The overarching goal of this application is to establish a Vermont Center on Tobacco Regulatory Science (VCTRS). This multidisciplinary center will be located at the University of Vermont but will work closely with collaborators and consultants from Brown University, Johns Hopkins University, University of Minnesota, and University of Pittsburgh. The VCTRS will address one of the crosscutting and two of the specific research priorities of the Food and Drug Administration (FDA) Center for Tobacco Products. The crosscutting priority will be researching tobacco products in vulnerable populations, including women of childbearing age/pregnant women, individuals with comorbid other substance use disorders, and individuals with comorbid serious mental illness. Each of these populations is at increased risk for tobacco use and dependence or tobacco-related adverse health outcomes. Yet despite these serious vulnerabilities, these populations are typically excluded from tobacco regulatory studies. For the FDA to effectively execute its tobacco regulatory responsibilities, having sound scientific evidence on how new tobacco products impact vulnerable populations is critically important. Our goal is for the VCTRS to assist in providing the FDA with that evidence. Regarding specific priorities, the VCTRS will research (a) reducing the addiction potential of cigarettes and other tobacco products by reducing their nicotine content and (b) examining the impact of new products on biomarkers of exposure and health outcomes in vulnerable populations. Regulating the nicotine content of cigarettes and other products is an important responsibility of the FDA that has tremendous potential to reduce smoking prevalence and improve the U.S. public health. The VCTRS will be organized around four primary aims. First, we will establish an Administrative Core that will provide the leadership, administrative and intellectual infrastructure, and organizational oversight necessary to develop and sustain a multidisciplinary center of research and training excellence. Second, we will complete three multi-site research projects evaluating the effects of very low nicotine content (VLNC) cigarettes in vulnerable populations. Third, we will establish a program to support developmental studies in tobacco regulatory science and respond to time-sensitive research priorities. Fourth, we will develop an exemplary predoctoral and postdoctoral training program in tobacco regulatory science. Overall, this proposal has the potential to establish a multidisciplinary center capable of providing the FDA with critically important empirical evidence relevant to its regulatory responsibilities, while also contributing new scientific knowledge on reducing the addictiveness of tobacco products and associated adverse health consequences in vulnerable populations.