Comments to the Secretary's Advisory Committee on Genetics Health and Society

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Good afternoon. My name is Gail Javitt and I am Law and Policy Director with the Genetics and Public Policy Center at Johns Hopkins University. I appreciate the opportunity to address you today about the Center's concerns with respect to genetic testing quality and pharmacogenetics.

As this Committee has recognized, pharmacogenetics holds great promise to improve the public's health by improving the safety and effectiveness of pharmaceuticals.

But the success of pharmacogenetics depends on the availability of a robust pipeline of genetic tests to accurately and reliably detect variations in DNA. This pipeline, in turn, requires that genetic testing laboratories have the capability to perform the tests accurately and reliably, that the tests themselves provide clinically valid information, and that health care providers are able to interpret the results.

We are concerned that the current regulation of genetic testing is shaky, and does not appear sturdy enough to support the promise of pharmacogenetics. Although the public widely believes that the government regulates the quality of genetic tests, this assumption is largely unfounded.

There is today no specialty area for genetic testing laboratories under the Clinical Laboratory Improvement Amendments of 1988. This situation exists despite the fact that this Committee's predecessor -- the SACGT -- recommended that such a specialty be created by the Centers for Medicare and Medicaid Services, that CMS's own advisory committee developed a proposal for a specialty, and that CMS announced its intention in 2000 to create such a specialty.

We were curious as to possible causes for the delay. We wondered whether perhaps the comments submitted to the agency in response to its announcement were uniformly negative, causing the agency to change it mind. We therefore undertook a thorough review of the comments. Instead of overwhelming opposition, we found significant support for the creation of a specialty, with specific concerns about certain elements of the proposal – elements we believe are not central to the key goal of laboratory competence. Indeed, on the issue of proficiency testing – the laboratory's ability to

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reliably and accurately get the right answer in performing a genetic test – there was strong support for the creation of a specialty.

In November 2005 we sent a White Paper containing our analysis to CMS Administrator Mark McClellan along with a letter urging him to issue a proposed rule for a genetic testing specialty under CLIA. Subsequently, the Genetic Alliance sent a similar letter.

Turning to the regulation of genetic tests themselves, here too there are troubling gaps in oversight. There are today two paths by which a genetic test can be offered. Genetic testing laboratories can perform tests using "test kits" or they can make the test in-house using their own proprietary methods. The vast majority of genetic tests are developed in-house.

If a laboratory uses a test kit, then the manufacturer of the test kit must first obtain approval from FDA. FDA assesses both the analytical and clinical validity of the test kit, ensures that the labeling is adequate and that claims are supported by the data, and requires postmarket reporting of adverse events related to the test kit.

In contrast, if a laboratory uses an in-house test, there is no premarket review of that test. While some components of the test must conform to FDA labeling and good manufacturing practice requirements, no expert body reviews the test to ensure that it actually detects what it claims to detect and that the mutations detected are clinically relevant.

Not surprisingly, of the more than 900 genetic tests currently available, only a handful have gone the test-kit path, and even fewer for pharmacogenetics. To compound the regulatory inequity, even once a test kit is approved by FDA, there is nothing to prevent a clinical laboratory from developing its own assay and making the same claims made by the test kit manufacturer. Indeed, this has already occurred in the case of pharmacogenetic testing.

FDA has in the past few years recognized the potential value of pharmacogenetics to achieving the agency's mission of public health protection. FDA's several guidance documents demonstrate that although the precise regulatory framework is evolving, the agency anticipates regulating pharmacogenetic test kits. FDA's diligent efforts will be undermined, however, unless FDA's requirements apply to all pharmacogenetic tests, regardless of the means by which they are produced.

Additionally, in the absence of adequate oversight for pharmacogenetic tests, physicians and the public are hard-pressed to distinguish the good performers from the bad, and have little assurance that the tests they use to guide their healthcare decisionmaking are reliable and relevant predictors of their disease risk or treatment outcome.

If pharmacogenetics is to gain the public's trust – and, equally important, the trust of health care payers – and deliver on its promise of improving health, there must be a sufficient level of confidence that the laboratories offering these tests are performing

them correctly and that the tests themselves yield information that is relevant to healthcare decisionmaking. That confidence today is unwarranted.

Getting to a system worthy of public trust will require the Department of Health and Human Services to give the necessary direction to the agencies charged with overseeing laboratory and test quality to ensure that they implement needed changes to ensure quality.

We would encourage this Committee to make a recommendation to the Secretary that CMS issue a proposed regulation for a genetic testing specialty under CLIA. Further, we would encourage this Committee to recommend to the Secretary that a regulatory framework be established for genetic tests that ensures they are clinically valid regardless of whether they are performed using a test kit or an in-house developed method.