• Date the Form FDA 483 issued (from the Form FDA 483);
• Firm establishment inventory (FEI) number, if available (from the Form FDA 483);
• Names and titles of FDA employees who conducted inspection (from the Form FDA 483);
• Office responsible for the inspection, e.g., district office, as listed on the Form FDA 483;
• Application number if the inspection was a preapproval inspection;
• Comprehensive statement of each issue to be resolved:
• Identify the observation in dispute.
• Clearly present the manufacturer's scientific position or rationale concerning the issue under dispute with any supporting data.
• State the steps that have been taken to resolve the dispute, including any informal dispute resolution that may have occurred before the issuance of the Form FDA 483.
• Identify possible solutions.
• State expected outcome.
• Name, title, telephone and fax number, and e-mail address (as available) of manufacturer contact.

*Description of Respondents*: Pharmaceutical manufacturers of veterinary and human drug products and human biological drug products.

*Burden Estimate*: FDA has reviewed the total number of informal disputes that currently arise between manufacturers and investigators (and FDA district offices) when a manufacturer disagrees with the scientific or technical basis for an observation listed on a Form FDA 483. FDA estimates that approximately 12 such disputes occur annually. FDA believes that the number of requests for formal dispute resolution under the draft guidance would be higher because manufacturers have expressed reluctance to dispute with the agency scientific or technical issues raised in an investigation in the absence of a formal mechanism to resolve the dispute. In addition, manufacturers have requested the formal mechanisms in the draft guidance to facilitate the review of such disagreements. Therefore, FDA estimates that approximately 25 manufacturers will submit approximately 25 requests annually for a tier-one dispute resolution. FDA also estimates that approximately five manufacturers will appeal approximately five of these requests to the DR Panel (request for tier-two dispute resolution).

Based on the time it currently takes manufacturers to prepare responses to FDA concerning issues raised in a Form FDA 483, FDA estimates that it will take manufacturers approximately 30 hours to prepare and submit each request for a tier-one dispute resolution and approximately 8 hours to prepare and submit each request for a tier-two dispute resolution.

Based on the methodology and assumptions in the previous paragraphs, table 1 of this document provides an estimate of the annual reporting burden for requests for a tier-one dispute resolution and requests for a tier-two dispute resolution under the draft guidance. FDA requests comments on this analysis of information collection burdens.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

| | No. of Respondents | Number of Responses per Respondent | Total Annual Responses | Hours per Response | Total Hours |
|---|---|---|---|---|---|
| Requests for Tier-One Dispute Resolution | 25 | 1 | 25 | 30 | 750 |
| Requests for Tier-Two Dispute Resolution | 5 | 1 | 5 | 8 | 40 |
| Total | | | | | 790 |

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

## IV. Electronic Access

Persons with access to the Internet may obtain the draft guidance document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm* or*http://www.fda.gov/cber/guidelines.htm*

Dated: August 27, 2003.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

[FR Doc. 03–22575 Filed 9–3–03; 10:00 am]

BILLING CODE 4160–01–S

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket Nos. 2003D–0060]**

### Guidance for Industry on ''Part 11, Electronic Records; Electronic Signatures—Scope and Application;'' Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Part 11, Electronic Records; Electronic Signatures—Scope and Application.'' The guidance explains FDA's current thinking regarding the requirements and application of part 11 (21 CFR part 11). FDA has begun to reexamine part 11 as it applies to all FDA regulated products. This guidance explains that we will narrowly interpret the scope of part 11. While the reexamination of part 11 is under way, we intend to exercise enforcement discretion with respect to certain part 11 requirements. With respect to systems that were operational before August 20, 1997, the effective date of the final rule establishing part 11, we intend to exercise enforcement discretion with respect to all part 11 requirements under certain circumstances.

**DATES:** Submit written or electronic comments on agency guidances at any time.

**ADDRESSES:** Submit written requests for single copies of this guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and

Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

**FOR FURTHER INFORMATION CONTACT:** Joseph C. Famulare, Center for Drug Evaluation and Research (HFD–320), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852, 301–827–8940, or *part11@cder.fda.gov*; or David Doleski, Center for Biologics Evaluation and Research (HFM–676), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–3031, *doleski@cber.fda.gov*; or John Murray, Center for Devices and Radiological Health (HFZ–340), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–4659, *jfm@cdrh.fda.gov*; or Vernon D. Toelle, Center for Veterinary Medicine (HFV–234), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–0312, *vtoelle@cvm.fda.gov*; or JoAnn Ziyad, Center for Food Safety and Applied Nutrition (HFS–206), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740–3835, 202–418–3116, *jziyad@cfsan.fda.gov*; or Scott MacIntire, Office of Regulatory Affairs (HFC–240), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857–1706, 301–827–0386, *smacinti@ora.fda.gov*.

**SUPPLEMENTARY INFORMATION:**

## I. Background

FDA is announcing the availability of a guidance for industry entitled ''Part 11, Electronic Records; Electronic Signatures—Scope and Application.'' The guidance explains FDA's current thinking regarding the requirements and application of part 11.

In March 1997, FDA issued final part 11 regulations that provided criteria for acceptance by FDA, under certain circumstances, of electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records, and handwritten signatures executed on paper (62 FR 13430, March 20, 1997). These regulations, which apply to all FDA program areas, were intended to permit the widest possible use of electronic technology, consistent with FDA's responsibility to protect the public health.

After part 11 became effective in August 1997, significant discussions ensued among industry, contractors, and the agency concerning the scope, interpretation, and implementation of the regulations. Concerns have been raised that some interpretations of the part 11 requirements would have the following effects: (1) Unnecessarily restrict the use of electronic technology in a manner that is inconsistent with FDA's stated intent in issuing the rule, (2) significantly increase the costs of compliance to an extent that was not contemplated at the time the rule was drafted, and (3) discourage innovation and technological advances without providing a significant public health benefit. These concerns have been raised particularly in the areas of part 11 requirements for validation, audit trails, record retention, record copying, and legacy systems.

As an outgrowth of its current good manufacturing practice (CGMP) initiative for human and animal drugs and biologics, FDA has begun to re-examine part 11 as it applies to all FDA regulated products. We may revise provisions of part 11 as a result of that examination. This guidance explains that we will narrowly interpret the scope of part 11. While the re-examination of part 11 is under way, we intend to exercise enforcement discretion with respect to certain part 11 requirements. However, with respect to legacy systems we intend to exercise enforcement discretion with respect to all part 11 requirements under certain circumstances. As announced on February 25, 2003, in the **Federal Register** document announcing the availability of the draft version of this guidance (68 FR 8775), we have withdrawn Compliance Policy Guide 7153.17 and previously published part 11 draft guidance documents on validation, glossary of terms, time stamps, and maintenance of electronic records. Also, in the **Federal Register** of February 4, 2003 (68 FR 5645), we announced the withdrawal of the previously published part 11 draft guidance on electronic copies of electronic records.

FDA received a number of comments when it issued the February 2003 draft version of this guidance. We have considered the comments on the draft carefully and have made some changes to address those comments. Among other things, we have revised the guidance by making the following changes:

1. Emphasize that part 11 remains in effect and that enforcement discretion applies only to certain requirements or circumstances as identified in the guidance;
2. Clarify the term 'enforcement discretion';
3. Explain that time stamps should be clearly referenced;
4. Remove the National Institute of Standards and Technology risk management guide as a reference and add the ISO 14971 risk management guide as a reference;
5. State that the FDA currently has no plans to re-issue the withdrawn part 11 draft guidance documents; and
6. Clarify the meaning of 'part 11 legacy system.'

This guidance provides recommendations to persons who, in fulfillment of a requirement in a statute or another part of FDA's regulations to maintain records or submit information to FDA, have chosen to maintain the records or submit designated information electronically and, as a result, have become subject to part 11.

This guidance announces that we intend to exercise enforcement discretion with respect to the validation, audit trail, record retention, and record copying requirements of part 11. We also intend to exercise enforcement discretion and do not intend to recommend or take enforcement action to enforce any part 11 requirements with regard to systems that were operational before August 20, 1997, the effective date of part 11 (commonly known as existing or legacy systems) while we are re-examining part 11. However, records must still be maintained or submitted in accordance with the underlying predicate rules.

It is important to note that FDA's exercise of enforcement discretion as described in this guidance is limited to specified part 11 requirements (setting aside legacy systems, as to which the extent of enforcement discretion, under certain circumstances, will be more broad). We intend to enforce all other provisions of part 11 including, but not limited to, certain controls for closed systems in § 11.10, the corresponding controls for open systems (§ 11.30), and requirements related to electronic signatures (e.g., §§ 11.50, 11.70, 11.100, 11.200, and 11.300). We expect continued compliance with these provisions, and we will continue to enforce them. Where the interpretation of part 11 in this guidance differs from the interpretation in the preamble to part 11, the interpretation in this guidance will apply.

This level 1 guidance is being issued consistent with FDA's good guidance

practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking on ''Part 11, Electronic Records; Electronic Signatures—Scope and Application.'' It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

**II. Comments**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the guidance at any time. Two paper copies of mailed comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

**III. Electronic Access**

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: August 27, 2003.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

[FR Doc. 03–22574 Filed 9–03–03; 10:00 am]

**BILLING CODE 4160–01–S**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. 2003D–0380]**

### Draft Guidance for Industry: Process Analytical Technology — A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled ''Guidance for Industry: PAT — A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance.'' The draft guidance explains a science-based, risk-based framework, ''Process Analytical Technology, or PAT,'' for developing and implementing innovative manufacturing technology. The guidance is intended to encourage innovative pharmaceutical manufacturing and quality assurance. Working with existing regulations, this guidance also describes a regulatory approach that will enable the agency and the pharmaceutical industry to address technical and regulatory issues and questions anticipated during introduction of new manufacturing and quality assurance technologies.

**DATES:** Submit written or electronic comments on this draft guidance on paper or electronically, by November 4, 2003. General comments on agency guidance documents are welcome at any time.

**ADDRESSES:** Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or to the Office of Communication, Training, and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Divison of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:**

Rajendra Uppoor, Center For Drug Evaluation and Research (HFD–003), 5600 Fishers Lane, Rockville, MD 20857, 301–594–5615, or

Dennis Bensley, Center for Veterinary Medicine (HFV–143), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–6956, or

Robert Coleman, Office of Regulatory Affairs, Food and Drug Administration, 60 8th Street North East, Atlanta, GA 30309, 404–253–1200, ext. 1295.

**SUPPLEMENTARY INFORMATION:** FDA is announcing the availability of a draft guidance entitled ''Guidance for Industry: PAT — A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance.'' The draft guidance explains a science-based, risk-based framework, ''Process Analytical Technology, or PAT,'' for developing and implementing innovative manufacturing technology. The guidance is intended to encourage innovative pharmaceutical manufacturing and quality assurance.

**I. Background**

Conventional pharmaceutical manufacturing is generally accomplished using batch processing with testing conducted on collected samples to ensure quality. This conventional approach has been successful in providing quality pharmaceuticals to the public. However, significant opportunities now exist for improving the efficiency of pharmaceutical manufacturing and quality assurance through the innovative application of modern process development and control technologies, including modern PAT. Unfortunately, the pharmaceutical industry generally has been hesitant to introduce new technologies and innovative systems into the manufacturing sector for a number of reasons. For example, one reason often cited is regulatory uncertainty, which may result from the perception that our existing regulatory system is unfavorable to the introduction of new technologies.

In August 2002, recognizing the need to free industry from its hesitant perspective, FDA launched a new initiative entitled ''Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach.''

Pharmaceutical development and manufacturing is evolving with increased emphasis on science and engineering principles. Effective use of pharmaceutical science and engineering principles and knowledge, throughout the life cycle of a product, can improve the efficiencies of both manufacturing and regulatory processes. FDA's initiative is designed to do just that using an integrated systems approach to regulating pharmaceutical product quality. This approach is based on science and engineering principles for assessing and mitigating risks related to poor product and process quality. The desired future state of pharmaceutical manufacturing may be characterized as: (1) Product quality and performance achieved and ensured through the design of effective and efficient manufacturing processes, (2) product and process specifications based on a mechanistic understanding of how formulation and process factors affect product performance, (3) continuous real time quality assurance, (4) regulatory policies and procedures tailored to recognize the level of scientific knowledge supporting products and processes, (5) risk-based regulatory approaches that recognize the