Evaluation of Human Tolerance and Safety in Clinical Trials: FIM Trials and Beyond

1 PHARMACEUTICAL DEVELOPMENT PROCESS AND SAFETY

As introduced in the beginning of this volume, the pharmaceutical development process is a long (6–16 years from drug inception to market approval) and costly ($100 million to $1 billion, depending on how one allocates costs) process, even when successful. It is shaped by medical needs, regulatory requirements, economics, our understanding of sciences and diseases, and limitations of technology. All of these interact to shape a process which serves to iteratively reduce risks (both economic and human safety), with the probability of failure being reduced in a stepwise fashion (Matoren, 1984; PhRMA, 2000). Figure 1 briefly summarizes this process.

For our purposes (that is, for a safety assessment perspective), the purpose of all nonclinical (animal and in vitro) testing is to reduce the risks and probability of adverse events in humans. But between initial nonclinical testing (and concurrent with additional animal testing) and a drug reaching the marketplace, the potential for having adverse effects in the general patient population it is intended for is further guarded against by a scheme of increasingly more powerful human (or "clinical") trials (Piantadosi, 1997). How safety is

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