Immunotoxicology in Drug Development

1 INTRODUCTION

Unlike many of the other areas covered in this volume, immunotoxicity evaluation of drugs has undergone fundamental changes since the first edition. Before, there was no specific guidance. Now, with the International Conference on Harmonisation (ICH) S8A in place and in force, there is both a requirement and a roadmap for immunotoxicity evaluations, though biologics are excluded from coverage.

This is in particular a concern as biologics have attained their therapeutic promise with their hyperpharmacology providing the largest portion of safety concern for them [from the "cytokine storm" of TGN-1412 to the unintended immune issues associated with most monoclonal antibodies (mAbs)]. With immune modulation of some form being the primary intended therapeutic effects and one-third of all new approved therapeutics being biologics, this is particularly a concern, while specifically not covered by ICH guidances, approaches and requirements for immunotoxicity evaluations of these moieties are addressed, however, in this chapter.

All three ICH regions have made strong efforts to harmonize the immunotoxicity risk assessment for investigational new drugs. These efforts culminated in the release of the ICH S8 guideline, which was adopted by the CHMP (Committee for Medicinal Products for Human Use) in October 2005 and came into force in the United States in April 2006, as well as the MHLW (Ministry of Health, Labor and Welfare, Japan) in April 2006. According to this current

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