Molecular Diagnostics Regulation: Shifting from a Biomarker-Based Approach to an Algorithm-Based Approach

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A profound shift is underway in the regulation of molecular diagnostics as we enter the era of personalized medicine and rapid, low-cost genomic sequencing. The traditional regulatory approach involved the relatively simple task, at least by comparison, of evaluating a test for a single biomarker – whether it be a gene, a protein or some other biological marker. This single biomarker-based approach is quickly becoming obsolete as researchers and clinicians move to more complex tests that include a panel of multiple markers, that can range from a few to hundreds or thousands of individual genes or other biomarkers. For an increasing number of conditions, a test combining assays for anywhere from a few to hundreds of individual markers, with the results combined and presented using a (often proprietary) algorithm allows medical professionals to predict the future risk of the condition, to diagnose the condition, to evaluate the prognosis of the condition, or to guide and monitor treatment of the condition. The ultimate example of this multi-marker testing is whole exome and whole genome sequencing, which are rapidly moving into the clinic.

The relatively simple single biomarker tests of the past were relatively simple to regulate in that they involved a single biological relationship or pathway, and the components and uses of that test remained static. Thus, once approved, they rarely if ever changed. In contrast, new, complex tests are based on algorithms and knowledge that is constantly being updated with new findings, and thus are dynamic rather than static. This presents an enormous regulatory challenge for the U.S. Food and Drug Administration (FDA), making a single pre-market comprehensive evaluation impossible given the complexity and ongoing modifications in the new types of tests.

In this presentation, we document this shift in the nature of molecular diagnostic tests, show why the existing regulatory paradigm of a one-time pre-market assessment is no longer viable, and propose a new regulatory approach that fits the complex, dynamic nature of these tests.

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