A novel low-loss programmable microwave waveguide is demonstrated. The waveguide is developed for applications in field-programmable microwave circuits with similar levels of programmability as that seen in field-programmable gate arrays. The waveguide is realized with a field-programmable microwave substrate (FPMS). The substrate consists of small unit cells that can be individually reconfigured to have a range of positive dielectric constants or a negative dielectric constant. The substrate is contained in a metal parallel plate structure. Programming a positive material sandwiched between two negative material sidewalls results in a waveguide that behaves in a way that is described by the slab waveguide equations. Miniaturization and increased density of unit cells can result in lower loss and better performance. Two implementations of the FPMS are presented. One implementation is on FR4 using all industry standard processes and components. The other implementation uses low-temperature cofired ceramic and custom designed CMOS chips. The FR4 implementation is used to demonstrate programmable waveguides, amplifiers, and oscillators from 0.9 to 3 GHz. The LTCC implementation is used to demonstrate miniaturization of the FPMS. The proposed FPMS concept promises a new era of programmable microwave circuit design for cognitive radio, the Internet of things, and self-healing/adaptive systems.