DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2011–N–0729]

Microbiology Devices; Classification of In Vitro Diagnostic Device for Yersinia Species Detection

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to classify in vitro diagnostic devices for *Yersinia* species (spp.) detection into class II (special controls), in accordance with the recommendation of the Microbiology Devices Advisory Panel (the panel). FDA is publishing in this document the recommendation(s) of the panel regarding the classification of this device. After considering public comments on the proposed classification, FDA will publish a final regulation classifying this device.

DATES: Submit either electronic or written comments by February 6, 2012. See section IV of this document for the proposed effective date of a final rule based on this proposed rule.

ADDRESSES: You may submit comments, identified with the FDA docket number found in brackets in the heading of this document, 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–N–0729 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 ''Request for 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: Beena Puri, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5553, Silver Spring, MD 20993–0002, (301) 796–6202.

SUPPLEMENTARY INFORMATION:

I. Background

A. Legal Authority

The Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (Pub. L. 101–629), the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105–115), the Medical Device User Fee and Modernization Act (Pub. L. 107–250), and the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110–85), among other amendments, established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval). Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability for comment of the draft guidance document that FDA proposes to designate as a special control for this device. In addition, the proposed rule would establish as a special control limitations on the distribution of this device.

Under section 513 of the FD&C Act, FDA refers to devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), as ''preamendments devices.'' FDA classifies a device after it: (1) Receives a recommendation from a device classification panel (an FDA advisory committee); (2) publishes the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) publishes a final regulation classifying the device type (see section 513(d) of the FD&C Act). FDA has classified most preamendments devices under these procedures.

FDA refers to devices that were not in commercial distribution before May 28, 1976, as ''postamendments devices.'' These devices are classified automatically by statute (section 513(f) of the FD&C Act) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless and until: (1) FDA reclassifies the device into class I or II; (2) FDA issues an order classifying the device into class I or II in accordance with section 513(f)(2) of the FD&C Act, as amended by the FDAMA; or (3) FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to previously offered devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and 21 CFR part 807 of the regulations.

A person may market a preamendments device that has been classified into class III through premarket notification procedures, without submission of a premarket approval application until FDA promulgates a final regulation under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval.

Consistent with the FD&C Act and the regulations, FDA consulted with the panel, regarding the classification of this device.

B. Regulatory History of In Vitro Diagnostic Devices for Yersinia spp. Detection

After the enactment of the Medical Device Amendments of 1976, FDA undertook to identify and classify all preamendments devices, in accordance with section 513(b) of the FD&C Act. However, in vitro diagnostic devices for *Yersinia* spp. detection were not identified and classified in this initial effort. FDA subsequently identified several preamendments devices for *Yersinia* spp. detection, including *Yersinia* spp. antisera conjugated with a fluorescent dye (immunofluorescent reagents) used to presumptively identify *Yersinia*-like organisms in clinical specimens, antigens used to identify antibodies to *Y. pestis* (Fraction 1) in serum, and bacteriophage used for differentiating *Y. pestis* from other

Yersinia spp. based on susceptibility to lysis by the phage.

Consistent with the FD&C Act and the regulations, FDA held a panel meeting on March 7, 2002, regarding the classification of the preamendments in vitro diagnostic devices for *Yersinia* spp. detection. After the panel meeting FDA found one additional in vitro diagnostic device for *Yersinia* spp. detection to be substantially equivalent to a preamendment device within that type. The additional device has the same intended use as its predicate device but makes use of newer nucleic acid amplification technology (NAAT). While it exhibits technological differences from the preamendments *Yersinia* spp. detection devices, FDA has determined that it is as safe and effective as, and does not raise different questions of safety and effectiveness from its predicate (see section 513(i) of the FD&C Act).

II. Panel Recommendation

At a public meeting held on March 7, 2002, the panel recommended that in vitro diagnostic devices for *Yersinia* spp. detection (Ref. 1) be classified into class II.

A. Identification

FDA is proposing the following identification based on the panel's recommendation and the available information. An in vitro diagnostic device for *Yersinia* spp. detection is used to detect and differentiate among *Yersinia* spp. and presumptively identify *Y. pestis* and other *Yersinia* spp. from cultured isolates or clinical specimens as an aid in the diagnosis of plague and other diseases caused by *Yersinia* spp. This device may consist of *Yersinia* spp. antisera conjugated with a fluorescent dye (immunofluorescent reagents) used to presumptively identify *Yersinia*-like organisms in clinical specimens or bacteriophage used for differentiating *Y. pestis* from other *Yersinia* spp. based on susceptibility to lysis by the phage or antigens used to identify antibodies to *Y. pestis* (Fraction 1) in serum. Diseases caused by *Yersinia* infections include three different forms of plague (bubonic, pneumonic, and septicemic), caused by *Y. pestis,* and gastrointestinal infection, caused by *Y. pseudotuberculosis* and *Y. enterocolitica.*

B. Classification Recommendation

The panel recommended that in vitro diagnostic devices for *Yersinia* spp. detection be classified into class II. The panel believed that class II with special controls (guidance document and limitations on the distribution) would provide reasonable assurance of the safety and effectiveness of the device.

C. Summary of Reasons and Data To Support the Recommendation

The panel considered information from the literature presented by FDA (Refs. 2 to 7), information presented at the meeting by representatives from the United States Army Medical Research Institute for Infectious Diseases who shared the historical perspective on their institution's use of devices for the detection of *Y. pestis* and their personal experience using these devices, and the panel's personal knowledge and experience.

Evidence presented to the panel addressed how the preamendments devices of this type work and some of their limitations. Bacteriophage tests are used for differentiating *Y. pestis* from *Y. pseudotuberculosis.* The test is performed at 20–25 °C because the bacteriophage can lyse *Y. pseudotuberculosis* at 37 °C but not at lower temperatures. Lysis at 22–25 °C provides presumptive evidence that a culture isolate is *Y. pestis.* The fluorescent antibody reagent is a fluorescein-labeled antibody against Fraction 1 (F1) antigen that is used to microscopically visualize specific binding with cultured bacteria. A protein from the capsular envelope of *Y. pestis* is used to microscopically visualize specific binding with cultured bacteria. The test can be performed with culture growth or can be done on clinical specimens that have gram-negative bacteria resembling *Y. pestis.* The presence of F1 antigen is presumptive evidence of *Y. pestis,* which must be confirmed with other testing. F1 antigen can be used to sensitize sheep erythrocytes for hemagglutination testing to detect antibody responses to F1 in human sera. Significant levels of human antibody to this antigen can be retrospective confirmation of *Y. pestis* infection or can be presumptive of *Y. pestis* infection when a single serum sample is tested.

The panel discussed considerations about use of these devices, including the training, experience, and facilities necessary for safe handling of test materials and specimens, and for appropriate test execution and interpretation of test results. They also discussed the desirability of coordination by public health Agencies, including the Centers for Disease Control and Prevention, to ensure that appropriate performance standards and use guidelines are developed for these tests and to encourage that test results be reported to public health authorities.

The panel recommended that in vitro diagnostic devices for *Yersinia* spp. detection should be classified into class II because they concluded that special controls, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance.

D. Risks to Health

Based on the panel's discussion and recommendations, and FDA's experience with these devices, we believe the following are risks to health associated with the use of the device type.

Failure of in vitro diagnostic devices for *Yersinia* spp. detection to perform as indicated or an error in interpretation of results may lead to misdiagnosis and improper patient management or inaccurate epidemiological information that may contribute to inappropriate public health responses. FDA believes that this type of device presents risks associated with a false-negative test result and a false-positive test result, as explained in this document. In addition, there may be risks to laboratory workers resulting from handling positive cultures and control materials.

A false-positive result may lead to a medical decision causing a patient to undergo unnecessary or ineffective treatment, as well as inaccurate epidemiological information on the presence of plague disease in a community. A false-negative result may lead to delayed recognition by the physician of the presence or progression of disease and inaccurate epidemiological information to control and prevent additional infections. A false-negative result could potentially delay diagnosis and treatment of infection caused by *Y. pestis* or other *Yersinia* spp.

Additionally, exposure to organisms potentially present in test specimens and those used as control materials poses a risk of infection of *Yersinia* to laboratory workers.

E. Special Controls

Based on the panel's discussion and recommendations, FDA believes that, in addition to general controls, the proposed special controls discussed in this document are adequate to address the risks to health.

FDA believes that the draft guidance document entitled ''Class II Special Controls Guidance Document: In Vitro Diagnostic Devices for *Yersinia* spp. Detection'' and limitations on distribution of these devices, set forth in the proposed classification regulation,

will address the risks identified previously in this document and provide a reasonable assurance of safety and effectiveness of the device. The class II special controls guidance document provides information on how to meet premarket (510(k)) submission requirements for the assays in sections that discuss performance studies and labeling. The guidance document provides specific recommendations for NAAT tests and tests using the technologies employed by the preamendments devices. The performance studies section of the guidance describes studies to demonstrate appropriate performance and control against assays that may otherwise fail to perform to acceptable standards. The labeling section of the guidance addresses factors such as directions for use, quality control, and precautions for use and interpretation. The special controls guidance recommendations will allow the manufacturer to identify the causes of false-positive and false-negative test results and appropriately label their device to limit the occurrence of false positives and false negatives.

In addition, FDA proposes as a special control that distribution of these devices be limited to laboratories with experienced personnel who have training in principles and use of microbiological culture identification methods and infectious disease diagnostics, and with appropriate biosafety equipment and containment. As noted, the panel was concerned about improper use of these devices and recommended that these devices be used only by personnel sufficiently skilled to maximize their performance and to appropriately interpret and make use of test results. FDA believes that this proposed distribution limitation will appropriately help assure the safe and effective use of these devices and that it is consistent with the intent of the panel in its discussion of limitations on the use of the devices and on monitoring of test results.

TABLE 1—RISKS TO HEALTH AND MITIGATION MEASURES

Identified risks	Mitigation measures
A false-negative test result may lead to delay of therapy and progression of disease and epidemiological failure to promptly recognize disease in the community.	Device description—recommended. Performance studies—recommended. Labeling—recommended. Limited distribution—required.
A false-positive test result may lead to unnecessary treatment and incorrect epidemiological information that leads to unnecessary prophylaxis and management of others.	Device description—recommended. Performance studies—recommended. Labeling—recommended. Limited distribution—required.
Biosafety and a risk of transmission of *Yersinia* infection to laboratory workers handling test specimens and control materials.	Labeling—recommended. Limited distribution—required.

III. Proposed Classification

FDA agrees with the panel's recommendation that in vitro diagnostic devices for *Yersinia* spp. detection should be classified into class II because special controls, in addition to general controls, will provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance.

IV. Proposed Effective Date

FDA proposes that any final regulation based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

V. Environmental Impact

The Agency has determined that under 21 CFR 25.34(b) this classification 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.

VI. Analysis of Impacts

A. Introduction

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 (Pub. L. 104–4). Executive Orders 12866 and 13563 direct 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 12866.

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 would create no new burdens, 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 $136 million, using the most current (2010) 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.

B. Need for Regulation

In vitro diagnostic devices used to identify and differentiate among *Yersinia* spp. are currently unclassified preamendment devices. Heightened interest in biological warfare and bioterrorism has generated interest in devices that would identify *Y. pestis,* the pathogen responsible for plague and other diseases. FDA has identified information for the safe and effective use of such devices and has applied this information in its clearance of a device that identifies *Y. pestis.* However, the lack of a formal device classification and published guidance may deter additional firms from entering the market for such devices. Devices are typically classified, and these designations are published in the **Federal Register**.

Market failure can occur when market participants lack important information or when they possess incorrect information. Because this device lacks a

formal classification and published data recommendations, potential manufacturers may be unable to assess whether to enter this market. Even manufacturers in possession of these standards that would otherwise enter this market might interpret the absence of a formal classification as FDA uncertainty about its premarket review requirements or that FDA may be about to change these requirements, making market entry seem riskier than it is. The market failure we intend to address is one of imperfect information. Classifying this device would provide valuable information to manufacturers about what is needed to obtain FDA clearance. Manufacturers lacking this information might choose not to enter the market for this device when a well-informed manufacturer would. Moreover, the submission process may be unclear to both manufacturers and FDA because the data requirements are not clearly articulated.

C. Background

Y. pestis, the causative agent of plague, is associated with over 100 million deaths worldwide during three historical pandemics. Rodents and other mammals have historically served as reservoirs of plague, while fleas feeding on these animals are vectors that can transmit the disease to humans. Improved urban sanitary conditions, including improved rodent control, has dramatically reduced the incidence of plague, while availability of antibiotics has dramatically lowered the mortality rate.

Plague has been endemic in the continental United States since at least 1900. The United States averaged 18 cases of plague per year in the 1980s and 9 cases per year since 1990. In 2006, a total of 13 human plague cases were reported among residents of four states. This is the largest number of cases reported in a single year in the United States since 1994. Two of the 13 cases were fatal.

Those infected with plague are likely to survive if they are treated with antibiotics soon after the symptoms appear. Treatment generally consists of taking antibiotics for at least 7 days. Without treatment, mortality is 60 percent for bubonic plague and 100 percent for pneumonic and septicemic plague. The primary public health issue associated with plague, however, would be its potential use in warfare or in an act of terrorism, where hundreds or thousands of individuals could be infected. Effective treatment would require rapid diagnosis, the timely administration of antibiotics, and public health measures to minimize the risk of further infection.

In the event of a potential massive plague outbreak, one would want to be able to test for *Y. pestis* quickly and accurately. Rapid identification of *Y. pestis* and diagnosis of plague would improve the ability to treat infected individuals and minimize the chances of infecting others. Reducing the likelihood of false-negative testing results would minimize the possibility that infected individuals would be left untreated and that the disease would go undetected by public health officials. Reducing the likelihood of false-positive testing results would minimize potential costs associated with unnecessary therapy and unnecessary infection control measures.

The Microbiology Devices Panel met March 7, 2002, to recommend a classification for in vitro diagnostic products for the identification of *Yersinia* spp. The panel recommended that the devices be classified as class II, without exemption from premarket notification requirements, and that special controls include testing guidelines, performance characteristics, and restrictions on distribution. FDA generally concurs with these recommendations.

In vitro diagnostic devices for *Yersinia* spp. detection are preamendment, unclassified devices. As such, manufacturers of new devices for *Yersinia* spp. detection may market these devices through premarket notification procedures and are not required to submit premarket approval applications. In 2007, a manufacturer obtained FDA clearance for a device to detect *Y. pestis* through the 510(k) premarket notification procedures. Throughout the process, FDA advised the applicant on the studies that would establish the performance characteristics of the device, device labeling, and distribution restrictions to demonstrate substantial equivalence to a preamendment device. This data submission was consistent with the recommendations of the 2002 panel. Absent this rulemaking effort, FDA would continue to regulate this device in this fashion.

D. Description of the Proposed Rule

Through this proposal, FDA intends to follow the recommendations of the 2002 Microbiology Devices Panel. This proposed rule would place devices used for the in vitro identification of *Yersinia* spp. into class II (special controls). General controls alone would be inadequate for safe and effective use, and the class III premarket application process would be unnecessary. The proposed special controls are consistent with the principle of applying the appropriate regulatory control necessary to provide reasonable assurance of safety and effectiveness. The application of this intermediate level of regulatory oversight and these specific special controls would be consistent with FDA's treatment of other devices with similar risk profiles. Reagents for detection of specific novel influenza A viruses, for example, are class II devices.

In addition to the general controls, FDA would require special controls in the form of a guidance document that would include recommendations for the types of information that should be included in premarket submissions and restrictions on device distribution. The guidance document would include a section on performance characteristics, describing studies to demonstrate appropriate device performance, and a section on labeling that would include device intended use, instructions for use of the device, precautions, and the interpretation and reporting of test results. The special controls would also include the restricted distribution of these devices. Under these special controls, the device would be limited to laboratories with experienced personnel who have training in principles and use of microbiological culture identification methods and infectious disease diagnostics, and with appropriate biosafety equipment and containment. These specific special controls are needed because of the public health issues associated with *Y. pestis* infection.

Erroneous test results when testing for *Y. pestis* can result in serious public health consequences. Individuals infected with *Y. pestis* are unlikely to survive if they are not treated in a timely manner. In the case of a potential massive outbreak of *Y. pestis,* such as might occur with the use of the pathogen as an instrument of bioterrorism, the potential consequences could be substantial. False negatives or otherwise mishandled test results could not only delay the treatment of infected individuals, but also could prevent public health officials from taking steps to prevent the transmission of plague to others. False positives could lead to unnecessary use of antibiotics and patient isolation, and would have serious economic and public health consequences if the reporting of these results were to contribute to a public health panic.

FDA intends to address risks to public health not adequately controlled by general controls through special controls. The device description section of the special controls guidance

document would explain to manufacturers the need to include in the premarket submission information on the nature of the device and its proper use. The section on performance studies would recommend the types of information and data manufacturers need to collect in order to establish the performance of their device, clarifying regulatory requirements. The special control on labeling would provide users with information on the device's intended use, directions for use, interpretation of results, and potential precautions. The control on distribution would ensure that those using this device would have the training and equipment needed to perform the test safely and effectively, and that test results would be appropriately reported to the public health authorities.

E. Costs and Benefits of the Proposed Regulation

This proposed rule would not create any additional burdens or directly result in significant benefits. Both current practice and this proposed rule are applications of the recommendations of the 2002 Microbiology Devices Advisory Panel. The requirements associated with class II and the chosen special controls do not change the requirements FDA imposes on manufactures. Indirectly, however, the classification of this device and publication of the special controls would benefit both manufacturers and FDA. Manufacturers would benefit from published regulatory requirements in that they would know the burdens associated with entering this market before starting the premarket notification process, and they would submit premarket notification submissions containing the appropriate information. Improved knowledge of the submission requirements would reduce the need for consultation with FDA during the clearance process to facilitate FDA review and accelerate product availability. Classification of this device and publication of the requirements would also reduce FDA resources consumed in these consultations and improve premarket review consistency.

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 would impose no new burdens, the Agency proposes to certify that this proposed rule would not have a significant economic impact on a substantial number of small entities.

VII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. Section 4(a) of the Executive order requires agencies to ''construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Federal law includes an express preemption provision that preempts certain state requirements ''different from or in addition to'' certain federal requirements applicable to devices. 21 U.S.C. 360k; See *Medtronic* v. *Lohr,* 518 U.S. 470 (1996); *Riegel* v. *Medtronic, Inc.* 552 U.S. 312 (2008). The special controls established by this proposed rule, if finalized, would create ''requirements'' to restrict the distribution of these devices and to address each identified risk to health presented by these specific medical devices under 21 U.S.C. 360(k), even though product sponsors may have flexibility in how they meet those requirements Cf. *Papike* v. *Tambrands, Inc.,* 107 F.3d 737, 740–42 (9th Cir. 1997).

VIII. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed rule contains no collection of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required. FDA also concludes that the special controls guidance document identified by this rule refers to previously approved collections of information found in FDA regulations. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the availability of a guidance entitled ''Class II Special Controls Guidance Document: In Vitro Diagnostic Devices for *Yersinia* spp. Detection.'' The notice contains an analysis of the paperwork burden for the guidance.

IX. 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.

X. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. Transcript of the FDA Microbiology Devices Panel meeting, March 7, 2002 (*http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfAdvisory/details.cfm?mtg=348*).
2. Bibel, D.J. and T.H. Chen, ''Diagnosis of Plague: An Analysis of the Yersin-Kitasato Controversy,'' vol. 40, pp. 633–651, *Bacteriological Reviews,* 1976.
3. Cavanaugh, DC and S.F. Quan, ''Rapid Identification of *Pasteurella pestis* Using Specific Bacteriophage Lyophilized on Strips of Filter Paper; a Preliminary Report,'' vol. 23, pp. 619–620, *American Journal of Clinical Pathology,* 1953.
4. Chen, T.H. and K.F. Meyer, ''An Evaluation of *Pasteurella pestis* Fraction-1–Specific Antibody for the Confirmation of Plague Infections,'' vol. 34, pp. 911–918, *Bulletin of the World Health Organization,* 1966.
5. Marshall, J.D., Jr., J.A. Mangiafico, and D.C. Cavanaugh, ''Comparison of the Reliability and Sensitivity of Three Serological Procedures in Detecting Antibody to *Yersinia pestis* (Pasteurella pestis),'' vol. 24, pp. 202–204, *Applied Microbiology,* 1972.
6. Perry, R.D. and J.D. Fetherston, ''*Yersinia pestis*—Etiologic Agent of Plague,'' vol. 10, pp. 35–66, *Clinical Microbiology Reviews,* 1997.
7. Rust J.H., Jr., S. Berman, W.H. Habig, et al., ''Stable Reagent for the Detection of Antibody to the Specific Fraction 1 Antigen to *Yersinia pestis,''* vol. 23, pp. 721–724, *Applied Microbiology,* 1972.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

1. The authority citation for 21 CFR part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 866.3945 is added to subpart D to read as follows:

§ 866.3945 In vitro diagnostic device for Yersinia spp. detection.

(a) *Identification.* An in vitro diagnostic device for *Yersinia* spp.

detection is a device that is used to detect and differentiate among *Yersinia* spp. and presumptively identify *Y. pestis* and other *Yersinia* spp. from cultured isolates or clinical specimens as an aid in the diagnosis of plague and other diseases caused by *Yersinia* spp. Diseases caused by *Yersinia* infections include three different forms of plague (bubonic, pneumonic, and septicemic), caused by *Y. pestis,* and gastrointestinal infection, caused by *Y. pseudotuberculosis* and *Y. enterocolitica.* This device may consist of *Yersinia* spp. antisera conjugated with a fluorescent dye (immunofluorescent reagents) used to presumptively identify *Yersinia*-like organisms in clinical specimens or bacteriophage used for differentiating *Y. pestis* from other *Yersinia* spp. based on susceptibility to lysis by the phage; or antigens used to identify antibodies to *Y. pestis* (Fraction 1) in serum.

(b) *Classification.* Class II (special controls). The special controls are:

(1) ''Class II Special Controls Guidance Document: In Vitro Diagnostic Devices for *Yersinia* spp. Detection; Guidance for Industry and Food and Drug Administration Staff.'' See § 878.1(e) for availability information of this guidance document; and

(2) Distribution is limited to laboratories with experienced personnel who have training in principles and use of microbiological culture identification methods and infectious disease diagnostics, and with appropriate biosafety equipment and containment.

Dated: November 1, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011–28724 Filed 11–4–11; 8:45 am]

BILLING CODE 4160–01–P