Vaccination has been the most effective medical intervention in the history of mankind. Infectious diseases that used to kill or cause disability in millions of people annually such as diphtheria, tetanus, smallpox, polio, measles, mumps, and rubella were conquered during the last century with the first wave of vaccines. The second wave of vaccination started during the 1980s and consisted of vaccines that were made possible by the new technologies such as recombinant DNA, conjugation, genomics, that allowed the development of vaccines against Hepatitis B, papillomavirus, *Haemophilus influenzae*, pneumococcus, and meningococcus. Thanks to the advances in understanding of the structure of the antigens and their epitopes and how they interact with the human immune system we are now entering the third wave of vaccine development, characterized by optimal design antigens, adjuvants and delivery systems. This new phase is expected to tackle diseases such as tuberculosis, malaria, and HIV and STIs that have, so far, been refractory to vaccine development.