An *in vivo* study designed to assess the level of risk associated with a particular compound under various dosing regimens typically employs telemetry equipped animals. Surgical implantation of telemetry equipment capable of detecting changes in parameters such as heart rate, blood pressure, contractile force, and ejection fraction is followed by a recovery period (2–4 weeks) to allow healing. Once the animals have healed, they can be treated with various doses of the compound in question to determine whether or not the candidate compound has any impact of cardiovascular function. Animals can be subjected to a single dose of a candidate compound to in an effort to identify acute cardiovascular safety issue. Alternatively, animals can be dosed with multiple doses of the same compound over an extended period of time in order to assess the risk associated with chronic exposure. In either event, the implanted telemetry equipment will provide significant insight into the cardiovascular risks associated with the candidate compound under review.[43] Cardiovascular studies of this type can take weeks, or even months to complete, and throughout the study the test subjects (the lab animals) must be properly housed, fed, and treated humanely. Given the length of time required, the significant cost, and the difficulties associated with properly caring for study animals, it should come as no surprise that *in vivo* cardiovascular safety studies are reserved for only the most promising candidate compounds.

CENTRAL NERVOUS SYSTEM SAFETY AND TOXICOLOGY STUDIES

There are many drugs on the market specifically designed to modulated central nervous systems functions, such as antidepressant, antipsychotic agents, and antiseizure medication. The lives of millions of patients have been improved as a result of advances in the treatment of CNS diseases. It is important to understand, however, that modulation of CNS functions can produce a range of negative effects that may preclude advancement of candidate compounds. Off-target CNS-mediated effects can include hallucinations, insomnia, sedation, seizures, increases sensitivity to pain, impaired memory function, depression, and even an increased risk of suicide. Popular drugs such as Prozac® (fluoxetine, antidepressant, Figure 8.21(a)),[44] Effexor® (venlafaxine, antidepressant, Figure 8.21(b)),[45] Chantix® (Varenicline, smoking cessation, Figure 8.21(c)),[46] and Accutane® (Isotretinoin, acne treatment, Figure 8.21(d))[47] have been linked to an increased risk of suicidal thoughts and tendencies. While the level of risk associated with each of these drugs was not high enough to warrant withdrawal from the market, these examples highlight the importance of monitoring for CNS-mediated side effects.

CNS-mediated side effects can also complicate the drug discovery process. Consider, for example, a program focused on the development of