

# *Bulk Pharmaceuticals Task Force*

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June 21, 2004

## **Via Facsimile and Mail**

Dockets Management Branch (HFA-305)

Food and Drug Administration

5630 Fishers Lane

Room 1061

Rockville, MD 20852

**Re: Docket Nos. 2003D-0060; Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures -- Scope and Application;" Availability.**

Dear Sir or Madam:

The Bulk Pharmaceutical Task Force (BPTF) of the Synthetic Organic Chemical Manufacturers Association appreciates the opportunity to provide comments on the Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures – Scope and Application." BPTF is committed to aiding in the promotion of public health and would like to work closely with the Food and Drug Administration (FDA) as it develops regulations and guidance materials for Part 11.

We would like to begin by introducing our organization to FDA. BPTF is an association for manufacturers of active pharmaceutical ingredients (APIs), excipients, and intermediates committed to excellence in cGMP compliance and regulatory solutions. One of our primary goals is to seek clarification of the status and treatment of APIs, which is often uncertain under current regulation and policy. The Task Force coordinates these efforts on behalf of SOCMA, the leading trade association of the specialty-batch and custom chemical industry. The association represents 300 member companies with more than 2,000 manufacturing sites and 100,000 employees. The membership includes representatives from each segment of the industry – from small specialty producers to large multinational corporations.

The following comments are submitted in response to the publication of the Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures – Scope and Application." BPTF welcomes this guidance on the scope and application of Part 11. However, BPTF is concerned about the applicability of Part 11 to API manufacturers.

The 28<sup>th</sup> International Good Manufacturing Practices Conference was held at the University of Georgia College of Pharmacy during the week of March 15-18. The program included speakers from the FDA, pharmaceutical industry, and academe. Joe Famulare of FDA's Center for Drug Evaluation and Research (CDER) contributed a presentation regarding "Quality Systems/Part 11." As part of the program, Mr. Famulare received the following question: What is FDA's current position on the applicability of 21 C.F.R. 11 to active pharmaceutical ingredient (API) producers in light of the fact that the rule applies to Part 211 and APIs do not fall under part 211? He replied to the effect that the

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statutory cGMP obligation for API manufacturers constituted a predicate rule for the purposes of determining the applicability of Part 11. This assertion has ramifications in terms of whether Part 11 is viewed as a source of guidance for API manufacturers or is an enforceable obligation.

As Part 11 is currently written, finding a legal basis for such an assertion of authority is difficult. The rule states at 21 C.F.R. §11.1(b) that “[t]his part applies to records in electronic form that are created ... under any records requirements set forth in agency regulations.” We note that, as a legal matter, a statute is not an agency regulation.

The rule, in the same paragraph, goes on to state that “[t]his part also applies to electronic records submitted to the agency under requirements of the Federal Food, Drug, and Cosmetic Act [the Act] and Public Health Service Act [PHS Act], even if such records are not specifically identified in agency regulations.” This language is such that FDA might contend that it encompasses any records that are “accessed” by an inspector in the course of an inspection in order to determine whether the facility was operating in accordance with cGMPs. However, such claims by FDA would be in direct conflict with both the plain language and the purpose of that language as explained by FDA when it was added to the final rule. The stated purpose was addressed in the preamble to the final rule as follows:

29. Several comments requested clarification of which FDA records are required to be in paper form, and urged the agency to allow and promote the use of electronic records in all cases. One comment suggested that proposed Sec. 11.1(d) be revised to read, in part, “\* \* \* unless the use of electronic records is specifically prohibited.”

The agency intends to permit the use of electronic records required to be maintained but not submitted to the agency (as noted in Sec. 11.2(a)) provided that the requirements of part 11 are met and paper records are not specifically required. The agency also wishes to encourage electronic submissions, but is limited by logistic and resource constraints. The agency is unaware of “maintenance records” [*e.g.*, documentation required by a cGMP regulation] that are currently explicitly required to be in paper form (explicit mention of paper is generally unnecessary because, at the time most regulations were prepared, only paper-based technologies were in use) but is providing for that possibility in the future. For purposes of Part 11, the agency will not consider that a regulation requires “maintenance” records to be in paper form where the regulation is silent on the form the record must take. FDA believes that the comments’ suggested wording does not offer sufficient advantages to adopt the change.

However, to enable FDA to accept as many electronic submissions as possible, the agency is amending Sec. 11.1(b) to include those submissions that the [A]ct and the PHS Act specifically require, even though such submissions may not be identified in agency regulations. An example of such records is premarket

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submissions for Class I and Class II medical devices, required by section 510(k) of the act (21 U.S.C. 360(k)).

62 Fed. Reg. 13464, 13438 (March 20, 1997).<sup>1</sup>

There is nothing in the preamble discussion to suggest that the “maintenance records” reference was intended to extend beyond those records required to be maintained by a regulation. Furthermore, it seems clear that the broad reference to FDA’s enabling legislation was not intended to encompass every record “maintained” in conjunction with compliance efforts but was intended to provide a basis for, and eliminate potential obstacles to, the electronic filing of submissions required only by statute. Indeed, the interpretation offered at the University of Georgia conference renders moot the reference to a “specific” statutory requirement since there are no specific submission requirements associated with cGMP compliance or “maintenance records” in general.

The statutory obligation with respect to API cGMPs is provided by section 501 of the Act regarding adulterated drugs and devices. Section 501(a)(1)(B) states that a product will be deemed adulterated when “the methods used in, or the facilities or controls used for, [the API's] manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.” As a practical matter, the words have come to mean that the API manufacturer is responsible for documenting everything that has been done in the manufacture of the API. This cannot be accomplished with records that are unreliable, be they electronic or written in pencil, but deviations from Part 11 do not, *per se*, render records unreliable.

In short, we view Part 11 as relevant guidance, but not a predicate rule. In our view the Guidance merely reaffirms Part 11’s applicability only to records in electronic form subject to a predicate record keeping requirement by Agency regulation, the Act, or the PHS Act, and that API cGMPs lack such a predicate basis for recordkeeping.

BPTF strongly feels that FDA should consider the unique perspective of the API and intermediates industry as part of issuing guidance related to its re-examination of Part 11. The depth and expertise of this industry sector are vital components of the U.S. chemical industry and contribute significantly to U.S. global competitiveness.

Once again, BPTF appreciates the opportunity to comment on the Guidance document. We look forward to continuing to work with FDA in the development of standards for Part 11.

Sincerely,

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<sup>1</sup> Curiously, a regulation had already been promulgated well before 1977 that repeated the statutory obligation. 21 C.F.R.807.81 (initially published at 42 Fed Reg. 42526 (August 23, 1977).

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Brant Zell, Chairman  
Bulk Pharmaceutical Task Force

CC: BPTF membership  
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