



**Association for Molecular Pathology**  
*Promoting Clinical Practice, Basic Research, and Education in Molecular Pathology*

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April 23, 2009

Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Comments to Docket No. FDA-2008-P-0638-0001/CP

Dear Sir or Madam:

The Association for Molecular Pathology (AMP) submits these comments in response to the Citizen Petition filed by Genentech, Inc. on December 9, 2008 that requests FDA review and clearance of all laboratory developed tests (LDTs) used in therapeutic decision-making.

AMP is an international medical and professional association representing approximately 1,700 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Our members are dedicated to the development and implementation of molecular pathology testing, including genetic testing, in a manner consistent with the highest standards established by the Clinical Laboratory Improvement Amendments (CLIA), the College of American Pathologists (CAP), the American College of Medical Genetics (ACMG), and the Food & Drug Administration (FDA). AMP members populate the majority of clinical molecular diagnostics laboratories in the United States, and their efforts are central to the generation of novel, high quality, molecular tests that are applied daily in medical decision-making. Assays designed and validated within these laboratories are used for diagnosis, prognosis and patient management in all medical areas including cancer, infectious diseases, heritable disorders, and histocompatibility testing. In addition to developing and implementing such tests, AMP members are experts in their interpretation.

AMP understands the concerns set forth in Genentech's Citizen Petition, and agrees that only high quality, clinically and analytically valid diagnostic tests should be performed in clinical laboratories. For the vast majority of molecular pathology tests the CLIA program, laboratory accreditation by professional societies such as the CAP, and board-certification and licensure of laboratory directors provide the most effective, appropriate, and patient-oriented oversight system for clinical diagnostic laboratories. The recommendations proposed in Genentech's petition, if adopted, would be detrimental to patient care and have adverse consequences for the healthcare system as a whole.

### **Access to High Quality Laboratory Developed Tests**

The use of LDTs has historically been an essential and central component of medical practice. Anatomic and clinical pathologists as well as other laboratory professionals who perform such tests have, and will continue to have, vital roles in therapeutic decision-making and other aspects of patient management.

In addition to ensuring necessary access to innovative tests, the current oversight system allows clinical laboratorians to rapidly incorporate new findings into practice, and to modify existing LDTs in accordance with advances in our understanding of clinical utility and disease pathogenesis. Laboratory developed molecular pathology tests have played key roles in the major advancements we have made in the diagnosis and management of diseases like AIDS, leukemia, lymphoma, and other types of cancer. LDTs identify suitable bone marrow donors, and allow us to monitor the disease course in transplant recipients.

Most molecular tests have their origins as LDTs. The vast majority of the thousands of molecular pathology tests listed in the AMP Test Directory ([www.amptestdirectory.org](http://www.amptestdirectory.org)) are offered as LDTs, as are most of the tests included in the heritable disorders website, GeneTests.org. Indeed Genentech in its Citizen Petition acknowledges the importance of LDTs, stating that the Company “fully support[s] the development of LDTs and other diagnostic tests that help inform clinical practice and recognizes the important role they can play in modern medicine.”

Adding a greater regulatory burden to the extensive oversight system currently in place would strain the limited resources of many molecular laboratories, particularly in university and hospital settings. Such action would obstruct medical practice, decrease the availability of tests, and deny thousands of patients access to accurate, rapid, and potentially lifesaving diagnostic services.

### **Adherence to CLIA and Professional Guidelines**

The current system of regulation and oversight is effective and appropriate. First, all laboratories that perform clinical diagnostic testing in the United States are required to comply with the mandates of the Clinical Laboratory Improvement Amendments and accompanying regulations. Only laboratories that are certified to perform high complexity testing are permitted to design and perform laboratory developed tests. The extensive training and experience required of high complexity laboratory directors and the professionals who perform tests at the bench, combines with the remainder of the CLIA regulations to ensure accurate, reliable, timely, high quality patient test results, proper test performance and accurate reporting ([www.cms.hhs.gov](http://www.cms.hhs.gov)). Of note, CLIA requires regular performance assessment of all assays offered by clinical laboratories.

AMP’s laboratory director members are pathologists or other physicians and board-certified doctoral scientists, who have undergone extensive and specialized training in the design and development of LDTs as well as their analytic and clinical validation and

appropriate utilization. Our director members are experts in assay quality control and quality assurance methods and procedures.

Importantly, the CLIA oversight system incorporates flexibility that enables pathologists to properly and effectively practice their medical specialty. The Secretary of HHS established separate processes for test complexity categorization for commercial manufacturers of test kits and clinical laboratories in 42 C.F.R. 493.17(c). Classification of commercial test kits falls within the jurisdiction of FDA, while classification of laboratory developed tests has been delegated to CDC. In so doing, the Secretary clearly demonstrated that CLIA was the primary means by which the Agency intended to regulate clinical laboratory performance.

Second, most laboratories that perform genetic testing are accredited by the CAP. CAP accreditation standards far exceed those of CLIA, and require assessments of clinical validity and appropriate test utilization. In addition, the CAP requires formal proficiency testing for the most commonly performed molecular tests.

Third, most laboratories that solicit samples nationwide receive New York State approval for their tests. New York State requirements are also more stringent than those of CLIA. Significantly, New York assay approvals routinely take many months, and delays of two years or more are commonplace. FDA's implementation of a similar system of review would deny or delay access of thousands of patients to beneficial diagnostic advances.

Finally, there is no evidence that the comprehensive system of oversight already in place has been inadequate, or that there are systemic problems with the quality of U.S. laboratory tests generally or LDTs specifically.

### **Participation in Deliberative Process**

AMP members are primary providers of molecular LDTs. We bring a practical perspective, real world experience, and accurate, up-to-date information on the development and validation of laboratory developed tests. With this in mind, AMP respectfully requests an invitation from the FDA to share its insights. We also extend an offer to the Agency to provide assistance as you consider the Citizen Petition submitted by Genentech, or in any future deliberations regarding molecular tests or their oversight. AMP looks forward to continuing this dialogue with the FDA, and to serving as an authoritative and reliable resource for the FDA, other federal agencies, and public and private stakeholders.

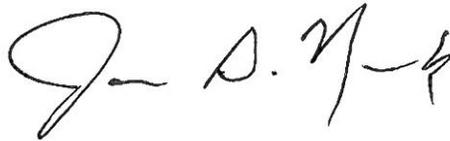
### **Conclusion**

Thank you very much for your consideration of our comments in response to Genentech's Citizen Petition. AMP and its membership strongly believe that all diagnostic tests should be of the highest quality, reliability, and safety, and that each test must provide valid and useful information for clinical decision-making. Moreover, we believe that claims accompanying any and all laboratory tests should be truthful and accurate.

Adoption of the recommendations contained in Genentech's petition would significantly hinder the ability of laboratories to provide access to many tests critical to patient care. Moreover, this would curtail the innovative impact that laboratory developed tests have on the advancement of personalized medicine, a concept that the FDA and numerous other federal agencies strongly support.

AMP members are confident that existing regulatory, accreditation, and professional standards provide safe, medically appropriate oversight and effective quality controls for the laboratory developed tests we design. Additional FDA regulation would result in delays in the development and introduction of medically valuable new diagnostics, and limit our ability to expand and improve upon currently offered tests. As such, any efforts to modify the current system of oversight must be treated with extreme caution. AMP is pleased to serve as a resource for the FDA. We look forward to the FDA's response to our comments.

Sincerely,

A handwritten signature in black ink, appearing to read "Jan Nowak". The signature is fluid and cursive, with a large initial "J" and a distinct "N".

Jan Nowak, MD, PhD  
President