

## Crystal Structures of Large-Volume Commercial Pharmaceuticals

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As part of a continuing project, the challenging room-temperature crystal structures of four commercial pharmaceutical APIs have been solved by Monte Carlo simulated annealing techniques using synchrotron X-ray powder diffraction data (11-BM at APS), and optimized using density functional techniques. Atorvastatin calcium trihydrate (Lipitor®), (C<sub>33</sub>H<sub>34</sub>FN<sub>2</sub>O<sub>5</sub>)<sub>2</sub>Ca(H<sub>2</sub>O)<sub>3</sub> crystallizes in space group P1 (#1) with a = 5.44731(4), b = 9.88858(16), c = 29.5925(10) Å, α = 95.859(3)°, β = 94.211(1)°, γ = 105.2790(1)°, V = 1521.277(10) Å<sup>3</sup>, and Z = 1. The structure was solved by removing the O atoms from the carboxylate groups of the anion, and using a CaO<sub>6</sub> fragment. Pimecrolimus (Elidel), C<sub>43</sub>H<sub>68</sub>ClNO<sub>11</sub>, crystallizes in space group P2<sub>1</sub> (#4) with a = 15.28864(7), b = 13.31111(4), c = 10.95529(5) Å, β = 96.1542(3)°, V = 2216.649(9) Å<sup>3</sup>, and Z = 2. By default, simulated annealing programs did not give enough torsional degrees of freedom, so the macrocycle was broken, and re-formed at a low success rate. Ivermectin hemihydrate ethanolate, (C<sub>48</sub>H<sub>74</sub>O<sub>14</sub>)(H<sub>2</sub>O)<sub>0.5</sub>(C<sub>2</sub>H<sub>5</sub>OH)<sub>0.68</sub>, crystallizes in space group I2 (#5) with a = 14.94878(15), b = 9.26938(4), c = 39.27263(30) Å, β = 94.4017(7)°, V = 5425.80(5) Å<sup>3</sup>, and Z = 4. A reduced cell search yielded another solvate, and the guest species were identified using difference Fourier and spectroscopic techniques. Ceftriaxone sodium hemiheptahydrate (Rocefin), C<sub>18</sub>H<sub>16</sub>N<sub>8</sub>O<sub>7</sub>S<sub>3</sub>Na<sub>2</sub>(H<sub>2</sub>O)<sub>3.5</sub>, crystallizes in space group C2 (#5) with a = 30.56495(19), b = 4.75245(3), c = 18.55021(18) Å, β = 90.3551(7)°, V = 2694.521(24) Å<sup>3</sup>, and Z = 4. Some of the water molecules were difficult to locate conventionally, and were placed by progressively searching for smaller voids. Other new structures may be discussed as they become available.