Members of the spore-forming genus Bacillus have long been used as probiotic supplements for human and animal use. Species such as *Bacillus clausii*, *Bacillus coagulans*, *Bacillus subtilis* and *Bacillus licheniformis* are found in a number of products and some, such as *B. clausii* that are produced as GMP products with proven efficacy in the prevention of gastrointestinal illness. The compelling aspect of spore forming bacteria is the spore which is produced at the end of the life cycle of this organism and enables a product to be produced that is both heat and desiccation resistant. This enables a product to be produced that can be stored indefinitely at ambient temperature and survive passage through the gastro-intestinal tract. This in turn simplifies storage and distribution of these products and enables spores to be used in ways that are not possible with the more common products such as the lactobacilli etc. For example, spores can be stored in aqueous solution, incorporated in foods included baked products and used in animal feed products where the formulation process requires extensive incubation at high temperatures. Despite these attributes our understanding of spores and how they exert a probiotic effect is less apparent. What we do know and which will be covered in this presentation is as follows: Innate Immunity: Spores are able to interact with Toll-like Receptors and induce an innate immune response leading to the production of IFN-γ and other cytokines. In animal studies as few as two nasal doses of *B. subtilis* spores can provide 100% protection to influenza (H5N2). Interestingly, this protection can be achieved using inactivated or killed spores. *Clostridium difficile*: *B. subtilis* spores have been used to evaluate protection against *C. difficile* infection in animal models. Our data shows that pre-dosing and concurrent dosing of mice infected with *C. difficile* provides varied levels of protection and illuminates the potential of using spores for treatment of this important nosocomial infection.