Cystic Fibrosis is the most common autosomal recessive disease in Caucasians. Latin American populations, including Argentine, are ethnically heterogeneous due to a mixture of European descendants and Native Americans. For this reason, a national panel of mutations is difficult to define. **OBJECTIVE:** The aim of this study was to describe genetic mutations found in patients attending an Argentine CF Reference Center, and to assess the sensitivity of the different genetic methods used. **METHODS:** the genetic data from patients with confirmed CF diagnosis were analyzed. During the 2006-2016 period, a panel of 29 mutations was used. Since 2016, Next Generation Sequencing (NGS) and Multiplex Ligation dependent Probe Amplification (MLPA) was introduced. We reviewed all patients with this technique. **RESULTS:** 164 patients were included. The most common mutations in our cohort were: p.F508del: 60% (CI95% 54.5-65.4), G542X: 4.5% (CI95% 2.6-7.4), W1282X: 1.5% (CI95% 0.5-3.5), R334W: 1.2% (CI95%0.3-3.1), 1811+1.6 Kb: 1.2% (CI95% 0.3-3.1), 1717 1G-A: 0.9% (CI95% 0.2-2.7) and 2789+ 1G-A: 0.9% (CI95% 0.2-2.7). With the 29 mutation panel and NGS with MLPA, we identified 80.7% (CI95% 76.1-84.9) (265 alleles) and 91.4% (CI95% 87.9-94.3) (300 alleles), respectively. We found both mutations for 67% (CI95% 59.3-74.2) and 86% (CI95% 79.7-90.9) of patients, using the 29 mutation panel and NGS with MLPA, respectively (McNemar test, p<0.01). We were not able to identify the both mutations in 6 patients (3.6%) (CI95% 1.3-7.8). **CONCLUSIONS:** NGS with MLPA was more sensitivity than the 29 mutation panel to identify both mutated alleles in each confirmed CF patient. Argentine CF patients have a heterogeneous genetic profile.