

# *Histopathology in Nonclinical Pharmaceutical Safety Assessment*

## **1 INTRODUCTION**

Toxicological pathology is the study of the molecular, cellular, tissue, and/or organ responses of a living organism when exposed to injurious chemical or physical agents. These responses represent a spectrum of cellular changes ranging from cell death to malignant transformations, tissue and organ responses (including regeneration inflammation), and organization and overall response as identified by clinical changes and alterations in body fluids (Arnold et al., 1990; MHLW, 1990; EEC, 1992; EMEA, 2000; Rousseaux et al., 2002; Prince and Wilson, 2003; ICH, 2005, 2006). It starts from recognition of the fact that the cell constitutes the basic unit of life. Accordingly, morphological changes in organs and tissues arise as a result of injury beginning with the responses of underlying cells to the toxic insult. A proper evaluation and understanding of related pathology must start at the cellular level. Some cellular components whose alterations have been reported to be critically associated with cell injury include the plasma membrane, site of osmotic, electrolyte,