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## **21st Century Cures: Examining the Regulation of Laboratory Developed Tests**

**Testimony Before  
Committee on Energy and Commerce  
Subcommittee on Health  
United States House of Representatives**

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# **21st Century Cures: Examining the Regulation of Laboratory Developed Tests**

## **Testimony of Charles L. Sawyers, MD, Chair, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center**

Good morning, Mr. Chairman and distinguished Members of the Subcommittee. I am the immediate past president of the American Association for Cancer Research (AACR), and serve as Chair of the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center. I am honored to appear before you today to provide you with a perspective from the AACR on the recent notification offered by the Food and Drug Administration regarding the regulation of Laboratory Developed Tests (LDTs). Specifically, I will address the ways in which we believe this potential framework for regulatory oversight will protect patients, incentivize innovation, and advance the practice of personalized or precision medicine.

The mission of the AACR is to prevent and cure cancer through research, education, communication, and collaboration. Founded in 1907, the AACR is the world's oldest and largest cancer organization dedicated to accelerating advances in cancer research to benefit patients. The AACR's membership includes more than 35,000 basic, translational, and clinical researchers, health care professionals, patients and patient advocates residing in the U.S. as well as 96 other countries.

Because the AACR encompasses the entire continuum of cancer research and biomedical science – from the laboratory to the clinic including public policy – we are able to marshal the full

spectrum of expertise in the cancer community to accelerate progress in the prevention, detection, diagnosis, and treatment of cancer.

Cancer researchers today are leading the way in the exciting area of personalized or precision medicine, where scientists are increasingly developing treatments that are precisely targeted to the unique molecular and genetic characteristics of an individual's cancer. However, the success of these personalized treatments depends in no small measure on diagnostic tests that are reliable.

### ***The Promise of Personalized or Precision Medicine***

The knowledge of cancer's underlying biological causes, enabled through sustained investment by the federal government, primarily through the National Institutes of Health, has catalyzed a shift from the classification of cancer by site of origin, like lung or breast cancer, to classification by molecular subtype. This means that we are rapidly moving away from the era of one-size-fits-all cancer treatments that involve surgery, radiation, and chemotherapy, and are instead utilizing more sophisticated and highly innovative DNA sequencing technologies to provide patients with more opportunities for targeted treatments and personalized or precision medicine. More and more, we are treating cancer patients based on the specific molecular characteristics of his or her tumor(s), which is increasingly determined using highly complex DNA sequencing technologies. The promise of this approach is immense, and we are now ensuring that these advances are being applied to various forms of cancer with increasing speed and success.

I know the impact of molecularly targeted cancer therapy from firsthand experience, having led the first clinical trial of a drug called Gleevec that is highly effective in a form of blood cancer known as chronic myeloid leukemia. Patients with this formerly devastating disease now live for decades simply by taking a pill once a day that precisely targets the cancer cells. In fact, many of the patients I treated on the first clinical trial in 1999 are still alive and well today.

Since the approval of Gleevec in 2001, many additional targeted therapies have been developed and approved for a range of cancers; including previously deadly cancers -45 such personalized or precision medicines have gained FDA approval as of July 31 this year<sup>1</sup>. The benefit of targeted cancer therapy is that we are able to hone in on specific mutations that drive the growth of a patient's tumor cells, thereby enhancing the chance of a successful treatment response without the side effects of chemotherapy or radiation. However, this sophisticated mechanism of action also means that these drugs are only effective in those patients whose tumors carry these mutations. Therefore, the success of these personalized or precision medicine treatments depends on accurately identifying patients with a particular mutation before treating them with the appropriately matched drug. This is why the sophisticated new diagnostic tests that enable physicians to match the right drugs to the right patients play such a critical role in cutting-edge cancer care.

### ***Importance of Accurate and Effective Diagnostics in Cancer Care***

That over 40 targeted cancer therapies have gained FDA approval over the past 10 years is a testament to the fact that we have a streamlined and effective regulatory process in the U.S. To ensure that the right patients receive a targeted drug, the FDA approves targeted therapies in

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<sup>1</sup> US Food and Drug Administration. Hematology/Oncology (Cancer) Approvals; accessed on Sep. 5, 2014  
<http://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm>

conjunction with a diagnostic tool called a *companion diagnostic*, which provides physicians and patients with information that is essential for the safe and effective use of the therapy<sup>2</sup>. Drugs that are effective in a specific sub-population of patients are approved with the stipulation that the corresponding diagnostic test must be used to identify the appropriate patients for treatment. Thus, it follows that the diagnostic tools used to detect the molecular alterations that form the basis of tailored or personalized cancer treatments are crucial for the safe and effective practice of personalized medicine. A safe, reliable, accurate, and sensitive diagnostic test is as important as a safe, reliable, and effective drug.

### ***Different Paths to Market for Diagnostics***

In contrast to the single regulatory path to market for drugs, there are two very different paths to market for a diagnostic<sup>3</sup>. The first path is by gaining approval or clearance from the FDA which requires a sponsor to demonstrate proof of analytic and clinical validity as well as clinical utility of the test in some cases. *This is the path by which companion diagnostics are currently approved, in conjunction with approval of a targeted therapy.* The second path to market is when a test developer designs, manufactures and offers the test within a single laboratory as a laboratory developed test or an LDT. Because LDTs are not subject to the same level of scrutiny as diagnostics approved through the first regulatory path, there is less certainty and confidence in the accuracy of these products. This is particularly relevant for the highly sophisticated DNA sequencing technology based tests that generate the information from tumor cells that form the basis for many companion diagnostic tests.

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<sup>2</sup> US Food and Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools); accessed on Sep. 5, 2014

<sup>3</sup> Sawyers CL, and van 't Veer, LJ. Reliable and Effective Diagnostics Are Keys to Accelerating Personalized Cancer Medicine and Transforming Cancer Care: A Policy Statement from the American Association for Cancer Research. Clin Can Res; Published Online First September 9, 2014; doi: 10.1158/1078-0432.CCR-14-2295.

For a cancer patient, the consequences of an incorrect treatment recommendation made on the basis of a faulty diagnostic test are unacceptable, since the patient may lose the opportunity to receive an effective treatment or may be exposed to side effects from a treatment that has little to no chance of benefit. Physicians and patients must be able to trust the claims made by developers of health care products, especially products that determine the treatment regimen for a cancer patient.

### ***A Single Regulatory Standard to Ensure Patient Safety and Reliability of Diagnostics***

Given the importance of diagnostic tests to personalized cancer treatments, the AACR believes it is imperative that all diagnostic tests used to make high-risk treatment decisions, including the tailoring of an individual's cancer treatment regimen, must be FDA-approved to ensure that these diagnostic tests are held to the highest regulatory and approval standards<sup>4</sup>. Having a single, strict regulatory approval standard will reassure the American public that the tests used in high-risk health care decision-making, regardless of origin, are safe, accurate, and effective.

### ***The FDA's Proposed Framework for Regulatory Oversight of LDTs***

The AACR welcomes the recent notification to Congress by FDA of its intent to phase-in a risk-based framework for regulatory oversight of laboratory developed tests<sup>5</sup>. We commend the FDA for taking a regulatory approach that puts patients first by proposing a classification of LDTs

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<sup>4</sup> Sawyers CL, and van 't Veer, LJ. Reliable and Effective Diagnostics Are Keys to Accelerating Personalized Cancer Medicine and Transforming Cancer Care: A Policy Statement from the American Association for Cancer Research. Clin Can Res; Published Online First September 9, 2014; doi: 10.1158/1078-0432.CCR-14-2295.

<sup>5</sup> US Food and Drug Administration. Notification to Congress and Anticipated Details of the Draft Guidance for Industry, Food and Drug Administration Staff and Clinical Laboratories; Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs); accessed on Sep 5, 2014

<http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407409.pdf>

based on the risk posed by the test to the *patient*. We also note that the FDA plans to focus its efforts and appropriately utilize its resources by continuing to exert its policy of enforcement discretion over low-risk and routine laboratory procedures such as blood and urine analysis. As an organization of cancer scientists and physicians, we strongly support efficient and evidence-based regulatory policy making, and we look forward to doing the same with this proposal.

The proposed framework strikes a thoughtful balance between protecting patient safety while promoting research and innovation in this rapidly evolving field in the following ways:

- By prioritizing FDA's initial oversight efforts to ensure that high-risk LDTs undergo pre-market review to assess the accuracy and safety of the test especially when there is an FDA-approved/cleared equivalent currently on the market;
- By ensuring that this proposal will not adversely affect the ability of researchers at academic medical research centers to develop new tests or conduct clinical research;
- By ensuring that patient access to tests that have not yet undergone FDA review will not be obstructed in cases where there is not an equivalent FDA-approved or cleared test
- By requiring adverse event reporting of LDTs and
- By providing adequate time for laboratories and providers to be in compliance by phasing in the requirements over a period of nine years after the guidance is finalized.

### ***Conclusion***

Diagnostic tests are evolving to become more technically complex, and the complexity of these tests will only grow with the increasing use of next-generation sequencing or NGS-based tests. Further, clinicians are increasingly relying on these complex test results to make treatment

decisions. Therefore, patients and physicians should be confident in the test results that are forming the basis of high-risk treatment decisions, whether these tests are developed as an LDT or are kits approved by the FDA. Implementation of a risk-based framework by the FDA that would provide for evaluation of all high-risk molecular diagnostic tests would balance the need for encouraging innovative medical product development with the need for ensuring patient safety. Having a predictable and reliable regulatory environment is important for patients and for developers of diagnostic and drugs, since the success of a targeted therapy is inextricably linked to the successful development of its companion diagnostic test. Therefore, a single regulatory standard for high-risk diagnostic tests is crucial to ensuring the safety and efficacy of molecular diagnostic tests and the key to advancing personalized medicine. We are in the midst of an extremely promising age of innovative new cancer treatments. Genome sequencing and targeted treatments are revolutionizing the way we treat cancer patients and the way we develop cancer treatments. A robust, predictable, and reliable evidence-based regulatory framework will ensure that these 21<sup>st</sup> century cures will reach patients in an efficient and expeditious manner.

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### **About the American Association for Cancer Research**

Founded in 1907, the American Association for Cancer Research (AACR) is the world's oldest and largest professional organization dedicated to advancing cancer research and its mission to prevent and cure cancer. AACR membership includes more than 35,000 laboratory, translational, and clinical researchers; population scientists; other health care professionals; and cancer advocates residing in more than 90 countries. The AACR marshals the full spectrum of expertise of the cancer community to accelerate progress in the prevention, biology, diagnosis, and treatment of cancer by annually convening more than 20 conferences and educational workshops, the largest of which is the AACR Annual Meeting with more than 18,000 attendees. In addition, the AACR publishes eight peer-reviewed scientific journals and a magazine for cancer survivors, patients, and their caregivers. The AACR funds meritorious research directly as

well as in cooperation with numerous cancer organizations. As the scientific partner of Stand Up To Cancer, the AACR provides expert peer review, grants administration, and scientific oversight of team science and individual grants in cancer research that have the potential for near-term patient benefit. The AACR actively communicates with legislators and policymakers about the value of cancer research and related biomedical science in saving lives from cancer. For more information about the AACR, visit [www.AACR.org](http://www.AACR.org).