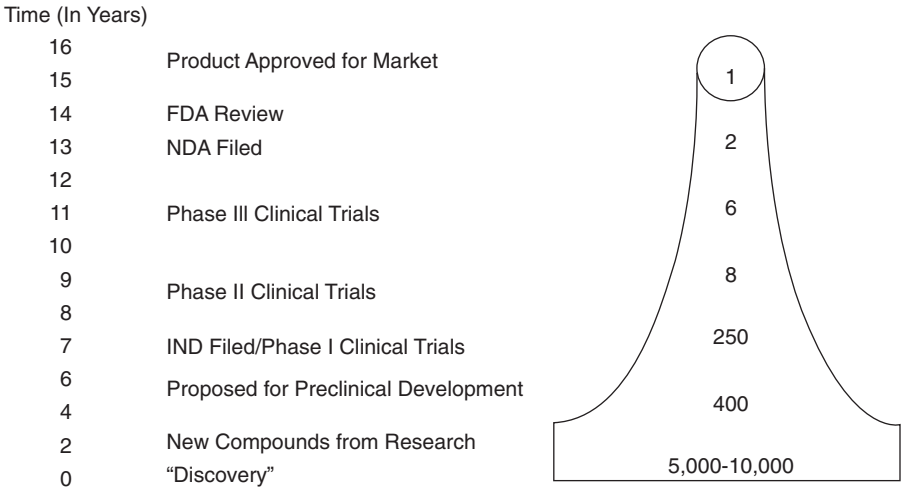

Figure 1 Attrition during the development of new molecules with a promise of therapeutic potential. Over the course of taking a new molecular entity through scale-up, safety, and efficacy testing, and, finally, to market, typically only 1 out of every 9000 to 10,000 will go to the marketplace.

providing new tools for use in both early screening and the understanding of mechanisms of observed toxicity in preclinical and clinical studies [2, 3], particularly with the growing capabilities and influence of genomic and proteomic technologies. This is increasingly important as the societal concern over drug prices has grown [4]. Additionally, the marketplace for new drugs is exceedingly competitive. The rewards for being either early (first or second) into the marketplace or achieving a significant therapeutic advantage are enormous in terms of eventual market share. Additionally, the first drug approved sets agency expectations for those drugs that follow. In mid-2004, there were 263 pharmaceutical products awaiting approval (93 of these biotech products)—the "oldest" having been in review 10 years) and some 2300 additional agents in the IND stage. Not all of these (particularly the oldest) will be economically successful).

The usual way in which transition (or "flow") of new molecules between the different phases is handled in drug discovery/development is to use a tiered screening or testing approach. Each tier generates more specific data (and costs more to do so) and draws on the information generated in earlier tiers to refine the design of new studies. Different tiers are keyed to the support of successive decision points (go/no-go points) in the development process, with the intent of reducing risks (as to efficacy bioavailability and safety) as early as possible.

The first real critical decisions concerning the potential advancement of a compound to evaluation in clinical trials are the most difficult. They require an understanding of how well particular in vitro or in vivo work in predicting