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Preface

At the end of 2011, roughly 200 biologics were approved for therapeutic applications and more than 600 were under clinical development. Many of these protein drugs, such as hormones, growth factors, cytokines, coagulation factors, and enzymes, are small in size and are rapidly cleared from circulation. Half-life extension strategies have therefore become increasingly important to improve the pharmacokinetic and pharmacodynamic properties of protein therapeutics, but also for reasons of compliance. Several half-life extension strategies are already utilized in approved drugs, including PEGylation, hyperglycosylation, binding to human serum albumin, and fusion to an immunoglobulin G (IgG) Fc region. However, there is a strong need for new strategies not only to further improve the pharmacokinetic properties but also to facilitate production and application of these half-life extended drugs. These strategies include those that increase the hydrodynamic radius of the drug, thus aiming at reducing the renal clearance, but also strategies that implement recycling by the neonatal Fc receptor (FcRn), which is responsible for the extraordinary long half-life of IgG molecules and serum albumin. In the past 5 to 10 years the field has experienced a rapid growth in the establishment of novel half-life extension strategies, including the application of novel hydrophilic polymers, the generation of recombinant PEG mimic polypeptide chains, and the development of various albumin-binding molecules. Furthermore, the half-life of IgG molecules was altered by engineering of the Fc region, which opens new opportunities for the development of next-generation antibody drugs.

This book is written by renowned experts in the field and is intended to provide a comprehensive overview of the various established but also emerging half-life extension strategies. It can be expected that in the near future many of these technologies will be evaluated in clinical trials and become established strategies to prolong the half-life and thus to improve the pharmacokinetic and pharmacodynamic properties of therapeutic proteins.

Stuttgart, October 2011

Roland Kontermann