Single-Dose (Acute) and Pilot (DRF) Toxicity Testing in Drug Safety Evaluation

1 INTRODUCTION

Acute toxicity testing is the defining and evaluation of the toxic syndrome (if any) produced by a single or a few doses over the course of a day, such as twice or three times per day (bid or tid, in the case of continuously infused intravenous formulation in a 24-h course of treatment) of a drug. Historically, the main focus of these tests has been lethality determinations and the identification of overt signs and symptoms of overdosage. For a complete historical perspective, see Deichmann and Gerarde (1969), Piegorsh (1989), Auletta (1998), Gad and Chengelis (1999), or Rhodes (2000). A more enlightened and modern view holds that, especially for pharmaceutical agents, lethality in animals is a relatively poor predictor of hazard (other than lethality) in humans (Gad and Chengelis, 1999). The current trend is toward gaining increasing amounts of more sophisticated data from these tests. The various types of acute study designs, their utility in pharmaceutical product testing, their limitation, and the resultant sample data are discussed in this chapter.

For new product approvals (and first in human clinically trials), single-dose toxicity studies are required by regulatory authorities though this requirement

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