transport of the Samsung Galaxy Note 7 device, in particular, immediately prior to boarding is no longer warranted, due to the extensive efforts by Samsung and U.S. wireless providers to recall all Samsung Galaxy Note 7 devices and to make users aware the Samsung Galaxy Note 7 device is forbidden from transportation by air. Moreover, on December 9, 2016, Samsung reported on its Web site that more than 93 percent of all recalled Samsung Galaxy Note 7 devices had been returned to Samsung and that it would release a software update starting on December 19, 2016 that would prevent U.S. Samsung Galaxy Note 7 devices from charging and eliminate their ability to work as mobile devices.[1] We understand that major U.S. wireless providers will push out this update on or before January 8, 2017. T Mobile reported that it would push the software update on December 27, 2016.[2] Verizon Wireless and AT&T both reported that they would push the software update on January 5, 2017,[3] and Sprint reported that it would push the update on January 8, 2017.[4] We think that these efforts to render U.S. Samsung Galaxy Note 7 devices inoperable, in addition to the ongoing recall and notification efforts, will decrease the likelihood that Samsung Galaxy Note 7 devices will be brought on board aircraft. In addition, the hazardous materials regulations (HMR; 49 CFR parts 171–180) provide a systematic framework to protect the safe transportation of hazardous materials that includes procedures for notification, handling, and reporting of discrepancies and incidents at air passenger facilities and cargo facilities.

Remedial Action

To eliminate or abate the imminent hazard:

(1) Persons covered by this Amended Order shall not transport, nor offer for transportation, via air any Samsung Galaxy Note 7 device.

(2) Air carriers are required to handle Samsung Galaxy Note 7 devices consistently with other forbidden hazardous materials under 49 CFR parts 173 and 175, and to deny boarding to a passenger in possession of a Samsung Galaxy Note 7 device unless and until the passenger divests themselves and carry-on or checked baggage of the Samsung Galaxy Note 7 device.

(3) Persons covered by this Amended Order who inadvertently bring a prohibited Samsung Galaxy Note 7 device aboard an aircraft must immediately power off the device, leave it powered off until no longer aboard the aircraft, not use or charge the device while aboard the aircraft, protect the device from accidental activation, including disabling any features that may turn on the device, such as alarm clocks, and keep the device on their person and not in the overhead compartment, seat back pocket, nor in any carry-on baggage, for the duration of the flight.

(4) When a flight crew member identifies that a passenger is in possession of a Samsung Galaxy Note 7 device while the aircraft is in flight, the crew member must instruct the passenger to power off the device, not use or charge the device while aboard the aircraft, protect the device from accidental activation, including disabling any features that may turn on the device, such as alarm clocks, and keep the device on their person and not in the overhead compartment, seat back pocket, nor in any carry-on baggage, for the duration of the flight.

Rescission of This Amended Order

This Amended Order remains in effect until the Secretary determines that an imminent hazard no longer exists or a change in applicable statute or federal regulation occurs that supersedes the requirements of this Amended Order, in which case the Secretary will issue a Rescission Order.

Failure To Comply

Any person failing to comply with this Amended Order is subject to civil penalties of up to $179,933 for each violation for each day they are found to be in violation (49 U.S.C. 5123). A person violating this Order may also be subject to criminal prosecution, which may result in fines under title 18, imprisonment of up to ten years, or both (49 U.S.C. 5124).

Right To Review

Pursuant to 49 U.S.C. 5121(d)(3) and in accordance with section 554 of the Administrative Procedure Act (APA), 5 U.S.C. 500 *et seq.,* a review of this action may be filed. Any petition seeking relief must be filed within 20 calendar days of the date of this order (49 U.S.C. 5121(d)(3)), and addressed to U.S. DOT Dockets, U.S. Department of Transportation, 1200 New Jersey Avenue SE., Room W12–140, Washington, DC 20590 (*http://Regulations.gov*). Furthermore, a petition for review must state the material facts at issue which the petitioner believes dispute the existence of an imminent hazard and must include all evidence and exhibits to be considered. The petition must also state the relief sought. Within 30 days from the date the petition for review is filed, the Secretary must approve or deny the relief in writing; or find that the imminent hazard continues to exist, and extend the original Emergency Order. In response to a petition for review, the Secretary may grant the requested relief in whole or in part; or may order other relief as justice may require (including the immediate assignment the case to the Office of Hearings for a formal hearing on the record).

Emergency Contact Official

If you have any questions concerning this Amended Emergency Restriction/Prohibition Order, you should call PHMSA Hazardous Materials Information Center at 1–800–467–4922 or email at *phmsa.hm-infocenter@dot.gov.*

Issued in Washington, DC, on January 9, 2017.

Reginald C. Govan,

Chief Counsel, Federal Aviation Administration.

[FR Doc. 2017–00555 Filed 1–9–17; 4:15 pm]

BILLING CODE 4910–13–P

[1] *https://news.samsung.com/us/2016/12/09/samsung-taking-bold-steps-to-increase-galaxy-note7-device-returns/; see also http://www.samsung.com/us/note7recall/.*

[2] *https://explore.t-mobile.com/samsung-galaxy-note7-recall.*

[3] *https://www.verizonwireless.com/support/samsung-galaxy-note7-recall-faqs/; https://www.att.com/esupport/article.html#!/wireless/KM1122948.*

[4] *https://support.sprint.com/support/article/FAQs-about-the-Samsung-Galaxy-Note7-recall/817d4190-b2e2-43c8-b549-97b3553d5c24.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2014–N–0440]

Microbiology Devices; Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly With Clinical Specimens

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying antigen based rapid influenza virus antigen detection test systems intended to detect influenza virus directly from clinical specimens that are currently regulated as influenza virus serological reagents from class I into class II with special controls and into a new device classification regulation.

DATES: This order is effective February 13, 2017. See further discussion in section IV, ''Implementation Strategy.''

FOR FURTHER INFORMATION CONTACT: Stefanie Akselrod, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5438, Silver Spring, MD 20993–0002, 301–796–6188.

SUPPLEMENTARY INFORMATION:

I. Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (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) (Pub. L. 105–115), the Medical Device User Fee and Modernization Act of 2002 (Pub. L. 107–250), the Medical Devices Technical Corrections Act (Pub. L. 108–214), the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110–85), and the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144), 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, reflecting 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).

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

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as ''postamendments devices''), are automatically classified by 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, the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval.

Under section 513(i) of the FD&C Act, a device is substantially equivalent if it has the same intended use and technological characteristics as a predicate device, or has the same intended use as the predicate device and has different technological characteristics, but data demonstrate that the new device is as safe and effective as the predicate device and does not raise different questions of safety or effectiveness than the predicate device. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification (510(k)) procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDAMA added section 510(m) to the FD&C Act. Section 510(m) of the FD&C Act provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the FD&C Act, if the Agency determines that premarket notification is not necessary to assure the safety and effectiveness of the device.

On July 9, 2012, FDASIA was enacted. Section 608(a) of FDASIA amended section 513(e) of the FD&C Act, changing the mechanism for reclassifying a device from rulemaking to an administrative order. Section 513(e) of the FD&C Act provides that FDA may, by administrative order, reclassify a device based upon ''new information.'' FDA can initiate a reclassification under section 513(e) of the FD&C Act or an interested person may petition FDA to reclassify an eligible device type. The term ''new information,'' as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time. See, *e.g., Holland-Rantos Co.* v. *U.S. Dep't of Health, Educ., and Welfare,* 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn* v. *Finch,* 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard,* 366 F.2d 177 (7th Cir. 1966).

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent action where the reevaluation is made in light of newly available authority. See *Bell,* 366 F.2d at 181; *Ethicon, Inc.* v. *FDA,* 762 F. Supp. 382, 388–91 (D.D.C. 1991), or in light of changes in ''medical science'' (*Upjohn,* 422 F.2d at 951). Whether data before the Agency are old or new data, the ''new information'' to support reclassification under section 513(e) of the FD&C Act must be ''valid scientific evidence,'' as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2). See, *e.g., Gen. Med. Co.* v. *FDA,* 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Mfrs. Ass'n.* v. *FDA,* 766 F.2d 592 (D.C. Cir.), cert. denied, 474 U.S. 1062 (1986).

Section 513(e)(1) of the FD&C Act sets forth the process for issuing a final order for reclassifying a device under that section. Specifically, prior to the issuance of a final order reclassifying a device, the following must occur: (1) Publication of a proposed order in the **Federal Register**; (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments to a public docket. FDA published a proposed order to reclassify this device type in the **Federal Register** of May 22, 2014 (79 FR 29387). FDA has held a meeting of a device classification panel described in section 513(b) of the FD&C Act with respect to antigen based rapid influenza diagnostic test (RIDT) systems and has also received and considered comments on the proposed order, as discussed in section II. Therefore, FDA has met the requirements under section 513(e)(1) of the FD&C Act.

II. Public Comments in Response to the Proposed Order

On May 22, 2014, FDA published a proposed order to reclassify antigen based RIDTs intended to detect influenza virus antigen directly from clinical specimens that are currently regulated as influenza virus serological reagents under § 866.3330 (21 CFR 866.3330) from class I into class II with special controls and into a new device classification regulation (79 FR 29387).

The Agency received comments on the proposed order from several entities. Comments were received from device industry manufacturers, a consumer group, professional organizations, a health care organization, a device manufacturers association, and an individual consumer.

To make it easier to identify comments and our responses, the word ''Comment'' and a comment number appear in parentheses before each comment's description, and the word ''Response'' in parentheses precedes each response. Similar comments are grouped together under the same number. Specific issues raised by the comments and the Agency's responses follow.

A. General Comments

(Comment 1) Commenters expressed support for the proposed order to reclassify antigen based RIDTs from class I to class II with special controls, noting that there is evidence that the currently available antigen based RIDTs, which are widely used in non-clinical laboratory settings such as physician office laboratories, are performing poorly, resulting in many misdiagnosed cases of influenza. Commenters noted that a misdiagnosis of influenza may have serious consequences, including: Inappropriate use of antibiotics and failure to use antiviral therapy, which may be critical for some patients, following false negative results; the unnecessary or inappropriate prescribing of antiviral drugs following false positive results; ineffective infection control measures; and an overall increased public health burden, such as increased rate of hospitalization and return doctor visits. Several commenters expressed a concern regarding frequent antigenic changes in the circulating strains as the influenza virus evolves and agreed with the new requirement that manufacturers conduct annual analytical testing of circulating strains in an effort to monitor the performance of these tests over time. Overall, there was a general consensus among the commenters that the proposed special controls address and mitigate the risks to health.

(Response) FDA agrees that reclassification of antigen based RIDTs into class II as outlined in this order will help to improve the overall quality of testing for influenza. The new minimum performance requirements for these tests detecting influenza virus antigens are expected to lower the number of misdiagnosed influenza infections by increasing the number of devices that can reliably detect the influenza virus. In addition, the special controls requiring annual and emergency analytical reactivity testing provide a process for continued monitoring of the performance of antigen based RIDTs. As part of that process, the Centers for Disease Control and Prevention (CDC) and FDA will collaborate in efforts to ensure that there is an influenza virus analytical reactivity test panel available to all manufacturers of antigen based RIDTs for evaluation of the analytical reactivity of their assays with circulating viruses on an annual basis.

(Comment 2) One commenter noted that under the FD&C Act, as amended by FDASIA, FDA is able to reclassify a device via an ''order rather than rulemaking,'' but the commenter expressed a concern that FDA seems to consider holding a panel meeting after the issuance of a proposed order as ''discretionary rather than mandatory.'' The commenter urged FDA to hold panel meetings after the issuance of proposed reclassification orders in order to allow the panel to discuss the proposal after it has been issued. The commenter stated that holding a panel meeting following issuance of a proposed reclassification order is a critical element of the process reforms enacted by Congress. In addition, the commenter expressed a concern that the Agency has not obtained sufficient feedback from physicians who commonly use the rapid influenza tests in their practice. Therefore, the commenter suggested that FDA should convene another panel meeting and include these physicians to provide critical expertise and perspective on the overall evaluation of FDA's proposed plans on test reclassification, including the analytical reactivity testing protocol, specifications, and qualification of specimens.

(Response) The June 13, 2013, Microbiology Advisory Panel (''Panel'') meeting considered all relevant scientific issues associated with the proposed order for the antigen based RIDTs and recommended reclassifying these devices into class II (special controls). The Panel included six physicians and seven researchers who provided input that FDA considered for purposes of the proposed order, including the proposed special controls. Each of the Panel members is considered an authority on matters of influenza infection, treatment, epidemiology, and/or biology. Representatives from CDC and the Association of Public Health Laboratories presented extensive data on the use of the currently available antigen based RIDTs and the outcomes related to patients that support the conclusion that there has been poor performance of antigen based RIDTs in the medical practice. The Panel recommended the reclassification of antigen based RIDTs. FDA is not aware of any significant changes in benefits or risks relating to the antigen based RIDTs that have been identified since the June 13, 2013, Panel meeting. Stakeholders had an opportunity to provide feedback to the proposed order in their comments, and that feedback has been largely positive. The public comments are addressed here and are also available to view by request or on *https://www.regulations.gov.*

The process followed by FDA in reclassifying antigen based RIDTs is in accordance with the applicable statutory provisions, which were amended by FDASIA. Section 608 of FDASIA amended section 513(e) of the FD&C Act by changing the reclassification process from rulemaking to an administrative order process. The amendments to section 513(e) of the FD&C Act made by FDASIA require, in relevant part, that issuance of an administrative order reclassifying a device be preceded by a proposed order and a meeting of a device classification panel.

As amended, section 513(e) of the FD&C Act does not prescribe when these two events (the panel meeting and proposed order) must occur in relation to each other. Therefore, under this provision, the Agency may hold a panel meeting either before or after the issuance of a proposed reclassification order. This approach is consistent with the prior panel provision in section 513(e) of the FD&C Act, which provided for FDA, at its discretion, to secure a panel recommendation prior to the promulgation of a reclassification rule. Generally, for future reclassifications under section 513(e) of the FD&C Act for which a meeting of a device classification panel has not yet occurred, FDA expects a proposed reclassification order will be issued prior to the panel meeting required under section 513(e).

B. Transition Period

(Comment 3) While one commenter expressed agreement that the proposed 1 year timeframe should be sufficient for manufacturers to bring devices already on the market into compliance with the special controls, another commenter suggested that FDA consider providing additional transition time for the implementation of the final order. The commenter suggested that this would assist manufacturers who are working in good faith to meet the new requirements to prepare submissions in advance of the influenza season and would provide for product continuity among health care providers. The commenter did not identify why 1 year would be an insufficient period of transition time.

(Response) The Panel recommended and FDA made the determination that special controls, including the new minimum performance requirements, are needed, in addition to general controls, to provide reasonable assurance of safety and effectiveness for antigen based RIDTs. We, therefore, do not believe, given the risk that poor performance of antigen based RIDTs pose to public health, a delay in implementation of more than 1 year is appropriate. FDA also understands the need for a balanced approach that takes into account the time it will take for

manufacturers to come into compliance with the special controls and seeks to avoid disruption of access to these devices. With these considerations in mind, FDA believes that a period of 1 year from the publication date of this final order is appropriate for manufacturers to come into compliance with the special controls and for those manufacturers whose currently legally marketed devices do not meet the minimum performance criteria to prepare and submit a 510(k) for a new or significantly changed or modified device. Therefore, FDA does not intend to enforce compliance with the special controls with respect to currently legally marketed antigen based RIDT devices until 1 year after the date of publication of this final order. FDA believes this approach will help ensure the efficient and effective implementation of the final order.

C. Clinical Performance Standards and Comparator Methods

(Comment 4) One comment recommended a transition to one common reference method comparator: A molecular nucleic acid-based method. The reasons cited for this recommendation included: (1) A level playing field for all manufacturers and (2) better clarity for users, industry, and the Agency. Another comment raised concerns about the unreliability of the culture results due to non-standardized culture practices. In addition, a commenter cautioned that providing two minimum performance standards, one when compared to viral culture and another when compared to a nucleic acid-based method, may have unintended consequences: (1) Users may make false assumptions and choose a method based strictly on the presented estimates of sensitivity and specificity without noting the comparator reference method that was used to derive the performance measures and (2) manufacturers may elect to conduct the method comparison using both types of reference methods and submit the results in support of a 510(k) even if only one of the comparisons meets the minimum performance bar.

(Response) FDA appreciates the concern over the potential consequences of allowing for the two performance levels based on different comparator methods. The Agency carefully considered the public feedback as well as the implications of eliminating the viral culture comparator method as an acceptable comparator method used in the evaluation of clinical performance of antigen based RIDTs. Some important considerations were: (1) A lack of standardization of viral culture methods among various laboratories, (2) an increasing difficulty in procuring the services of a laboratory that is equipped to perform viral culture procedures, (3) the wide availability of FDA-cleared nucleic acid-based comparator methods among laboratories, (4) the demonstrated high sensitivity of the nucleic acid-based methods when compared to viral culture method (when properly performed) for the detection of the influenza viruses, and (5) the reliability of the viral culture method when performed properly.

In addition, we recognize that performance evaluation based on two different comparators where each detects a different analyte (viral culture methods detect viable virus particles while nucleic acid-based methods detect the viral ribonucleic acids) requires two sets of performance criteria resulting in performance measures that may not allow for direct comparison between some devices. However, viral culture method, when performed correctly, has been shown historically to be accurate and remains a valid reference method for the detection of influenza viruses. There are many influenza detecting devices currently on the market that have been evaluated based on comparison with viral culture comparator methods and met the performance criteria set forth in § 866.3328(b)(1)(ii) (21 CFR 866.3328). FDA has also stated expressly in the special controls that a viral culture comparator method used to demonstrate that a device meets the minimum performance criteria at § 866.3328(b)(1)(ii) must be correctly performed.

At this time, the only currently appropriate and FDA accepted comparator methods are: (1) An FDA-cleared nucleic acid-based test or (2) a correctly performed viral culture method. However, FDA recognizes that a comparator method at least as accurate as FDA-cleared nucleic acid-based tests in the detection of the influenza viruses may be established in the future. Based on that recognition and the available information, the final order clarifies that other comparator methods, if currently appropriate and FDA accepted, could be used to demonstrate that the performance criteria requirements in § 866.3328(b)(1)(i) have been met. Therefore, if FDA determines at some point in the future that another comparator method at least as accurate as FDA-cleared nucleic acid-based tests has been established as a currently appropriate comparator method, sponsors of premarket submissions for antigen based RIDTs would have the option of demonstrating that their devices meet the minimum performance criteria at § 866.3328(b)(1)(i) based on a comparison to that additional currently appropriate and FDA-accepted comparator method.

(Comment 5) Another commenter cautioned that the performance estimates shown in the package inserts for these tests may be biased due to the fact that the data have been generated under closely controlled clinical trial procedures that use optimal sample types, a time of sample collection post onset of symptoms, proper sample storage, and time to testing. Because these conditions are often not maintained in daily clinical use, the true performance of these assays in ''real life'' settings may be different.

(Response) FDA acknowledges that the performance data in the device labeling are estimates. All assays are subject to variation under real-life circumstances when the assays are used in clinical practice. However, FDA believes that premarket studies demonstrating performance for these devices should include a variety of testing sites representative of the settings in which the device will be used and that a sufficient number of clinical specimens should be tested to arrive at reasonable measures of confidence in the calculated performance estimates (*i.e.,* the lower bound of the two-sided 95 percent confidence interval (calculated by the Score method)), as outlined in the guidance document entitled ''Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Influenza Viruses'' (*http://www.fda.gov/RegulatoryInformation/Guidances/ucm079171.htm*) (''2011 Influenza Guidance document'').

(Comment 6) One commenter suggested that the proposed sensitivity criteria for influenza A for antigen based RIDTs, when using a molecular method as a comparator method, are less stringent than those recorded in the 2011 Influenza Guidance document. The commenter stated that it:

> [I]s not clear . . . why the Special Controls for comparison to a molecular method has become less stringent (sensitivity/PPA estimate for Influenza A reduced from a point estimate of 90 percent with a 95 percent CI lower bound of 80 percent, to a point estimate of 80 percent with a 95 percent CI lower bound of 70 percent) when the intention of a Special Controls document would presumably be thought to make comparative criteria tighter overall.

The commenter made a reference to the statement in section 9.B.iii, pages 26–27 of the 2011 Influenza Guidance

document (3d bullet), that states: ''Nucleic acid-based tests should demonstrate at least 90% sensitivity for each analyte and each specimen type with a lower bound of the two-sided 95% CI greater than 80%.'' The commenter also questioned whether this determination was discussed and used to scientifically justify the different criteria for sensitive molecular methods, including polymerase chain reaction, which detect inactive virus in the absence of viable viral particles in a sample, and for viral detection in general when using a molecular comparative method.

(Response) The quoted statement from the 2011 Influenza Guidance document refers to the performance of nucleic acid-based devices, while the performance criteria stated in the May 22, 2014, proposed order (79 FR 29387 at 29390) (Section VIII. Special Controls: . . . If the manufacturer chooses to compare the device to an appropriate molecular comparator method: The positive percent agreement for the device when testing for Influenza A and Influenza B must be at least at the 80 percent point estimate with a lower bound of the 95 percent confidence interval that is greater than or equal to 70 percent) refer to RIDTs based on antigen detection, which are historically known to have a more limited sensitivity due to the properties of the enzyme immunoassay (EIA) technology. The relevant citation pertaining to the performance of the rapid devices detecting influenza virus antigens may be found in section 9.B.iii, pages 26–27 (1st and 2d bullet) of the 2011 Influenza Guidance document, which states:

> For rapid devices detecting influenza A virus antigen, we recommend that you include a sufficient number of prospectively collected samples for each specimen type claimed to generate a sensitivity result with a lower bound of the two-sided 95% CI greater than 60%. . . . For rapid devices detecting influenza B virus antigen, we recommend that you include a sufficient number of samples for each claimed specimen type to generate a result for sensitivity with a lower bound of the two-sided 95% CI greater than 55%.

Nucleic acid-based assays that test for influenza are regulated under § 866.3980, *Respiratory viral panel multiplex nucleic acid assay,* and have been held to higher performance criteria than antigen based RIDTs because of their demonstrated ability to reach higher sensitivity for viral detection. By establishing special controls with minimum performance criteria for antigen based RIDTs, this final order raises the required minimum performance criteria for viral detection by the EIA based tests beyond the recommendations set forth in the 2011 Influenza Guidance Document. Nucleic acid-based tests continue to be subject to the document entitled ''Class II Special Controls Guidance: Respiratory Viral Panel Multiplex Nucleic Acid Assay'' (*http://www.fda.gov/RegulatoryInformation/Guidances/ucm180307.htm*), except when the device detects and differentiates Influenza A subtype H1 and subtype H3, in which case they are also subject to the document entitled ''Class II Special Controls Guidance Document: Testing for Detection and Differentiation of Influenza A Virus Subtypes Using Multiplex Nucleic Acid Assays'' (*http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm180310.pdf*).

(Comment 7) One commenter criticized FDA for providing no specifications for how to design a clinical performance study for antigen based RIDT systems in terms of the proportion of samples that should be presented for each age group. In addition, the comment suggested that the performance estimates of different devices presented in their package inserts may be biased due to the actual proportions of age groups in the study (*i.e.,* children vs. adults) and may not be truly reflective of the performance in the population overall. The commenter further suggested that the number of positive samples as well as sensitivity and specificity (or positive percent agreement (PPA)/negative percent agreement (NPA)) for each age group be presented in each device's Instructions for Use to ensure transparency.

(Response) FDA's current recommendations for appropriate study design can be found in the 2011 Influenza Guidance document, where section 9.B.ii mentions that there should be a representative number of positive samples (determined by the reference method) from each age group and [the data should be presented] stratified by age (*e.g.,* pediatric populations aged birth to 5 years, 6 to 21 years, . . . adults aged 22–59, and greater than 60 years old) in addition to the overall data summary table.

In addition, the 2011 Influenza Guidance document recommends diversifying the location of the selected clinical sites and the anticipated prevalence of influenza at the time of the study. Depending on the site selection, the age composition of the subjects will vary, but it is difficult to predict the different age groups at the outset of a study. FDA evaluates assay performance estimates stratified by age groups and determines whether the performance among different age groups is similar before making the final decision regarding 510(k) clearance. FDA encourages sponsors to use the pre-submission program to discuss the premarket submission strategy and study design for their specific devices. The pre-submission program is described in the guidance document titled ''Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff'' found on FDA's Web site at *http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf.*

(Comment 8) A commenter also suggested that the proposed special controls do not clearly state that data demonstrating that a device meets the clinical performance criteria be obtained using prospective, fresh samples and that this may be easily remedied by adding a statement in the final special controls document indicating that ''clinical performance studies should be carried out on fresh, prospective samples.''

(Response) The 2011 Influenza Guidance Document, in section 9.B.iii *Specimens,* on p. 27, states that: ''[w]e recommend that you assess the ability of your device to detect influenza viruses in fresh specimens collected from patients suspected of having an influenza infection who have been sequentially enrolled in the study (all-comers study)''. The guidance further states that ''[f]rozen archived specimens may be useful for analytical performance evaluations, but are not recommended for studies to calculate clinical sensitivity or specificity''.

As the incidence of influenza varies from year to year and also from region to region, testing of archived specimens may be acceptable where fresh positive specimens are difficult to obtain. Performance data obtained from testing retrospective archived samples are generally evaluated and presented separately from data obtained with prospectively collected specimens in the final device labeling.

(Comment 9) A further recommendation was made that the proposed special controls include explicit wording to clarify that clinical performance criteria must be met for each sample type claimed in the proposed labeling submitted for clearance.

(Response) FDA agrees with this recommendation. The proposed special controls have been modified to clarify that clinical performance criteria must be met for each specimen type claimed in the intended use of the device.

(Comment 10) One commenter asserted that the proposed acceptance criteria for devices choosing to use viral culture as a comparator have been determined using certain generalizations that can confound the data. Referring to the Executive Summary document prepared for the Panel meeting (Ref. 1), the commenter states that, for example, all sample types and age ranges were included in the overall presentation of sensitivity for various devices. The commenter objected that the performance criteria, as presented in the Executive Summary document, appear to have been subjectively defined. The commenter further suggested that the purpose of tables 1 and 2 in the Executive Summary was to imply that any device cleared prior to 2008 is assumed to have variable and unacceptable performance, and that the performance criteria for antigen based RIDTs were chosen specifically with the intention of removing those devices from use. Additionally, the commenter stated that the information, as presented in the publicly available Executive Summary, did not make it clear that the data were confounded and created an unfair marketing advantage for some manufacturers.

(Response) The summary data tables presented in the Executive Summary document submitted to the Panel in June 2013 were compiled to illustrate the range in clinical performance among the antigen based RIDTs available on the market in support of the reclassification effort and were not aimed to remove devices cleared before 2008 from the market, as the commenter suggests. The data for each assay presented in table 1 in the Executive Summary document were based on the information provided to FDA in support of the 510(k) submissions for those devices and included results from all prospectively collected samples during the clinical study conducted by the manufacturer, regardless of the specimen type or the age of the patient (Ref. 1). The information in this table shows a wide range of assay performances.

The data presented in table 2 in the Executive Summary document were intended to illustrate the even broader range in sensitivity of these assays as reported in the scientific literature and derived from postmarket studies conducted in the field. The data in table 2 were also based on combined results, regardless of sample type, patient age and even influenza virus type. Although the commenter may consider the data ''confounded,'' they were not meant to demonstrate statistical validity but rather to illustrate that some of the currently available antigen based RIDTs have clinically poor sensitivity even under the controlled conditions of a clinical study conducted in support of a regulatory submission. More importantly, the clinical performance of these assays in the field, as reported in peer reviewed publications, is considerably worse for some of these assays than was demonstrated in the studies submitted to FDA to support their clearance. Overall, the data contained in the two tables were intended to help illustrate the sensitivity of the antigen based RIDTs available on the market, taking into consideration the limitations of the available technology. The data presented in both tables in the Executive Summary document support that improved influenza detection devices are needed to benefit public health in detection, treatment, and infection control with regard to the influenza viruses.

(Comment 11) Some commenters inquired about the process for notifying manufacturers that their assays do not meet the new performance criteria and expressed concern that manufacturers should be allowed sufficient transition time to develop new or modified influenza detection devices and to submit new 510(k)s for those products.

(Response) A manufacturer will not be individually notified that its product does not comply with the new special controls; each manufacturer of an antigen based RIDT is responsible for compliance with these special controls, including the minimum performance criteria. If an antigen based RIDT device does not meet the new performance criteria set forth in this final order, the device may be considered adulterated under section 501(f)(1)(B) of the FD&C Act (21 U.S.C. 351(f)(1)(B)), and manufacturers must cease marketing of the device. However, as outlined in section IV, ''Implementation Strategy,'' FDA does not intend to enforce compliance with the special controls with respect to currently legally marketed antigen based RIDT devices until 1 year after the date of publication of this final order. A manufacturer may contact the Center for Devices and Radiological Health's (CDRH) Division of Microbiology Devices in the Office of In Vitro Diagnostics and Radiological Health (OIR) with any specific questions.

(Comment 12) One commenter inquired whether there will be an appeals mechanism for manufacturers and what specific steps would be available for manufacturers.

(Response) No new appeals mechanisms will be implemented for those manufacturers whose assays do not comply with the new special controls. However, there are processes available to outside stakeholders to request additional review of decisions or actions by the CDRH. For more information, see the FDA guidance document entitled ''Center for Devices and Radiological Health Appeals Processes—Guidance for Industry and Food and Drug Administration Staff'' (*http://www.fda.gov/RegulatoryInformation/Guidances/ucm284651.htm*).

D. Annual Analytical Reactivity Testing

1. Access to Strains

(Comment 13) Commenters expressed concerns about whether all manufacturers, regardless of their size or resources, will have equal access to the samples needed to conduct the annual analytical reactivity testing in compliance with the new special controls. One of the commenters noted that there may be challenges to specimen access for some manufacturers under the World Health Organization (WHO) Pandemic Influenza Preparedness (PIP) Framework as well as potential impact on accessing the influenza strains sourced by the WHO Global Influenza Surveillance and Response System (GISRS). The commenter asked if manufacturers required to perform the annual testing would need to participate in the PIP framework to access GISRS specimens. The commenter further stated that unless all companies are able to access specimens in a fair, timely and non-cost restrictive manner to comply with the new postmarket requirements, some innovators may be unable to continue to develop new influenza diagnostics.

(Response) CDC intends to make available an annual analytical reactivity test panel, which is an annual standardized seasonal influenza virus test panel, so that manufacturers can comply with the annual analytical reactivity testing requirement. If the annual strains are not available from CDC, FDA will identify an alternative source for obtaining the requisite strains. The selection of viruses in the CDC annual analytical reactivity test panels is expected to be largely based on the strains selected by WHO for the annual vaccine and will be distributed for annual analytical reactivity testing or analytical validation in support of new 510(k) submissions for antigen based RIDT devices. We expect that the panel will primarily consist of human viruses that circulated in the recent influenza seasons. FDA and CDC do not believe that manufacturers will need to enter

agreements under the PIP Framework to access influenza viral strains in the manner described in this final order for the sole purpose of conducting testing to comply with the special controls at § 866.3328(b)(3) and (4). The annual analytical reactivity test panel will be made available to manufacturers at the same time, including those that require it for the annual analytical reactivity testing as well as those who are developing new or modified influenza assays. CDC and FDA are committed to facilitating equal access for manufacturers to the annual analytical reactivity test panel and are prepared to consider any unforeseen circumstances in an equitable manner.

(Comment 14) Another commenter expressed a concern regarding whether the requisite strain(s) will be made available in sufficient time to allow manufacturers to conduct the studies and have the data available in the labeling or on the manufacturer's Web site within the timeframe specified for both annual and emergency analytical reactivity testing. The comment stated that for most manufacturers, the process of testing and making a change in labeling would take a minimum of 90 days from receipt of samples.

(Response) Under the new special controls, the results of the last 3 years of annual analytical reactivity testing conducted from the date that the device was given marketing authorization by FDA must be incorporated into the device's labeling in the manner discussed in § 866.3328(b)(3)(iii) by July 31 of each calendar year. CDC and FDA are committed to making available or designating an alternative source for the annual analytical reactivity test panel with sufficient time for all manufacturers to conduct the testing and include the results in their device's labeling within the required timeframe.

Similarly, in the case of emergency analytical reactivity testing, as described in the special controls at § 866.3328(b)(4), after CDC makes the viral samples available for testing, FDA will notify the manufacturers of the availability of the samples. The manufacturers will have 60 days to perform the testing of the viral samples and to incorporate the results into the device's labeling in the manner discussed in § 866.3328(b)(4)(ii). If a manufacturer is concerned about meeting these timelines due to time needed to amend device labeling that physically accompanies the device, the manufacturer may pursue the § 866.3328(b)(3)(iii)(B) and (b)(4)(ii)(B) alternatives, which allow manufacturers to provide the results as electronic labeling via the manufacturer's public Web site that can be reached via a hyperlink found in the device's label or in other labeling that physically accompanies the device. If a manufacturer chooses the option to post analytical reactivity testing results on its Web site, it would be subject to the requirements of section 502(f) of the FD&C Act (21 U.S.C. 352(f)) that provides that required labeling for prescription devices intended for use in health care facilities or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments may be made available solely by electronic means as long as the labeling complies with the law, and that the manufacturer affords users the opportunity to request the labeling in paper form, and that after a request, promptly provides the requested information without additional cost.

If a manufacturer provides the hyperlink to a public Web site at which annual analytical reactivity and emergency testing data may be viewed, generally no updates would be needed to the labeling that physically accompanies the device when meeting the annual analytical reactivity testing requirements under § 866.3328(b)(3) or the emergency analytical reactivity testing requirements under § 866.3328(b)(4). If annual or emergency analytical reactivity testing reveals that the device is unable to detect one or more strains, the manufacturer would need to include a limitation in the device labeling, as further discussed in our response to Comment 21.

2. Acquisition of the Annual Analytical Reactivity Test Panel and Reporting of Results

(Comment 15) Commenters expressed concern about the logistics of the implementation of the new requirement for the annual analytical reactivity testing. One commenter stated that a clear mechanism was not outlined in the proposed order for activities leading to the reporting of results.

(Response) The activities leading to the reporting of results will include acquisition of the annual analytical reactivity test panel and analytical reactivity testing following the standardized protocol included with the test panel, which will be a standardized protocol considered and determined by FDA to be acceptable and appropriate. Results must be reported by updating the device's labeling in accordance with § 866.3328(b)(3)(iii). As previously stated, CDC and FDA are committed to working with the manufacturers of the influenza tests to facilitate timely and equitable access to the influenza virus annual analytical reactivity test panel. CDC has developed a Web site (*http://www.cdc.gov/flu/dxfluviruspanel/index.htm*) where the manufacturers can affirm their need for the annual analytical reactivity test panel, referred to by CDC as the ''CDC Influenza Virus Panel,'' to comply with the annual analytical reactivity testing requirement. The CDC panel will be distributed along with certificates of analyses for the viruses and a standardized testing protocol, considered and determined by FDA to be acceptable and appropriate, instructing the user on handling and testing of the provided virus stocks in the test panel. There are currently no plans to post the analytical reactivity testing data generated by the manufacturers on the CDC Web site. For any questions related to the test procedure, manufacturers may contact CDC or FDA as specified in the information included with the influenza virus analytical reactivity test panel. CDC will serve as the contact for questions pertaining to viruses, and FDA will serve as the contact for all regulatory and reporting issues.

(Comment 16) Commenters expressed concern about the continued availability of the test panel from CDC due to the future potential for limited resources at CDC or FDA.

(Response) In a case where the influenza virus analytical reactivity test panel is not available from CDC due to unforeseen limitations in resources, an alternate source of influenza strains for use in conducting the annual analytical reactivity testing will be identified by FDA, in consultation with CDC. An example of an alternate source could be a commercial vendor that specializes in acquisition, authentication, production, and preservation of microorganisms.

(Comment 17) Commenters suggested that the industry should be engaged for feedback in the development of the standardized testing protocol.

(Response) A standardized protocol has been developed by CDC in consultation with FDA and will be provided to manufacturers with the annual analytical reactivity test panel. The protocol uses basic principles for working with virus stocks and is general enough to allow for use with various devices. For any questions related to the testing procedure, manufacturers can contact CDC or FDA. CDC will serve as the contact for questions pertaining to viruses, and FDA will serve as the contact for all regulatory and reporting issues.

(Comment 18) One commenter inquired whether the analytical reactivity testing could be conducted using a modified limit of detection

(LoD) protocol, where 60 replicates are tested over 3 dilutions with positivity rates between 80 and 99 percent followed by linear regression to calculate the specific concentration that corresponds to a positivity rate of 95 percent.

(Response) This approach is acceptable to use in the determination of a LoD of an antigen based RIDT assay. However, manufacturers must follow the protocol included with the influenza virus analytical reactivity test panel, which will be a standardized protocol considered and determined by FDA to be acceptable and appropriate. We believe the standardized protocol will be less burdensome than this commenter's proposal and will help ensure that the results generated allow for comparability between different devices, as all devices will have followed a common standardized testing protocol.

(Comment 19) One commenter asked whether interested manufacturers would have an option to have the testing conducted by an independent laboratory, such as a laboratory at a university.

(Response) Yes, a manufacturer may contract an outside laboratory to conduct the testing on its behalf.

(Comment 20) One commenter raised a concern that customers without access to a manufacturer's Web site may not be able to access the annual and/or emergency analytical reactivity testing information; therefore, the commenter suggested that an alternate method of contact should be provided in the product labeling.

(Response) All in vitro diagnostic devices are required by regulation to state on the label and in the product labeling the name and place of business of the manufacturer, packer, or distributor § 809.10(a)(8) and (b)(14) (21 CFR 809.10(a)(8) and (b)(14)), except where such information is not applicable, or as otherwise specified in a standard for a particular product class.

In addition, in accordance with § 866.3328(b)(3)(iii) the results of the annual analytical reactivity testing must either be in the § 809.10(b) compliant labeling that physically accompanies the device or be provided as electronic labeling via the manufacturer's public Web site that can be reached via a hyperlink prominently found in the device's label or in other labeling that physically accompanies the device. If the manufacturer chooses the Web site option, it would be subject to the requirements of section 502(f) of the FD&C Act, which provides that required labeling for prescription devices intended for use in health care facilities or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments may be made available solely by electronic means, as long as the labeling complies with the law, and that the manufacturer affords users the opportunity to request the labeling in paper form, and that after a request, promptly provides the requested information without additional cost. Therefore, a manufacturer is already required to provide an opportunity for a health care professional to request the annual analytical reactivity test results in paper form.

(Comment 21) One commenter raised a question about notifying the public when a test is non-reactive with any of the strains included in the influenza virus analytical reactivity test panel provided by CDC and whether the product labeling will be updated annually. In particular, the commenter questioned how labeling changes to reflect absence of reactivity would be communicated to users who have already purchased the test.

(Response) This final order requires that the results of the last 3 years of annual analytical reactivity testing conducted from the date that the device was given marketing authorization by FDA be included as part of the device's labeling by July 31 of each calendar year. Modification of the labeling solely to incorporate analytical reactivity testing results required under § 866.3328(b)(3)(iii) or (b)(4)(ii) can be made without an official submission to FDA. In a case where one or more strains are shown not to be detected by the device during annual analytical reactivity testing under § 866.3328(b)(3) or emergency analytical reactivity testing under § 866.3328(b)(4), the manufacturer will need to include a limitation in the device labeling regarding reactivity with the specific strain(s) that were not detected by the device. Without such a limitation, the device would not meet the labeling requirements of § 809.10(b).

(Comment 22) One commenter raised a question about whether there will be a guidance document issued on a yearly basis to interpret the results of the analytical reactivity testing for that year.

(Response) FDA does not intend to issue a guidance document on how to interpret the results of the analytical reactivity testing each year, as the result interpretations are stated in the CDC information sheet that will be distributed with the CDC annual analytical reactivity test panel. The annual analytical reactivity testing is intended to evaluate whether the assay detects each strain included in the annual analytical reactivity test panel; however, that testing does not provide direct information about how the assay performs when used with clinical specimens that are collected directly from patients. Any positive result obtained during analytical reactivity testing performed with the annual influenza virus analytical reactivity test panel, at any viral concentration/dilution, indicates that the assay is reactive with that virus; however, the minimal concentration of the virus that is needed for the detection (assay sensitivity) may vary. Since the difference in analytical reactivity does not necessarily translate into an appreciable difference in performance when testing clinical specimens, it is important to emphasize that the results should not be over-interpreted for clinical purposes.

(Comment 23) One commenter suggested further collaboration between the Agency and influenza test manufacturers in establishing the regulatory process for implementing the labeling change before a final ''Notice to Industry'' or other document is published. The commenter further recommended that FDA specify an interactive process, whereby individual manufacturers can seek guidance, particularly if they encounter issues that may impede timely publication of annual and emergency analytical reactivity testing data (*e.g.,* if the matrix used in the preparation of the virus strains in the test panel causes invalid results with a particular device).

(Response) Interactive communication with manufacturers is common practice among the reviewers and the managers in CDRH. Manufacturers are encouraged to contact CDRH's OIR with questions or about issues related to the new requirements. In addition, the CDRH pre-submission program is designed to allow sponsors the opportunity to obtain targeted FDA feedback in response to specific questions related to product development, including planned non-clinical evaluations, proposed clinical study protocols, or data requirements prior to making a submission to the Agency.

E. Timely Testing of Newly Emergent Strains

(Comment 24) Similar concerns to those surrounding the annual reactivity testing requirement were raised in regard to the emergency testing of emergent strains. In addition, one comment expressed support for specifying a timeline for reporting the results after the samples become available.

(Response) Section 866.3328(b)(4)(ii) requires that, in certain emergency or potential emergency situations involving an influenza viral strain, the results of analytical reactivity testing with the emerging virus(es) must be made available within 60 days from the date that FDA notifies antigen based RIDT manufacturers that characterized viral samples are available. The results of the influenza emergency analytical reactivity testing must be disclosed in a tabular format in a similar manner as the results of the annual analytical reactivity testing (*i.e.,* either by placing the table directly in the device's § 809.10(b) compliant labeling that physically accompanies the device in the section of the labeling devoted to analytical reactivity testing, or in a section of the device's label or in labeling that physically accompanies the device, by prominently providing a hyperlink to a part of the manufacturer's Web site where the analytical reactivity testing data can be found). As previously discussed, modification of the labeling solely to incorporate annual analytical reactivity testing results under § 866.3328(b)(3)(iii) or emergency analytical reactivity testing results under § 866.3328(b)(4)(ii) can be made without an official submission to FDA. In a case where one or more strains are shown not to be detected by the device during annual analytical reactivity testing under § 866.3328(b)(3) or emergency analytical reactivity testing under § 866.3328(b)(4), the manufacturer will need to include a limitation in the device labeling regarding reactivity with the specific strain(s) that were not detected by the device. Without such a limitation the device would not meet the labeling requirements of § 809.10(b).

FDA is also clarifying the special controls to be more precise regarding the situations in which emergency analytical reactivity testing is required. Under section 564(a)–(b) of the FD&C Act (21 U.S.C. 360bbb–3(a)–(b)), the Secretary of Health and Human Services (HHS) may authorize the introduction into interstate commerce of a drug, device, or biologic product intended for use in an actual or potential emergency (referred to as ''emergency use'') after making a declaration, under section 564(b)(1) of the FD&C Act, that circumstances exist justifying the authorization. Such a declaration must be based on one of the following actions listed at section 564(b)(1)(A)–(D) of the FD&C Act:

- A determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a chemical, biological, radiological, or nuclear (CBRN) agent or agents;
- A determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to U.S. military forces of attack with a CBRN agent or agents;
- A determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of U.S. citizens living abroad, and that involves a CBRN agent or agents, or a disease or condition that may be attributable to such agent or agents; or
- The identification of a material threat, by the Secretary of Homeland Security under section 319F–2 of the Public Health Service (PHS) Act, that is sufficient to affect national security or the health and security of U.S. citizens living abroad.

If one of these four actions that can provide the basis for the Secretary of HHS to make a declaration under section 564(b)(1) of the FD&C Act occurs with respect to an influenza viral strain, then, after being notified that characterized viral samples are available from CDC, antigen based RIDT manufacturers must conduct analytical reactivity testing with those samples and make the results available in their device labeling within the timeframes set forth in § 866.3328(b)(4).

In addition, the Secretary of HHS may determine under section 319(a) of the PHS Act (42 U.S.C. 247d(a)) that a disease or disorder presents a public health emergency or that a public health emergency otherwise exists. In the event of such a determination under section 319(a) of the PHS Act with respect to an influenza viral strain, then, after being notified that characterized viral samples are available from CDC, antigen based RIDT manufacturers would also need to conduct analytical reactivity testing with those samples and make the results available in their device labeling within the timeframes set forth in § 866.3328(b)(4).

The final order also modifies the special controls to require that any emergency reactivity test results added to antigen based RIDT device labeling under § 866.3328(b)(4)(ii) remain in the labeling for a period of 3 years. Emerging influenza strains may still be circulating after the statutory actions described under section 564(b)(1)(A)–(D) of the FD&C Act and section 319(a) of the PHS Act have terminated. The change will align the period that emergency analytical reactivity test results must remain in device labeling with the requirement in § 866.3328(b)(3)(iii) that manufacturers provide the last 3 years of annual analytical reactivity testing in the device labeling. FDA believes that this makes the labeling requirements in the special controls more clear and consistent for industry.

As discussed previously, after reviewing the comments received along with the proposed order and the Panel's recommendations, FDA is making a few clarifications and modifications to the special controls for antigen based RIDTs. These include: (1) Clarifying that clinical performance criteria must be met for each specimen type claimed in the intended use of the device; (2) clarifying that manufacturers of future antigen based RIDT devices may use a currently appropriate and FDA accepted comparator method other than comparison to an FDA-cleared nucleic acid based-test or viral culture methods to demonstrate that those devices meet the clinical performance criteria, if such a comparator method is established; (3) clarifying that a manufacturer choosing to provide analytical reactivity testing results via its public Web site must prominently provide hyperlink to that Web site in the device's label or in other labeling that physically accompanies the device; (4) clarifying the circumstances in which emergency analytical reactivity testing is required under § 866.3328(b)(4); and (5) requiring results of such emergency analytical reactivity testing to remain in the device labeling for a period of 3 years.

III. The Final Order

Under section 513(e) of the FD&C Act, FDA is adopting its findings as published in the preamble to the proposed order, with the modifications discussed in section II of this final order. FDA is issuing this final order to reclassify antigen based rapid influenza virus antigen detection test systems intended to detect influenza virus antigen directly from clinical specimens that are currently regulated as influenza virus serological reagents under § 866.3330 from class I into class II with special controls and into a new device classification regulation for ''influenza virus antigen detection test systems.'' Currently, antigen based RIDTs are mostly found under product codes GNX and GNT. However, any antigen based rapid influenza virus antigen detection test system intended to detect influenza virus antigen directly from clinical specimens that is currently regulated as influenza virus serological reagents under § 866.3330 is subject to this

reclassification regardless of the product code to which it is currently assigned.

Section 510(m) of the FD&C Act provides that a class II device may be exempt from the premarket notification requirements under section 510(k) of the FD&C Act, if the Agency determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this device, FDA believes that premarket notification is necessary to provide reasonable assurance of safety and effectiveness. Therefore, this type of device is not exempt from premarket notification requirements.

In addition, FDA believes that special controls that: (1) Identify the minimum acceptable performance criteria; (2) require use of a currently appropriate and FDA accepted comparator method for establishing performance of new antigen based RIDTs; (3) require annual analytical reactivity testing of contemporary influenza strains; and (4) require analytical reactivity testing of newly emerging strains under certain situations involving an emergency or potential for an emergency, are necessary to provide reasonable assurance of safety and effectiveness of these devices.

IV. Implementation Strategy

The special controls identified in this final order are effective February 13, 2017.

- For antigen based RIDTs that have not been legally marketed prior to February 13, 2017, or that have been legally marketed but are required to submit a 510(k) under 21 CFR 807.81(a)(3) because the device is about to be significantly changed or modified, manufacturers must obtain 510(k) clearance, among other relevant requirements, and demonstrate compliance with the special controls included in this final order, before marketing their new or changed device. If a manufacturer markets such a device after February 13, 2017 without obtaining 510(k) clearance and demonstrating compliance with the special controls included in this final order, then FDA would consider taking action against such a manufacturer under its usual enforcement policies.
- For antigen based RIDTs that have been legally marketed prior to February 13, 2017, FDA does not intend to enforce compliance with the special controls until January 12, 2018. If a manufacturer markets such a device after January 12, 2018, and that device does not comply with the special controls, then FDA would consider taking action against such a manufacturer under its usual enforcement policies.

FDA believes that a period of 1 year from the publication date of this final order is appropriate for manufacturers to come into compliance with the special controls and for those manufacturers whose currently legally marketed devices do not meet the minimum performance criteria to prepare and submit a 510(k) for a new or significantly changed or modified device. FDA believes this approach will help ensure the efficient and effective implementation of the order.

V. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this reclassification 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. Paperwork Reduction Act of 1995

This administrative order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information 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 collections of information in part 807, subpart E, regarding premarket notification submissions have been approved under OMB control number 0910–0120; the collections of information in 21 CFR part 812 regarding investigational device exemptions have been approved under OMB control number 0910–0078; the collections of information in 21 CFR part 801 and § 809.10 have been approved under OMB control number 0910–0485; and the collections of information regarding pre-submissions have been approved under OMB control number 0910–0756.

VII. Codification of Orders

Prior to the amendments by FDASIA, section 513(e) of the FD&C Act provided for FDA to issue regulations to reclassify devices. Although section 513(e) of the FD&C Act, as amended, requires FDA to issue final orders rather than regulations, FDASIA also provides for FDA to revoke previously issued regulations by order. FDA will continue to codify classifications and reclassifications in the Code of Federal Regulations (CFR). Changes resulting from final orders will appear in the CFR as changes to codified classification determinations or as newly codified orders. Therefore, under section 513(e)(1)(A)(i) of the FD&C Act, as amended by FDASIA, in this final order, we are codifying the reclassification of antigen based RIDTs into class II (special controls).

VIII. Reference

The following reference is on display in the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, and is available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; it is also available electronically at *https://www.regulations.gov.* FDA has verified the Web site addresses, as of the date this document publishes in the **Federal Register**, but Web sites are subject to change over time.

1. Transcript and other meeting materials of FDA's Microbiology Devices Panel Meeting held on June 13, 2013, are available on FDA's Web site at: *http://www.fda.gov/AdvisoryCommittees/ucm351035.htm.*

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 part 866 continues to read as follows:

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

■ 2. Add § 866.3328 to subpart D to read as follows:

§ 866.3328 Influenza virus antigen detection test system.

(a) *Identification.* An influenza virus antigen detection test system is a device intended for the qualitative detection of influenza viral antigens directly from clinical specimens in patients with signs and symptoms of respiratory infection. The test aids in the diagnosis of influenza infection and provides epidemiological information on influenza. Due to the propensity of the virus to mutate, new strains emerge over time which may potentially affect the performance of these devices. Because influenza is highly contagious and may lead to an acute respiratory tract infection causing severe illness and even death, the accuracy of these

devices has serious public health implications.

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

(1) The device's sensitivity and specificity performance characteristics or positive percent agreement and negative percent agreement, for each specimen type claimed in the intended use of the device, must meet one of the following two minimum clinical performance criteria:

(i) For devices evaluated as compared to an FDA-cleared nucleic acid based-test or other currently appropriate and FDA accepted comparator method other than correctly performed viral culture method:

(A) The positive percent agreement estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 80 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 70 percent.

(B) The negative percent agreement estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 95 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 90 percent.

(ii) For devices evaluated as compared to correctly performed viral culture method as the comparator method:

(A) The sensitivity estimate for the device when testing for influenza A must be at the point estimate of at least 90 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 80 percent. The sensitivity estimate for the device when testing for influenza B must be at the point estimate of at least 80 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 70 percent.

(B) The specificity estimate for the device when testing for influenza A and influenza B must be at the point estimate of at least 95 percent with a lower bound of the 95 percent confidence interval that is greater than or equal to 90 percent.

(2) When performing testing to demonstrate the device meets the requirements in paragraph (b)(1) of this section, a currently appropriate and FDA accepted comparator method must be used to establish assay performance in clinical studies.

(3) Annual analytical reactivity testing of the device must be performed with contemporary influenza strains. This annual analytical reactivity testing must meet the following criteria:

(i) The appropriate strains to be tested will be identified by FDA in consultation with the Centers for Disease Control and Prevention (CDC) and sourced from CDC or an FDA-designated source. If the annual strains are not available from CDC, FDA will identify an alternative source for obtaining the requisite strains.

(ii) The testing must be conducted according to a standardized protocol considered and determined by FDA to be acceptable and appropriate.

(iii) By July 31 of each calendar year, the results of the last 3 years of annual analytical reactivity testing must be included as part of the device's labeling. If a device has not been on the market long enough for 3 years of annual analytical reactivity testing to have been conducted since the device received marketing authorization from FDA, then the results of every annual analytical reactivity testing since the device received marketing authorization from FDA must be included. The results must be presented as part of the device's labeling in a tabular format, which includes the detailed information for each virus tested as described in the certificate of authentication, either by:

(A) Placing the results directly in the device's § 809.10(b) of this chapter compliant labeling that physically accompanies the device in a separate section of the labeling where the analytical reactivity testing data can be found; or

(B) In the device's label or in other labeling that physically accompanies the device, prominently providing a hyperlink to the manufacturer's public Web site where the analytical reactivity testing data can be found. The manufacturer's home page, as well as the primary part of the manufacturer's Web site that discusses the device, must provide a prominently placed hyperlink to the Web page containing this information and must allow unrestricted viewing access.

(4) If one of the actions listed at section 564(b)(1)(A)–(D) of the Federal Food, Drug, and Cosmetic Act occurs with respect to an influenza viral strain, or if the Secretary of Health and Human Services (HHS) determines, under section 319(a) of the Public Health Service Act, that a disease or disorder presents a public health emergency, or that a public health emergency otherwise exists, with respect to an influenza viral strain:

(i) Within 30 days from the date that FDA notifies manufacturers that characterized viral samples are available for test evaluation, the manufacturer must have testing performed on the device with those viral samples in accordance with a standardized protocol considered and determined by FDA to be acceptable and appropriate. The procedure and location of testing may depend on the nature of the emerging virus.

(ii) Within 60 days from the date that FDA notifies manufacturers that characterized viral samples are available for test evaluation and continuing until 3 years from that date, the results of the influenza emergency analytical reactivity testing, including the detailed information for the virus tested as described in the certificate of authentication, must be included as part of the device's labeling in a tabular format, either by:

(A) Placing the results directly in the device's § 809.10(b) of this chapter compliant labeling that physically accompanies the device in a separate section of the labeling where analytical reactivity testing data can be found, but separate from the annual analytical reactivity testing results; or

(B) In a section of the device's label or in other labeling that physically accompanies the device, prominently providing a hyperlink to the manufacturer's public Web site where the analytical reactivity testing data can be found. The manufacturer's home page, as well as the primary part of the manufacturer's Web site that discusses the device, must provide a prominently placed hyperlink to the Web page containing this information and must allow unrestricted viewing access.

Dated: January 4, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017–00199 Filed 1–11–17; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

24 CFR Part 15

[Docket No. FR–5986–F–01]

RIN 2501–AD81

Revision of Freedom of Information Act Regulation

AGENCY: Office of the Secretary, HUD.

ACTION: Final rule.

SUMMARY: This final rule amends HUD's Freedom of Information Act (FOIA) regulation to implement the FOIA Improvement Act of 2016. The FOIA Improvement Act enacted a range of procedural issues, including requirements that agencies establish a minimum of 90 days for requesters to file an administrative appeal, and codifies the foreseeable harm standard.