



January 29, 2014

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

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the November 25, 2013 final guidance "*Distribution of In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only Guidance for Industry and Food and Drug Administration Staff.*" We support the FDA's efforts to ensure that manufacturers appropriately sell, and clinical laboratories correctly use, these reagents. We are requesting that the FDA clarify aspects of this policy that may affect the use of laboratory developed tests (LDTs) and access to new technologies.

### **General Comments**

The problem, as defined by the agency, is that the use of RUO/IUO products "for purposes other than research or investigation (for example, for clinical diagnostic use), has led, in some cases, to the clinical diagnostic use of products with unproven performance characteristics, and with manufacturing controls that are inadequate to ensure consistent manufacturing of the finished product. Use of such tests for clinical diagnostic purposes may mislead healthcare providers and cause serious adverse health consequences to patients, who are not aware that they are being diagnosed with or treated based on the results of the test with research or investigational products."

Although we appreciate the FDA's concern, it's important to note that the vast majority of laboratories using RUO/IUO reagents already comply with stringent federal and private sector requirements for using such products. These laboratories conduct rigorous validation studies, establish appropriate performance controls, and participate in regular proficiency testing to ensure test performance. If a laboratory fails to comply with any of these requirements, the regulatory agency or accrediting body can impose a series of penalties, including revocation of their certificate. AACC urges the FDA to work closely with the medical device and laboratory communities to ensure that responsible laboratories continue to have access to these reagents.

### **Laboratory Developed Tests**

Although there have been improvements from the previous guidance, we still have a number of questions. In the June 1, 2011 draft guidance, the FDA stated that LDTs were not covered by the document. This statement was deleted from the November 25, 2013 final guidance. AACC would like clarification on how this policy affects LDTs.

#### ***Questions:***

1. Does this document apply to clinical laboratories? Laboratory developed tests?
2. If it applies to laboratories, will laboratories be considered a “manufacturer” of a diagnostic if they actively market or promote a test in their test menu catalogue?
3. Would laboratories be interpreted in the same manner as manufacturers with respect to appropriate and inappropriate labeling if the results of an LDT (being utilized for patient care and medical decision-making) contains a disclaimer comment using the RUO or IUO language?

### **New Technology/Orphan Tests**

In the updated draft, the FDA deleted a sentence directing manufacturers not sell to “clinical laboratories that the manufacturer knows, or has reason to know, use the IVD product in clinical diagnostics use in an investigation or otherwise, and support (including technical support) for those activities.” AACC agrees with the deletion. In its place, the FDA has listed a number of practices that “would appear to conflict with RUO or IUO labeling.” The agency ‘suggests’ that manufacturers avoid these situations. We are still concerned that manufactures complying with some of these recommendations may limit laboratory access to RUO/IUO products. We seek clarification on the following questions:

#### ***Questions:***

1. Clinical laboratories use instruments that are not FDA approved (spectrophotometers, pH meters, mass spectrometers, etc.) and are often labeled as RUO. How does this guidance impact the sale and use of these instruments?
2. Would FDA grandfather LDTs that use RUO product components and that have no IVD counterpart so that patient care is not adversely impacted due to the sudden withdrawal of such tests?
3. If a lab uses a RUO/IUO product and carries it through their CLIA '88/CAP-required method validation, is that sufficient?

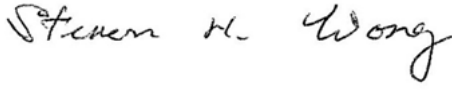

FDA

January 29, 2014

Page Three

By way of background, AACC is the principal association of professional laboratorians--including MDs, PhDs and medical technologists. AACC's members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and practice in hospitals, independent laboratories and the diagnostics industry worldwide. The AACC provides international leadership in advancing the practice and profession of clinical laboratory science and medicine and its applications to health care. If you have any questions, please call me at (336) 716-2639, or Vince Stine, PhD, Director, Government Affairs, at (202) 835-8721.

Sincerely,

Steven H. Wong, Ph.D., DABCC (TC), FACB  
President, AACC