In the clinical setting, polyvinyl chloride (PVC) accounts for 25% of all polymers used in medical device applications. However, medical devices fabricated with PVC suffer from thrombosis and infection. Mortality associated with HAIs exceed 100,000 deaths each year. One method to overcome these challenges is to develop bioactive polymers with nitric oxide (NO) release. Nitric oxide exhibits many physiological roles including, antibacterial, antithrombic, anti-inflammatory activity. In this study, Tygon® PVC tubing was impregnated with an NO donor molecule, S-nitroso-N-acetylpenicillamine (SNAP), via a simple solvent-swelling method, where polymer samples were submerged in a solvent mixture (SNAP, plasticizer, methanol, acetone). An additional topcoat of a biocompatible CarboSil 2080A (CB) was applied to reduce SNAP leaching and prolong NO release. The SNAPâ€“PVCâ€“CB was characterized for NO release using chemiluminescence, leaching with UVâ€“Vis, surface properties via SEM, mechanical properties, stability during storage and sterilization, and antimicrobial properties in vitro. The SNAPâ€“PVCâ€“CB released physiological levels of NO for up to 14 days (incubated in PBS at 37 °C). The addition of CBâ€“topcoat reduced the total SNAP leaching by 86% during incubation. Mechanical properties and surface topography remained similar to control PVC after SNAPâ€“impregnation and application of CBâ€“topcoat. After ethylene oxide sterilization and 1-month storage, SNAPâ€“PVCâ€“CB demonstrated excellent SNAP stability (ca. 90% SNAP remaining). In a 24 h antibacterial assay, SNAPâ€“PVCâ€“CB reduced viable bacteria colonization (ca. 1 log reduction) of S. aureus and E. coli compared to PVC controls. This novel method for SNAPâ€“impregnation of medical grade plasticized PVC holds great potential for improving the biocompatibility of post-fabricated PVC medical devices.