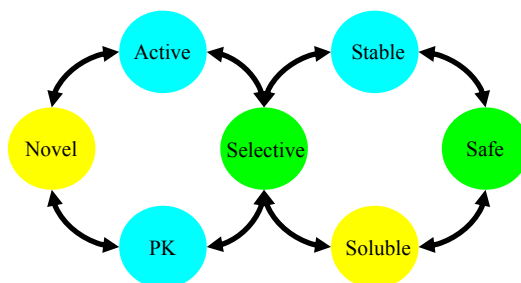


new data are produced as changes in the molecular structure are made to the “lead” compounds, and these data are used to design the next generation of compounds. This cycle of generating structure–activity relationship data continues until a compound suitable for clinical evaluation has been identified. The nature of this process and the associated medicinal chemistry will be discussed in greater detail in Chapter 5.

## IDENTIFY A CLINICAL CANDIDATE: JUGGLING THE PROPERTIES

Simply identifying a compound that is potent at the target of interest is a difficult task to begin with, but sheer potency is not enough to allow a compound to be considered for clinical development and ultimately commercialization. The process of discovering a suitable drug candidate is, in many ways, a juggling act performed by drug discovery scientists (Figure 1.17). As programs progress from hit and lead identification to



**FIGURE 1.17** The identification of a clinical candidate requires consideration of a variety of properties beyond activity at the biological target of interest. Drug discovery and development programs seek to optimize as many of these properties as possible in order to identify the best opportunity for success.

lead optimization and an eventual clinical study, hundreds if not thousands of compounds will be examined. It is the drug discovery scientist’s responsibility to identify a compound that will not only modulate the target of interest but also possesses the correct balance of properties required to create a usable drug. Potency at a biological target is only the beginning of a long series of screening processes that must be performed in order to demonstrate that a compound will survive the rigors of a discovery program. The specific strategies employed are different for each program, but in general they can be mapped in a screening cascade (Figure 1.18) that sets gating guidelines for each level of the screening process, from initial activity screening through *in vivo* animal efficacy studies. The screening cascade is designed to decrease the number of