The human body is colonized by trillions of microbes, collectively referred to as the endogenous microbiota. These microorganisms protect us against pathogens and promote wellbeing, but when the microbiota is disrupted it becomes a risk factor for disease and frailty. Intervention with certain beneficial microbes may restore alterations of the microbiota composition, and thereby reduce the risk of disease and advance human health. These beneficial microbes are called ‘probiotics’ (for life) and fuel a multi-billion-dollar market that benefits healthy consumers and patients globally. In recent years, however, it became increasingly evident that the innovation process for probiotics is hampered considerably, since probiotics are not consistently used in clinical practice, no (European) health claim has been approved to date and there remains a lack of fundamental knowledge on probiotics and their interaction with the host. As this curtails the therapeutic and socioeconomic potential of probiotics for consumers and patients, this thesis sets out study persistent barriers to the probiotic innovation process to advance research & development on live microorganisms for the promotion of human health.