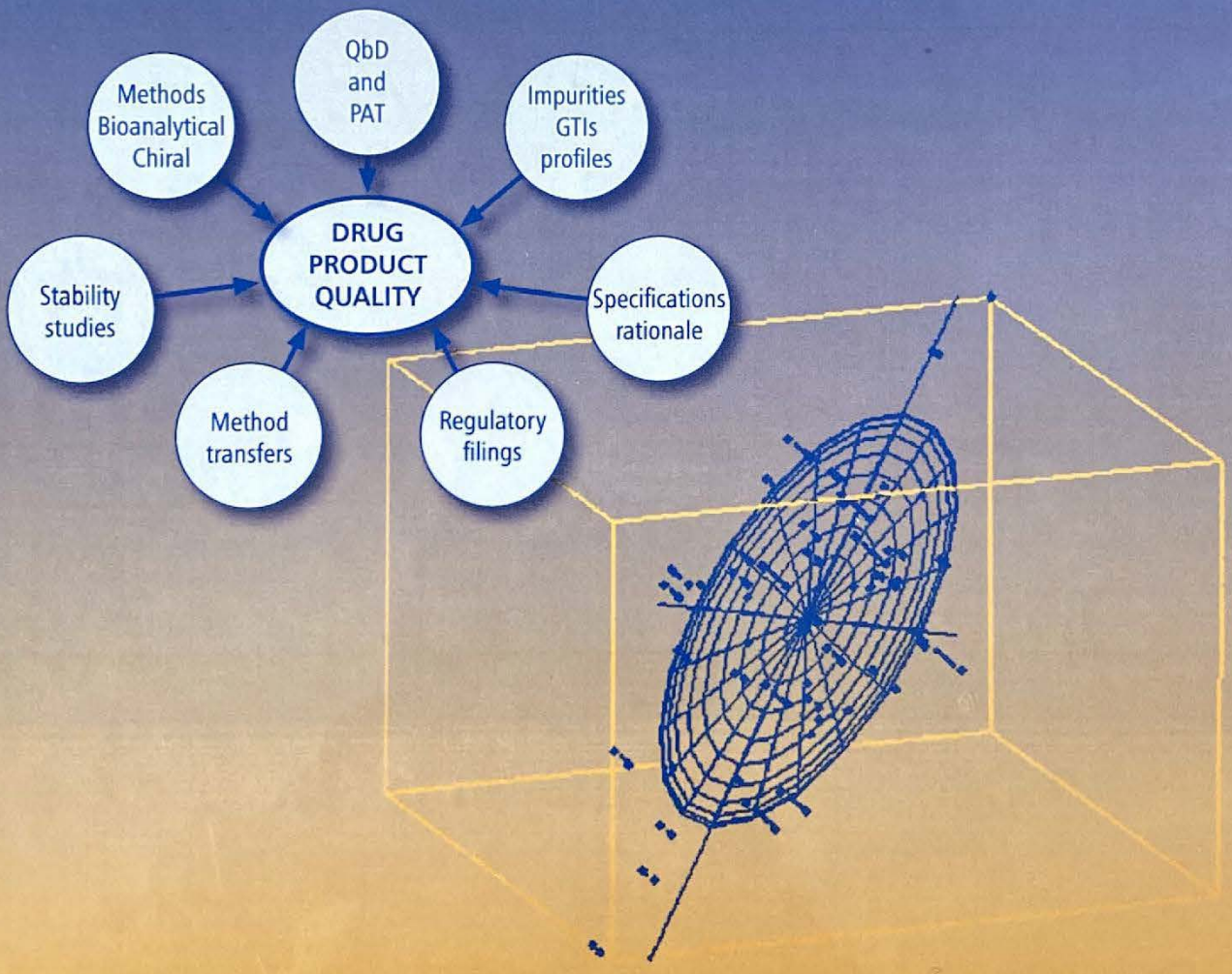
SECOND EDITION

HANDBOOK OF MODERN PHARMACEUTICAL ANALYSIS

Edited by
Satinder Ahuja and Stephen Scypinski



SEPARATION SCIENCE AND TECHNOLOGY
VOLUME 10
Series Editor Satinder Ahuja

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

HANDBOOK OF MODERN PHARMACEUTICAL ANALYSIS
2nd Edition

Edited by

Satinder Ahuja

Ahuja Consulting
Calabash, NC, USA

Stephen Scypinski

Analytical Research & Development, Bristol-Myers Squibb Company
New Brunswick, NJ, USA

ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO
Academic Press is an imprint of Elsevier

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

Academic Press is an imprint of Elsevier
30 Corporate Drive, Suite 400, Burlington, MA 01803, USA
525 B Street, Suite 1900, San Diego, CA 92101-4495, USA
84 Theobald's Road, London WC1X 8RR, UK
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands

First edition 2001
Second edition 2011

Copyright © 2011 Elsevier Inc. All rights reserved.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means electronic, mechanical, photocopying, recording, or otherwise without the prior written permission of the publisher

Permissions may be sought directly from Elsevier's Science & Technology Rights Department in Oxford, UK: phone (+44) (0) 1865 843830; fax (+44) (0) 1865 853333; e-mail: permissions@elsevier.com. Alternatively you can submit your request online by visiting the Elsevier Web site at http://elsevier.com/locate/permissions, and selecting *Obtaining permission to use Elsevier material.*

Notice
No responsibility is assumed by the publisher for any injury and/or damage to persons or property as a matter of products liability, negligence, or otherwise or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made

Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

ISBN: 978-0-12-375680-0

ISSN: 0149-6395

For information on all Academic Press publications
visit our website at www.books.elsevier.com

Printed and bound by CPI Group (UK) Ltd, Croydon, CR0 4YY

Transferred to digital print 2012

Working together to grow
libraries in developing countries
www.elsevier.com | www.bookaid.org | www.sabre.org
ELSEVIER BOOK AID International Sabre Foundation

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

CONTENTS

PREFACE xi
CONTRIBUTORS xiii

1. Overview of Modern Pharmaceutical Analysis
SATINDER AHUJA

I. Introduction 1
II. Solid-State Studies 3
III. Degradation and Impurities Studies 3
IV. Analytical Considerations for Genotoxic and Other Impurities 4
V. Quality by Design and Process Analytical Technology 4
VI. Novel Dosage Forms 4
VII. Method Development for Chiral Compounds 5
VIII. Characterization and Analysis of Biopharmaceutical Proteins 5
IX. Preformulation and Early Phase Method Development 6
X. In-Process Control Testing 6
XI. Method Validation 7
XII. Stability Studies 7
XIII. Method Transfer 7
XIV. Documentation 8
References 9

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

2. Characterization of Pharmaceutical Compounds in the Solid State

HARRY G. BRITTAIN

I. Introduction 11
II. Properties Associated with the Molecular Level 13
III. Properties Associated with the Particulate Level 26
IV. Properties Associated with the Bulk Level 36
V. Summary and Conclusions 49
References 49

3. Degradation and Impurity Analysis for Pharmaceutical Drug Candidates

KAREN M. ALSANTE, STEVEN W. BAERTSCHI, MICHAEL COUTANT, BRIAN L. MARQUEZ, THOMAS R. SHARP, AND TODD C. ZELESKY

I. Forced Degradation Studies 60
II. Isolation of Impurities/Degradants 80
III. Mass Spectrometry in the Identification of Impurities 100
IV. NMR 126
V. Case Studies 147
VI. Summary 157
References 158

4. Analytical Considerations for Genotoxic and Other Impurities

RODNEY L. PARSONS AND SCOTT A. MILLER

I. Introduction 171
II. Concept of GTI Relative to Standard Impurities and the Current Regulatory Thinking 172
III. Viracept® GTI Contamination Issue 173
IV. GTI Risk Assessment and Control Strategy Design 174
V. Analytical Challenges 179
VI. Summary and Conclusions 191
References 191

5. Quality by Design and the Importance of PAT in QbD

ROBERT W. BONDI, Jr. AND JAMES K. DRENNEN, III

I. Introduction 195
II. The Role of PAT in QbD 200

DOCKET ALARM

Find authenticated court documents without watermarks at docketalarm.com.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.