# CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREFACE</td>
<td>xi</td>
</tr>
<tr>
<td>FOREWORD</td>
<td>xiii</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>xv</td>
</tr>
<tr>
<td>CONTRIBUTORS</td>
<td>xvii</td>
</tr>
<tr>
<td><strong>PART I  INTRODUCTION</strong></td>
<td>1</td>
</tr>
<tr>
<td><em>Philip Marder and Virginia Litwin</em></td>
<td></td>
</tr>
<tr>
<td>1 Introduction to Flow Cytometry</td>
<td>3</td>
</tr>
<tr>
<td><em>Elizabeth Raveche, Fatima Abbasi, Yao Yuan, Erica Salerno, Siddha Kasar, and Gerald E. Marti</em></td>
<td></td>
</tr>
<tr>
<td>2 Recent Advances in Flow Cytometry: Platforms, Tools, and Challenges for Data Analysis</td>
<td>23</td>
</tr>
<tr>
<td><em>Paul J. Smith, Roy Edward, and Rachel J. Errington</em></td>
<td></td>
</tr>
<tr>
<td>3 Introduction to Biomarkers</td>
<td>55</td>
</tr>
<tr>
<td><em>Ole Vesterqvist and Manjula P. Reddy</em></td>
<td></td>
</tr>
</tbody>
</table>
PART II FLOW CYTOMETRY IN THE DRUG DEVELOPMENT PROCESS

Virginia Litwin and Philip Marder

4 HTS Flow Cytometry, Small-Molecule Discovery, and the NIH Molecular Libraries Initiative

Larry A. Sklar and Bruce S. Edwards

5 A Multiparameter Approach to Cell Cycle Analysis as a Standard Tool in Oncology Drug Discovery

Carmen Raventos-Suarez and Byron H. Long

6 Flow Cytometry in Preclinical Toxicology/Safety Assessment

David McFarland and Kristi R. Harkins

7 Use of Flow Cytometry to Study Drug Target Inhibition in Laboratory Animals and in Early-Phase Clinical Trials

David W. Hedley

8 CD4 T Cell Assessments in Evaluation of HIV Therapeutics

Thomas N. Denny, Raul Louzao, John Wong, and Brooke Walker

9 Monitoring the Cellular Components of the Immune System During Clinical Trials: A Translational Medicine Approach

Virginia Litwin and James Andahazy

10 Immunogenicity Testing Using Flow Cytometry

Denise M. O’Hara and Valerie Theobald

11 Pharmacokinetics by Flow Cytometry: Recommendations for Development and Validation of Flow Cytometric Method for Pharmacokinetic Studies

Yuanxin Xu and Susan M. Richards

PART III VALIDATION AND REGULATORY COMPLIANCE

Virginia Litwin and Philip Marder

12 Regulatory Compliance and Method Validation

Carla G. Hill, Dianna Y. Wu, John Ferbas, Virginia Litwin, and Manjula P. Reddy
CONTENTS

13 Instrument Validation for Regulated Studies 267
   John Ferbas and Michelle J. Schroeder

PART IV FUTURE DIRECTIONS 279
   Virginia Litwin and Philip Marder

14 Probability State Modeling: A New Paradigm for
   Cytometric Analysis 281
   C. Bruce Bagwell

15 Phospho Flow Cytometry: Single-Cell Signaling Networks in
   Next-Generation Drug Discovery and Patient Stratification 303
   Peter O. Krutzik, Sean C. Bendall, Matthew B. Hale,
   Jonathan M. Irish, and Garry P. Nolan

INDEX 335