High concentrations of histamine are associated with subacute ruminal acidosis, a common disease in high-producing lactating dairy cows. Therefore, the accurate detection of low histamine levels is a strategy to monitor and diagnose ruminal acidosis in early stages. In this work, we developed an impedimetric histamine biosensor based on an organic compound, poly (3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS). It can be utilized to detect low concentrations of histamine in a phosphate-buffered saline buffer (PBS) and McDougall’s buffer solution (MDBS) with an impedimetric readout technique. With PEDOT:PSS film as the sensing medium, the device displayed a limit of detection of 0.1 µM and an impedance of ~82 Ω at low frequencies in MDBS. The impedance is correlated with the concentration of histamine: the R² values in the PBS (pH = 5.5 and pH = 7.4) and the MDBS (pH = 8.4) are 0.95, 0.95 and 0.99, respectively. The sensor is fabricated using large-area solution processing technology, opening the door to low-cost, high-volume commercial sensor production.