(Lat. 42°54′29″ N., long. 106°27′52″ W.)

Within a 4.3-mile radius of Natrona County International Airport. This Class E airspace area is effective during the specific dates and times established in advance by a Notice to Airmen. The effective date and time will thereafter be continuously published in the Airport/Facility Directory.

Paragraph 6004 Class E airspace designated as an extension to a Class D surface area.

* * * * *

ANM WY E4 Casper, WY [Amended]

Casper, Natrona County International Airport, WY
(Lat. 42°54′29″ N., long. 106°27′52″ W.)
Muddy Mountain VORTAC
(Lat. 43°05′27″ N., long. 106°16′37″ W.)
Johno LOM
(Lat. 42°54′26″ N., long. 106°34′12″ W.)

That airspace extending upward from the surface within 4.3 miles each side of the Muddy Mountain VORTAC 216° radial extending from the VORTAC to 29 miles southwest of the VORTAC, and within 2.7 miles each side of the ILS localizer west course extending from .9 miles east to 9 miles west of the Johno LOM. This Class E airspace area is effective during the specific dates and times established in advance by a Notice to Airmen. The effective date and time will thereafter be continuously published in the Airport/Facility Directory.

Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface of the earth.

* * * * *

ANM WY E5 Casper, WY [Amended]

Casper, Natrona County International Airport, WY
(Lat. 42°54′29″ N., long. 106°27′52″ W.)
Muddy Mountain VORTAC
(Lat. 43°05′27″ N., long. 106°16′37″ W.)
Casper ASR
(Lat. 42°55′16″ N., long. 106°27′15″ W.)

That airspace extending upward from 700 feet above the surface within a 23.5-mile radius of the Casper ASR; that airspace extending upward from 1,200 feet above the surface within the 37.5-mile radius of the Casper ASR, and within an area extending from the 37.5-mile radius to the 36.6-mile radius of the Muddy Mountain VORTAC, bounded on the north by the Muddy Mountain VORTAC 060° radial and on the south by the Muddy Mountain VORTAC 111° radial; that airspace extending upward from 11,500 feet MSL extending from the 37.5-mile radius to the 52.2-mile radius of the Muddy Mountain VORTAC, bounded on the east by the west edge of V–19 and on the south by the north edge of V–298.

Paragraph 6006 En route domestic airspace areas.

* * * * *

ANM WY E6 Casper, WY [New]

Casper, Natrona County International Airport, WY
(Lat. 42°54′29″ N., long. 106°27′52″ W.)

That airspace extending upward from 1,200 feet above the surface within a 85-mile radius of Natrona County International Airport; excluding existing controlled airspace 7,100 feet MSL and above.

Issued in Seattle, Washington, on June 14, 2011.

William Buck,

Acting Manager, Operations Support Group, Western Service enter.

[FR Doc. 2011–15393 Filed 6–20–11; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 600, 610, and 680

[Docket No. FDA–2011–N–0080]

Amendments to Sterility Test Requirements for Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) proposes to amend the sterility test requirements for biological products. This proposed rule is intended to provide manufacturers of biological products greater flexibility and to encourage use of the most appropriate and state-of-the-art test methods for assuring the safety of biological products. We are taking this action as part of our continuing effort to review and, as necessary, update the biologics regulations.

DATES: Submit either electronic or written comments on this proposed rule by September 19, 2011. See section X of this document for the proposed effective date of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. FDA–2011–N–0080, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

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

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.

Instructions: All submissions received must include the Agency name and Docket No. FDA–2011–0080 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* 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.regulations.gov* and insert the docket number, 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: Paul E. Levine, Jr., Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION:

I. Background

Any product that purports to be sterile should be free of viable contaminating microorganisms to assure product safety (§ 600.3(q) (21 CFR 600.3(q)). Absolute sterility of a lot cannot be practically demonstrated without complete destruction of every finished article in that lot (United States Pharmacopeia (USP) Chapter 1211). Therefore, sterility assurance is accomplished primarily by validation of the sterilization process or of the aseptic processing procedures under current good manufacturing practice (CGMP), and is supported by sterility testing using validated and verified test methods. (See *e.g.,* USP Chapter 71>, European Pharmacopeia 2.6.2.)

In the **Federal Register** of November 20, 1973 (38 FR 32048), we reorganized and republished the biologics regulations, which included regulations governing sterility testing, as title 21 of the Code of Federal Regulations (CFR), subchapter F, parts 600 through 680 (21 CFR parts 600 through 680). Section 610.12 currently requires manufacturers to perform sterility tests for both bulk and final container material of most biological products [1] for the detection of

[1] Sterility tests are not currently required to be performed for Whole Blood, Cryoprecipitated Antihemophilic Factor (AHF), Platelets, Red Blood Cells, Plasma, Source Plasma, Smallpox Vaccine, Reagent Red Blood Cells, Anti-Human Globulin, or Blood Grouping Reagents; or in cases where the Director of the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER), as appropriate, determines that the mode of administration, method of

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viable contaminating microorganisms (*e.g.,* bacteria, molds, and/or yeasts).

Over the years, FDA has amended the biologics regulations, as necessary, to clarify and update the sterility test requirements. On March 11, 1976 (41 FR 10427) and March 2, 1979 (44 FR 11754), we updated § 610.12 to clarify the procedures for repeat testing. On April 18, 1984 (49 FR 15186), we amended § 610.12 by removing and reserving paragraph (g)(3) previously entitled *Different Tests Equal or Superior* and by adding § 610.9 entitled *Equivalent methods and processes* to provide manufacturers of licensed biological products the flexibility to use alternate test methods or manufacturing processes that provide assurances of safety, purity, potency, and effectiveness equal or greater than those provided by the methods or processes specified in the regulations under parts 610 through 680. On December 15, 1986 (51 FR 44903), we clarified and updated certain requirements for sterility testing to ensure the reliability of the growth-promoting qualities of the sterility test culture media and to provide greater consistency with the requirements of USP Chapter XXI. Finally, on September 15, 1997 (62 FR 48174), we incorporated by reference the 1995 ed. of the USP concerning the procedures for the membrane filtration test method.

Section 610.12 currently requires that the sterility of most licensed biological products [2] be demonstrated through the performance of tests prescribed in § 610.12(a) and (b). Specifically, § 610.12 requires that the sterility of each lot of each product, with the exception of certain products,[3] be demonstrated by the performance of prescribed sterility tests for both bulk and final container material, unless different sterility tests are prescribed in the license (see § 610.12(g)(1)) or the manufacturer submits adequate data [4] establishing that the mode of administration, the method of preparation, or the special nature of the product precludes or does not require a sterility test, or that the sterility of the lot is not necessary to assure the safety, purity, and potency of the product (§ 610.12(g)(4)(ii)).

The regulation, under § 610.12, also specifies the test method and culture media to be used. For instance, the prescribed sterility test methods rely upon culture media (either Fluid Thioglycollate Medium or Soybean-Casein Digest Medium) to detect growth of microorganisms (§ 610.12(a)(1) and (a)(2)). Moreover, § 610.12 specifies criteria, such as incubation conditions (time and temperature) to be used during testing, suitable test organisms for the evaluation of the growth-promoting qualities of the culture media, storage and maintenance of test organism cultures, and storage and condition of media.

Manufacturers of innovative products, such as cell and gene therapy products, as well as manufacturers of currently approved products, may benefit from sterility test methods with rapid and advanced detection capabilities. Advances in technology in recent years have allowed the development of new sterility test methods that yield accurate and reliable test results in less time and with less operator intervention than the currently prescribed methods. Some examples of novel methods with the potential to detect viable contaminating microorganisms include the Adenosine Triphosphate (ATP) bioluminescence, chemiluminescence, and carbon dioxide head space measurement.

We are proposing to amend § 610.12 to promote improvement and innovation in the development of sterility test methods, to address the challenges of novel products that may be introduced to the market in the future, and to potentially enhance sterility testing of currently approved products. This proposed revision would provide manufacturers the flexibility to take advantage of modern methods as they become available, provided that these methods meet certain criteria.

II. Highlights of This Proposed Rule

We are proposing to amend the sterility test requirements for biological products to provide manufacturers with greater flexibility to encourage use of the most appropriate and state-of-the-art test methods. The most significant proposed changes include the following:

- Elimination of specified sterility test methods, culture media formulae (or formulations), and culture media test requirements;
- Elimination of specified membrane filtration procedure requirement for certain products;
- Elimination of specified sterility test requirements for most bulk material; [5]
- Modification of the repeat sterility test requirements, so that repeat tests would occur only once for each lot. These tests would be limited to situations when the quality control unit conclusively determines, after conducting an investigation upon detection of viable microbial contamination during the initial test of the lot, that the contamination is the result of laboratory error or faulty materials used in conducting the sterility test;
- Replacement of the storage and maintenance requirements for cultures of test organisms used to determine the ''growth-promoting qualities'' of culture media with: (1) Validation requirements specifying that any sterility test used is able to consistently detect the presence of viable contaminating microorganisms and (2) verification of ''growth-promoting properties'' [6] or microorganism-detection capabilities of test and test components;
- Replacement of the sample size or amount requirement with a requirement that the sample be appropriate to the material being tested;
- Replacement of the *Interpretation of test results* paragraph under § 610.12(c) with a requirement that manufacturers establish, implement, and follow written procedures for sterility testing that describe, at a minimum, the test method used, the method of sampling, and the written specifications for acceptance or rejection of each lot; and
- Simplification of the *Exceptions* paragraph under § 610.12(c).

III. Description of This Proposed Rule

This proposed rule is intended to promote improvement and innovation in the development of sterility test methods by allowing manufacturers flexibility needed for sterility testing of some novel products that may be introduced to the market, to enhance sterility testing of currently approved products, and to encourage manufacturers to benefit from scientific and technological advances in sterility test methods as they become available.

A. When is sterility testing required?

Currently, sterility testing must be performed, with certain limited

preparation, or special nature of the product precludes or does not require a sterility test or that the sterility of the lot is not necessary to assure the safety, purity, and potency of the product. (See 21 CFR 610.12(g)(4).)

[2] See list of exemptions in § 610.12(g)(4).

[3] Whole Blood, Cryoprecipitated AHF, Platelets, Red Blood Cells, Plasma, Source Plasma, Smallpox Vaccine, Reagent Red Blood Cells, Anti-Human Globulin, or Blood Grouping Reagents (§ 610.12(g)(4)(i)).

[4] The Director of CBER or CDER, as appropriate, will determine the adequacy of the data (§ 610.12(g)(4)(ii)).

[5] See section III.A of this document for a detailed discussion of when sterility testing of bulk material may be necessary and appropriate.

[6] We are proposing to refer to ''growth-promoting properties'' rather than ''growth-promoting qualities'' as we believe ''growth-promoting properties'' may reflect more accurate and current terminology. However, we invite comments on which term is most appropriate.

exceptions, on both bulk and final container material for each lot of each biological product prior to release of that lot (§§ 610.1 and 610.12). A lot is defined as that quantity of uniform material identified by the manufacturer as having been thoroughly mixed in a single vessel (§ 600.3(x)).

We propose to eliminate the sterility test requirement for most bulk materials. We have determined that, in most cases, for purposes of sterility testing, the most appropriate test material is the final container material. We recognize that, due to the nature of some biological products, testing the final container material may not always be feasible or appropriate. Thus, proposed § 610.12 would require that prior to release, manufacturers of biological products must perform sterility testing of each lot of each biological product's final container material or other material (*e.g.,* bulk material or active pharmaceutical ingredient (API), in-process material, stock concentrate material) as appropriate and as approved in the biologics license application (BLA) or BLA supplement. For example, certain allergenic and cell and gene therapy products may need to be tested for sterility at an in-process stage or some other stage of the manufacturing process (*e.g.,* intermediate, API, bulk drug substance) instead of the final container material, because the final container material may interfere with the sterility test. Likewise, some cell therapy products and cell-based gene therapy products may need to be tested for sterility at an in-process stage or some other stage of manufacturing process because low production volumes may result in an insufficient final container material sample for sterility testing or a short product shelf-life may necessitate administration of the final product to a patient before sterility test results on the final container material are available. If it is determined that sterility testing needs to be performed on material other than the final product, due to the nature of the final product, we would expect the manufacturer, in its BLA or BLA supplement, to: (1) Describe the details of the sterility test method, including the procedure for testing the alternate material instead of the final container material and (2) provide the scientific rationale for selecting the specific test material.

If this proposed rule is finalized, a manufacturer who desires to utilize an alternate sterility test method other than the one approved in its BLA must submit a BLA supplement in accordance with § 601.12(b).

B. What are the sterility test requirements?

1. Test Methods

Currently, § 610.12(a), (b), and (e) prescribe the culture-based test method to be used for sterility testing, including the acceptable culture media (either Fluid Thioglycollate Medium or Soybean-Casein Digest Medium) and incubation conditions (time and temperature) to be used during testing, with exceptions provided in § 610.12(g). In addition, § 610.12(f) provides that a membrane filtration test method, set forth in (USP 23d revision, 1995), may be used to test bulk and final container materials or products containing oil products in water-insoluble ointments. We propose to eliminate references to specific test methods and culture media for sterility testing, and instead require that the sterility test be appropriate to the material being tested such that the material does not interfere with or otherwise hinder the test. We believe that this revision recognizes current practices and provides manufacturers the flexibility to take advantage of suitable modern sterility test methods and keep pace with advances in science and technology. Because we are proposing to expand potentially acceptable sterility test methods to include non-culture-based methods in addition to culture-based methods, we also propose to remove the definition of a lot of culture medium currently defined in § 610.12(e)(2)(i) as ''* * * that quantity of uniform material identified as having been thoroughly mixed in a single vessel, dispensed into a group of vessels of the same composition and design, sterilized in a single autoclave run, and identified in a manner to distinguish one lot from another. * * *'' Although we still consider this definition to apply, we believe that this concept is captured by the definition of ''lot'' in § 600.3(x). This change also reflects our recognition that prepared culture media may be purchased, in which case a lot may be predetermined by the vendor.

Section 610.12(e)(2)(i) currently provides an exception to the growth-promoting test requirements for dehydrated culture media provided that the manufacturer has an approved validation program for autoclaves used to sterilize these media and the manufacturer has received approval for this practice from the Director of CBER or CDER, as appropriate. We propose to eliminate this exception. Proposed § 610.12(h)(2) provides that all manufacturers seeking an exemption from the sterility test requirements must submit, in their BLA or BLA supplement, data that adequately establish that the route of administration, the method of preparation, or any other aspect of the product precludes or does not necessitate a sterility test.

Additionally, current § 610.12(e)(2)(ii) stipulates the test organisms, strains, characteristics, identity, and verification to be used. We propose to eliminate the requirement to test culture media with specific test organisms and to eliminate the requirement regarding the number of organisms that must be used to demonstrate the growth-promoting qualities of the culture media. This flexibility would allow manufacturers to use sterility test methods that are either culture-based or non-culture-based, which may necessitate different verification activities. Thus, instead of specifying the number and type of test organisms, proposed § 610.12(b) would require the following: (1) Use of a sterility test method that is appropriate to the material being tested such that the material does not interfere with or otherwise hinder the test; (2) validation studies to demonstrate that the sterility test method used is capable of consistently detecting the presence of viable contaminating microorganisms; and (3) verification that the sterility test method and test components used can detect the presence of viable contaminating microorganisms.

Due to the variety of currently available and potential future sterility test methods, we propose to eliminate specified incubation conditions (time and temperature) and visual examination requirements currently prescribed in § 610.12. Because we propose to allow any validated sterility test method that is appropriate to the material being tested, rather than specifying the test and the media used, we also propose to eliminate the Fluid Thioglycollate Medium incubation temperatures prescribed in § 610.12(a)(1)(ii) for the final container material containing a mercurial preservative.

2. Validation

The International Conference on Harmonisation (ICH) Q2(R1) ''Validation of Analytical Procedures: Text and Methodology'' dated November 2005, states that ''[t]he objective of validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose.'' [7]

[7] This text was previously named ''Text on Validation of Analytical Procedures'' (Q2A) (approved by the Steering Committee in October 1994). An accompanying ''Guideline on Validation of Analytical Procedures: Methodology'' (Q2B) was

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Similarly, USP General Chapter 1223, ''Validation of Alternative Microbiological Methods,'' states: ''Validation of a microbiological method is the process by which it is experimentally established that the performance characteristics of the method meet the requirements for the intended application.'' For sterility testing, this means that the test can consistently detect the presence of viable contaminating microorganisms.

We propose to eliminate the prescribed sterility test methods found in current § 610.12 and instead allow the use of sterility test methods that are validated in accordance with established protocols, to be capable of consistently detecting the presence of viable contaminating microorganisms. If an established USP compendial sterility test method is used, a manufacturer must verify that this established method is suitable for application to the specific product; however, FDA considers established USP compendial sterility test methods to already have been validated using an established validation protocol, so their accuracy, specificity, and reproducibility need not be re-established to fulfill the proposed validation requirement. In contrast, novel methods and any methods that deviate from the USP compendial sterility test methods would require the detailed validation discussed in the following paragraphs.

Proposed § 610.12 allows the use of a material sample that does not interfere with or otherwise hinder the sterility test from detecting viable contaminating microorganisms. This requirement is crucial, because the material itself or substances added to the material during formulation may make some sterility tests inappropriate for use. A validated sterility test method is a critical element in assuring the safety and quality of the product. USP General Chapter 1223, as well as the ICH Guideline for Industry (Text on Analytical Procedures), provide general descriptions of typical validation parameters, how they are determined, and which subset of each parameter is required to demonstrate validity, based on the method's intended use. Validation of each test method should be performed on a case-by-case basis, to ensure that the parameters are appropriate for the method's intended use. In the context of reviewing sterility test methods as part of BLAs and BLA supplements, FDA may decide, as appropriate, to encourage the use of the compendial method as a benchmark or starting point for validation of novel methods and certain other methods. FDA is specifically seeking comments on whether the proposed requirements are sufficient to ensure adequate validation of novel sterility test methods or whether additional criteria or guidance is needed.

It is important to consider validation principles, such as limit of detection, specificity, ruggedness, and robustness, while developing the validation protocol and performing validation studies. These terms are defined as follows:

- The limit of detection reflects the lowest number of microorganisms that can be detected by the method in a sample matrix. This is necessary to define what is considered contaminated.
- Specificity is the ability of the test method to detect a range of organisms necessary for the method to be suitable for its intended use. This is demonstrated by challenging the sterility test with a panel of relevant organisms in the sample matrix.
- Ruggedness is the degree of reproducibility of results obtained by analysis of the same sample under a variety of normal test conditions, such as different analysts, different instruments, and different reagent lots.
- Robustness is the capacity of the test method to remain unaffected by small, but deliberate variations in method parameters, such as changes in reagent concentration or incubation temperatures.

Under 21 CFR 211.160(b), laboratory controls must include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. We consider such laboratory controls to be needed for both culture-based and non-culture-based sterility test methods. The manufacturer must establish and document the test method's accuracy, sensitivity, specificity, and reproducibility (§ 211.165(e) (21 CFR 211.165(e)), as specified in the BLA or BLA supplement (§§ 601.2 and 601.12). For sterility tests, FDA believes that a validation protocol that would meet these standards would, at a minimum, include samples of the material to be marketed, and incorporate appropriate viable contaminating microorganisms to demonstrate the sterility test's growth-promoting properties or the method's detection system capabilities, depending on the type of test method used. In addition, validation protocols for culture-based methods should include both aerobic and anaerobic microorganisms when selecting test organisms and include microorganisms that grow at differing rates so that manufacturers can establish that the test media are capable of supporting the growth of a wide range of microorganisms.

When utilizing culture-based methods, validation protocols should require that challenge organisms be added directly to the product prior to membrane filtration or direct inoculation. If this is not possible due to inhibition by the product, then validation protocols should require that the challenge organism be added to the final portion of sterile diluent used to rinse the filter if a membrane filtration test method is used, or directly to the media containing the product if a direct inoculation test method is used. For non-culture-based methods, the feasibility of identifying microorganisms from a contaminated sample should be evaluated during validation. If a method does not have the capability to identify microorganisms to the species level, the validation protocol should require that an additional method for species identification be utilized for investigation of detected contaminants. The test organisms selected should reflect organisms that could be found in the product, process, or manufacturing environment.

The validation study design should contain the appropriate controls to evaluate the product sample's potential to generate false positive and false negative results. Validation of the sterility test should be performed on all new products, and repeated whenever there are changes in the test method that could potentially inhibit or enhance detection of viable contaminating microorganisms.

3. Verification

Verification is the confirmation that specified requirements have been fulfilled as determined by examination and provision of objective evidence. While validation of a sterility test method is the initial process of demonstrating that the procedure is suitable to detect viable contaminating microorganisms, verification occurs over the lifetime of the sterility test method and is the process of confirming that the sterility test and test components continue to be capable of consistently detecting viable

subsequently developed and approved by the Steering Committee in November 1996. The parent guideline is now renamed Q2(R1) as the Guideline Q2B on Methodology has been incorporated into the parent guideline. See *http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q2_R1/Step4/Q2_R1__Guideline.pdf.*

contaminating microorganisms in the samples analyzed. This verification activity may be necessary periodically or each time a sample is tested, depending upon the test method used. We propose to require that the sterility test and test components be verified, as appropriate, to demonstrate that they can continue to consistently detect viable contaminating microorganisms. (See section III.E.2 of this document for a more detailed discussion of verification.)

C. What information is needed in written procedures for sterility testing?

We propose to replace the requirement for *Interpretation of test results* in § 610.12(c) with the requirement that manufacturers establish, implement, and follow written procedures for sterility testing. Written procedures are essential to ensure consistency in sampling, testing, and interpretation of results, and to provide prospective acceptance criteria for the sterility test. Written procedures should include all steps to be followed in the sterility test method for initial and repeat tests. Procedures should be detailed and clear to eliminate ambiguity. Under the CGMP regulations, manufacturers are required to document that a drug product satisfactorily conforms to final specifications for the drug product (§ 211.165(a)). As such, scientifically sound and appropriate specifications, standards, sampling plans, and test procedures must be designed and written to ensure that materials conform to appropriate standards of sterility; and written procedures must include a description of the sampling method and the number of units per batch to be tested. (See § 211.165(c).)

Proposed § 610.12 allows the use of either culture-based or non-culture-based sterility test methods to evaluate material for sterility. There are marked differences between culture-based and non-culture-based sterility tests. Proposed § 610.12(c) provides the following minimum critical considerations that must be included in written procedures for both culture-based and non-culture-based sterility tests:

- The sterility test method to be used;
- The method of sampling, including the number, volume, and size of articles to be tested;
- Written specifications for the acceptance or rejection of each lot; and
- A statement of any other function critical to the particular sterility test method to ensure consistent and accurate results.

For culture-based sterility test methods, FDA believes the minimum critical considerations include the composition of media, growth promotion test requirements, and incubation conditions (time and temperature). For non-culture-based sterility test methods, the Agency believes critical considerations include the composition of test components, test parameters, and the controls used to verify the test method's ability to consistently detect the presence of viable contaminating microorganisms.

D. What is an appropriate sample for sterility testing?

Selection of an appropriate sample of a lot is critical for purposes of sterility testing. Current § 610.12(d) prescribes the number of samples for testing bulk and final container material. Due to the variety of products covered under § 610.12, including innovative products that may be introduced to the market in the future, such as cell and gene therapy products, we propose to eliminate the sample number requirement and instead require that the sample be appropriate to the material being tested. In selecting an appropriate sample size, proposed § 610.12(d) requires that the following minimal criteria be considered:

- The size or volume of the final product lot. For example, a final product lot size of 100,000 units would necessitate a greater number of samples to be evaluated than a final product lot size of 5,000 units;
- The duration of manufacturing of the drug product.[8] For example, samples should be taken at different points of manufacture, which, at a minimum should include the beginning, middle, and end of manufacturing, in an effort to provide evidence of sterility of the drug product throughout the duration of the manufacturing process;
- The final container configuration and size. We believe this will ensure appropriate representation of the lot;
- The quantities or concentrations of inhibitors, neutralizers, and preservatives, if present, in the test material;
- For a culture-based test method, the volume of test material that results in a dilution of the product that was determined not to be bacteriostatic or fungistatic; and
- For a non-culture-based test method, the volume of test material that results in a dilution of the product that does not inhibit or otherwise hinder the detection of viable contaminating microorganisms.

[8] See 21 CFR 210.3(b)(4) for definition of ''drug product.''

E. What is required to verify the sterility test?

Verification activities are necessary to demonstrate that sterility test methods can continue to reliably and consistently detect viable contaminating microorganisms. The degree of verification necessary depends upon the sterility test method employed. Depending upon the sterility test method, verification of each individual test might be appropriate. On the other hand, some sterility test methods may only need verification activities performed on the selected culture media or test organisms. We propose under § 610.12(e) that manufacturers perform verification activities appropriate for the sterility test method chosen as follows:

1. For culture-based test methods, manufacturers must conduct tests to demonstrate that the performance of the test organisms and culture media are acceptable to consistently detect the presence of viable contaminating microorganisms, including tests for each lot of culture media to verify its growth-promoting properties over the shelf-life of the media. Growth-promotion testing is important to demonstrate that the culture media are capable of supporting the growth of microorganisms.

2. For non-culture-based test methods, manufacturers must include, within the test itself, appropriate controls to demonstrate the ability of the test method to continue to reliably and consistently detect the presence of viable contaminating microorganisms.

F. Can a sterility test be repeated?

Current regulations in § 610.12(b) allow one time repeat testing of the bulk material to verify results after a positive initial test. Repeat testing for final container sterility testing is permitted twice, provided there was no evidence of growth in any test of the bulk material. Under current § 610.12(c), a lot meets the test requirements for sterility if no growth appears during the repeat tests. We propose to eliminate the reference to repeat testing of bulk material, because we are proposing that sterility testing will not be required on bulk material in most instances.[9] We further propose to modify the provision for repeat testing to harmonize our regulatory expectations with current scientific understanding of quality manufacturing controls by eliminating the use of a second repeat test for final container material.

Consistent with USP Chapter 71, we propose that if the initial test indicates

[9] See section III.A of this document for discussion of when sterility testing of bulk material may be appropriate.

the presence of microorganisms, then the product being examined does not comply with the sterility test requirements, unless a thorough investigation by the quality control unit can conclusively ascribe the initial evidence of microbial presence to a laboratory error or faulty materials used in conducting the test. If the test of the initial sample is found to be invalid, due to laboratory error or faulty test materials, the sterility test may be repeated one time. If no evidence of microorganisms is found in the repeat test, the product examined complies with the test requirements for sterility; if evidence of microorganisms is found in the repeat test, the product examined does not comply with the test requirements for sterility (USP Chapter 71).[10]

We further propose that for repeat testing, comparable product that is reflective of the initial sample in terms of sample location and the stage in the manufacturing process from which it was taken, and the same sterility test method must be used for both the initial and repeat tests. This is intended to ensure that the same volume of material is used for the initial test and each repeat test, and that the interpretation of the results is conducted in the same manner.

This proposed rule, if finalized, could result in the need for some manufacturers to modify their repeat test procedures. We consider these modifications to be minor changes in accordance with § 601.12(d) and to have a minimal potential for an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. Therefore, such changes must be reported in an annual report within 60 days of the anniversary date of approval of the BLA.

G. What records must be kept relating to sterility testing?

Currently, § 610.12(h) incorporates by reference the recordkeeping and maintenance requirements contained in 21 CFR 211.167 and 211.194. We propose to continue to maintain these requirements. This is intended to assure that data derived from sterility tests comply with established specifications. This includes describing the samples received for testing, stating the method used to test the samples, identifying the location of relevant validation or verification data, recording all calculations performed, and stating how the results of tests performed compare to set specifications.

H. Are there any exceptions to sterility test requirements?

We propose to maintain the current exceptions to the sterility test requirements in § 610.12(g)(4)(i) for Whole Blood, Cryoprecipitated AHF, Platelets, Red Blood Cells, Plasma, Source Plasma, Smallpox Vaccine, Reagent Red Blood Cells, Anti-Human Globulin, and Blood Grouping Reagent. However, we request comment on whether any of these current exceptions should be removed. For example, we specifically request comment on whether to remove the exemption for platelets. Bacterial contamination of platelets is a recognized public health risk and the blood collection industry has already called for and implemented methods to detect and limit or inactivate bacteria in platelet components. Requiring testing for platelets would be consistent with these industry practices.

We propose to make minor modifications to the current exception in § 610.12(g)(4)(ii), under which the Director of CBER or CDER, as appropriate, determines that data submitted adequately establish that the mode of administration, the method of preparation, or the special nature of the product precludes or does not require a sterility test or that the sterility of the lot is not necessary to assure the safety, purity, and potency of the product. Specifically, we refer to the ''route of administration'' rather than the ''mode of administration'' and to the ''any other aspect of the product'' rather than ''the special nature of the product'' in proposed § 610.12(h)(2) so as to account for novel products that may be introduced to the market in the future, such as cell and gene therapy products. This proposed exception allows the Director of CBER or CDER, as appropriate, to exempt biological material from the sterility test requirements of this section if, based upon the scientific evidence presented in the BLA or BLA supplement, the data adequately establish that the route of administration, method of preparation, or any other aspect of the product precludes or does not necessitate a sterility test to assure the safety, purity, and potency of the product. This proposed exception also would allow the Director of CBER or CDER, as appropriate, to require sterility testing of the bulk material subject to any conditions necessary to assure the safety, purity, and potency of the product.

We propose to eliminate the current exceptions under § 610.12(g)(1) and (g)(2) because they are no longer necessary given the flexibility built into this proposal. Specifically, the current exception in § 610.12(g)(1) allows for the use of different sterility test methods prescribed for certain products. We further propose to eliminate the current exception under § 610.12(g)(2), for using two sterility tests, one at incubation temperatures of 18° to 22 °C and one at 30° to 37 °C, in lieu of performing one test using an incubation temperature of 30° to 35 °C. The proposed language in § 610.12(b) requires the sterility test used to be ''* * * appropriate to the material being tested * * *'' and proposed § 610.12(c) requires manufacturers to specify incubation conditions (time and temperature) in written procedures for sterility testing when culture-based media are used. These proposed changes are intended to provide sufficient flexibility for the use of different sterility test methods, as appropriate.

We propose to eliminate the current exceptions for *Number of final containers more than 20, less than 200* (§ 610.12(g)(5)), *Number of final containers—20 or less,* (§ 610.12(g)(6)), *Samples—large volume of product in final containers,* (§ 610.12(g)(7)), and *Immune globulin preparations.* (§ 610.12(g)(9)). Instead, we propose to require manufacturers to determine the appropriate sample volume and size for the material being tested. (See proposed § 610.12(d).) Similarly, we propose to eliminate the special requirements in the *Diagnostic biological products not intended for injection* exception (§ 610.12(g)(8)). We believe the special requirements in current § 610.12(g)(8) are no longer necessary because proposed § 610.12(b)(1) requires the sterility test to be ''appropriate to the material being tested'' and proposed § 610.12(d) requires manufacturers to determine the appropriate sample volume and size for the material being tested.

IV. Proposed Revisions to Other Regulations

In addition to the revisions to the sterility regulation in § 610.12, we are also proposing revisions to two other FDA regulations as a result of this proposed rule. These proposed revisions are as follows:

- Section 600.3(q): Current § 600.3(q) defines ''sterility'' to mean ''* * * freedom from viable contaminating microorganisms, as determined by the

[10] See also Barr, Fish, and Schwemer, *Application of Pharmaceutical CGMPs,* the Food and Drug Law Institute, p. 149, (''In the case of a clearly identified laboratory error, the retest results substitute for the original test results * * * If, on the other hand, no laboratory error could be identified in the first test, then there is no scientific basis for discarding the initial out-of-specification results in favor of passing retest results''), 1997.

tests prescribed in § 610.12 of this chapter.'' We are proposing to reword this definition to eliminate the term ''prescribed'' since, as proposed, § 610.12 would not prescribe specific test methods. Thus, we are proposing to amend § 600.3(q) to define ''sterility'' as ''* * * freedom from viable contaminating microorganisms, as determined by tests conducted under § 610.12 of this chapter.''

• Section 680.3(c): Currently, § 680.3(c) states that: ''A sterility test shall be performed on each lot of each Allergenic Product, as prescribed in § 610.12 of this chapter, with the following exceptions: * * * When bulk material is not prepared, the sterility test prescribed for bulk material shall be performed on each container of each stock concentrate at the time a stock concentrate is prepared, and the test sample shall be no less than 1 ml. from each stock concentrate container. * * * For lots consisting of no more than 5 final containers, the final container test shall be performed in accordance with § 610.12(g)(6) of this chapter using the sample therein prescribed or using a sample of no less than 0.25 ml. of product from each final container, divided in approximately equal proportions for testing in Fluid Thioglycollate and Soybean-Casein Digest Media. The test sample in the later alternative method may be an overfill in the final container. * * * For products prepared in sets of individual dilution series, a test sample of 0.25 ml. shall be taken from a final container of each dilution, which samples may be pooled and one half of the pooled material used for the test with Fluid Thioglycollate Medium and one half used for the test with Soybean-Casein Digest Medium. * * * Tablets and capsules need not be tested for sterility provided aseptic techniques are employed in their manufacture.''

We are proposing to amend § 680.3(c) to eliminate the term ''prescribed''. As proposed, § 680.3(c) would say that ''a sterility test shall be performed on each lot of each Allergenic Product, as required by § 610.12 of this chapter.'' Additionally, we are proposing to eliminate § 680.3(c)(1) through (c)(4), because these exceptions would no longer be necessary under the proposed revisions to § 610.12. As proposed § 610.12 would eliminate the sterility test requirement on most bulk material, so the exception in § 680.3(c)(1) of how to test allergenic products when bulk material is not prepared, would no longer be needed. To the extent it is appropriate to perform the sterility test on bulk product for allergenics, the approach for such testing will be explained in the BLA or BLA supplement that is submitted by the manufacturer and approved by FDA. Moreover, § 610.12, as proposed, would not prescribe a specific sample number and would not contain the specific exemption in § 610.12(g)(6) referenced in § 680.3(c)(2). The proposed requirement that the sample be appropriate to the materials being tested would accommodate the situation envisioned by current § 680.83(c)(2) for lots consisting of no more than five final containers. Current § 680.83(c)(3) should similarly be accommodated by the flexible language of the proposal such that sterility tests for sets of individual dilution series can be done on test samples that are appropriate to these material and thus a specific exception would no longer be needed for the sterility testing of these products. Finally, current § 680.83(c)(4) would be accommodated by the general exception in proposed § 610.12(h)(2) and thus this fourth exception would also be rendered unnecessary.

V. Legal Authority

FDA is issuing this regulation under the biological products provisions of the Public Health Service Act (42 U.S.C. 262 and 264) and the drugs and general administrative provisions of the Federal Food, Drug, and Cosmetic Act (sections 201, 301, 501, 502, 503, 505, 510, 701, and 704) (21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 371, and 374). Under these provisions of the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act, we have the authority to issue and enforce regulations designed to ensure that biological products are safe, effective, pure, and potent, and to prevent the introduction, transmission, and spread of communicable disease.

VI. Analysis of Impacts

FDA has examined the impacts of the 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.

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 generally increases flexibility for sterility testing and codifies an approach for retesting similar to the approach prescribed by the USP, and does not add any new regulatory responsibilities, the Agency proposes to certify that the final rule will 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 $135 million, using the most current (2009) 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.

These amendments would generally provide manufacturers of biological products with more flexibility as to how they evaluate the sterility of their products and reduce the number of evaluations required. The net effect would be to reduce costs.

One part of these proposed amendments might impose some additional costs on manufacturers, however. Under the current regulations, if a biological product fails a sterility test, the test may be repeated. If the product passes a subsequent test, it is inferred that the first test was flawed and only the later results are used. Under the new regulations, the test may be repeated only if it is possible to ''ascribe definitively'' the initial failure to ''a laboratory error or faulty materials used in conducting the sterility testing.''

This change could increase costs for manufacturers because of the additional products that would be discarded. The size of the increase would be determined by the number of additional lots discarded, the lot sizes and the production costs per unit. Some or all of the costs of this change would be mitigated by the reduction in losses associated with the provision of contaminated products.

This change is expected to affect few manufacturers. The method for sterility testing described in Chapter 71 of USP 33–NF 28 already limits the repetition of tests to circumstances similar to those described in these amendments. It is

anticipated that, in the absence of these amendments, the majority of manufacturers would limit the repetition of sterility tests in order to comply with USP Chapter 71. The Agency invites comment on the frequency with which manufacturers diverge from the retesting protocol of these amendments and the costs that limiting retests will impose.

The benefit of limiting retests would be fewer illnesses caused by contaminated biological products. We are unable to quantify the value of the reduction in illnesses because we do not have an estimate of the risk of illness from contaminated biological products or the decline in that risk associated with limiting retests.

VII. Environmental Impact

The Agency has determined under 21 CFR 25.31(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. The Paperwork Reduction Act of 1995

This proposed rule refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). The collections of information in §§ 211.165 and 610.12 have been approved under OMB control number 0910–0139. Therefore, FDA tentatively concludes that the proposed requirements in this document are not subject to review by OMB because they do not constitute a ''new collection of information'' under the PRA.

IX. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed 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 concluded that the proposed 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.

X. Proposed Effective Date

FDA is proposing that any final rule that may issue based on this proposal be effective 90 days after the date of its publication in the **Federal Register**.

XI. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments 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 600

Biologics, Reporting and recordkeeping requirements.

21 CFR Part 610

Biologics, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 680

Biologics, Blood, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 600, 610, and 680 be amended as follows:

PART 600—BIOLOGICAL PRODUCTS: GENERAL

1. The authority citation for 21 CFR part 600 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 360i, 371, 374; 42 U.S.C. 216, 262, 263, 263a, 264, 300aa–25.

§ 600.3 [Amended]

2. Section 600.3 is amended in paragraph (q) by removing the phrase ''prescribed in'' and by adding in its place the phrase ''conducted under''.

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

3. The authority citation for 21 CFR part 610 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360c, 360d, 360h, 360i, 371, 372, 374, 381; 42 U.S.C. 216, 262, 263, 263a, 264.

4. Section 610.12 is revised to read as follows:

§ 610.12 Sterility.

(a) *The test.* Except as provided in paragraph (h) of this section, manufacturers of biological products must perform sterility testing of each lot of each biological product's final container material or other material, as appropriate and as approved in the biologics license application or supplement for that product.

(b) *Test requirements.* (1) The sterility test must be appropriate to the material being tested such that the material does not interfere with or otherwise hinder the test.

(2) The sterility test must be validated to demonstrate that the test is capable of reliably and consistently detecting the presence of viable contaminating microorganisms.

(3) The sterility test and test components must be verified to demonstrate that the test method can consistently detect the presence of viable contaminating microorganisms.

(c) *Written procedures.* Manufacturers must establish, implement, and follow written procedures for sterility testing that describe, at a minimum, the following:

(1) The sterility test method to be used;

(i) If culture-based test methods are used, include, at a minimum:

(A) Composition of the culture media;

(B) Growth-promotion test requirements; and

(C) Incubation conditions (time and temperature).

(ii) If non-culture-based test methods are used, include, at a minimum:

(A) Composition of test components;

(B) Test parameters, including acceptance criteria; and

(C) Controls used to verify the method's ability to detect the presence of viable contaminating microorganisms.

(2) The method of sampling, including the number, volume, and size of articles to be tested;

(3) Written specifications for the acceptance or rejection of each lot; and

(4) A statement of any other function critical to the particular sterility test method to ensure consistent and accurate results.

(d) *The sample.* The sample must be appropriate to the material being tested, considering, at a minimum:

(1) The size and volume of the final product lot;

(2) The duration of manufacturing of the drug product;

(3) The final container configuration and size;

(4) The quantity or concentration of inhibitors, neutralizers, and preservatives, if present, in the tested material;

(5) For a culture-based test method, the volume of test material that results in a dilution of the product that is not bacteriostatic or fungistatic; and

(6) For a non-culture-based test method, the volume of test material that results in a dilution of the product that does not inhibit or otherwise hinder the detection of viable contaminating microorganisms.

(e) *Verification.* (1) For culture-based test methods, studies must be conducted to demonstrate that the performance of the test organisms and culture media are suitable to consistently detect the presence of viable contaminating microorganisms, including tests for each lot of culture media to verify its growth-promoting properties over the shelf-life of the media.

(2) For non-culture-based test methods, within the test itself, appropriate controls must be used to demonstrate the ability of the test method to continue to consistently detect the presence of viable contaminating microorganisms.

(f) *Repeat Test Procedures.* (1) If the initial test indicates the presence of microorganisms, the product does not comply with the sterility test requirements unless a thorough investigation by the quality control unit can ascribe definitively the microbial presence to a laboratory error or faulty materials used in conducting the sterility testing.

(2) If the investigation described in paragraph (f)(1) of this section finds that the initial test indicated the presence of microorganisms due to laboratory error or the use of faulty materials, a sterility test may be repeated one time. If no evidence of microorganisms is found in the repeat test, the product examined complies with the sterility test requirements. If evidence of microorganisms is found in the repeat test, the product examined does not comply with the sterility test requirements.

(3) If a repeat test is conducted, the same test method must be used for both the initial and repeat tests, and the repeat test must be conducted with comparable product that is reflective of the initial sample in terms of sample location and the stage in the manufacturing process from which it was obtained.

(g) *Records.* The records related to the test requirements of this section must be prepared and maintained as required by 21 CFR 211.167 and 211.194 of this chapter.

(h) *Exceptions.* Sterility testing must be performed on final container material or other appropriate material as defined in the approved biologics license application or supplement and as described in this section, except as follows:

(1) Sterility testing is not required for Whole Blood, Cryoprecipitated Antihemophilic Factor, Platelets, Red Blood Cells, Plasma, Source Plasma, Smallpox Vaccine, Reagent Red Blood Cells, Anti-Human Globulin, and Blood Grouping Reagents.

(2) A manufacturer is not required to comply with the sterility test requirements if the Director of the Center for Biologics Evaluation and Research or the Director of the Center for Devices and Radiological Health, as appropriate, determines that data submitted in the biologics license application or supplement adequately establish that the route of administration, the method of preparation, or any other aspect of the product precludes or does not necessitate a sterility test to assure the safety, purity, and potency of the product.

PART 680—ADDITIONAL STANDARDS FOR MISCELLANEOUS PRODUCTS

5. The authority citation for 21 CFR part 680 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371; 42 U.S.C. 216, 262, 263, 263a, 264.

6. Section 680.3 is amended by revising paragraph (c) to read as follows:

§ 680.3 Tests.

* * * * *

(c) *Sterility.* A sterility test shall be performed on each lot of each Allergenic Product as required by § 601.12 of this chapter.

Dated: June 16, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011–15346 Filed 6–20–11; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF JUSTICE

28 CFR Part 104

[Docket No. CIV 151]

RIN 1105–AB39

James Zadroga 9/11 Health and Compensation Act of 2010

AGENCY: Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: On January 2, 2011, President Obama signed into law the James Zadroga 9/11 Health and Compensation Act of 2010 (Zadroga Act). Title II of the Zadroga Act reactivates the September 11th Victim Compensation Fund of 2001 and requires a Special Master, appointed by the Attorney General, to provide compensation to any individual (or a personal representative of a deceased individual) who suffered physical harm or was killed as a result of the terrorist-related aircraft crashes of September 11, 2001, or the debris removal efforts that took place in the immediate aftermath of those crashes. This rule proposes to amend the regulations implementing the Fund to reflect the changes made by the Zadroga Act.

DATES: Written comments must be postmarked and electronic comments must be submitted on or before August 5, 2011. Comments received by mail will be considered timely if they are postmarked on or before that date. The electronic Federal Docket Management System (FDMS) will accept comments until Midnight Eastern Time at the end of that day.

ADDRESSES: Comments may be mailed to Kenneth L. Zwick, Director, Office of Management Programs, Civil Division, U.S. Department of Justice, Main Building, Room 3140, 950 Pennsylvania Avenue, NW., Washington, DC 20530. However, the Department encourages commenters to submit their comments using *http://www.regulations.gov.*

FOR FURTHER INFORMATION CONTACT: Kenneth L. Zwick, Director, Office of Management Programs, Civil Division, U.S. Department of Justice, Main Building, Room 3140, 950 Pennsylvania Avenue, NW., Washington, DC 20530, telephone 855–885–1555 (TTY 855–885–1558).

SUPPLEMENTARY INFORMATION:

Comment Period: The Department of Justice has allocated 45 days for public comment. This timeline is appropriate in light of the proposed regulations' substantial incorporation of the regulations that were previously used, the Department's experience in operating the Victim Compensation Fund, and the public interest in beginning operation of the Fund as soon as possible.

Posting of Public Comments: Please note that all comments received are considered part of the public record and made available for public inspection online at *http://www.regulations.gov.* Such information includes personal identifying information (such as your name and address) voluntarily submitted by the commenter.

You are not required to submit personal identifying information in order to comment on this rule. Nevertheless, if you want to submit personal identifying information (such