Guided by rigorous methodology and a life-course perspective, the goal of this research is to address a gap in current knowledge on whether, when, and how strongly intergenerational continuity of substance use exists when examining age-equivalent and developmentally specific stages of the life course. Annual self-reported substance use measures were analyzed from a prospective, longitudinal, and nationally representative sample that originally consisted of 1,725 respondents and their families, who were then interviewed over a 27-year period from 1977 to 2004. Findings from multi-level random-intercept regression models provide support for intergenerational continuity when substance use occurs in emerging adulthood but not when limited to adolescence. Implications, limitations, and future research directions are discussed.