Preface

The inspiration for this text was the 1988 volume by Alder and Zbinden*, written before the ICH harmonization process for drug safety evaluation (or its ISO analog for device biocompatibility evaluation) had been initiated or come to force. Since then, much has changed in both the world and the practice of medicine and regulation of drugs. The intent of this volume is to provide similar guidance as to what nonclinical safety assessment tests need to be performed to move a drug into man, through development and to market approved (this intent was subsequently extended to cover the closely related medical device biotechnology and combination product fields) in a concise, abbreviated manner for all the major world market countries.

As when teaching on the subject of drug safety evaluation, the approach I have taken here is to first address the broadest scope "general case" for the regulatory nonclinical safety evaluation by ICH and ISO adhering countries, then to branch out to cover the differences in requirements associated with specific therapeutic areas (such as oncology), major routes of administration (with oral being the general case, other routes starting with parenteral, dermal, and inhalation are addressed). Large molecules biotechnology products are then considered, followed by special courses of product marketing approval, and finally the remaining national differences.

As will be seen, even for ICH countries there is (in mid-2009) continuing modification of the basic M3 guidance for small molecule drugs (R2 being released in step 2 in August of 2008) and S6 (for protein therapeutics) series guidances, and it is not expected that the situation captured and guidance offered in this volume will long withstand the need for regular updating. The drivers for such need will be new science, new ways of using therapeutic products, new concerns, and the influence of new major markets. Also, there will be new real or perceived drug safety concerns. Much of these effects translate to "regulatory creep" (unpublished changes in practice and expectations by different parts of regulatory agencies that proceed in an

* Alder, S. and Zbinden, Z. (1988) National and International Drug Safety Guidelines, M.T.C. Verlay Zollikon, Zollikon, Switzerland.

undocumented fashion almost from the moment a new regulatory guidance comes out), and tracking these changes in a published text approaches is a hopeless task.

It is also not intended that this volume addresses the specifics of study design and interpretation. There are several current texts which perform these tasks well (Gad and McCord, 2008 for devices, Gad 2009 for drugs, and Cavanaro 2008 specifically for biotechnology products) and in the details required. Adequate references are provided to guide the reader (user) of this volume directly to the details required.

Cary, North Carolina

Shayne C. Gad
Gad Consulting Services