ICH and the process by which ICH operates to propose and approve guidances for the pharmaceutical industry.

The second section is a presentation of the non-clinical toxicity guidances in the overall safety designation of ICH topics. Among the topics included in this particular section are ICH guidance for single and repeated-dose toxicity studies, reproductive toxicity studies, genotoxicity and carcinogenicity studies, and the safety assessment of biotechnology-derived pharmaceuticals.

The third section provides a short presentation of the non-clinical safety topics that fall outside of the traditional toxicology realm. These non-clinical ICH safety guidances are in the area of pharmacokinetics (PK)/toxicokinetics (TK) and evaluation of systemic exposures in non-clinical studies and in the area of safety pharmacology, an area of intense recent interest.

The fourth and final section is a presentation of case studies involving a series of non-clinical toxicology packages of studies that were submitted to support the marketing approval of specific drugs. These case studies of Celebrex™, Herceptin®, Rituxan®, and Remicade®, are each illustrative of the unique nature of the different drug development programs. It is my hope that the case studies, together with the ICH guidances, provide a constructive starting point for the design of the package of non-clinical toxicity studies that may be required for a new drug.

2. INTRODUCTION

The ICH is a regulatory and scientific undertaking initiated with the goal of improving the drug development process in the three major regions, Europe, Japan, and the United States, through harmonization of the regulatory guidances among these regions. Established in 1990, ICH is an ongoing joint project between governmental regulatory authorities and pharmaceutical industry experts from each of the three major regions. These six parties to ICH meet with the goal of reaching scientific consensus on various regulatory issues, thereby standardizing the regulatory guidances globally. This standardization of regulatory guidances should significantly reduce the duplication of development activities that might occur when a company desires to obtain worldwide marketing approval. The positive influence of the ICH process is readily apparent in the improved relationship among government regulators and the pharmaceutical industry. The industry is now more able to implement strategies for drug development that allow registration in multiple regions. Much of the credit for the success of ICH has been the end result of the commitment of the regulatory authorities to implement the tripartite harmonized recommendations and guidelines in each of three regions.