Multidrug-resistant tuberculosis (MDR-TB), defined as TB resistant to at least isoniazid and rifampicin, is posing a substantial threat to TB control in the Pacific Island countries and territories (PICTs), due to its complex diagnostic and treatment challenges. If available data indicate overall low levels of drug resistance in the southern Pacific, the resistance levels are already alarmingly high in some PICTs, especially the Micronesian. Recent survey data from Northern Mariana Islands show a prevalence of MDR-TB among new TB cases as high as 11.1%. Chukot State of the Federated States of Micronesia (FSM) recently experienced an MDR-TB outbreak with six laboratory confirmed MDR-TB cases resulting in four deaths and a total of six patients currently isolated for treatment of MDR-TB with IV and oral medications. Four MDR-TB have also been reported since 2005 on Ebeye, a small islet in Kwajalein atoll, Republic of Marshall Islands. Most of the cases have been managed on an informal basis, and major constraints have been timely provision of second-line drugs, long-term management of patients on isolation and laboratory services support. Hence, there is an urgent need to support the development of a framework of response to drug-resistant TB in the Pacific that will link the three critical aspects of case management of drug-resistant TB, i.e., laboratory services, technical/clinical support for case management, and the timely provision of second-line drugs.