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RE: Docket No. FDA-2018-N-0467 Joint Meeting of the Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee

On behalf of the Association of Public Health Laboratories (APHL), please accept the following comments concerning docket no. FDA-2018-N-0467 Joint Meeting of the Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee. APHL supports the proposed reclassification of nucleic acid and serology-based point-of-care and laboratory-based in vitro diagnostic devices for use as aids in the diagnosis of human immunodeficiency virus (HIV) and hepatitis C virus (HCV). APHL supports the reclassification of these devices from Class III to Class II to achieve urgently needed improved accessibility to the latest HIV and HCV testing technologies in the US. Improving access to state of the art HIV and HCV tests will improve patient diagnosis, laboratory efficiency, patient management, and public health surveillance. We believe that designating HIV and HCV diagnostic assays as Class II devices with general controls, and potentially special controls will be sufficient to provide reasonable assurance of the safety and efficacy of the assays.

The decision to regulate these devices under Class III controls was made decades ago when the infections caused by these viruses were a death sentence. Since that time we have made significant gains in our knowledge about these viruses and our ability to treat the infections they cause through research and epidemiological studies. This increased knowledge, including a vast amount of information on genetic variation of these viruses has led to the creation of more robust tests. The standards for validation of tests have also evolved to ensure the diverse array of circulating genotypes and subtypes are detected. Additionally, the outcome of infection by these viruses has changed dramatically with the advent of highly effective anti-retroviral therapy.

APHL believes that reclassification to Class II devices for HIV and HCV diagnostics would increase access to HIV and HCV testing at a time when there is increased incidence of HCV and co-incident HIV infection being driven by the opioid epidemic and a strong need to identify infections earlier to prevent future transmission. The reclassification could help with this by 1) decreasing the burden of submission criteria, 2) shortening delays to market of newly developed HIV and HCV assays, and 3) increasing competition in the market. APHL contends that reclassification would not increase the risk of adverse outcomes to safety and efficacy of assays.

1. APHL does not believe that the down classification would result in any adverse safety of efficacy outcomes.

- a. FDA down-classified Hepatitis A virus devices from Class III to Class II in 2006 with special controls and there have not been any adverse outcomes reported to date.
 - b. Diagnosis of HIV and HCV relies on a multi-step algorithm which by design mitigates risk. The potential risk from down classification of a single device from Class III to Class II could be mitigated by the requirement of multiple devices being used to make the diagnosis.
2. Currently, there is virtually no competition in the diagnostic testing market for HIV-1/2 antibody differentiating tests (the second step in the recommended laboratory algorithm) or for HIV-1 nucleic acid amplification tests (NAT) approved for aiding diagnosis. Additionally, there is not a single FDA-approved diagnostic HIV-2 NAT.
 - a. A down-classification of these devices, as outlined previously, could enable the development and quicker approval of additional devices.
 - b. It would also increase the variety and types of assays available which would add to the competition and better data on test effectiveness as there would be other devices to compare performance against.
3. A decreased burden of submission criteria would reduce the size and cost of clinical trials as well as the cost of submission fees.
 - a. Current 2018 standard user fees for Medical Device Users are \$300,000 greater for a PMA submission than a 510K submission, \$310,764 versus \$10,566. This is in addition to the additional costs of a clinical trial for PMA submission
 - b. This could incentivize current manufacturers to include additional specimen types (i.e. dried blood spots) in the clinical trial design since it would be less costly to do so.
 - c. This could allow smaller manufacturer's with novel products to enter the arena that have not been able to meet the burden of a PMA submission but have a valuable product.
4. A down-classification could also shorten delays to market of newly developed HIV and HCV assays.
 - a. Newly developed HIV and HCV assays typically receive a CE-mark for testing and marketing in the European Union well before they are FDA-approved. For example the HIV-1/2 Antigen-Antibody combination assays were available in the European Union up to seven years before they were FDA-approved for use in the US.
 - b. Down-classification would therefore allow tests that can diagnose HIV and HCV infections earlier in the course of the infection to reach the US market in a shorter time frame. This would in turn improve the US diagnostic capability to detect and diagnose these infections and thereby enable us to decrease transmission.
 - c. APHL partners with over 40 public health laboratories that follow the CDC/APHL HIV diagnostic algorithm and now have access to an HIV RNA test for HIV diagnosis required to identify acute infections through two referral laboratories. While this service enables these sites access to the diagnostic HIV RNA test, the turnaround time from sample collection to NAT result is 12 days on average with only 80% of samples being tested within 2 weeks. This delay may result in additional transmissions. Increased commercial



availability of diagnostic HIV RNA assays, including simplified nucleic acid tests with a diagnostic claim could significantly reduce this window.

We are at a time when the stringent requirements for a Class III device should be re-evaluated. Additionally, it should be noted that even though these two viruses are under Class III controls, from an outside perspective, it would seem that the HIV devices face additional barriers compared to HCV devices with respect to obtaining approval from the FDA for diagnostic claims. The evidence to support this apparent difference was the recent change in HCV nucleic acid tests where they were approved with “dual-claims” for both diagnosis and monitoring whereas for HIV this is not currently an option. APHL therefore also suggests that FDA handle all devices within a classification with the same standard and approaches.

APHL believes that the proposed reclassification, if adopted, will help improve critical access to quality HIV/HCV tests and this in turn will improve patient diagnosis, laboratory efficiency, patient management, and public health surveillance. In addition it could significantly improve our ability to reach national goals of HIV and HCV elimination. These diseases impact disadvantaged populations disproportionately, and yet all persons deserve access to the best diagnostics available.

Sincerely,

A handwritten signature in black ink that reads "Scott J. Becker".

Scott J. Becker, MS
Executive Director
Association of Public Health Laboratories

APHL works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.