



June 8, 2000

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

Re: Docket No. 99N-4783; Administrative Practices and Procedures; Good Guidance Practices; Proposed Rule (65 Federal Register 7321-7330, February 14, 2000); Addendum to Comments Previously Submitted

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is submitting this set of comments on the proposed rule on Good Guidance Practices (GGPs) as an addendum to those filed earlier. While PhRMA recognizes that the comment period has closed, we trust that these additional comments will be reviewed as the FDA moves forward to finalize this critical regulation.

Comments on the Proposed Rule

As noted in our earlier comments, PhRMA members have benefited from many FDA guidance documents that provide constructive and thoughtful insight into FDA's current thinking on various topics. PhRMA supports FDA's effort to establish a transparent system for the development, issuance, timely revision, and appropriate use of guidance documents. PhRMA also supports the concept that the scope and content of guidance documents will benefit from meaningful opportunities for constructive input and participation of all stakeholders. Finally, PhRMA supports the concept that the process for development, issuance, timely revision, and use of guidance documents should be consistent across all parts of FDA.

Preamble of Good Guidance Practices (GGPs):

PhRMA's member companies have had significant operational experience with the many FDA guidance documents, including the guidance documents issued in draft or final form in the post-FDAMA era. As FDA strives to issue new guidances on appropriate topics, as

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well as revise and re-issue outdated guidances, PhRMA recommends that FDA include in the preamble to the final rule on GGP's of generally accepted principles of "good" guidances. We believe that PhRMA, FDA, and other stakeholders can embrace the following generally accepted principles of a "good" guidance document:

- The guidance provides insight into FDA's current thinking, as well as FDA's regulatory, scientific, and administrative intent for the guidance.
- The guidance is consistent with contemporary knowledge in science and medicine.
- The guidance is prepared with public participation, except in rare and extraordinary circumstances.
- The guidance is written with full awareness of other widely recognized and relevant sources of scholarly thinking (such as ICH guidelines, CPMP documents, or pharmacopoeial standards) so that the guidance will either be consistent with these other sources or have clearly justifiable inconsistencies.
- The guidance is practical in its operational implications, i.e., it describes activities that can be made operational on a routine basis.

PhRMA asserts that guidances with such properties will facilitate both efficient drug development and appropriate implementation of regulation.

Finally, with respect to general principles, PhRMA recommends that FDA make explicit the point that a guidance document applies to all parties who may undertake work in the area addressed by the guidance. Historically, situations have arisen where apparently different guidance has been applied to work undertaken by different sponsors (e.g., large pharmaceutical companies, start-up companies, academic sponsors, etc.). FDA guidance should be uniformly applicable to all.

Proposed § 10.115 (f)(4): Annual Publication of List:

FDA's current practice is to publish a list of proposed guidances semi-annually. However, in the proposed rule, FDA proposes to publish, once a year, a comprehensive list of guidance documents under development or revision. This annual frequency would be reasonable if supplemented by two things:

- the status of each item (i.e., whether each guidance has issued in draft or final form).
- FDA's identification of the highest priority guidance documents for the next year (e.g., identification of the top 10 guidance documents for action in each Center).

Such proactive identification of the highest priority guidance documents would facilitate alignment of stakeholders with FDA and thereby enable stakeholders with special expertise on a specific topic to develop and submit early input to FDA. In PhRMA's

view, such early input comprises an opportunity for FDA to take advantage of potential synergies with stakeholders; Dr. Henney recently solicited ideas for such synergies through meetings with stakeholders in Palo Alto, CA (March 2000) and Durham, NC (April 2000).

Proposed § 10.115 (g)(1)(v): Issuing a Second Draft of a Guidance for Public Comment:

The proposed rule allows FDA the option to issue a second draft guidance, but no circumstances are described where this is likely. In our view, two particular situations usually merit issuance of a second draft guidance, with an additional request for comments, prior to finalization of the guidance.

First, a second draft guidance may be necessary when the first draft guidance on a medical or scientific topic is highly controversial, as reflected by the comments to the Docket and multiple explicit requests for a second draft, particularly when requested by multiple stakeholders. Such first draft guidances may be the subject of consultation by FDA with one of its Advisory Committees. PhRMA recommends that such guidances will usually merit preparation and issuance of a second draft guidance.

Second, comments demonstrating that aspects of first draft guidance are in conflict with other widely recognized sources of scholarly guidance (such as ICH guidelines, CPMP documents, or pharmacopoeial standards) will usually merit preparation and issuance of a second draft guidance.

Proposed § 10.115 (g)(2): Issuance of a Level 1 Guidance with No Prior Public Participation:

The proposed rule gives FDA the authority to issue a Level 1 guidance, in final form, in situations where prior public participation is "not feasible or appropriate." Based on information in the preamble (pages 7324 and 7326), PhRMA understands that FDA has identified the following three circumstances in which FDA may issue a Level 1 guidance as final, without prior public participation:

- (1) There are public health reasons for immediate implementation of the guidance document;
- (2) There is a statutory requirement, executive order, or court order that requires immediate implementation; or
- (3) The guidance document presents a less burdensome policy that is consistent with public health.

Importantly, the proposed rule also states that FDA “reserves the authority to provide for other exceptions that are consistent with section 701(h)(1)(C) of the act, if the need arises.”

PhRMA recommends that FDA make clear in the proposed rule that, consistent with Congressional intent, the Agency may waive the requirement for prior public participation “only in rare and extraordinary circumstances where there is a compelling rationale,” including “reasons such as public health.” H. Rep. 105-310, at 74 (1997). The current preamble language stating that FDA will follow the statute is insufficiently clear in this regard and lacks this important detail that stakeholders reasonably expect in this rule.

In summary, lack of public participation in the guidance development process is undesirable, and should be reserved for rare and extraordinary circumstances.

Proposed § 10.115 (g)(4): Issuance of a Level 2 Guidance:

The proposed rule describes it as the exception, rather than the routine, that FDA will seek public comment on Level 2 guidances prior to issuance. The preamble (page 7325) notes that FDA may, in its discretion, seek public comment on a Level 2 guidance before it is implemented. In addition, the proposed rule states that the availability of Level 2 guidances will be known by virtue of posting on FDA's internet site, rather than publication of a notice in the Federal Register.

PhRMA believes that the quality of Level 2 guidances would benefit from participation by the public, prior to issuance as a final guidance. Level 2 guidances can include revisions of substantive guidances for development of disease-specific therapies; such work, that may result in minor or greater changes in a guidance which a sponsor is already following for development of an investigational drug, is of keen interest to PhRMA members. In such circumstances, particularly when an existing guidance may be superseded, the formal opportunity for comment following a notice in the Federal Register provides an important and well-established means of formal notice to the sponsor (and other stakeholders) about the change in FDA's current thinking. Therefore, PhRMA recommends that FDA provide notice and an opportunity for comment.

Proposed § 10.115(i): Standard Elements in a Guidance Document:

In addition to the other elements identified in the proposed rule, PhRMA suggests that each guidance document (and draft guidance) include a statement identifying its “Level.” Moreover, if the guidance is a “Level 1” guidance, and has been issued without prior public participation, the guidance should set forth the reasons for FDA’s determination that prior public participation was “not feasible or appropriate.” This information will

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assist all stakeholders by indicating whether public input was sought before a guidance's issuance; whether FDA intends the guidance as a means for communicating new or different regulatory policies or interpretations; and whether FDA believes there to be an urgency or other circumstance justifying implementation of the guidance without prior public participation.

Early Input into Development of Guidances:

PhRMA strongly supports FDA's recognition, as stated in the preamble (pages 7324 and 7326), that it is important to solicit and accept early input on guidances to be developed, including acceptance of actual draft guidances from stakeholders.

PhRMA hopes that you find these comments useful and constructive. PhRMA members would be pleased to discuss these comments with you in person or via teleconference, at your request. PhRMA welcomes future opportunities to work with you and other colleagues to contribute to the development of ever improving guidance documents. Thank you for your consideration of these comments.

Sincerely,



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PhARMA

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