Reagents for Detection of Specific Novel Influenza A Viruses - Class II Special Controls Guidance for Industry and FDA Staff

Document issued on: March 22, 2006

See additional PRA statement in Section 9 of the guidance.

For questions about this document, contact the Division of Microbiology Devices (DMD) and at 301-796-5460 or Tamara Feldblyum at 301-796-6195 or Tamara.Feldblyum@fda.hhs.gov (mailto:Tamara.Feldblyum@fda.hhs.gov) and Claudia Gaffey at 301-796-6196 or Claudia.Gaffey@fda.hhs.gov (mailto:Claudia.Gaffey@fda.hhs.gov).

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to Regulations.gov (http://www.regulations.gov). Please identify your comments with the docket number 2006D-0099. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov (mailto:CDRH-Guidance@fda.hhs.gov) to receive a copy of the guidance. Please use the document number 1596 to identify the guidance you are requesting.

Table of Contents

Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Reagents for Detection of Specific Novel Influenza A Viruses

1. Introduction

This document was developed as a special control to support the classification of reagents for detection of specific novel influenza A viruses into class II (special controls). Reagents for detection of specific novel influenza A viruses are devices intended for use in a nucleic acid amplification test to directly detect specific virus RNA in human respiratory specimens or viral cultures. Detection of virus RNA aids in the diagnosis of influenza caused by specific novel influenza A viruses in patients with clinical risk of infection with these viruses, and also aids in the presumptive laboratory identification of specific novel influenza A viruses to provide epidemiological information on influenza. These reagents include primers, probes, and specific influenza A virus controls. They are used for detecting a specific influenza A virus (for example, a particular subtype or lineage), as opposed to devices that are used in detecting influenza A virus generally, without detecting the presence of specific influenza A viruses.

Novel influenza A viruses are new or re-emergent human strains of influenza A that cause cases or clusters of human disease, as opposed to those human strains commonly circulating that cause seasonal influenza and to which human populations have residual or limited immunity (either by vaccination or previous infection).

This guidance is issued in conjunction with a *Federal Register* notice announcing the classification of reagents for detection of specific novel influenza A viruses. Any firm submitting a 510(k) premarket notification for reagents for detection of specific novel influenza A viruses will need to address the issues covered in the special control guidance. However, the firm need only show that its device meets the recommendations of the guidance, or in some other way provides equivalent assurances of safety and effectiveness. In addition, the device must satisfy the additional special control specified in the classification regulation (See Section 3 – Scope).

The firm must show that its device addresses the issues of safety and effectiveness identified in this guidance, either by meeting the recommendations of this guidance or by some other means that provides equivalent assurances of safety and effectiveness.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe should be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in The Least Burdensome Provisions: Concept and Principles: Guidance for Industry and FDA Staff (/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles).

Top

2. Background

FDA believes that special controls, when combined with the general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of reagents for detection of specific novel influenza A viruses. A manufacturer who intends to market a device of this type should (1) conform to the general controls of the Federal Food, Drug & Cosmetic Act (the Act), including the premarket notification requirements described in 21 CFR 807

(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=807&showFR=1)Subpart E, (2) address the specific risks to health associated with reagents for detection of specific novel influenza A viruses identified in this guidance, (3) satisfy the other special control designated in 21 CFR 866.3332, the classification regulation for this type of device, and (4) obtain a substantial equivalence determination from FDA prior to marketing the device.

This guidance document identifies the classification regulation and product code for reagents for detection of specific novel influenza A viruses. (Refer to Section 3 – Scope). In addition, other sections of this guidance document list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with the general controls and other special controls designated for this device type, will generally address the risks associated with these assays and lead to a timely premarket notification [510(k)] review and clearance. This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=807.87) and other FDA documents on this topic, such as "Premarket Notification 510(k) (/premarket-notification-510k)".

Top

3. Scope

The scope of this document is limited to the following devices, described in 21 CFR 866.3332 (product code NXD):

21 CFR 866.3332 - Reagents for detection of specific novel influenza A viruses.

(a) Identification. Reagents for detection of specific novel influenza A viruses are devices that are intended for use in a nucleic acid amplification test to directly detect specific virus RNA in human respiratory specimens or viral cultures. Detection of specific virus RNA aids in the diagnosis of influenza caused by specific novel influenza A viruses in patients with clinical risk of infection with these viruses, and also aids in the presumptive laboratory identification of specific novel influenza A viruses to provide epidemiological information on influenza. These reagents include primers, probes, and specific influenza A virus controls.

In addition to this guidance document, these devices are subject to a special control requiring that distribution be limited to laboratories with (i) experienced personnel who have training in standardized molecular testing procedures and expertise in viral diagnosis, and (ii) appropriate

biosafety equipment and containment. (21 CFR 866.3332(b)(2)).

This special control guidance recommends specific information for mitigating risks identified in the following section (Section 4 - Risks to Health). It supplements other applicable guidances. General recommendations for fulfilling premarket notification (510(k)) requirements, including recommendations on descriptive information, demonstrating performance, and labeling to establish substantial equivalence are specified in the document, “Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s”, issued August 12, 2005. [Ref. 1]. In addition, FDA has developed draft guidance regarding the type of information generally recommended for inclusion in a 510(k) for reagents used in nucleic acid amplification tests. We suggest that manufacturers consult this guidance when final [Ref. 2].

4. Risks to Health

Top

Influenza illness caused by commonly circulating influenza A viruses can have high morbidity and mortality, particularly in special populations like the elderly and the very young. Acquired immunity to seasonal influenza viruses is limited because influenza viruses mutate in small but important ways from year to year (a process known as antigenic drift). Novel influenza viruses present even greater likelihood of morbidity and mortality, with the potential to cause widespread disease and/or disease of unusually high severity, because few people (or none at all) have prior immunologic exposure to surface glycoproteins of these viruses. In addition, other pathogenicity factors may increase virulence.

Failure of reagents for detection of specific novel influenza A viruses to perform as expected, or failure to interpret results properly may lead to incorrect patient management decisions and inappropriate public health responses. In the context of individual patient management, a falsely negative report could lead to delays in providing (or even failure to provide) definitive diagnosis, appropriate treatment, and infection control and prevention measures, while a falsely positive report could lead to unnecessary or inappropriate treatment, or unnecessary control and prevention actions. In the context of public health, a falsely negative report could lead to a delay in recognition of an outbreak or cluster of influenza due to a novel influenza A virus, while a falsely positive report could lead to unnecessary public health actions (e.g., unnecessary or inappropriate treatment and management of others in the community).

Several factors may negatively affect performance of these reagents, or lead to improper interpretation of results. First, improper testing and inaccurate reporting may result when testing is not performed by trained and experienced laboratory personnel. Because use of these

reagents requires specialized techniques, testing by laboratory personnel without experience and proper training in both preanalytical (specimen processing and extraction) and analytical molecular procedures increases the risk of obtaining inaccurate results. Likewise, if laboratory personnel lack expertise in viral diagnosis, there is an increased risk of providing inadequate or inaccurate interpretation of testing results.

Second, the propensity of all influenza A viruses to mutate (viral RNA changes) may affect the performance of reagents for detection of specific novel influenza A viruses. Primers and probes for detection of novel influenza viruses are selected for their homology with highly conserved regions within viral RNA segments. With continued mutations over time, annealing of primer and probe reagents with viral targets can diminish. This may significantly reduce performance of the reagents.

Third, test performance can be affected because the epidemiology and pathology of disease caused by a specific novel influenza A virus is not fully known. For example, clinicians and laboratories may not know the optimum types of specimens to collect, and when during the course of infection these specimens are most likely to contain levels of virus that can be readily detected.

In addition to the risks that the test will not perform as expected or that results will not be interpreted properly, testing with these reagents is associated with a potential for transmission of novel influenza A viruses. Controls that are not adequately inactivated may themselves be a source of infection. Testing with these devices by inexperienced or untrained laboratory personnel, as well as use of these reagents in laboratories that do not have appropriate biosafety equipment and containment procedures, increases risk of laboratory-acquired infection caused by novel influenza A virus and potential for spreading infection to others outside the laboratory.

Additionally there is the risk that a novel influenza virus may reassort with other influenza viruses if not properly contained. Influenza viruses, including novel viruses such as the H5N1 avian influenza virus, have the capability to reassort with influenza viruses circulating in other animal species. Reassortment of a novel influenza A virus with a human influenza virus, may lead to significant changes in the virus, such as changes in host range, virulence, and antigenicity, which can lead to the virus acquiring the ability for sustained person-to-person transmission. This change is believed necessary to precipitate pandemic influenza. Conditions that favor reassortment are more likely to occur if testing is done by inexperienced or untrained personnel, or without appropriate biosafety equipment and containment procedures.

In the table below, FDA has identified the risks to health generally associated with the use of reagents for detection of specific novel influenza A viruses. Measures recommended to mitigate these identified risks are given in this guidance document, as shown in the table below. (In addition, the classification regulation for this type of device designates an additional special control intended to mitigate these risks, indicating that distribution of these devices is limited to laboratories with (i) experienced personnel who have training in standardized molecular testing procedures and expertise in viral diagnosis, and (ii) appropriate biosafety equipment and containment. See 21 CFR 866.3332(b)(2).)

We recommend that you conduct a risk analysis, prior to submitting your premarket notification, to identify any other risks specific to your device. The premarket notification should describe the risk analysis method. If you elect to use an alternative approach to address a particular risk identified in this document, or have identified risks additional to those in this document, you should provide sufficient detail to support the approach you have used to address that risk.

Identified risk	Recommended mitigation measures
Failure of testing to perform properly • Failure of the reagents to perform as expected, including inability to detect mutated viral RNA • Inability to optimize testing when epidemiology or pathology of viral/host factors is not fully understood	Sections 5-8
Failure to properly interpret test results	Sections 5-8
Laboratory-acquired infection and reassortment	Sections 5 and 7

Top

5. Device Description

Intended Use

Your 510(k) must include labeling that describes the intended use of your product. (See 21 CFR 807.87(e)). You should ensure that all elements of the intended use are clearly stated, particularly regarding the specific viruses the device is intended to detect (for example, influenza A/H5 (Asian lineage)). The intended use includes the viral RNA region detected (analyte), the patient population to be tested, specimen types for which testing will be indicated, and any specific conditions of use.

In your 510(k), you should clearly describe the following information related to the intended use of your product:

- The identity, phylogenetic relationship, or other recognized characterization of a specific novel influenza virus that your device is designed to detect.
- How the device test results will be used in a diagnostic algorithm and other measures that would be needed for a definitive laboratory identification of a specific novel influenza A virus.
- Clinical and epidemiological parameters that are relevant to a patient case diagnosis. The World Health Organization (WHO) and other public health entities provide criteria that may be used as a guide for defining patient cases.

Note: Recognized laboratory methods for definitive identification of certain novel influenza viruses are available (e.g., WHO Manual on Animal Influenza Diagnosis and Surveillance) [Ref. 3.]; sequencing of DNAs generated by subtype-specific primers may also be used to definitively identify a specific novel influenza virus [Ref. 4].

Reagents and other device components

When describing reagents and other device components in your 510(k), we recommend you follow general guidance provided in other FDA guidance documents. FDA has developed draft guidance regarding Nucleic Acid Amplification Testing, which will be particularly relevant when final [Ref. 2]. Additionally, for reagents for detection of specific novel influenza A viruses, you should describe design requirements for your device that address or mitigate risks associated with primers, probes, and controls used in a nucleic-acid based test procedure to detect viral RNA segments from a specific novel influenza A virus. Examples include:

- Designing your reagent for use in a closed tube test system, to minimize false positives due to contamination or carryover.
- Providing multiple probes that enable detection of virus variants appearing due to mutations within the target RNA segment(s), or variants within a designated novel influenza virus strain (or lineage).

- Developing a positive virus control that minimizes the risk that the control itself will be a source of infection or of reassortment with other influenza A viruses handled or maintained in the type of clinical laboratory where testing is intended to be done.
- Developing methods for extraction and purification that yield suitable quality and quantity of viral RNA from different specimen types for use in the test system with your reagents.
- Optimizing your reagents and test procedure for recommended instruments.

We expect that appropriate literature references will not likely be available to detail reliable RNA targets within any viral RNA region (e.g., H 0 within the hemagglutinin RNA) characteristic for a specific novel influenza A virus. In your 510(k), you should provide performance information that supports the conclusion that your design requirements have been met. You should also provide information to verify the design of your reagents (e.g., rationale for selection of specific conserved target sequences and the methods used to design primers and probes). (See Section 6 – Performance).

You should assure acceptable reproducibility and efficiency of the recommended extraction procedure(s) from respiratory specimen types you recommend for testing (e.g., swabs, aspirates, and viral culture media).

Testing Procedures using your device

In your 510(k), you should describe, in detail, the principles of operation applicable to your device in detecting and differentiating a specific novel influenza A virus. For reagents for detection of specific novel influenza A viruses, you should specifically describe testing conditions, procedures and controls designed to provide safeguards for conditions that can cause false positive and false negative results, or present a biosafety hazard. These include, but are not limited to:

- Overall design of the testing procedure, including control elements incorporated into the recommended testing procedures. These controls should approximate the lower range of clinically relevant viral RNA levels and should be extracted as a clinical sample.
- Recommendations for additional controls that monitor for contamination and extraction efficiency (e.g., a blank extracted with each specimen test, and concurrent amplification of an endogenous human gene in the sample, as a control for nucleic acid extraction and inhibition).
- Features and additional controls that reduce failure to recognize procedural errors or factors (e.g., degradation of master mix) that adversely affect amplification and detection conditions.

- Biological Safety Level (BSL) under which testing procedures should be performed.

We recommend that you include a description of all additional procedures, methods, and practices incorporated into your directions for use (See Section 7 - Labeling) that mitigate risks associated with testing for a specific novel influenza A virus.

Interpreting Test Results/Reporting

In your 510(k), you should describe how presumptive positive, equivocal, and negative results are determined and how they should be interpreted. There should be clear explanations for how interpretative algorithms have been determined. In addition, please see Section 8 (Postmarket Measures) for monitoring results over time to identify changes in performance due to biological changes with the virus, or changes in performance when prevalence changes from the existing prevalence at the time your product is evaluated.

Top

---

6. Performance

In your 510(k), you should provide descriptive information on the studies done to support performance of your reagents for detection of specific novel influenza A viruses. FDA has developed draft guidance elsewhere making general recommendations for this information [Ref. 2].

Your 510(k) should include performance information demonstrating:

- Detection of a specific novel influenza A virus (e.g., influenza A/H5 (Asian lineage)) directly in respiratory specimens from patients who were identified clinically and epidemiologically, and were laboratory confirmed patient cases (using WHO recommended criteria) [Ref. 3].
- Low likelihood of presumed false positive results when testing specimens from patients who were known to have other influenza A or influenza B virus infections, or who have no influenza viruses detected by WHO-recommended methods (primarily virus culture) [Ref. 4].
- Detection of known variant novel influenza A viruses (e.g., clades, lineages).
- Lack of cross-reactivity with other broadly representative influenza A viruses that are known to cause human infections (e.g., influenza A/H3N2), with other respiratory viruses (e.g., respiratory syncytial virus, human metapneumovirus, etc.) and with relevant bacterial species (e.g., *Streptococcus pneumoniae, Staphylococcus aureus*).

- Rare unexpected positivity when testing is done on a large group of specimens from individuals with respiratory symptoms, and from viral cultures.
- Reproducible and efficient extraction procedure(s) for respiratory specimen types that you recommend for testing (e.g., swabs, aspirates, and viral culture media).
- Reproducible results without unexpected false positive or false negative test results in multiple clinical laboratories. Samples should include those representing the lower end of the viral level range that is clinically relevant (e.g., 101-106 TCID50/mL viral levels have been documented in respiratory specimens from patients with influenza A/H5 infections; thus samples should represent that lower range for A/H5 viruses).

Clinical studies

FDA recommends that you assess the ability of your device to detect the specific novel influenza A virus in specimens from patients who are case-confirmed, in accordance with WHO criteria for laboratory-confirmed cases. Fresh samples are preferred and testing multiple specimen types is helpful for positive case determinations. Any additional testing that is done to qualify presumptive positives and equivocal test results should include WHO-recommended methods for characterizing and identifying a novel influenza A virus, including sequencing as needed.

When evaluating your device with specimens from patients not suspected to have a novel influenza virus infection, fresh samples are preferred. However, archived samples may be useful to expand representation of specimens (e.g., geographically diverse, different specimen types recommended). Archived samples may be useful to provide the variety of specimen types from patients who have other respiratory infections, and from whom fresh specimens may not be readily available (e.g., S-coronavirus positive samples).

Top

7. Labeling

IVD devices for direct detection of specific novel influenza A viruses in human specimens, like other devices, are subject to statutory requirements for labeling (Federal Food, Drug and Cosmetic Act (the Act), Sections 502(a), 201(n); 21 USC §§ 352(a), 321(n)). Reagents for detection of specific novel influenza A viruses must provide adequate directions for use and adequate warnings and precautions. (Section 502(f); 21 USC § 352(f)). Specific labeling requirements for all IVD devices are set forth in 21 CFR 809.10.

Although final labeling is not required for 510(k) clearance, final labeling for in vitro diagnostic devices must comply with the requirements of 21 CFR 809.10 before an in vitro diagnostic device is introduced into interstate commerce.

To ensure compliance with section 502 of the Act and 21 CFR 809.10, FDA recommends that labeling for these devices (reagents for detection of specific novel influenza A viruses) address the items identified below. These labeling recommendations also help to mitigate the risks identified previously in this guidance to ensure safe and effective use of these devices, particularly when a novel influenza A virus may be emerging.

Your labeling should clearly describe the identity, phylogenetic relationship, or other recognized characterization of a specific novel influenza virus that your device is designed to detect, and the associated clinical aspects of human infection.

Your labeling should also include a statement such as the following: “If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.”

Intended Use

In addition to specific elements that describe the analyte detected, your intended use[1] should specify indications for testing respiratory specimens from patients with symptoms of respiratory illness and a risk of exposure, and that these reagents should be used in conjunction with other laboratory testing and clinical observations. FDA also recommends that your statement of intended use be clarified by a warning statement such as: “Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions.”

You should also prominently provide the following statement immediately below your intended use: “For use by experienced personnel who have training in standardized molecular testing procedures and expertise in viral diagnosis, in laboratories with appropriate biosafety equipment and containment procedures.”

Directions for use

You should provide clear and concise instructions that delineate the clinical and epidemiological relevance of the particular novel influenza strain that is detected, technological features of the specific device, procedures for using reagents, and types of controls that will minimize risks of

inaccurate results. Instructions should encourage use of additional control measures and testing of control material to ensure use in a safe and effective manner.

If your reagents will not include reagents for extraction and preparation, you should provide specifications for the extraction and preparation reagents that users will need to perform testing. You should also provide specifications for assessing the quality of extracted/purified samples.

Quality Control

We recommend that you provide a description of quality control recommendations, types of procedures and material that can be used as additional quality control measures, and the expected results for acceptability of control testing.

Precautions for interpretation

We recommend that you incorporate directions for reporting results into the Results section,[2] including a reminder to report results to state or local public health departments. Additionally you should provide the following types of statements in the Limitations[3] section:

- Negative results (e.g., no novel viral RNA detected) do not exclude influenza infection with other influenza A or B viruses.
- Additional testing for influenza A or B, or other respiratory infections may be required.
- Results that are positive for a novel influenza A virus do not definitively identify a specific influenza A virus subtype.
- Optimum specimen types and timing for peak viral levels during infections caused by a novel influenza A virus have not been determined. Collection of multiple specimens from the same patient may be necessary to detect the virus.
- False negative results may occur if a specimen is improperly collected, transported or handled. False negative results may occur if inadequate numbers of organisms are present in the specimen.
- Positive and negative predictive values are highly dependent on prevalence. False positive test results are likely when prevalence of disease due to a novel influenza A virus is low or non-existent in a community.
- If the virus mutates in the target region, a specific novel influenza A virus may not be detected or may be detected less predictably.
- Inhibitors or other types of interference may produce a false negative result.

Performance Characteristics[4]

We recommend that in your labeling, you describe the population(s) (i.e., geographical location, specimen types, and age groups) whose specimens were tested to support performance characteristics. You should separately represent testing done on specimens from patient cases that are laboratory-confirmed with influenza due to the novel influenza A virus that your device is intended to detect.

You should include a description of the design and evaluation of results for all studies that would aid users in interpreting test results.

Top

8. Postmarket measures

We recommend that you obtain and analyze data postmarket to ensure the continued reliability of your device in detecting the specific novel influenza A virus that it is intended to detect, particularly given the propensity for influenza viruses to mutate and the potential for changes in disease prevalence over time. We recommend the following measures:

- As updated influenza viral sequences become available (from WHO, NIH and other public health entities), you should compare them with your primer/probe sequences and incorporate the result of these analyses into your Quality Management System, as required by 21 CFR 820.100(a)(1), Corrective and Preventive Action. Further, these analyses should be evaluated against the device design validation and risk analysis required by 21 CFR 820.30(g), Design Validation, to determine if any design changes may be necessary.
- If the prevalence of influenza caused by the specific novel influenza A virus that your device is intended to detect changes, compared to the prevalence existing when the clinical evaluation(s) described in your 510(k) were conducted, you should collect data on the clinical performance of your device under the new prevalence conditions. The prevalence of infection with the specific novel influenza virus that your device is intended to detect may change significantly with time, possibly affecting your device performance. The labeling of your device may need to be revised to reflect the new clinical performance data.

To demonstrate how you will address this aspect of the special control, we recommend that you provide a plan that describes how you intend to address the postmarket elements described above with your 510(k) submission. FDA will evaluate whether this plan will help to mitigate the

risks presented by the device and therefore help to provide continued reasonable assurance of the safety and effectiveness of the device.

Top

9. Paperwork Reduction Act of 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 10 hours per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

FDA PRA Staff,
Office of Operations,
Food and Drug Administration,
PRAStaff@fda.hhs.gov (mailto:PRAStaff@fda.hhs.gov)

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information in 21 CFR Part 809 have been approved under OMB Control No. 0910-0485; the collections of information in 21 CFR Part 807 have been approved under OMB Control No. 0910-0120; the collections of information in 21 CFR Part 820 have been approved under OMB Control No. 0910-0073.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0584 (expires 07/31/2025).

References

[1] Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s, issued August 12, 2005. Available at

[2] Nucleic Acid Based In Vitro Diagnostic Devices for Detection of Microbial Pathogens - Draft Guidance for Industry and FDA Staff, DRAFT GUIDANCE, issued on: December 8, 2005

[3] WHO (2002). *WHO manual on animal influenza diagnosis and surveillance ,* 2002, Geneva, World Health Organization (document WHO/CDS/CSR/NCS/2002.5

[4] WHO (2005). *Recommended laboratory tests to identify avian influenza A virus in specimens from humans,* 2005, Geneva, World Health Organization.

_1. 21 CFR 809.10(a)(2); 21 CFR 809.10(b)(2).

_2. 21 CFR 809.10(b)(9).

_3. 21 CFR 809.10(b)(10).

_4. 21 CFR 809.10(b)(12).