

the manufacturing area after completion of cleaning and decontamination.

Under revised § 600.11(e)(3)(ii), processing and propagation of spore-forming microorganisms must be conducted in areas and using systems that are not used for any other purpose at the same time. Prior to processing and propagation of any organism, procedures must be designed and in place to prevent contamination with pathogenic and/or toxic agents, as well as to decontaminate, sterilize and/or disinfect, as appropriate, all affected areas and systems. It is important to demonstrate control over and containment of spore-forming microorganisms during their propagation and processing in order to prevent contamination of the product. Products derived from spore-forming microorganisms should not be removed from designated areas unless this can be done in a manner that prevents contamination of other products. These containment procedures will provide a level of assurance that products made using spore-forming microorganisms remain safe, pure, and of high quality.

The agency anticipates developing a guidance document to assist manufacturers in complying with these more flexible provisions on work with spore-forming microorganisms.

B. Substitution of "Spore-Forming" for "Spore-Bearing"

As noted previously in this document, we are replacing the term "spore-bearing" in our regulations with the term "spore-forming" because the latter has become the more commonly used term to describe these microorganisms. Accordingly, in addition to § 600.11(e)(3), we are revising §§ 600.10(c)(3) (21 CFR 600.10(c)(3)) and 600.11(e)(1) and (e)(2) by substituting the term "spore-forming" for the term "spore-bearing".

III. Rulemaking Action

In the **Federal Register** of November 21, 1997 (62 FR 62466), FDA described its procedures on when and how the agency will employ direct final rulemaking. We have determined that this rule is appropriate for direct final rulemaking because we believe that it includes only noncontroversial amendments and we anticipate no significant adverse comments. Consistent with our procedures on direct final rulemaking, FDA is publishing elsewhere in this issue of the **Federal Register** a companion proposed rule to revise the biologics regulations to allow greater flexibility in production facilities and procedures for work with spore-forming microorganisms. The

companion proposed rule provides a procedural framework within which the rule may be finalized in the event that the direct final rule is withdrawn because of any significant adverse comments. The comment period for the direct final rule runs concurrently with the companion proposed rule. Any comments received in response to the companion proposed rule will be considered as comments regarding the direct final rule.

We are providing a comment period on the direct final rule of 75 days after date of publication in the **Federal Register**. If we receive any significant adverse comments, we intend to withdraw this direct final rule action before its effective date by publication of a notice in the **Federal Register**. A significant adverse comment is defined as a comment 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. In determining whether an adverse comment is significant and warrants terminating a direct final rulemaking, we will consider whether the comment raises an issue serious enough to warrant a substantive response in a notice-and-comment process in accordance with section 553 of the Administrative Procedure Act (5 U.S.C. 553). Comments that are frivolous, insubstantial, or outside the scope of the rule will not be considered significant or adverse under this procedure. A comment recommending a regulation change in addition to those in the rule would not be considered a significant adverse comment unless the comment states why the rule would be ineffective without the additional change. In addition, if a significant adverse comment applies to an amendment, paragraph, or section of this rule and that provision can be severed from the remainder of the rule, we may adopt as final those provisions of the rule that are not the subjects of a significant adverse comment.

If any significant adverse comments are received during the comment period, FDA will publish, before the effective date of this direct final rule, a document withdrawing the direct final rule. If we withdraw the direct final rule, any comments received will be applied to the proposed rule and will be considered in developing a final rule using the usual notice-and-comment procedures.

If FDA receives no significant adverse comments during the specified comment period, FDA intends to publish a confirmation document,

before the effective date of the direct final rule, confirming the effective date.

IV. 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 the direct final rule under Executive Order 12866, 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). We believe that this direct final rule is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the direct final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze whether a rule may have a significant economic impact on a substantial number of small entities. Because the direct final rule allows for greater flexibility in production facilities and procedures for work with spore-forming microorganisms, it would not result in any increased burden or costs on small entities. Therefore, we certify that the direct final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

The Unfunded Mandates Reform Act requires that agencies prepare a written statement under section 202(a) of anticipated costs and benefits before proposing any rule that may result in an annual expenditure by State, local and tribal governments, in the aggregate, or by the private sector, of \$100 million (adjusted annually for inflation). Because the rule does not impose mandates on State, local, or tribal governments, or the private sector, that will result in an expenditure in any one year of \$100 million or more, FDA is not required to perform a cost-benefit analysis according to the Unfunded Mandates Reform Act.