



August 20, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

***Re: Docket No. FDA-2014-N-0440; Microbiology Devices; Proposed Order on
Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly
with Clinical Specimens***

Dear Sir or Madam:

On behalf of AdvaMedDx, a Division of the Advanced Medical Technology Association (AdvaMed), we provide these comments on the Food and Drug Administration (FDA) proposed order on “Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly with Clinical Specimens” (hereinafter “proposed reclassification order” or “proposed order”).

AdvaMedDx member companies produce advanced, *in vitro* diagnostic tests that facilitate evidence-based medicine, improve quality of patient care, enable early detection of disease and reduce overall health care costs. Functioning as an association within AdvaMed, AdvaMedDx is the only multi-faceted, policy organization that deals exclusively with issues facing *in vitro* diagnostic companies in the United States and abroad. Our membership includes manufacturers engaged in the development of innovative technologies supporting the advancement of the public health, including antigen based rapid influenza virus antigen detection test systems (or “rapid flu tests”).

GENERAL COMMENTS

AdvaMedDx appreciates the opportunity to provide comments on this proposal. At the same time, we respectfully request that FDA hold a panel meeting following the publication of this proposed order so that the panel can evaluate CDRH’s specific proposal for revision of classification and public stakeholders are allowed to participate in a meaningful way. This procedure was outlined in Section 608 of the Food and Drug Administration Safety and Innovation Act (FDASIA). While FDA obtained significant administrative efficiencies in the reclassification process as a result of FDASIA, which allows for use of an order rather than rulemaking, the holding of a panel meeting following issuance of a proposed reclassification order is a critical element of the process reforms enacted by Congress.

FDA issued this proposed order in conjunction with plans to reclassify these rapid flu tests. The proposed reclassification order outlines a number of new requirements for implementation by manufacturers, including mandatory annual analytical reactivity testing with contemporary influenza strains. A clear understanding of requirements and implications by manufacturers and

other members of the public and assurance of workable implementation of this proposal is critical in advance of reclassification. In particular, we note concern regarding the need to assure timely and accessible specimens for small and large innovators as well as clear testing program and reclassification roll-out to assure continuity in test access and sufficient time for any necessary testing, product modifications, and subsequent submissions. The proposed order suggests that the holding of an expert panel following the proposed order is discretionary rather than mandatory. FDA may hold additional panel meetings if it wishes to gain early input or help inform its thinking, but this should not take the place of a panel to discuss the proposal after it has been issued. FDA has appropriately held panels following proposed reclassification orders in a number of cases and we urge this to be a consistent practice rather than on a case-by-case basis at the discretion of FDA.

While we are not opposed to the reclassification of these products generally, we would like to relay several issues and questions related to scientific and practical application that are ripe for discussion and have been generated following issuance of the proposed order. These points are covered in our specific comments that follow. Recommendations are provided in many cases to address concerns and provide an optimal path forward.

SPECIFIC COMMENTS

AdvaMedDx's specific comments are below and provide more detailed comments and several points for clarification. Our comments are focused on process and implementation considerations that we believe are integral to successful reclassification of these products vital to patient care.

Assuring Appropriate Specimen Access and Consistent Transparent Annual Testing Process

FDA plans to require annual analytical reactivity testing with contemporary flu strains. As previously discussed, we believe there are some challenges with obtaining timely and appropriately accessible specimens for this testing and have some questions regarding how this program would be implemented. Details of this requirement are not well outlined in this proposal and do not describe how this can be practically accomplished apart from reference to "a standardized protocol considered and determined by FDA to be acceptable and appropriate" and tested with "appropriate strains...identified by FDA in consultation with CDC and sourced from CDC or a CDC-designated source." The proposed rule also generally references that in the event that "annual strains are not available from CDC, FDA will identify an alternative source for obtaining the requisite strains." There are also proposed requirements for reporting by the manufacturer of the results, but there is no clear mechanism outlined for activities leading up to such posting. For such a fundamentally new requirement, there will be relative capacities of innovators to acquire such specimens considering time constraints, resources, and administrative challenges to specimen access through current networks (e.g., World Health Organization Pandemic Influenza Preparedness or "PIP" Framework and potential impact on access to influenza strains sourced by the WHO Global Influenza Surveillance and Response System or "GISRS"). These details should be discussed and resolved with CDC, FDA, and industry prior to finalizing this reclassification. Companies must be able to access specimens in a fair, timely,

and non-cost restrictive manner and comply with these postmarket requirements. Otherwise, innovators may be unable to continue to develop new influenza diagnostics that meet public health needs.

Questions that require clarification prior to issuing any final order include:

- If manufacturers are required to perform this annual testing, will they need to participate in the WHO PIP Network in order to access specimens through the GISRS?
- Will specimens be available through venues other than the GISRS for this testing?
- Could there be an option for testing to be conducted by an independent lab, such as at a university, for interested manufacturers?
- Can a standardized panel be provided for use with annual strain testing? This would allow for the same concentration for testing and would benefit the public health.
- What will be the process for notifying manufacturers that their assay meets or does not meet the new performance requirements?
- Will there be an appeals mechanism for manufacturers? What specific steps would be available for manufacturers?
- With respect to the “standardized protocol,” will industry be engaged for feedback prior to roll-out and in what capacity? How will this protocol be developed and made available to manufacturers?

Allowing Sufficient Transition Time To Accommodate Flu Season and Subsequent Submissions

We appreciate FDA’s allotment of a transition period for manufacturers. Under the proposed order, FDA suggests an effective date of one year from the publication of the final rule.

One key question that requires clarification prior to issuing any final order and is integral to product continuity for healthcare professionals:

- Will FDA consider providing additional transitional time to accommodate timing sufficiently in advance of the flu season and to allow time for completion and review of submissions?

Such additional time will provide for much smoother implementation and assist manufacturers who are working in good faith to meet new requirements.

Further Engaging Physician Users of Rapid Flu Tests to Participate at Panel

As part of next steps, we would recommend inclusion of physicians who use rapid flu tests in their practice to be included along with academic and lab-based investigators in the reclassification panel to discuss this proposed order. This will lend critical expertise and perspective. Further, it will aid overall evaluation of FDA's proposed plans on test reclassification, including test protocol, specifications, and qualification of specimens.

We appreciate FDA's effort to issue this proposed order and welcome additional dialogue to ensure smooth implementation. Our comments are intended to support the reclassification process and development of flu diagnostics that support the public health. Thank you for consideration of our comments.

Sincerely,

/s/

Khaterh Calleja
Vice President
Technology and Regulatory Affairs