To repeat, the medical device that was the subject of the 510(k) submission was purified DNA.

Validation of the medical device (the genomic DNA) included the following tests. The tests measured integrity of the DNA, and stability under various storage conditions. Integrity of the DNA was measured by sequencing the DNA, and where validation took the form of assaying under different formats. As stated in the 510(k) Substantial Equivalence Determination Decision Summary, the FDA reviewer referred to these formats, writing that, "the correct genotype results were reproducible from lab-to-lab, lot-to-lot, and from run-to-run."

Referring to tests for integrity, the FDA reviewer wrote that "stability of three different lots of the ... material were [sic] evaluated ... by four methods ... agarose gel, generation of PCR amplicon, bi-directional sequencing, and additional methodologies to evaluate specific alleles."

Moreover, stability of the genomic DNA was assessed under various storage conditions, that is, at 2–8°C, −30°C, at room temperature in a vial that was opened and closed at least 10 times, heated at 45°C for 5 days, and three freeze/thaw cycles.

To summarize, validation of the in vitro diagnostics reagent (the medical device) took three general approaches:

1. Testing in different laboratories, testing of different lots.
2. Testing using various assay methods to assess DNA integrity or structure, such as, agarose gels, DNA sequencing, and the ability to amplify the sequence by PCR.
3. Stability testing using various storage conditions (222).

Although the medical device in question was relatively simple (just a reagent in a vial), this author points out that the same principles of validation are applicable to more complex reagents and procedures involving biomarkers, such as a device and method for conducting multiplex PCR analysis, or a device and method for detecting chromosomal mutations by FISH.

c. Validation PCR Reaction Diagnostic Test in a 519(k) Submission

To provide another example, the 510(k) no. k073014 submission concerned a medical device that comprised an array made of polyester film coated with spots, where each spot was designed to detect a specific sequence of DNA, a liquid reagent for conducting a PCR reaction, and a machine that comprises a microscope, where the machine conducts multiplex PCR reactions (223). This 510(k) submission assessed run-to-run variability, stability testing, the determination of the lowest level of detection, and the potential of chemicals found in blood to interfere with the test. These bullet points outline the approaches used for this 510(k) submission:

- Run-to-run variability, variability found with three different machines, site-to-site variability, variability with different operators.

[222]The author (Tom Brody) conducted the same type of quality control tests, on small-molecule biologicals, and instrumentation at Athena Neurosciences, South San Francisco, CA, in 1993–94. Hence, the author knows that the tests set forth by the FDA's 510(k) Substantial Equivalence Determination Decision Summary are generally applicable to reagents that are small molecules, biologicals, and machines or instrumentation.

[223]510(k) Substantial Equivalence Determination Decision Summary for 510(k) no. k073014. Approval letter of Jan. 28, 2008. Approved by Jean M. Cooper, Office of In Vitro Diagnostic Device Evaluation and Safety, FDA. Documents accessed from FDA website on Mar. 1, 2015.