August 3, 2011

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

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the June 1, 2011 "Draft Guidance for Industry and Food and Drug Administration Staff/Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions." We applaud the FDA's efforts to ensure that clinical laboratories are appropriately using these reagents. AACC is concerned, however, that the agency's draft guidance, if strictly implemented, may adversely affect patient care by hindering the development of new tests and limiting access to specialized testing for rare disorders.

General Comments
The problem, as defined by the agency, is that the use of RUO/IUO products *"for purposes other than research or investigations…has led in some cases to diagnostic use of laboratory tests with unproven performance characteristics and 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 research or investigational products."*

AACC shares the agency's concern. We agree that clinical laboratories should not market tests that utilize RUO/IUO reagents without first validating the test. AACC believes that the federal agencies and private sector accrediting bodies responsible for overseeing clinical laboratories should work together to identify and educate those laboratories and, if necessary, impose appropriate sanctions. We particularly urge CMS, as the agency responsible for testing-related issues, to devote more time and resources during inspections to discovering and addressing these tests.

It's important to note that the vast majority of laboratories using RUO/IUO reagents comply with the 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 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.

New Technology
The FDA states that manufacturers who label their IVD products "For Research Use Only" or "For Investigational Use Only," should not sell these products to clinical laboratories that "they know" or have "reason to know" are using them for clinical diagnostic use. We are concerned that this second provision will place manufacturers in the untenable position of speculating about a laboratory's intentions and possibly lead to new, unwarranted restrictions on the sale of these reagents.

Although we understand the FDA's concerns regarding the use of some RUO/IUO products, the agency needs to balance this concern with the potential impact its new policy may have on the development of new assays. Limiting laboratory access to these products may hinder the development of new assays, since RUO/IUO reagents are often the key building blocks in the creation of these tests. This is particularly true in the field of molecular diagnostics where new tests, such as assays detecting new viral and bacterial pathogens, as well as genetic rearrangements in cancer, are greatly improving clinicians' ability to diagnosis and treat disease.

Patient Access to Care/Orphan Tests
AACC is also concerned that the FDA's draft policy may adversely affect patient care. For example, all 50 states now screen infants for at least 30 inborn metabolic errors. Follow-up testing to confirm and define these disorders relies almost exclusively on RUO/IUO reagents for mass spectrometry. Tests monitoring immunosuppression in transplant patients and detecting exposure to toxic substances also commonly depend on these same instruments and reagents. There are many other orphan tests that are only available in RUO and IUO formats. The commercial appeal of these tests is so limited that unless an exception is made for these specialty tests, they are likely to be discontinued. Limiting access to these reagents will have serious consequences for patient care.

AACC urges the FDA to revise this draft guidance to ensure that it more accurately reflects the agency's intent, namely to sanction those few laboratories inappropriately marketing assays that utilize RUO/IUO reagents. We are concerned that the current language may cause confusion among manufacturers and lead to unnecessary restrictions on the sale of RUO/IUO products to responsible laboratories, which could hinder patient access to care. AACC looks forward to working with the FDA on this issue.

By way of background, AACC is the principal association of professional laboratory scientists--including MDs, PhDs and medical technologists. AACC's members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work 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 its application to health care. If you have any questions, please call me at (314) 362-0194, or Vince Stine, PhD, Director, Government Affairs, at (202) 835-8721.

Sincerely,

Ann M. Gronowski, PhD
President, AACC