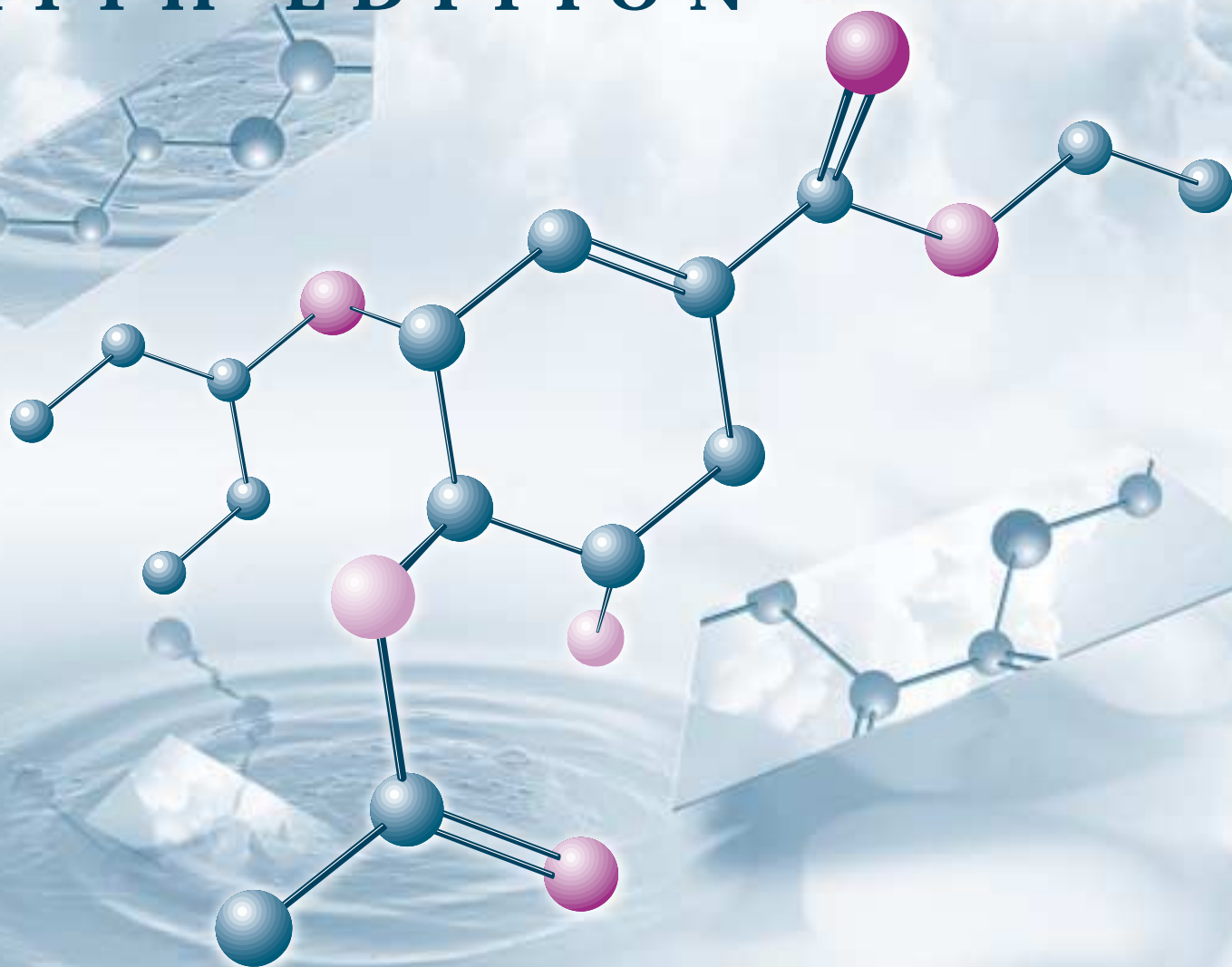


Optically Active Chemical Compounds

11TH EDITION



Worldwide Market and Technology Assessment

Competitive Intelligence

Chiral Compounds in Clinical Development

Optically Active Chemical Compounds

1 1 T H E D I T I O N

Chiral drugs continue to be a significant force in the global pharmaceutical market. Recent developments in the chiral-related industries indicate that a fundamental shift is occurring. Pharmaceutical companies are increasingly concentrating on their core strengths in drug discovery and marketing. Another trend is the increased consolidation in the pharmaceutical industry. These trends are resulting in the divestiture of chemical operations and plants by big pharma. For fine chemical companies this increases the requirement to develop a 'critical mass' and a full range of capabilities for continued participation.

The winners in the fine chemicals industry will be companies that achieve critical mass, develop good process technology and proprietary products, and secure value-added contracts with a number of customers.

The emergence of a new model for success is spurring significant merger and acquisition activity in the fine chemicals and pharmaceutical intermediates arena. Programs of acquisition, divestment, and joint venture have transformed some companies from having portfolios of virtually unrelated business into cohesive groupings of activities. New entrants into fine chemicals are seeking to acquire expertise and plants to achieve critical mass in this high margin business. Every chiral technology company that comes on the market has a number of bidders raising asset prices in this sector. Several companies, such as Elan, Novartis, Aventis, and Watson, have been very aggressively acquiring companies or technologies. New entrants, such as Great Lakes, are acquiring divested operations to create an immediate presence in this attractive market.

As markets for single-isomer drugs continue to blossom, both fine chemical companies and academic chemists are prospecting for new enantioselective technologies to produce them.

Companies are developing a full range of capabilities through alliance or acquisition. Recent alliances and acquisitions include:

- Glaxo Wellcome and SmithKline Beecham merged to create \$182 billion GlaxoSmithKline, one of the world's leading research-based pharmaceutical and healthcare companies.
- Warner-Lambert was acquired by Pfizer creating a \$230 billion pharmaceutical company.
- Teva Pharmaceutical Industries Ltd. completed its acquisition of Novopharm Ltd. for \$493 million.
- Vertex Pharmaceuticals Inc. and Novartis Pharma AG announced the formation of an alliance to discover, develop, and commercialize small molecule drugs directed at targets in the kinase protein family.
- Aventis Pharma and Millennium Pharmaceuticals, Inc. announced a unique alliance with the signing of agreements covering the joint development and commercialization of drugs for the treatment of inflammatory diseases; joint development of new drug discovery technologies; transfer of key elements of Millennium's technology platform to Aventis to enhance its existing capabilities; and purchase of an equity interest in Millennium by Aventis.
- Rhodia, a leading specialty chemicals company, entered into a definite agreement to acquire ChiRex Inc., a provider of advanced product development services and manufacturing to the pharmaceutical industry.
- Watson Pharmaceuticals, Inc. completed its acquisition of Schein Pharmaceutical, Inc. for \$740 million.

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- Catalytica, Inc. and DSM announced that DSM would acquire Catalytica's pharmaceuticals business through the purchase of Catalytica, Inc. for approximately \$750 million plus the assumption of debt, for a total current value of approximately \$800 million.
 - Elan Corporation completed its acquisition of Dura Pharmaceuticals, Inc. for \$1.8 billion.
 - Evotec Biosystems merged with Oxford Asymmetry International to become Evotec OAI in a £316 million deal.
 - Cambridge Antibody Technology and Human Genome Science established a \$67 million alliance for antibody drug development.
 - Cambrex Corporation and Synthron Chiragenics Corporation announced a four year collaborative agreement for the development, manufacture, and supply of advanced chiral compounds for use in therapeutic drugs.
 - Abbott Laboratories entered into a definitive agreement to acquire the pharmaceutical business of BASF, which includes the global operations of Knoll. Abbott will pay \$6.9 billion in cash.
 - The Dow Chemical Company announced that the company, through a wholly owned subsidiary, made an offer to acquire 100 percent of the shares of Ascot Plc, a publicly traded UK company.
 - Degussa AG declared an offer to take over the British specialty chemicals corporation Laporte plc.

Companies need to understand the technical and business strategies of competitors, suppliers and customers to take advantage of this fundamental shift. The report series, *Optically Active Chemical Compounds (OACC)*, provides current assessments of the technical and business implications of chirality. Subscribers will receive reports that provide in-depth analysis and evaluation of emerging chiral technologies, competitor activities and product developments.

The eleventh edition of OACC consists of three individual volumes:

- Volume I: Worldwide Market and Technology Assessment
- Volume II: Competitive Intelligence
- Volume III: Chiral Compounds in Clinical Development



Volume I

Worldwide Market and Technology Assessment

The *Worldwide Market and Technology Assessment* volume of this edition of *Optically Active Chemical Compounds* reviews recent developments within the fine chemical and pharmaceutical industries, with emphasis on single-enantiomer products, their intermediates, and the relevant technologies. Detailed sales data for enantiomerically-pure pharmaceuticals are provided by therapeutic category and company. Recent technology developments are reviewed and analyzed in this volume.

Total worldwide pharmaceutical sales were \$390 billion in 2000. The total sales value of single-enantiomer products continued to grow at a significantly faster rate than the overall pharmaceutical market. In 2000, worldwide sales of single-enantiomer drugs surged 13% in 2000 over 1999 to almost \$133 billion, mainly from advances in enantiomeric antiviral, gastro-intestinal, and anticancer drugs.

In the Market Assessment section of this volume, Technology Catalysts International provides details on why chiral chemistry-based pharmaceuticals continue to outpace the total market. The major product categories with the largest growth rates in 2000 are analyzed and the new launched chiral drugs in 1999 and 2000 are evaluated based on their market potential and process technologies used to make them. By analyzing the synthesis of these compounds, fine chemical companies are able to anticipate and prepare for future manufacturing technology needs.

In the Technology Assessment section of this volume, we provide details concerning recent technical developments in asymmetric synthesis, enantiomer resolution, and enzymatic transformation.

TABLE OF CONTENTS

I. Introduction and Executive Summary

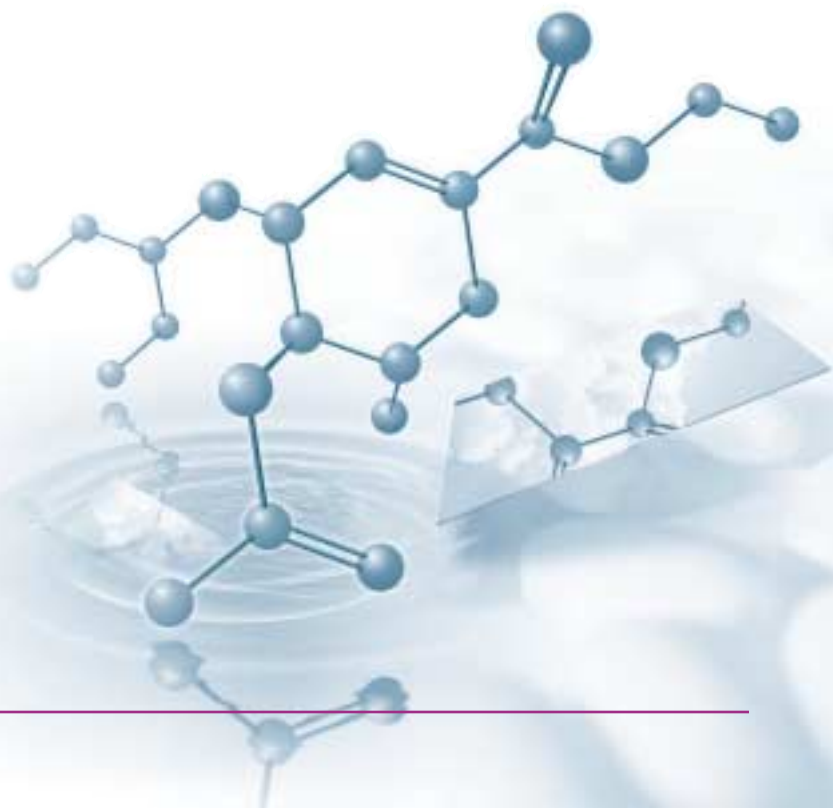
II. Worldwide Pharmaceutical Market Update

III. Racemic Switch Update and Forecast

1. Recent Developments
2. Forecast on market of racemic switches

IV. Worldwide Technology Update

1. Recent Developments in Asymmetric Synthesis Technology
2. Recent Developments in Resolution Technology
3. Recent Development in Enzymatic Transformation
4. Recent technology licensing activities in chiral field



Volume II

Competitive Intelligence

Technology Catalysts International continues its efforts to provide subscribers with the latest information on competitor activities, technology developments and product launches, and technological achievements. As in the past, the

Competitive Intelligence report focuses on leading-edge companies which are playing a leading role in shaping the future of chiral industry. The report presents current information on the leading pharmaceutical and fine chemical companies worldwide.

Global Competitive Intelligence

<i>New Companies in</i>	<i>Eleventh Edition</i>	<i>Tenth Edition</i>	<i>Ninth Edition</i>	<i>Eighth Edition</i>	<i>Seventh Edition</i>	<i>Sixth Edition</i>	<i>Fifth Edition</i>	<i>Fourth Edition</i>	<i>Third Edition</i>	<i>Second Edition</i>	<i>First Edition</i>
Asia	5	9	9	0	9	25	13	18	45	26	36
North America	7	4	6	2	16	24	13	31	48	21	35
Europe	6	4	11	4	7	26	22	48	50	24	36
Total (New)	18	17	26	6	32	75	48	97	143	71	107
<i>Updated Information</i>	82	83	74	94	71	47	103	87	58	38	N/A
TOTAL NUMBER OF COMPANIES	100	100	100	100	103	122	151	184	201	109	107

LIST OF COMPANIES

Abbott Laboratories, Inc.	Borregaard Synthesis
Aerojet Fine Chemicals	BioCatalytics, Inc.
Ajinomoto Co., Ltd.	Bristol-Myers Squibb
Alchemia Pty., Limited	Cambrex Corporation
Altus Biologics, Inc.	Celltech Chiroscience
American Home Products Corporation	Cheil Jedang Corporation
Amgen, Inc.	Chiral Quest, llc
AstraZeneca plc	Chong Kun Dang Pharmaceutical Corporation
Avecia Limited	Ciba Specialty Chemicals Corporation
Aventis SA	Cipla, Ltd.
Bachem AG	Clariant International Limited
BASF Group	Dabur India, Ltd.
Bayer Group	Daicel Chemical Industries, Inc.

Daiichi Pharmaceutical Co., Ltd.
Daiso Co., Ltd.
Degussa AG
Diversa Corporation
Dow Chemical Company
Dr. Reddy's Laboratory Ltd.
DSM N.V.
Dyax Corporation
Eastman Chemical Company
Eisai Co., Ltd.
Eli Lilly & Company
Evotec-OAI
Facilichem, Inc.
Ferro Corporation
Fujirebio, Inc.
Fujisawa Pharmaceutical Co., Ltd.
Genzyme Corporation
Gilead Sciences, Inc.
GlaxoSmithKline plc
Great Lakes Chemical Corporation
GroPep Limited
Isu Chemical Co., Ltd.
Johnson & Johnson
Johnson Matthey plc
K-Genix Group
Kaneka Corporation
KiralChem Ltd.
Kyowa Hakko Kogyo Co., Ltd.
Larova Biochemie GmbH
Lonza AG
Maxygen, Inc.
MediChem Research, Inc.
Mercian Corporation
Merck & Co.
Meristem Therapeutics
Mimotopes Pty., Ltd.
Mitsubishi Rayon Co., Ltd.
Neose Technologies, Inc.
Newport Synthesis Ltd.

Nissan Chemical Industries, Ltd.
Novartis AG
Novazyme Pharmaceuticals, Inc.
NPS Pharmaceuticals, Inc.
Opregen Pharma GmbH
Orion Group
Peptech Limited
Pfizer, Inc.
Pharmacia Corporation
PPG-Sipsy
R+S Biotec GmbH
Regis Technologies, Inc.
Rhodia
Roche Group
Rohner AG
Samsung Fine Chemicals Co., Ltd.
Sanofi-Synthelabo
Schering AG
Schering-Plough Corporation
Schwarz Pharma AG
Seloc France SA
Sepracor, Inc.
Shenzhen Boda Natural Product Co., Ltd.
SK Energy & Chemicals
Sumitomo Chemical Co., Ltd
Synchem, Inc.
Synetix
Synthon Chiragenics Corporation
Synthetech, Inc.
Takeda Chemical Industries, Ltd.
Toray Industries, Inc.
Triangle Pharmaceuticals, Inc.
Vertex Pharmaceuticals
Yamanouchi Pharmaceutical Co., Ltd.
Welfide Corporation

Volume III

Chiral Compounds in Clinical Development

INTRODUCTION

The report presents information on enantiomerically-pure chiral compounds which were in active clinical development at the time of publication. These compounds represent selections from the clinical pipelines of companies in North America, Europe, and Asia.

Each compound is presented in summary format which includes the following information (where known):

- Identity of developing company
- Compound development name
- Generic name
- CAS registry number
- Molecular formula

- Compound structure
- Primary indication
- Clinical trial status
- Most possible synthetic routes

In addition, a pharmaceutical materials purchasing agent or development contact is provided for each compound. These individuals are either key decision makers or contact points who can steer information from outside vendors to appropriate decision makers. The outsourcing contacts are provided as entry points for manufacturers of intermediates, synthons, catalysts, resolving agents, or separation systems. Direct approach to each pharmaceutical company to introduce these products is appropriate. In some cases, the outsourcing contact will serve as a conduit to project heads and development specialists that might be searching for the next generation of product(s).

LIST OF OPTICALLY ACTIVE CHIRAL COMPOUNDS

<i>Drug Name</i>	<i>Source</i>	<i>Phase</i>
A-216546	Abbott	CT 1
Ajulemic acid	Atlantic Pharmaceuticals	CT 1
Auristatin PE	Teikoku Hormone	CT 1
BI-397	Biosearch Italia	CT 1
BMS-184476	Bristol-Myers Squibb	CT 1
BMS-214662	Bristol-Myers Squibb	CT 1
BMS-247550	Bristol-Myers Squibb	CT 1
CEP-2563	Cephalon	CT 1
CI-1018	Pfizer	CT 1
DMP-851	DuPont Pharmaceuticals	CT 1
DMP-961	DuPont Pharmaceuticals	CT 1
ED-749	Merck	CT 1
GW-660511	Zambon	CT 1
GYKI-16084	Gedeon Richter	CT 1
Itriglumide	Rotta	CT 1

<i>Drug Name</i>	<i>Source</i>	<i>Phase</i>
Izonsteride	Lilly	CT 1
LY-444711	Lilly	CT 1
MX-68	Chugai	CT 1
Octreother	Novartis	CT 1
ONO-8711	Ono	CT 1
PNU-142721	Pharmacia	CT 1
PS-519	Millennium	CT 1
R-113281	Sankyo	CT 1
Ravuconazole	Eisai	CT 1
RGD-891	Aventis Pharma	CT 1
RIG-200	University of St. Andrews	CT 1
Ro-09-4889	Nippon Roche	CT 1
SS-750	SSP Co.	CT 1
Talnetant	GlaxoSmithKline	CT 1
AG-7088	Pfizer	CT 2
AMP-579	Aventis Pharma	CT 2
AP-1903	Ariad	CT 2
BIBN-4096BS	Boehringer Ingelheim	CT 2
BMS-189921	Bristol-Myers Squibb	CT 2
BN-80915	Biomeasure	CT 2
Capromorelin	Pfizer	CT 2
Cilengitide	Merck KGaA	CT 2
CKD-602	Chong Kun Dang	CT 2
CMI-977	Millennium	CT 2
Crobenetine HCl	Boehringer Ingelheim	CT 2
Darusentan	Abbott	CT 2
DPC-083	DuPont Pharmaceuticals	CT 2
DPP-728	Novartis	CT 2
Fiduxosin hydrochloride	Abbott	CT 2
Ganstigmine	Chiesi	CT 2
Harkoseride	Schwarz Pharma	CT 2
Implitapide	Bayer	CT 2
J-104132	Banyu (Merck & Co.)	CT 2
L-756423	Merck	CT 2
Merimempodib	Vertex	CT 2
PD-123497	Pfizer	CT 2
PS-341	Proscript	CT 2
Robalzotan tartrate hydrate	AstraZeneca	CT 2
Sch-66336	Schering-Plough	CT 2
SUN-C5174	Suntory	CT 2
TAK-637	Takeda	CT 2
TAK-778	Takeda	CT 2
Timcodar dimesilate	Vertex	CT 2

<i>Drug Name</i>	<i>Source</i>	<i>Phase</i>
Tonabersat	GlaxoSmithKline	CT 2
TR-14035	Tanabe Seiyaku	CT 2
ABT-773	Abbott	CT 3
Orbofiban	Pharmacia	CT 3
YM-905	Yamanouchi	CT 3
AP-22408	Aventis Pharma	Preclinical
BB-3497	British Biotech	Preclinical
BIIE-0246	Boehringer Ingelheim	Preclinical
BIM-46068	Biomeasure	Preclinical
Bradyzide	Novartis	Preclinical
CP-654743	Pfizer	Preclinical
CT-5219	Celltech Chiroscience	Preclinical
CV-1013	Cytovia (Maxim)	Preclinical
DM-232	Universit Odegli Studi di Firenze	Preclinical
Epcitabine	Novirio	Preclinical
FR-182024	Fujisawa	Preclinical
GW-4459	GlaxoSmithKline	Preclinical
GW-5950X	Vertex	Preclinical
HMR-1556	Aventis Pharma	Preclinical
IQM-97423	Universidad de Navarra	Preclinical
JE-2179	Japan Energy Corp.	Preclinical
L-779976	Merck	Preclinical
Levovirin	ICN	Preclinical
LF-16-0687	Fournier	Preclinical
LY-314177	Lilly	Preclinical
MC-002434	Microcide	Preclinical
NIP-142	Nissan Chemical	Preclinical
ONO-8815	Ono	Preclinical
PNU-171829	Pharmacia	Preclinical
R-103757	Janssen	Preclinical
R-116010	Janssen	Preclinical
Ro-27-0574	Roche AG	Preclinical
RPR-118031A	Aventis Pharma	Preclinical
RPR-208566	Aventis Pharma	Preclinical
RU-79115	Aventis Pharma	Preclinical
RWJ-56110	R. W. Johnson	Preclinical
S-33138	Servier	Preclinical
SB-239063	GlaxoSmithKline	Preclinical
SM-31900	Sumitomo Pharmaceuticals	Preclinical
SR-3785	SRI International	Preclinical
SUN-N8075	Suntory	Preclinical
TBC-3486	Texas Biotechnology	Preclinical
TH-1177	University of Virginia	Preclinical

Technology Catalysts International Corporation

Technology Catalysts International, founded in 1979, is a full-service strategic alliance consultancy specializing in technical and business research in pharmaceuticals, life sciences, chemicals, and advanced materials and processes. The company provides several distinct services.

Drug Delivery Information Services™ (DDIS) provide an assessment of new technologies, international competitive intelligence, and business opportunities on a worldwide basis. The annual subscription includes reports, a custom study, and unlimited “hot line” service. The “hot line” service allows immediate access to information being accumulated for the annual report.

The Licensing Locator™ service provides companies with unlimited requests for technology or products available for license, joint venture, or contract research. Searches are conducted on a worldwide basis. No brokerage fees or commissions are charged.

Late-Stage Product Acquisition Services assist companies in the identification of ethical or OTC (self-medication) pharmaceuticals which have pending registrations and can be acquired for cash and royalties.

Optically Active Chemical Information Services™ (OACIS) provide unpublished intelligence, technology assessments, and acquisition opportunities for the pharmaceutical industry and its suppliers. OACIS provides technical and economic evaluations of specific emerging technologies on chiral drugs which can be used to create a competitive advantage. The annual subscription includes reports, a custom study, and a “hot line” service.

Generic Drug Analysis Service (GxAS) enables fine chemical and drug delivery clients interested in making or marketing generic drugs to cost-effectively target those opportunities with the highest margins. Over 300 candidate generic drugs are analyzed according to strategic criteria developed with the

client. The end product is a prioritized list of candidate drugs for possible development by the client. With TCI guidance the client is then able to formulate a business plan and market-entry strategy.

Ask TCI Any Question™ (ATAQ) is a specialized information service designed to protect a client’s anonymity while providing unpublished, difficult-to-get, non-confidential information. ATAQ is designed to go beyond database searches, the information from which is frequently incomplete, inaccurate, or not timely. The service provides “essential to have” rather than “nice to know” information. Response time is fast, usually within two business days. Client requests are handled by senior staff specialists with access to worldwide resources. The service allows a client’s request to be billed in units of time. Each month the client is provided with an activity report.

Food Technology Consulting Practice is focused on specific client needs in the global food business. Food additives, products, ingredients, and processing are covered. TCI’s expertise includes novel technology identification and assessment, commercial evaluation, supply/demand forecasts, and regulatory impact. TCI professionals identify client problems, utilize appropriate methodologies, and provide actionable recommendations.

Contacts are listed on the back cover for further information on the above services, or contact us on the web:

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Optically Active Chemical Compounds

Eleventh Edition

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Tenth Edition

- | | | |
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