA exemption for confidential commercial information. There is nothing in the legislative history of FDAMA to suggest that Congress intended to make public information that would otherwise be exempt from disclosure under FOIA, except to the very narrow extent necessary to identify a sponsor and establish the status of a study. The assertion in the preamble to the proposed rule (64 Fed. Reg. at 67212) that FDAMA constitutes statutory authorization to disclose information that is otherwise nondisclosable is wholly unsupported.

Finally, the public disclosure provisions of the proposed rule also represent bad science. It is generally not appropriate to “peak” at results from a study before its scheduled completion. Sponsors will of course report adverse events to FDA as required. However, there is no public good to be served in releasing early, and more than likely incomplete, safety or efficacy data. If FDA has a specific reason to ask for additional information from an ongoing study, sponsors would ordinarily comply voluntarily, to the extent an ongoing study would not be jeopardized. But there is no added value, and indeed a potential downside, to requiring such disclosure as part of an ongoing update procedure.

³ This principle is recognized in the caselaw. See McDonnell Douglas Corp v. NASA, 180 F.3d 303, 305 (D.C. Cir. 1999); CNA Fin. Corp v. Donovan, 830 F.2d 1132, 1151 (D.C. Cir. 1987), cert. denied, 485 U.S. 977 (1988). It is also reinforced in the Department of Justice’s Freedom of Information Act Guide (Sept. 1998) (available at <www.usdoj.gov/oip/exemption4.htm>). The “practical effect” of the Trade Secrets Act is to limit an agency’s ability to make a discretionary release of otherwise exempt material, because to do so in violation of the Trade Secrets Act is not only a criminal offense, but constitutes “a serious abuse of agency discretion’ redressable through a reverse FOIA suit.” DOJ Guide.

In light of these serious concerns, PhRMA asserts that the proposed rule must be revised. First, in accordance with Section 130 of FDAMA and FOIA, the only information that should be required to be disclosed should be basic information to identify the study and sponsor, and the standardized information on the status of a study (or, if applicable, a brief explanation of why a study was not conducted).⁴ Second, an efficient procedure should be established to identify the information that is disclosable. PhRMA suggests that sponsors be instructed to include a section in their postmarketing status reports that is specifically intended for public disclosure. This approach is consistent with that adopted recently by FDA for information provided by sponsors to advisory committees in connection with open advisory committee meetings. See Guidance for Industry, “Disclosing Information Provided to Advisory Committees in Connection with Open Advisory Committee Meetings Related to the Testing or Approval of New Drugs and Convened by the Center for Drug Evaluation and Research, Beginning on January 1, 2000” at 3-4 (Dec. 1999).⁵ If FDA disagrees with the sponsor’s designation of disclosable information, the agency should then consult with the sponsor.

⁴ This should also be the only information posted on FDA’s web site.

⁵ PhRMA objects to many aspects of this draft guidance and will be submitting comments accordingly. However, PhRMA agrees with the concept set forth in the draft guidance of identifying in advance the portions of a submission that may be released.

3. IMPLEMENTATION SCHEME AND EFFECTIVE DATE

Section 130 of FDAMA indicates that sponsors should have six months following the issuance of final regulations to submit initial reports on postmarketing study commitments. See FDCA § 506B(a)(2); 21 U.S.C. § 356b(a)(2). Consistent with this six-month implementation period, FDA should provide that the effective date of any final rule will be 120 days after publication of the rule in the Federal Register. FDA currently proposes that any final rule would become effective 90 days after publication in the Federal Register. See 64 Fed. Reg. at 67212. With a 90-day effective date, a sponsor could be required to submit an initial report five months following publication of the final rule, depending on the anniversary date of their products.⁶ This is not consistent with FDAMA, and PhRMA urges that it be modified to ensure that all sponsors will have at least six months to file reports under the new requirements.

PhRMA also recommends that FDA set some reasonable limit on how far back it will reach in requiring sponsors to report on studies they agreed to conduct years before enactment of Section 130, but that remain open for some reason or another. For example, FDA could provide that no reporting obligation exists for a study agreement entered into more than three years ago.

⁶ For example, if the anniversary of a product's approval occurred 91 days following publication of the final rule, the sponsor would have to submit a report within 60 days of that anniversary date. Thus, the sponsor would be required to submit an initial report within 151 days of issuance of the final rule. This is less than the six-month implementation period contemplated in section 130 of FDAMA.

4. AVOIDING DUPLICATIVE REPORTING

The proposed rule risks imposing duplicative reporting obligations on sponsors. Much of the information required to be submitted in an NDA annual report under the proposed rule must already be submitted to an IND. This risk of duplicative reporting burdens is exacerbated by the fact that NDA and IND anniversary dates may differ. Thus sponsors may essentially be required to collect and reconcile information for the same postmarketing studies twice a year.

PhRMA recommends that two main steps be taken to address this concern. First, FDA should scale back the scope of information required to be submitted to the NDA annual report. FDA has expanded the content of required status reports beyond that provided for by FDAMA, as discussed in Section 1 above, and this expanded scope exacerbates the problem of duplicative reporting. Second, FDA should specify in any final rule that an NDA annual report may reference pertinent sections of an IND and IND annual report. The IND information must be treated confidentially in accordance with FOIA and the Trade Secrets Act, as discussed in Section 2 above.

5. TERMINATION OF REPORTING REQUIREMENTS

The proposed rule provides that status reports must be submitted on postmarketing study commitments until FDA notifies the sponsor in writing that the requirement has been fulfilled, is no longer feasible, or would no longer provide useful information. Proposed 21 C.F.R. § 314.81(b)(2)(vii). The proposed rule should further provide that FDA will respond within a set time after the response to a commitment has been filed and notify the

sponsor whether the requirement has been fulfilled. A 60-day response time would be reasonable.

* * *

FDA's proposed rule effectively integrates the implementation of Section 130 of FDAMA with FDA's existing postmarketing study reporting regulations. However, the proposed rule also inappropriately expands the reporting obligations imposed on sponsors and risks the disclosure of confidential commercial information to the public. These aspects of the proposed rule deviate from the clear requirements of FDAMA, FDA's own existing postmarketing reporting regulations, and long-established FOIA law. None of these objectionable aspects of the proposed rule are needed to create a stronger and more complete program for FDA's oversight of phase IV study commitments, and they should be eliminated in any final rule.