• Approximately 70 comments were received regarding the proposed new § 211.240 on control of chemical and physical contaminants. Many of the comments stated that the rule should be revised to better describe how contaminants will be identified and to provide allowances for threshold levels or limits of contaminants.

Overall, the comments were constructive, informative, and addressed nearly every area of the May 1996 proposed rule. Although we do not plan to publish specific responses to each of these comments, we will take these comments into account as we proceed to make incremental changes to parts 210 and 211.

IV. Withdrawal of the Proposed Rule

For the reasons described in this document, FDA is withdrawing the proposed rule published on May 3, 1996 (61 FR 20103).

Dated: November 26, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E7–23271 Filed 12–3–07; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 210 and 211

[Docket No. 2007N–0280]

Amendment to the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals; Companion Document to the Direct Final Rule

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is publishing this companion proposed rule to the direct final rule, published elsewhere in this issue of the **Federal Register**, which is intended to amend certain sections of the regulations as the first phase of an incremental approach to modifying the current good manufacturing practice (CGMP) regulations for finished pharmaceuticals.

DATES: Submit written or electronic comments on or before February 19, 2008.

ADDRESSES: You may submit comments, identified by Docket No. 2007N–0280, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

• Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.

• Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

• FAX: 301–827–6870.

• Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described previously, in the **ADDRESSES** portion of this document under *Electronic Submissions*.

Instructions: All submissions received must include the agency name and Docket No(s). and Regulatory Information Number (RIN) (if a RIN number has been assigned) for this rulemaking. All comments received may be posted without change to *http://www.fda.gov/ohrms/dockets/default.htm*, including any personal information provided. For additional information on submitting comments, see the ''Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/ohrms/dockets/default.htm* and insert the docket number(s), found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Mary Malarkey, Center for Biologics Evaluation and Research (HFM–600), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6190, or

Dennis Bensley, Center for Veterinary Medicine (HFV–140), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–6956, or

Frederick Blumenschein, Center for Drug Evaluation and Research (HFD–326), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852, 301–827–9022.

SUPPLEMENTARY INFORMATION:

I. Background

Since the development of the CGMP regulations in 1962, FDA has balanced the need for easily understood minimum standards with the need to encourage innovation and the development of improved manufacturing technologies. We strive to give manufacturers latitude to determine how to achieve the level of control necessary for CGMP compliance, recognizing that, in some instances, more direction from FDA is necessary to provide a uniform standard to the entire industry or because of the potential for harm or the narrow range of acceptable means to accomplish a particular CGMP objective. FDA periodically reassesses and revises the CGMP regulations to accommodate advances in technology that further safeguard the drug manufacturing process and the public health. As technology and scientific knowledge related to CGMP evolve, so does understanding of the material, equipment, and process variables, as well as the operational procedures and oversight methods that must be defined and controlled to achieve assurance of drug product quality.

In 1996, as part of this reassessment process, FDA proposed to amend certain requirements of the CGMP regulations for finished pharmaceuticals to clarify certain manufacturing, quality control, and documentation requirements, and to ensure that the regulations more accurately encompass current industry practice (61 FR 20103, May 3, 1996) (1996 proposed rule)). Subsequently, as a part of the risk-based pharmaceutical CGMPs for the 21st century initiative, FDA created a CGMP Harmonization Analysis Working Group (CGMP Working Group) to analyze related CGMP requirements in effect in the United States and internationally, including those related to quality systems. The CGMP Working Group compared parts 210 amd 211 (21 CFR parts 210 and 211) with the GMPs of the European Union (EU), as well as other FDA regulations (e.g., the Quality Systems Regulation, 21 CFR part 820) to identify the differences and consider the value of supplementing or changing the current regulations. Based on the CGMP Working Group's analysis, we decided to take an incremental approach to modifying parts 210 and 211 (see *http://www.fda.gov/cder/gmp/gmp2004/GMP_finalreport2004.htm#_Toc84065744*).

Because of this change in approach, FDA decided not to finalize the 1996

proposed rule. Therefore, elsewhere in this issue of the **Federal Register**, we are publishing a notice withdrawing the 1996 proposed rule.

The amendments being proposed in this rule are intended to clarify and modernize the CGMP regulations, as well as harmonize the regulations with international GMP requirements and other FDA regulations. This proposed rule represents the first increment of modifications to parts 210 and 211.

II. Additional Information

This proposed rule is a companion to the direct final rule published in the final rule section of this issue of the **Federal Register**. The proposed rule and the direct final rule are substantively identical. This companion proposed rule provides the procedural framework to proceed with standard notice-and-comment rulemaking if the direct final rule receives significant adverse comment and is withdrawn. A significant adverse comment is one that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without a change. The comment period for the companion proposed rule runs concurrently with the comment period of the direct final rule. Any comments received on this companion proposed rule will also be treated as comments on the direct final rule and vice versa.

For additional information, see the corresponding direct final rule published in the final rules section of this issue of the **Federal Register**. All persons who may wish to comment should review the rationale for these amendments set out in the preamble discussion of the direct final rule. A comment recommending a rule change in addition to this rule will not be considered a significant adverse comment unless the comment states why this rule would be ineffective without the additional change. If no significant adverse comment is received in response to the direct final rule, no further action will be taken related to this companion proposed rule. Instead, we will publish a confirmation notice within 30 days after the comment period ends, and we intend the direct final rule to become effective 30 days after publication of the confirmation notice. If we receive significant adverse comments, we will withdraw the direct final rule. We will proceed to respond to all of the comments received regarding the direct final rule, treating those comments as comments to this proposed rule. The agency will address the comments in a subsequent final rule. We will not provide additional opportunity for comment.

III. Analysis of Impacts

A. Review Under Executive Order 12866, the Regulatory Flexibility Act, and the Unfunded Mandates Reform Act of 1995

FDA has examined the impacts of this proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is not a significant regulatory action as defined by the Executive order, because the rule, if finalized, would generally either clarify the agency's longstanding interpretation of, or increase latitude for manufacturers in complying with, preexisting CGMP requirements.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule, if finalized, would not impose any new regulatory obligations, the agency tentatively certifies that it would not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $122 million, using the most current (2005) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

The purpose of this proposed rule is to update the codified language to reflect current practice and to harmonize requirements in the CGMP regulations with requirements in other regulations. It would not impose any additional requirements; therefore, industry would not incur incremental compliance costs for these proposed changes.

B. Environmental Impact

It is FDA's tentative conclusion that issuing these clarifying amendments to the CGMP regulations would not have a significant impact on the human environment. Therefore, FDA believes that an environmental impact statement is not required.

C. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has tentatively concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IV. Paperwork Reduction Act of 1995

The provisions of this proposed rule contain requirements that were submitted for review and approval to the Director of the Office of Management and Budget (OMB), as required by section 3507(d) of the Paperwork Reduction Act of 1995. The requirements were approved and assigned OMB control number 0910–0139.

V. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. This comment period runs concurrently with the comment period for the direct final rule. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that any individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects

21 CFR Part 210

Drugs, Packaging and containers

21 CFR Part 211

Drugs, Labeling, Laboratories, Packaging and containers, Prescription

drugs, Reporting and recordkeeping requirements, Warehouses.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 210 and 211 be amended as follows:

PART 210—CURRENT GOOD MANUFACTURING PRACTICE IN MANUFACTURING, PROCESSING, PACKING, OR HOLDING OF DRUGS; GENERAL

1. The authority citation for 21 CFR part 210 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 355, 360b, 371, 374; 42 U.S.C. 216, 262, 263a, 264.

2. Section 210.3 is amended by revising paragraph (b)(6) to read as follows:

§ 210.3 Definitions.

(b) * * *

(6) Nonfiber releasing filter means any filter, which after appropriate pretreatment such as washing or flushing, will not release fibers into the component or drug product that is being filtered.

* * * * *

PART 211—CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

3. The authority citation for 21 CFR part 211 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 355, 360b, 371, 374; 42 U.S.C. 216, 262, 263a, 264.

4. Section 211.48 is amended by revising paragraph (a) to read as follows:

§ 211.48 Plumbing.

(a) Water supplied by the plumbing system of the facility must be safe for human consumption. This water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any drug product.

* * * * *

5. Section 211.67 is amended by revising paragraph (a) to read as follows:

§ 211.67 Equipment cleaning and maintenance.

(a) Equipment and utensils shall be cleaned, maintained, and sanitized and/or sterilized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.

* * * * *

6. Section 211.68 is amended by adding paragraph (c) to read as follows:

§ 211.68 Automatic, mechanical, and electronic equipment.

* * * * *

(c) Such automated equipment used for performance of operations addressed by §§ 211.101(c) or (d), 211.103, 211.182, or 211.188(b)(11) can satisfy the requirements included in those sections relating to the performance of an operation by one person and checking by another person if such equipment is used in conformity with this section and one person verifies that the operations addressed in those sections are performed accurately by such equipment.

7. Section 211.72 is revised to read as follows:

§ 211.72 Filters.

Filters for liquid filtration used in the manufacture, processing, or packing of injectable drug products intended for human use shall not release fibers into such products. Fiber-releasing filters may not be used in the manufacture, processing, or packing of these injectable drug products unless it is not possible to manufacture such drug products without the use of such filters. If use of a fiber-releasing filter is necessary, an additional nonfiber-releasing filter of 0.22 micron maximum mean porosity (0.45 micron if the manufacturing conditions so dictate) shall subsequently be used to reduce the content of particles in the injectable drug product.

8. Section 211.82 is amended by revising paragraph (b) to read as follows:

§ 211.82 Receipt and storage of untested components, drug product containers, and closures.

* * * * *

(b) Components, drug product containers, and closures shall be stored under quarantine until they have been tested or examined, whichever is appropriate, and released. Storage within the area shall conform to the requirements of § 211.80.

9. Section 211.84 is amended by revising paragraphs (c)(1), (d)(3), and (d)(6) to read as follows:

§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.

* * * * *

(c) * * *

(1) The containers of components selected shall be cleaned when necessary in a manner to prevent introduction of contaminants into the component.

* * * * *

(d) * * *

(3) Containers and closures shall be tested for conformity with all appropriate written specifications. In lieu of such testing by the manufacturer, a certificate of testing may be accepted from the supplier, provided that at least a visual identification is conducted on such containers/closures by the manufacturer and provided that the manufacturer establishes the reliability of the supplier's test results through appropriate validation of the supplier's test results at appropriate intervals.

* * * * *

(6) Each lot of a component, drug product container, or closure with potential for microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use.

* * * * *

10. Section 211.94 is amended by revising paragraph (c) as follows:

§ 211.94 Drug product containers and closures.

* * * * *

(c) Drug product containers and closures shall be clean and, where indicated by the nature of the drug, sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use. Such depyrogenation processes shall be validated.

* * * * *

11. Section 211.101 is amended by revising paragraphs (c) and (d) to read as follows:

§ 211.101 Charge-in of components.

* * * * *

(c) Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person to assure that:

(1) The component was released by the quality control unit;

(2) The weight or measure is correct as stated in the batch production records;

(3) The containers are properly identified. If the weighing, measuring, or subdividing operations are performed by automated equipment under § 211.68, only one person is needed to assure paragraphs (c)(1), (c)(2), and (c)(3) of this section.

(d) Each component shall either be added to the batch by one person and verified by a second person or, if the components are added by automated equipment under § 211.68, only verified by one person.

12. Section 211.103 is revised to read as follows:

§ 211.103 Calculation of yield.

Actual yields and percentages of theoretical yield shall be determined at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product. Such calculations shall either be performed by one person and independently verified by a second person, or, if the yield is calculated by automated equipment under § 211.68, be independently verified by one person.

13. Section 211.110 is amended by revising paragraph (a) introductory text and by adding paragraph (a)(6) to read as follows:

§ 211.110 Sampling and testing of in-process materials and drug products.

(a) To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. Such control procedures shall include, but are not limited to, the following, where appropriate:

* * * * *

(6) Bioburden testing.

* * * * *

14. Section 211.113 is amended by revising paragraph (b) to read as follows:

§ 211.113 Control of microbiological contamination.

* * * * *

(b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of all aseptic and sterilization processes.

15. Section 211.160 is amended by revising paragraph (b)(1) to read as follows:

§ 211.160 General requirements.

* * * * *

(b) * * *

(1) Determination of conformity to applicable written specifications for the acceptance of each lot within each shipment of components, drug product containers, closures, and labeling used in the manufacture, processing, packing, or holding of drug products. The specifications shall include a description of the sampling and testing procedures used. Samples shall be representative and adequately identified. Such procedures shall also require appropriate retesting of any component, drug product container, or closure that is subject to deterioration.

* * * * *

16. Section 211.182 is revised to read as follows:

§ 211.182 Equipment cleaning and use log.

A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed. If equipment is dedicated to manufacture of one product, then individual equipment logs are not required, provided that lots or batches of such product follow in numerical order and are manufactured in numerical sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record. The persons performing and double-checking the cleaning and maintenance (or, if the cleaning and maintenance is performed using automated equipment under § 211.68, just the person verifying the cleaning and maintenance done by the automated equipment) shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.

17. Section 211.188 is amended by revising paragraph (b)(11) to read as follows:

§ 211.188 Batch production and control records.

* * * * *

(b) * * *

(11) Identification of the persons performing and directly supervising or checking each significant step in the operation, or if a significant step in the operation is performed by automated equipment under § 211.68, the identification of the person checking the significant step performed by the automated equipment.

* * * * *

Dated: November 26, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E7–23292 Filed 12–3–07; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2007–0096]

RIN 1625–AA09

Drawbridge Operation Regulations; Pinellas Bayway Structure ''E'' (SR 679) Bridge, Gulf Intracoastal Waterway, mile 113, St. Petersburg Beach, Pinellas County, FL

AGENCY: Coast Guard, DHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Coast Guard proposes to change the drawbridge regulation of the Pinellas Bayway Structure ''E'' (SR 679) Bridge, Gulf Intracoastal Waterway, mile 113, St. Petersburg Beach, Pinellas County, Florida. This rule is needed to provide vehicular traffic relief during heavy vehicular traffic periods flowing into a nearby county park while still meeting the reasonable needs of mariners.

DATES: Comments and related material must reach the Coast Guard on or before January 18, 2008.

ADDRESSES: You may submit comments identified by Coast Guard docket number USCG–2007–0096 to the Docket Management Facility at the U.S. Department of Transportation. To avoid duplication, please use only one of the following methods:

(1) Online: *http://www.regulations.gov*.

(2) Mail: Docket Management Facility (M–30), U.S. Department of Transportation, West Building, Ground Floor, Room W12–140, 1200 New Jersey Avenue, SE., Washington, DC 20590–0001.

(3) Hand delivery: Room W12–140 on the Ground Floor of the West Building, 1200 New Jersey Avenue, SE., Washington, DC 20590, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. The telephone number is 202–366–9329.

(4) Fax: 202–493–2251.

FOR FURTHER INFORMATION CONTACT: If you have questions on this proposed rule, call Michael Lieberum, Seventh Coast Guard District, Bridge Branch, telephone number 305–415–6744. If you have questions on viewing or submitting material to the docket, call Renee V. Wright, Program Manager, Docket Operations, telephone 202–366–9826.

SUPPLEMENTARY INFORMATION: