After an introduction in which I will discuss the accuracy which can be expected from crystal structures determined using powder diffraction data, and the development of a correlation between the Mulliken overlap population and the energy of O-H...O hydrogen bonds, I will describe several crystal structures of large-volume pharmaceuticals which have been solved and refined using synchrotron powder data. The structures have also been optimized using density functional techniques. The structures will include (at least): paliperidone palmitate, 17alpha-dihydroequilin, atazanavir, doxepin hydrochloride, pantoprazole sodium, nilotinib, and sitagliptin hydrogen phosphate hydrate. The solution and refinement of all of these structures presented unusual problems, so the process for solving the structures as well as the structures themselves will be covered.