INTRODUCTION: Cystic fibrosis (CF) is the most common life-threatening autosomal recessive genetic disorder caused by mutations in the CF Transmembrane Conductance Regulator (CFTR) gene. A High Resolution Melting (HRM)-based test has been developed for the detection of 18 CF-causing mutations with high frequency in Cuba and Latin America. OBJECTIVE: To evaluate the analytical parameters of the HRM-based test in samples collected as dried blood spots (DBS) coming from CF patients and their relatives. METHODS: The HRM-based test allows the detection of mutations G85E, R334W, S466X, I507del, F508del, 1717-1G> A, G542X, R553X, 2183AA>G, 2789 + 5G> A, 3120 + 1G> A, 3272-26A> G, R1066C, Y1092X, R1162X, 3849 + 10KbC>T, W1282X and N1303K. It includes an internal control of PCR amplification. A post-PCR HRM step allows the identification of specific-amplified DNA fragment containing CFTR mutations. A total of 230 samples were evaluated in the HRM-based test and subsequently the results were confirmed by using the CF StripAssay 4-410 test or by automatic DNA sequencing as reference tests. The percentage of concordance between HRM-based test and the reference tests was determined. The clinical and analytical specificity were also evaluated. RESULTS: A total of 141 mutated alleles were detected, being F508del the predominant mutation. At least one CFTR gene mutation was detected in 88 samples. Out of these 88 samples, 53 had two mutations: 34 compound heterozygotes and 19 homozygous. It was obtained a 100% of agreement between the HRM-based test and the reference tests. The CFTR gene mutations could be detected without cross-reactions and a clinical specificity of 100% was obtained. CONCLUSIONS: The HRM-based test was able to detect with high specificity 18 mutations of the CFTR gene that cause CF. This method will allow increasing the scope of the molecular diagnosis of CF in Latin America; it is simple, fast and cost-efficient. The test can be used for the genetic characterization of individuals with clinical suspicion of CF and for carrier testing, reducing the risk of having a child with CF.