Cystic Fibrosis (CF) is an inherited multisystem disorder (autosomal-recessive disease) caused by mutations in the CF transmembrane conductance regulator (CFTR) gene that encodes a cyclic adenosine monophosphate–regulated chloride and bicarbonate channel expressed at the apical membrane of epithelial cells. It leads to a wide and variable array of presenting manifestations and complications. It is the most common life-threatening monogenic condition in the white population with an estimated birth prevalence of 1 in 1500–4000 newborns in European countries and European-derived populations. CF is responsible for most cases of exocrine pancreatic insufficiency in early life and is the major cause of severe chronic lung disease in children. It is also responsible for many cases of hypop5**natremic salt depletion, nasal polyps, pan sinusitis, rectal prolapse, pancreatitis, cholelithiasis, and non-autoimmune insulin-dependent hyperglycemia. The diagnosis of CF has been based on a positive quantitative sweat test (Cl− ≥60 m Eq/L) in conjunction with 1 or more of the following features: typical chronic obstructive pulmonary disease, documented exocrine pancreatic insufficiency, and a positive family history. With newborn screening, diagnosis is often made prior to obvious clinical manifestations such as failure to thrive and chronic cough. CF newborn screening is a complex procedure that uses multiple step combinations of tests on dried blood spots. The first tier is always a measurement of immunoreactive trypsinogen (IRT), followed in IRT-positive babies by other tests, which usually include mutation analysis of the CFTR gene. The aim is to identify neonates at high risk of having CF; these infants are then referred to a diagnostic service to confirm the diagnosis. Like any disease in screening process, there is the potential for indeterminate results. Infants with an indeterminate diagnosis present a treatment challenge to clinicians and a stress on families. Of those, there is a subset of infants with a positive newborn screen for CF, elevated immunoreactive trypsinogen and 1 or 2 copies of a CFTR mutation, but who have an initial negative sweat test and are asymptomatic. These infants have CFTR metabolic syndrome (CRMS) and should be followed in a CF center annually to ensure that they do not develop CF symptoms. Older children who did not have newborn CF screening available at birth can present the same way as those with CRMS but will be called CFTR Related Disorder (CFTR-RD) and not CRMS. All children with CRMS or CFTR Related Disorder need to have check-ups with a cystic fibrosis specialist doctor to be sure that any health problems are detected and treated properly. Objective: The goal of this presentation to review the Dilemma in neonatal screening for diagnosis of Cystic Fibrosis with new terminology of CFTR-Related Metabolic Syndrome (CRMS) and CFTR Related Disorders (CFTR-RD). Understanding the terminology of CFTR-RD and CRMS, increase awareness of close monitoring of these patients whether eventually develop further disease consistent with classical CF.