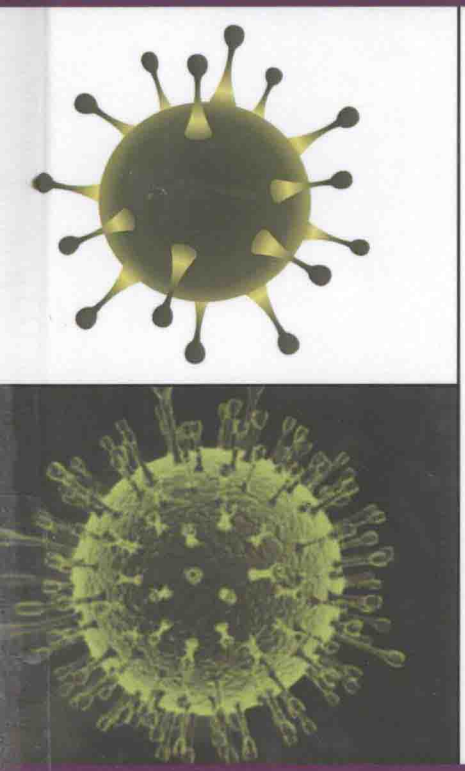
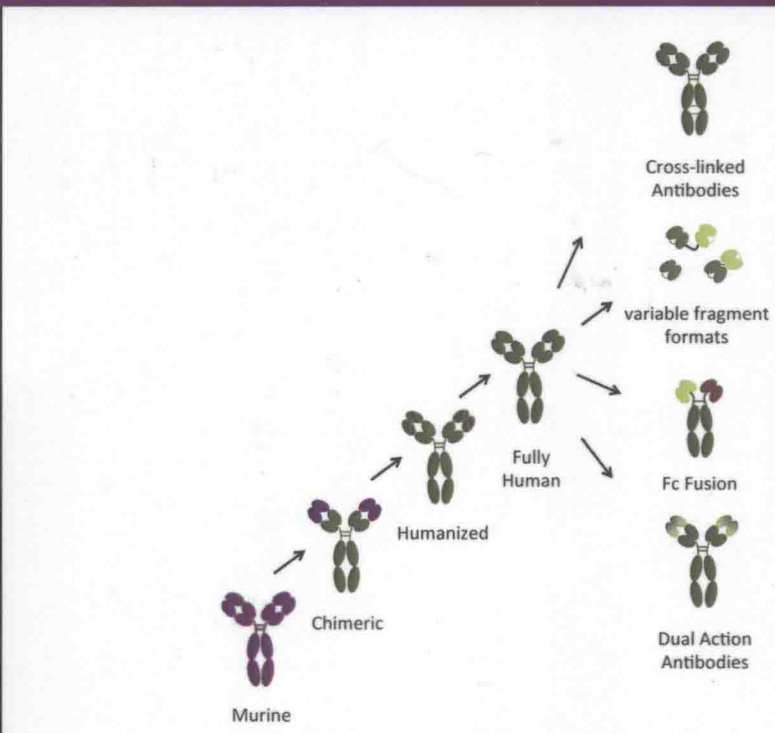
Nonclinical Development of Novel Biologics, Biosimilars, Vaccines and Specialty Biologics





Edited by
Lisa M. Plitnick
Danuta J. Herzyk

NONCLINICAL DEVELOPMENT OF NOVEL BIOLOGICS, BIOSIMILARS, VACCINES AND SPECIALTY BIOLOGICS

Edited by

LISA M. PLITNICK, MS, PHD

and

DANUTA J. HERZYK, PHD

Merck Research Laboratories, Merck & Co., Inc. West Point, PA, USA

ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier

Academic Press is an imprint of Elsevier
32 Jamestown Road, London NW1 7BY, UK
225 Wyman Street, Waltham, MA 02451, USA
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-394810-6

Typeset by TNQ Books and Journals Pvt Ltd.
www.tnq.co.in

Printed and bound in United States of America

13 14 15 16 17 10 9 8 7 6 5 4 3 2 1

NONCLINICAL DEVELOPMENT OF NOVEL BIOLOGICS, BIOSIMILARS, VACCINES AND SPECIALTY BIOLOGICS

Dedication

The Editors would like to dedicate this book to Peter J. Bugelski who passed away in 2011. Peter was not only a leader in the field of immunotoxicology and biologics but a friend, a mentor, and an invaluable collaborator to many authors of this book. Peter's contributions to the field, especially in the form of his numerous important publications, will be recognized and remembered long after his passing and he will remain in our hearts and memories for many years to come.

Preface

Biological medicines have been proven to be very effective both as prophylactic treatment in the form of vaccines and as a desirable solution for complex unmet medical needs in the form of biopharmaceuticals. Development of these medicines has been highly successful. Nevertheless, it remains very expensive, time-consuming, and requires many special considerations in comparison with small-molecule drugs. Although the nonclinical development of biological and small molecule drugs differ in many ways, the approaches for nonclinical evaluation have begun to converge. Development programs between biologics and small molecules are sometimes quite similar as the specificity of the latter increases and therapeutic targets for all types of novel drugs begin to involve similar molecular signaling pathways.

Since the discovery of early biologics such as vaccines and blood products, the field of biologics has evolved to include more advanced, target-specific modalities. *Nonclinical Development of Novel Biologics, Biosimilars, Vaccines and Specialty Biologics* is a testament to this evolution. The goal of this book and of all the many world-renowned experts who contributed to this effort is to educate and inform those interested in biopharmaceutical development, from students and academicians to those currently working in the biopharmaceutical industry. This book complements and builds upon the solid foundation provided in the first comprehensive book dedicated to nonclinical development of biopharmaceuticals edited by Joy Cavagnaro. In only a few short years the science has advanced sufficiently to warrant a second book on nonclinical development of biologics, which includes topics such as biosimilars and multispecific antibodies and fragments that were only an idea a few years ago, but have since become a reality. As those fields have progressed, so too have the regulatory guidelines such as the ICH S6 addendum, and specific documents for biosimilars, vaccines, gene therapy, and stem cells which aid researchers in the design of consistent and comprehensive nonclinical programs. The editors sincerely hope readers find the subject matter interesting and educational, and that the knowledge and enthusiasm of the authors will be appreciated.

Contributors

Vikram Arora, PhD, DABT Toxicology, Grifols Therapeutics, Inc., Research Triangle Park, NC, USA

Eugene P. Brandon, PhD ViaCyte, Inc., San Diego, CA, USA

Joy A. Cavagnaro, PhD, DABT, RAC Access BIO, L.C., Boyce, VA, USA

Anu V. Connor, PhD, DABT Department of Safety Assessment, Genentech Inc., South San Francisco, CA, USA

Justine J. Cunningham, PhD, DABT Allergan, Inc., Irvine, CA, USA

Maggie Dempster, PhD, DABT Nonclinical Safety Projects, Safety Assessment, GlaxoSmith-Kline, LLC., Philadelphia, PA, USA

Christina de Zafra, PhD, DABT Department of Safety Assessment, Genentech, Inc., South San Francisco, CA, USA

Thomas R. Gelzleichter, PhD, DABT Department of Safety Assessment, Genentech, Inc., South San Francisco, CA, USA

Wendy G. Halpern, DVM, PhD, DACVP Department of Safety Assessment, Genentech Inc., South San Francisco, CA, USA

Danuta J. Herzyk, PhD Merck Research Laboratories, Merck & Co., Inc., West Point, PA, USA

Beth Hinkle, PhD Comparative Biology and Safety Sciences, Amgen Inc., Thousand Oaks, CA, USA

Inge A. Ivens, PhD, DABT Toxicology, US Innovation Center Mission Bay, Bayer HealthCare, San Francisco, CA, USA

Amy Kim, MSPH, PhD, DABT Department of Safety Assessment, Genentech, Inc., South San Francisco, CA, USA

Donna W. Lee, PhD, DABT Department of Safety Assessment, Genentech Inc., South San Francisco, CA, USA

Timothy K. MacLachlan, PhD, DABT Novartis Institutes of Biomedical Research, Cambridge, MA, USA

Melinda Marian, MS Biologics Discovery DMPK and Bioanalytics, Merck Research Laboratories, Palo Alto, CA, USA

Barbara Mounho-Zamora, PhD ToxStrategies, Inc., Bend, OR, USA

Padma Kumar Narayanan, DVM PhD Comparative Biology and Safety Sciences, Amgen Inc., Seattle, WA, USA

Rania Nasis, MD, MBA Regenerative Medicine Strategy Group, LLC., Los Angeles, CA, USA

Deborah L. Novicki, PhD, DABT Novartis Vaccines and Diagnostics, Cambridge, MA, USA

Lisa M. Plitnick, MS, PhD Merck Research Laboratories, Merck & Co., Inc., West Point, PA, USA

Rafael Ponce, PhD Comparative Biology and Safety Sciences, Amgen Inc., Seattle, WA, USA

Rodney A. Prell, PhD, DABT Department of Safety Assessment, Genentech Inc., South San Francisco, CA, USA

Karen D. Price Bristol-Myers Squibb Company Department of Immunotoxicology, New Brunswick, NJ, USA

Gautham K. Rao Bristol-Myers Squibb Company Department of Immunotoxicology, New Brunswick, NJ, USA

Theresa Reynolds, BA, DABT Department of Safety Assessment, Genentech, Inc., South San Francisco, CA, USA

Wolfgang Seghezzi Bioanalytics, Biologics Discovery DMPK and Bioanalytics, Merck Research Laboratories, Palo Alto, CA, USA

Marque D. Todd, DVM, MS, DABT Regulatory Strategy & Compliance, Drug Safety Research & Development, Pfizer, Inc., La Jolla, CA, USA

Jayanthi J. Wolf, PhD Merck Research Laboratories, Merck & Co., Inc., West Point, PA, USA

Acknowledgments

The editors wish to thank all the authors who donated their time to share their expertise and greatly contributed to this effort. Without them, there would be no book. In addition, we would like extend special appreciation to Rodney Prell and Jayanthi Wolf for their inspiration for the cover art.

Contents

II

DEVELOPMENT OF BIOSIMILARS

III

VACCINES