

## NIST RM 8398: Standardizing Discoveries

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**S**TEEL, CONCRETE, PEANUT BUTTER, and genetic testing all have something in common: all have reference material established in the National Institute of Standards and Technology (NIST), an agency within the U.S. Department of Commerce (Pear, 2015). On May 21, 2015, NIST announced that they made “the world’s first reference material to help ensure laboratories accurately ‘map’ DNA for genetic testing, medical diagnoses, and future customized drug therapies” (“Measuring Stick’ Standard,” 2015). To do so, the FDA and NIST scientists facilitated a working relationship between NIST and stakeholders from the Genome in a Bottle consortium, a collection of professionals committed to reference standards, data, and methodology (Genome in a Bottle Consortium).

DNA sequencing techniques divide long strands of DNA into smaller segments. The segments are then reduced to their base sequences. By comparing the base sequences to a reference DNA sequence, researchers can discover mutations and describe the sequence in general. To be confident that the detected mutations are actually there, it is important to establish the accuracy of the test. The NIST reference material gives genetic testing laboratories the opportunity to test sequences against a standard to verify that the laboratory’s tests are accurate. This standard will ostensibly lead to a decrease in the number of false positives and negatives (“Measuring Stick’ Standard,” 2015). Dr. Jeffery E. Shuren, director of the FDA Center for Devices and Radiological Health, states that “an inaccurate genome-sequencing test can lead to patients receiving the wrong diagnosis, the wrong treatment or no treatment at all, even when effective therapy is available” (Pear, 2015).

The full name of this highly regarded “reference material” is NIST RM 8398. It originates from the cell line of a 1980s research participant, a female from Utah with European ancestry. NIST states that “the reference material is the first complete human genome to have been extensively sequenced and re-sequenced by multiple techniques, with the results weighted and analyzed to eliminate as much variation and error as possible (“Measuring Stick’ Standard,” 2015).” A NIST RM 8398 prototype was involved in the 2013 FDA certification and approval of some of the first commercial high-throughput DNA sequencers using the genome generated during the development of NIST RM 8398 (“Measuring Stick’ Standard,” 2015). For \$450, researchers and scientists can purchase 10 µg of the NIST material, proving that there is a price tag for reputability! (Pear, 2015).

Regulation of genetic testing is 2-fold. The FDA oversees the tests, and the Centers for Medicare and Medicaid Services (CMS) monitor and certify the clinical laboratories as stated by the 1988 legislation, Clinical Laboratory Improvement Amendments (CLIA). This reference material will most directly impact tests with downstream effects on laboratories. Marc L. Salit of NIST remarked that this newfound quality control for genetic testing will help laboratories to prove the value of their work and generate more confidence surrounding genome sequencing. In turn, this will hopefully encourage more affordable tests and health insurance coverage (Pear, 2015).

While some consider genetic testing to be the domain of the traditional laboratory, these techniques have recently generated significant buzz outside this conventional setting. For example, 23andMe, a company dedicated to the direct-to-consumer genomics approach, previously, supplied consumers with their saliva collection kit and personal genome service (PGS) and returned health reports to these customers on more than 200 diseases and ancestry information. However, in November 2013, the FDA stated that the kit and PGS were collectively a device and violated the Federal Food, Drug, and Cosmetic Act (Gutierrez, 2013). However, in February 2015, the FDA authorized 23andMe to market a rare genetic disorder carrier report for Bloom syndrome and exempt it from premarket approval (U.S. Food and Drug Administration, 2015). Although it is just the beginning, this is a huge step for direct to consumer and genetic testing at large.

Together these recent changes advance the caliber of genetic testing and thus increase testing options, coverage, and confidence.

These reference standards come at a pivotal time. In his State of the Union address this past January, President Obama introduced the precision medicine initiative. Dr. Francis S. Collins, director of the National Institutes of Health (NIH), and Dr. Harold Varmus, director of the National Cancer Institute (NCI), state that the core of the precision medicine initiative is “prevention and treatment strategies that take individual variability into account” (Collins and Varmus, 2015). NIST’s new reference material helps fuel this mission by tailoring treatment to target specific mutations. This initiative is backed by the proposed 2016 budget, which allocates \$215 million to the NIH (including the NCI), FDA, and the Office of the National Coordinator for Health Information and Technology (The White House, 2015). While standards

and variability intuitively oppose one another, here they work harmoniously as the reference material provides confidence that acknowledges when variability is mapped; it is done so with validity.

### References

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