

QUESTIONS

1. Why is Tamiflu® (Oseltamivir) sold as a prodrug?
2. Nitrofurantoin is an antibiotic marketed for the treatment of urinary tract infections, but it is known to be highly mutagenic, highly teratogenic, and highly carcinogenic. Why is this possible?
3. Seldane® (Terfenadine) was the first nonsedating antihistamine. Launched in 1985, it was removed from the market in 1997 even though it had been successfully used by over 100 million patients. Why was it removed from the market, and how did this event change the drug discovery process?
4. What does the development of Allegra® (Fexofenadine) teach about the importance of metabolism?
5. What does the development of Claritin® (Loratadine) and Clarinex® (Desloratadine) teach about the importance of metabolism?
6. Desmethyprodine (MPPP) is a potent μ -opioid receptor agonist that is not safe for clinical use? Why and how is this relevant to drug discovery and development as a whole?
7. Why were extended release and sustained release mechanisms important in the development of Bupropion?
8. What is the possible impact of a poorly written patent application?

References

1. Martin, P.; Martin-Granel, E. 2500-Year Evolution of the Term Epidemic. *Emerg. Infect. Dis.* **2006**, *12* (6), 976–980.
2. Mills, C. E.; Robins, J. M.; Lipsitch, M. Transmissibility of 1918 Pandemic Influenza. *Nature* **2004**, *432* (7019), 904–906.
3. Dawood, F. S.; Iuliano, A. D.; Reed, C.; Meltzer, M. I.; Shay, D. K.; Cheng, P. Y.; Bandaranayake, D.; Breiman, R. F.; Brooks, W. A.; Buchy, P.; et al. Estimated Global Mortality Associated with the First 12 Months of 2009 Pandemic Influenza A H1N1 Virus Circulation: A Modelling Study. *Lancet Infect. Dis.* **2012**, *12* (9), 687–695.
4. Maugh, T. H. Amantadine: An Alternative for Prevention of Influenza. *Science* **1976**, *192* (4235), 130–131.
5. Wintermeyer, S. M.; Nahata, M. C. Rimantadine: A Clinical Perspective. *Ann. Pharmacother.* **1995**, *29* (3), 299–310.
6. Kaiser, L.; Wat, C.; Mills, T.; Mahoney, P.; Ward, P.; Hayden, F. Impact of Oseltamivir Treatment on Influenza-Related Lower Respiratory Tract Complications and Hospitalizations. *Arch. Intern. Med.* **2003**, *163* (14), 1667–1672.
7. a. Meinal, P.; Bodo, G.; Palese, P.; Schulman, J.; Tuppy, H. Inhibition of Neuraminidase Activity by Derivatives of 2-deoxy-2,3-dehydro-*N*-acetylneuraminic Acid. *Virology* **1974**, *58* (2), 457–463.
8. von Itzstein, M. The War against Influenza: Discovery and Development of Sialidase Inhibitors. *Nat. Rev. Drug Discov.* **2007**, *6* (12), 967–974.
9. Varghese, J. N.; McKimm-Breschkin, J. L.; Caldwell, J. B.; Kortt, A. A.; Colman, P. M. The Structure of the Complex between Influenza Virus Neuraminidase and Sialic Acid, the Viral Receptor. *Proteins: Struct. Funct. Genet.* **1992**, *14*, 327–332.