Repeat-Dose Toxicity Studies

In the broadest sense, subchronic and chronic studies for pharmaceutical products can incorporate any of the routes used to administer a therapeutic agent, use any of a number of animal models, and conform to a broad range of experimental designs. They can be two weeks long (what used to be called "subacute" studies because they were conducted at dose levels below those employed for single-dose or acute studies) or last up to a year. Another name for these studies is repeat-dose studies (Ballantyne, 2000; Wilson et al., 2001; Gad, 2008a)—that is, those studies whereby animals have a therapeutic agent administered to them on a regular and repeated basis by one or more routes over a period of one year or less. There is great flexibility and variability in the design of such studies.

This chapter seeks to provide a firm grasp of the objectives for repeat-dose studies, the regulatory requirements governing them, the key factors in their design and conduct, and the interpretation of their results.

1 OBJECTIVES

As with any scientific study or experiment (but especially for those in safety assessment), the essential first step is to define and understand the reason(s) for the conduct of the study—that is, its objectives. There are three major (scientific) reasons for conducting subchronic and chronic studies, but a basic

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