



SEVENTH ANNUAL

Report and Survey of Biopharmaceutical Manufacturing Capacity and Production

A Study of Biotherapeutic Developers and Contract Manufacturing Organizations



APRIL 2010



7th Annual

Report and Survey of Biopharmaceutical Manufacturing Capacity and Production

*A Study of Biotherapeutic Developers and Contract
Manufacturing Organizations*

April 2010



BioPlan Associates, Inc.
2275 Research Blvd., Suite 500
Rockville, MD 20850 USA
301.921.5979

Copyright ©2010 by BioPlan Associates, Inc.
All rights reserved. Unauthorized reproduction prohibited.

7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production

*A Study of Biotherapeutic Developers and Contract
Manufacturing Organizations*

April 2010

BioPlan Associates, Inc.
2275 Research Blvd, Suite 500
Rockville MD 20850
301-921-5979
www.bioplanassociates.com

Copyright © 2010 by BioPlan Associates, Inc.

All rights reserved, including the right of reproduction in whole or in part in any form. 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 written permission of the publisher.

For information on special discounts or permissions contact
BioPlan Associates, Inc. at 301-921-5979, or info@bioplanassociates.com

Managing Editor: Eric S. Langer
Project Director: Krista E. Meisel
Layout and Cover Design: ES Design

ISBN 978-1-934106-20-4

ACKNOWLEDGMENT

We wish to acknowledge the contributions of our authors and subject matter experts. Without their thorough analysis of the data this project would not have been possible:

- E. Faye Coggins, Founder and Principal of BioTraction Associates, LLC
- Alfred C Dadson Jr, Sr Director, Manufacturing Operations, XOMA LLC
- Geoff Hodge, VP, Process Development & Technology, Xcellerex, Inc.
- David G. Jensen, Managing Director, Kincannon & Reed Global Executive Search
- Vladimir Kostyukovsky, Sr. Technical Manager, Kymanox
- Stephen M. Perry, President, Kymanox
- John L. Quick, Founder & Principal, Quick & Associates, Inc.
- Ronald A. Rader, President, Biotechnology Information Institute
- Rowena L. Roberts, PhD, Founder and Principal Biotraction Associates, LLC
- Abdul Wajid, Ph.D., Sr. Director, Process Sciences XOMA LLC
- Scott Wheelwright, President, Strategic Manufacturing Worldwide

We would also like to recognize our sponsoring organizations, and our media sponsor. Their efforts in assuring the cooperation and participation in the survey of their respective memberships helped guarantee the large group of survey participants to ensure data accuracy.

Our sponsoring institutions, all of whom contributed their time and effort to ensure the broad, international coverage of this project, include:

- ABO – Alliance of Bio-Box Outsourcing (China)
- AIBA (India)
- Ausbiotech (Australia)
- BayBio (San Francisco, CA)
- Beijing Pharma and Biotech Center (Beijing)
- BioForward (Madison, WI)
- BioMelbourne Network (Melbourne, Australia)
- BioProcessUK (London, United Kingdom)
- Massachusetts Biotechnology Council (Cambridge, MA)
- NC Biotechnology Center (RTP, NC)
- Bio-Process Systems Alliance (BPSA, Washington, DC)
- Strategic Manufacturing Worldwide, Inc. (CA)

To ensure global coverage for this project, this year we invited major media sponsors to support our outreach to biopharmaceutical decision-makers. This year, our media sponsors helped ensure broad and representative coverage of industry participation:

- BioProcess International, (Westborough, MA)
- Bioprocessing Journal (Williamsburg, VA)
- Biopharm Insight (Norwood, MA)
- Biopharm International (Iselin NJ)
- Contract Pharma, (Ramsey, NJ)
- CanBiotech (Mississauga, Canada)
- Genetic Engineering News (New Rochelle, NY)
- Media Gen
- Pharmaceutical Manufacturing (Itasca, IL)
- Pharmaceutical Technology (Iselin, NJ)

The early participation of our authors and sponsors in evaluating the areas and trends to be surveyed this year ensured the project was designed to cover the most relevant issues in biopharmaceutical manufacturing today. Their support was, again this year, critical to the success of the project.

Eric S. Langer
Editor

ABOUT BIOPLAN ASSOCIATES, INC.

BioPlan Associates, Inc. is a biotechnology and life sciences market analysis, research, and publishing organization. We have managed biotechnology, biopharmaceutical, diagnostic, and life sciences research projects for companies of all sizes since 1989. Our extensive market analysis, research and management project experience covers biotechnology and biopharmaceutical manufacturing, vaccine and therapeutic development, contract research services, diagnostics, devices, biotechnology supply, physician office labs and hospital laboratory environments.

We prepare custom studies, and provide public information our clients require to make informed strategic decisions, define objectives, and identify customer needs. With market information, our clients are better able to make informed, market-based decisions because they understand the trends and needs in high technology industries.

BioPlan Associates, Inc.
2275 Research Blvd., Suite 500
Rockville, MD 20850 USA
www.bioplanassociates.com
Tel: 301-921-5979

EDITOR:

Eric S. Langer, MS, President, BioPlan Associates, Inc.

Mr. Langer is President and Managing Partner and President of BioPlan Associates, Inc. a biotechnology and life sciences consulting company that has been providing management and market strategy services, and technology analysis to biopharmaceutical and healthcare organizations since 1989. He has over 20 years experience in biotechnology and life sciences management and market assessment. He is an experienced medical and biotechnology industry practitioner, strategist, researcher, and science writer. He has held senior management and marketing positions at biopharmaceutical supply companies. He teaches Biotechnology Marketing, Marketing Management, Services Marketing, Advertising Strategy, and Bioscience Communication at Johns Hopkins University, American University, and lectures extensively on pricing and channel management topics. Mr. Langer has a degree in Chemistry and Masters in International Business. He has written and consulted extensively for companies involved in: large scale biopharmaceutical manufacturing, global biotechnology in China, Asia, and the Middle East; he has expertise in cell culture markets, media, sera, tissue engineering, stem cells, diagnostic products, blood products, genetics, DNA/PCR purification, blood components, and many other areas.

ABOUT THE AUTHORS (ALPHABETICAL)

E. Faye Coggins, Founder and Principal of BioTraction Associates, LLC

Ms. Coggins has over 30 years experience in life science companies at executive level positions in both the diagnostics and biotechnology markets. She has extensive experience in management, business, marketing, sales, new product development and organizational coaching and development in life sciences companies. Ms. Coggins has held positions as VP Marketing for Fisher Biosciences LSR Division, Executive Director of Marketing, North America, QIAGEN Inc., Vice President of Marketing and Sales at Cylex, Inc. a venture based company focused on immune cell function; and Vice President of Worldwide Marketing at Life Technologies, Inc. In addition, Ms. Coggins has held several senior level business, marketing and sales positions, the last being Marketing Director of New Product Development at DuPont in its \$1 Billion Medical Products Division (now Siemens). Ms. Coggins received a B.S. in Medical Technology from East Carolina University and holds a MT (ASCP) certification. She has received special training in Marketing Management from Columbia University and Strategic Planning from the Wharton School of Business. In addition Ms. Coggins served as President Elect, President, and Past President of the Clinical Laboratory Managers Association (CLMA) from 1995-2001.

Alfred C Dadson Jr, Sr Director, Manufacturing Operations, XOMA LLC

Al has been with XOMA for over 7 years and is currently Sr Director, Manufacturing Operations of antibodies and proteins production. He has over 26 years of biotechnology experience with 20 years at Bayer Healthcare where he played a key role in the development of several biotechnology products including Kogenate®. While at Bayer Healthcare, he held positions from R&D to technology development. At Bayer Healthcare, Al was a Sr Staff Scientist/Manager of the Process Sciences Clinical Fermentation group.

David G. Jensen, Managing Director

Mr. Jensen has more than 25 years experience in executive search for biotechnology, pharmaceuticals, research products, medical devices, nutraceuticals, and academic research. He is the founder and former CEO of two executive search firms focused on life sciences -- Search Masters International (now a part of a \$4.4 billion human resources organization) and CareerTrax Inc. Prior to 1985, Jensen established a life sciences practice for a leading Arizona search firm. His monthly column "Managing Your Career" has been a visible part of the biotech industry for nearly twenty years and is now in each issue of Contract Pharma where Jensen is Contributing Editor. A popular speaker at biotechnology events, Jensen has delivered keynote presentations or workshops for NIH, the EPA, Karolinska Institute, Princeton, Harvard, and regional affiliates of BIO, such as MassBio, SoCalBio and BayBio. For more than a decade, Mr. Jensen has authored a popular monthly column for scientists at the AAAS website, publishers of SCIENCE. Phoenix, Arizona USA djensen@krsearch.net; (928) 274-2266; www.krsearch.com.

Vladimir Kostyukovsky, Sr. Technical Manager, Kymanox

Vladimir is leading Kymanox's Process Operations services. Prior to joining Kymanox, he served as a Sr. Director of Manufacturing with Artisan Pharma and worked as Director of Site Operations at BTEC which he helped design, build and start-up. Dr. Kostyukovsky worked as Director of Bioprocessing with Biolex in Pittsboro, NC, where he managed GMP and pre-clinical material manufacturing operations for a number of therapeutic proteins in transgenic plant system. Vladimir also managed contract manufacturing of viral vaccines and vectors at Bioreliance in Rockville, MD and served as Associate Director of Cell Culture with Diosynth (RTP). He also managed Cell Culture and Fermentation at DSM Biologics in Montreal, Canada and worked on developing recombinant protein processes at Allelix Biopharmaceutical (Toronto, Canada). Dr. Kostyukovsky worked for a number of Research Organizations in Russia, Czech Republic and Japan. He received Masters Degree in Animal Science from Ryazan School of Agriculture, Russia, and a Ph.D. degree in Microbiology from the Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences. www.kymanox.com

Geoff Hodge, Vice President, Process Development and Technology, Xcellerex

Geoffrey Hodge is Vice President, Process Development and Technology at Xcellerex, a contract manufacturing and development company based in Marlborough, Massachusetts. He is responsible for process development and the identification, development and integration of new technologies into the Xcellerex technology platform. Prior to joining Xcellerex, Mr. Hodge was Associate Director of Process Development at Millennium Pharmaceuticals, Cambridge, MA, with responsibility for the process development and clinical manufacturing of Millennium's biologics pipeline. In this role he pioneered the use of disposable manufacturing systems for the production of monoclonal antibodies and helped to develop a novel manufacturing platform and many of the high-throughput process development technologies subsequently licensed to Xcellerex. Mr. Hodge has also held positions in commercial manufacturing as Manufacturing Section Head at Genetics Institute (now Wyeth BioPharma), Andover, Massachusetts, and various management positions in process development, clinical manufacturing, manufacturing and validation at Alpha- Beta Technology, Worcester, Massachusetts. Mr. Hodge received his B.A. in Biology from Colgate University, and his M.S. in Biotechnology from Worcester Polytechnic Institute.

Stephen M. Perry, President, Kymanox

Stephen M. Perry is the founder of Kymanox – which helps biotechnology, pharmaceutical, and medical device companies achieve mission critical objectives. He has overseen the development of Kymanox's product offerings including CMOLocator™ – a search engine for biopharma CMOs, KymaPRO™ – a secure project website solution, and KymaSTORE – an online marketplace to download templates, procedures, and training packages. Stephen has extensive cGMP experience as a process engineer, technical project manager, quality manager, and regulatory advisor. Before starting Kymanox in 2004, Stephen had various leadership roles supporting scale-up, start-up, and commercialization initiatives at Abbott Laboratories, Covance Biotechnology Services, Diosynth Biotechnology, and Human Genome Sciences. Stephen has a bachelor's degree in Chemical Engineering from the University of Notre Dame and studied at the graduate level at Purdue University. Stephen is member of the ISPE and PDA, and is an industry trainer in several subject areas and speaks regularly at industry events throughout the country. 847-239-2710 Email: stephen.perry@kymanox.com

John L. Quick, MBA, Quick & Associates, Inc.

Over 44 years experience in the FDA regulated industry with extensive product development, manufacturing, quality and regulatory compliance experience. Undergraduate degree in Chemistry, MBA from Northwestern Kellogg School of Management. Involved in all FDA regulatory compliance and quality system matters. Thirty-seven years experience at Baxter International, Inc. running large medical device and drug related product development functions, and Quality/Regulatory Compliance. Responsible for 3500 quality professionals worldwide with over 150 operations; responsible for Corporate Sterility Assurance function and Quality Audit Process; Initiated Quality

Institute and Six Sigma Certified Engineer processes. As an independent consultant for quality/regulatory compliance, special emphasis is on solving problems for firms. Projects include API Mab Pre-approval inspection, adverse FDA inspections in preparing systematic approach to quality systems; 510(k) submissions. Career includes numerous presentations and patents. Quick & Associates, Inc. Genoa City, WI (847) 275-8770, JohnLQuick1@aol.com.

Ronald A. Rader, President, Biotechnology Information Institute

Mr. Ronald A. Rader has been President of his own publishing/consulting company, the Biotechnology Information Institute, since late 1990. Mr. Rader has a B.S. (Microbiology), M.L.S. (Library/Info. Sci.), and 30 years experience as a biotechnology and pharmaceutical information specialist, author, publisher and consultant. He is a world-class expert in biotechnology and pharmaceutical information, competitive intelligence, technology and market assessments, and information resources development; and concerning biopharmaceutical products and the industry Mr. Rader is author and publisher of BIOPHARMA: Biopharmaceutical Products in the U.S. and European Markets, reference concerning biopharmaceuticals. Mr. Rader is the Editor of Biopharmaceuticals, a new peer-reviewed periodical from Landes Biosciences concerning biopharmaceutical products. He also authored Biopharmaceutical Expression Systems and Genetic Engineering Technologies: Current and Future Manufacturing Platforms.

Rowena L. Roberts, PhD, Founder and Principal Biotraction Associates, LLC

Dr. Roberts has over 25 years of management experience in the life science research, medical device, and food diagnostics markets. Her experience includes marketing, product management, new product development, strategic planning, R&D management, basic and applied research, and market research. Dr. Roberts has held positions as Director of Marketing and Sales at BioInformatics, a market research consultancy, Senior Director of Marketing and R&D at KPL, Inc, a company specialized in antibodies and protein detection, Business Director at IGEN (now part of Roche Diagnostics) with responsibility for development of a food pathogen detection business, Product Line Business and Marketing Manager at Life Technologies (now Invitrogen) managing core molecular biology products, and Commercial Development Manager for biomedical products for the National Medical Care subsidiary (now Fresenius Medical Care) of W. R. Grace. Dr. Roberts holds a Ph.D. in Microbiology from the University of Texas and an M.B.A. in Marketing from the University of Maryland.

Abdul Wajid, Ph.D., Sr. Director, Process Sciences XOMA (US) LLC (Berkeley, CA)

Dr Wajid has been working for XOMA for the last eight years directing Fermentation development, Media development and Purification development processes with additional responsibility of scale-up and process transfer to Manufacturing. Wajid, has over 20 years experience in all facets of biologics development including clinical and commercial manufacturing. Prior to joining XOMA, he worked at Aventis Pasteur (Toronto, ON) as an Associate Director, Bacterial Manufacturing Operation, responsible for scale-up and manufacturing of Component Pertussis subunit vaccine.

Scott M. Wheelwright, Ph.D., Founder and Principal, Strategic Manufacturing Worldwide, Inc.

Dr. Wheelwright has over twenty years experience in bringing novel products to market, including new drug applications (BLAs and NDAs) in the US and Japan, numerous investigational applications (INDs) and commercial product launches. Dr. Wheelwright's work experience encompasses pharmaceutical firms and both large and small biotech companies, including Abbott, Chiron, Scios, Calydon, DURECT and Genitope. Dr. Wheelwright received his Ph.D. in chemical engineering from the University of California at Berkeley and continued post-doctoral studies at the Max Planck Institute for Biophysics in Frankfurt, Germany. He is the author of a book on protein purification and has published numerous articles on manufacturing and process development. Dr. Wheelwright's focus is on long-term strategic and near-term planning for development (CMC issues including process development, analytical testing and characterization), manufacturing and facilities. He has lead project teams that have conducted technology transfer within the US and overseas, supervised scale-up at CMOs and managed complex projects involving multiple outsource vendors.

7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production • April 2010

*A Study of Biotherapeutic Developers and Contract
Manufacturing Organizations*

CONTENTS

Overview	xxiii
Market Trends	xxiii
Market Potential	xxv
Methodology	xxvii
CHAPTER 1: Introduction and Discussion	1
Introduction.....	1
1-1 U.S. and World Biopharmaceutical and Recombinant Protein/Mab Markets	5
World Markets for Biopharmaceuticals	9
Analysis of Biosimilars	11
1-2 Expression Systems in Biopharmaceutical Manufacturing	14
1-3 Continuing Need for Production Improvements and Cost Containment	15
Biotherapeutic Developers.....	15
CMOs.....	16
Industry Suppliers	16
Government	16
CHAPTER 2: Demographics	17
Respondents' Area of Involvement	17
Respondents' Titles.....	19
Respondents' Facility Locations.....	20

Respondents' Areas of Biopharmaceutical Manufacturing Operations	22
Respondents' Production Operations, Phase of Development	23
Employees at Facility	24
Batches Run at Facility Per Year	25

CHAPTER 3: Emerging Issues in Biopharmaceutical Manufacturing 27

3-1 Budget Issues in 2010	27
Budget Change Comparisons	30
3-2 Operational Changes in 2010	32
Operational Changes: Biotherapeutic Developers vs CMOs	34
Operational Changes: Biotherapeutic Developers vs CMOs	35
3-3 New Product Development Opportunities in 2010	36
New Product Development Areas: Biotherapeutic Developers vs CMO's	38
New Product Development Areas: Biotherapeutic US vs Western Europe and ROW	40
3-4 Factors in Biomanufacturing Creating Improvements	42
Factors Improving Biomanufacturing Performance, Biotherapeutic Developers vs CMOs	43
Factors Improving Biomanufacturing Performance, US vs Western Europe, vs ROW	45
3-5 Perfusion Operations Issues	47
3-6 Discussion: Industry Trends and Issues	49
Budget Shifts	49
Maturing Internal Resources Strategies	49
Industry Growth and Adaptation	50

CHAPTER 4: Capacity Utilization 53

4-1 Capacity Utilization Trends	53
Capacity Utilization Definitions	53
Relevance of Capacity Utilization	54
Capacity Utilization in 2009	55
Capacity Utilization Changes Since 2003	56
Average Growth Rate in Capacity Utilization, 2005-2009	58
4-2 Capacity Utilization: CMOs vs. Biotherapeutic Developers	59
4-3 Capacity Utilization: US vs. Western European Manufacturers	61
4-4 Respondents' Current Total Production Capacity	62
Mammalian Cell Culture	62
Estimated Bioreactor Capacity Distribution, Biotherapeutic Developers and CMOs	64

Contract Manufacturing.....	65
Microbial Fermentation Capacity	67
Yeast Production Capacity	68
Insect Cells Production Capacity	69
4-5 Discussion: Current State of Capacity Utilization.....	70
4-6 Range of Titres for MAb Production	73
Future Capacity Issues	73
Capacity Utilization	76
4-7 Discussion: Capacity and Industry Trends	76

CHAPTER 5: Current Capacity Constraints 77

5-1 Current Capacity Constraints	77
Factors Creating Future Capacity Constraints.....	77
Respondents Experiencing No Capacity Constraints	79
Respondents' Perception of Capacity Constraints, 2003-2009.....	79
Perception of Capacity Constraints: Biotherapeutic Developers vs. CMOs	81
Capacity Constraints: US vs. European Biotherapeutic Developers & CMOs	82
5-2 Expected Capacity Constraints	84
Respondents' Expectations of Capacity Constraints in the Next Five Years	84
Expected Capacity Constraints by 2014: Comparing 2005 to 2009 Data.....	86
Expected Capacity Constraints by 2014: CMOs vs. Biotherapeutic Developers	88
Expected Capacity Constraints by 2014: U.S. vs Western Europe.....	89
5-3 Factors Impacting Future Production Capacity	90
Factors Creating Future Capacity Constraints.....	90
Factors Creating Future Capacity Constraints, 2007 vs 2009	92
Factors Creating Future Capacity Constraints: CMOs vs. Biotherapeutic Developers	94
CMO's Capacity Bottleneck Projections, in Retrospect	94
Biotherapeutic Capacity Bottleneck Projections, in Retrospect	95
Factors Creating Capacity Constraints: US vs. Western European Respondents.....	98
5-4 Key Areas to Address to Avoid Future Capacity Constraints.....	100
Avoiding Capacity Constraints	101
Analysis of Areas to Avoid Capacity Constraints: Changing Perspectives, 2005-2009.....	102

Key Areas to Address to Avoid Capacity Constraints:
U.S. vs Western Europe 108
5-5 Discussion 110

CHAPTER 6: Future Capacity Expansions 113

6-1 Planned Future Capacity Expansions 113
Planned Future Capacity Expansions, 2009 vs. 2014 116
Planned Future Capacity Expansions by 2014;
CMOs vs. Biotherapeutic Developers 117
Planned Five-Year Capacity Expansions;
US vs. Western European Manufacturers 119
Planned Future Capacity Expansions of >100%..... 121

CHAPTER 7: Outsourcing Trends in Biopharmaceutical Manufacturing .. 123

Why Outsource? 123
New Outsourcing Process & Risk Analysis 124
7-1 Current Outsourcing, by Production System 125
Summary of Findings: 125
Facilities Currently Outsourcing No Production
(All Production “In-house”), 2005-2009 127
7-2 Future Outsourcing..... 129
Biotherapeutic Developers’ Outsourcing, 2014 Projections,
by System..... 129
Outsourced Activities in Biopharmaceutical Manufacturing 133
Increased Outsourced Activities, 24-month Projections 135
Average Percentage of Activities Outsourced Today 137
7-3 Critical Outsourcing Issues..... 140
Selecting a CMO: 2009..... 140
Selecting a CMO, 2005-2009..... 143
Summary of Trends: 143
Changes in Critical Issues when Considering a CMO, 2005-2010 145
CMOs’ Problems with Clients..... 147
7-4 Country Selections for International Outsourcing..... 149
Country Selections for International Outsourcing of Biomanufacturing . 149
US vs Western European Respondents’ Outsourcing Destinations 151
Western European Respondents’ Outsourcing Destinations 154
Future of Outsourcing 158
7-5 Discussion 157

CHAPTER 8: Disposables and Single-Use Systems in Biopharmaceutical Manufacturing 161

8-1 Use of Disposables and Single-Use Systems	161
Disposables Applications in Biopharmaceutical Manufacturing	161
Trends in Disposable Applications: 2005-2009	163
Annual Growth Rate for Disposables Market Penetration / Usage	165
5-year Growth in Disposables Applications, Percentage-point Gains	168
Disposable Use by Stage of Production/Application	169
Newly Introduced Disposable Applications	172
Downstream Operations That Are Currently 100% Disposable	175
Leachables and Extractables.....	178
Cost Conscious L&E Testing.....	178
Use of Disposables: CMOs vs. Biotherapeutic Developers	180
8-2 Reasons for Increasing Use of Disposables & Single-Use Systems ...	183
Reasons for Increased Use of Disposables, 2005 through 2009.....	185
Summarizing trends:	185
Reasons for Increased Use of Disposables: Biotherapeutic Developers vs CMOs	188
Single Most Critical Reason for Increasing the Use of Disposables	191
Factors That May Restrict Use of Disposables: Trends 2005-2009.....	195
Factors that May Restrict Use of Disposables: CMO's vs. Biotherapeutic Developers	197
Most Critical Reasons for Restricting Use of Disposables.....	200
Most Important Reasons for Not Increasing Use of Disposables, 2008-2009.....	202
Top Reasons for Not Increasing the Use of Disposables: US vs. European Respondents	204
Most Important Reasons for Restricting Use of Disposables: Biotherapeutic Developer vs CMO	207
8-4 Current Spending on Disposable Systems.....	209
Budgets for on Disposable Systems, 2006-2009.....	211
Annual Growth Rate in Budgets for Single-use Components 2007-2010.....	213
1-year Change in Budgets for Single-use Components 2008-2010 Budget Year.....	215
Current Budget for Disposables: CMO's vs. Biotherapeutic Developers	216
8-5 Disposable Bioreactor Attributes	220
Waste Disposal of Single-use Devices	223
Single-Use Waste Disposal, U.S. vs Western Europe	226

8-6 Satisfaction with Vendors of Disposables for Biopharmaceutical Manufacturing.....	228
8-7 Discussion	231

CHAPTER 9: Downstream Purification233

9-1 Impact of Downstream Processing on Capacity	233
Impact of Downstream Processing on Capacity, Biopharmaceutical Developers vs. CMOs	236
Impact of Downstream Processing on Capacity, US vs. Western European Biomanufacturers.....	237
9-2 Specific Purification Step Constraints.....	238
Changes in Impact on Capacity of Purification Steps, 2007-2009.....	239
Specific Purification Step Constraints, US vs. Western European Biomanufacturers.....	240
9-3 Downstream Purification Issues Facing the Industry Today	242
Protein A and Alternatives	242
Changes in Perception of Protein A and Alternatives.....	243
Protein A Downstream Purification Issues, US vs Western Europe.....	245
9-4 Emerging Problems in Downstream Purification	246
9-5 New Downstream Processing Technologies	249
New Downstream Processing Technologies; Biotherapeutic Developers vs CMOs	252
New Downstream Processing Technologies; US vs Western Europe ...	254
9-6 Discussion	256

CHAPTER 10: Quality Issues, Batch Failures, and PAT in Biopharmaceutical Manufacturing257

Introduction	257
10-1 Process Analytical Technology.....	257
PAT Initiatives for Existing Processes	259
10-2 Hurdles to Implementing Process Analytical Technology.....	261
10-3 Batch Failure Frequency in Biopharmaceutical Manufacturing	263
10-4 Primary Cause of Batch Failures and Percentages of Failures	265
10-5 Quality Problems Traced to Vendors in BioManufacturing.....	268
10-6 Automation Implementation.....	270
Comparison of Implementation Plans 2008 vs 2009	272
10-7 Automation Impact on Production	273

10-8 “Quality By Design” Initiative Implementation	276
Quality Initiatives, Current and Within-the-Year	279
Comparison of Quality Initiative Implementation, 2008 vs 2009	281
10-9 Measuring Supplier Quality.....	282
Quality Factors Comparing CMOs and Biotherapeutic Developers.....	282

CHAPTER 11: Hiring, Employment Growth, and Training in Biopharmaceutical Manufacturing285

Introduction	285
11-1 Hiring in 2010.....	286
11-2 Hiring in 2014.....	287
11-3 Hiring Challenges Today.....	288
Hiring Difficulties, Comparison US vs W. Europe	291
11-4 Formal Education Requirements in Biopharmaceutical Workforce ...	294
Level of Biopharmaceutical Workforce Education, 2006 vs. 2011 Estimate	294
11-5 Training in Biopharmaceutical Manufacturing.....	295
11-6 Discussion	297

CHAPTER 12: Suppliers to Biopharmaceutical Manufacturing and Life Sciences299

Introduction	299
12-1 Demographics	299
Areas of Involvement	299
Vendors’ Years in Biopharmaceuticals Business	301
Location of Vendor Sales	302
Comparison of Vendors’ Export Business.....	303
Respondents’ Primary Job	305
12-2 Growth Rate of Sales by Suppliers	306
Average Industry Growth Rate, Distribution.....	306
Average Industry Growth Rate, By Segment	307
Vendor Sales Growth Rate, by Industry Segment, 2006 to 2009	308
Overall Vendor Sales Growth, 2006-2009	309
Vendor Annual Sales, Distribution.....	310
12-3 Discussion: Industry Growth Rates.....	311
12-4 Budget Issues and Problems Faced by Industry Supplier.....	312
Budget Challenges in 2010.....	312
Vendor Average Budget Changes for 2010 vs 2009.....	313

Vendor Pricing Changes	314
Projected Price Changes for 2010	315
CMO Price Changes	317
12-5 Problems Faced by Vendors.....	319
Sales Reps' Problems.....	320
Problems of Vendors in US and in Europe	321
Problems Faced by Vendors' Clients	322
Quality Measures in Business Relationships	323
Vendor Expansion Plans for 2010.....	325
12-6 Discussion: Supplier Issues	326
12-7 Sales Staff Training	328
Days of Training Provided	328
Areas Where More Training Needed, Sales Staff vs. All Staff	329

FIGURES AND TABLES:

Fig 1.1:	Investigational Drugs: Large Molecule (Protein Therapeutics), Worldwide, March 2010	3
Fig 1.2:	Current Worldwide Pipeline & Launched Products, Large Molecules, March 2010.....	5
Fig 2.1:	Area of Involvement in Biopharmaceutical Manufacturing	18
Fig 2.2:	Respondents' Job Responsibilities	19
Fig 2.3:	Facility Location	20
Fig 2.4:	Facility Location, by Region.....	21
Fig 2.5:	Biopharmaceutical Manufacturing Systems, 2007-2009.....	22
Fig 2.6:	Phase of Development of Surveyed Respondents	23
Fig 2.7:	Distribution of Employees at Facility, and Organization.....	24
Fig 2.8:	Distribution of Total Batches Run at Facility Last Year, by Scale of Production.....	25
Fig 3.1:	Biomanufacturers' Budget Shifts for 2010	28
Fig 3.2:	Approximate Average Change in Biomanufacturers' Budgets for 2010.....	29
Fig 3.3:	Approximate Average Change in Biomanufacturers' Budgets for 2010.....	31
Fig 3.4:	Operational Changes Due to Recent Global Economics	33
Fig 3.5:	Operational Changes Due to Recent Global Economics; Biotherapeutic developers vs CMO's	34
Fig 3.6:	Operational Changes Due to Recent Global Economics; US vs Western Europe	35
Fig 3.7:	New Product Development Focus Areas	37
Fig 3.8:	New Product Development Areas of Interest: Biotherapeutic Developers vs CMO's.....	39
Fig 3.9:	New Product Development Areas of Interest: US vs Western Europe and ROW.....	41
Fig 3.10:	Factors in Biomanufacturing Performance Creating "Significant" or "Some" Improvements.....	42
Fig 3.11:	Factors in Biomanufacturing Performance Creating "Significant" or "Some" Improvements: Biomanufacturers Vs CMOs.....	44
Fig 3.12:	Factors in Biomanufacturing Performance Creating "Significant" or "Some" Improvements: US Vs Western Europe Vs Rest of World	46
Fig 3.13:	Perfusion Operations Issues: Perfusion vs Batch-Fed Processes.....	48
Fig 4.1:	Capacity Utilization, By System, 2009	55
Fig 4.2:	Capacity Utilization, By System, 2003-2009	57
Fig 4.3:	Change in Capacity Utilization, CAGR, 2005-2009	58
Fig 4.4:	Capacity Utilization, By System, Biotherapeutic Developer vs CMOs	60
Fig 4.5:	Capacity Utilization By System, US vs. Western Europe	61
Fig 4.6:	Current Production Capacity Distribution, Mammalian Cell Culture	62
Fig 4.7:	Estimated Bioreactor Capacity Distribution, by Biotherapeutic	

	Developer (2006 vs 2010).....	66
Fig 4.8	Estimated Bioreactor Capacity Distribution, by Contract Manufacturing Organizations (CMO), 2006 vs 2010	66
Fig 4.9:	Current Production Capacity Distribution, Microbial Fermentation.....	67
Fig 4.10:	Current Production Capacity Distribution, Yeast.....	68
Fig 4.11:	Current Production Capacity Distribution, Insect Cells.....	69
Fig 4.12:	Mammalian Cell Culture Capacity Forecast (2003-2010).....	71
Fig 4.13:	Estimated Microbial Fermentation Capacity Forecast (2003-2009).....	72
Fig 4.14:	Range of Titres for Mabs Obtained at Various Production Scales, Distribution	74
Fig 4.15:	Annual Average Mab Titre Increase, 2007-2009	75
Fig 5.1:	Capacity Constraints, by Stage of Production.....	78
Fig 5.2:	Capacity Constraints, 2003 through 2009	80
Fig 5.3:	Capacity Constraints, Biotherapeutic Developers vs CMOs.....	81
Fig 5.4:	Capacity Constraints, US vs. Europe.....	83
Fig 5.5:	Expectations of Capacity Constraints; by Stage of Production; five-year Projections.....	85
Fig 5.6:	Expectations of Capacity Constraints: Five-year Projections Made in 2003-2009	87
Fig 5.7:	Five-year Projections for Capacity Constraints: Biotherapeutic Developers vs CMOs.....	88
Fig 5.8:	Five-year Projections for Capacity Constraints: US vs Western Europe	89
FIG 5.9:	Factors Creating Future Capacity Constraints	91
FIG 5.10:	Factors Creating Future Capacity Constraints, 2007-2009.....	93
Fig 5.11:	Factors Creating Future Capacity Constraints, CMOs vs Biotherapeutic Developers	96
Fig 5.12:	Factors Creating Future Capacity Constraints, US vs Western European Biomanufacturers.....	99
Fig 5.13:	Key Areas to Address to Avoid Capacity Constraints	101
Fig 5.14:	Key areas to Address to Avoid Capacity Constraints; 2005-2009.....	103
Fig 5.15:	Key areas to Address to Avoid Capacity Constraints; Biomanufacturers vs CMOs	106
Fig 5.16:	Key areas to Address to Avoid Capacity Constraints; U.S. vs Western Europe	109
Fig 6.1:	Industry Average Planned Production Increase by 2014	115
Fig 6.2:	Planned Future Capacity Expansion: 5-year Estimates, 2009 through 2014.....	116
Fig 6.3:	Planned Future Capacity Expansion: 5-year Estimates; Biotherapeutic Developers vs CMOs.....	118
Fig 6.4:	Planned Future Capacity Expansion: 5-year Estimates, 2009 through 2014, US vs Western Europe.....	120

Fig 6.5:	Percent of Respondents Projecting Production Increases of over 100% by 2014; 3-year Comparison	121
Fig. 7.1:	Current Percent Production Outsourced; by System, 2009	126
Fig 7.2:	Biopharmaceutical Manufacturing Facilities Outsourcing NO Production, 2005-2009	128
Fig 7.3:	Future Outsourcing: Percent Production Outsourced; by System, in 2014.....	130
Fig 7.4:	Five-year Projections: Percent Biotherapeutic Developers Planning to Outsource at Least <i>Some</i> Production; Projections made 2006-2009	132
Fig 7.5:	Percent of Biomanufacturers Outsourcing <i>at Least Some</i> Activity Today	134
Fig 7.6:	Outsourcing Activities Projected to be Done at 'Significantly Higher Levels' in 2 Years.....	136
Fig 7.7:	Current Outsourcing: Average Percentage of Activity Outsourced Today	138
Fig 7.8:	Outsourcing Issues: BioManufacturing by Contract Manufacturing Organizations.....	141
Fig 7.9:	Important Outsourcing Issues: BioManufacturing by Contract Manufacturing Organizations, Trends 2005-2009.....	144
Fig 7.10:	Important Outsourcing Issues: Response Shifts Over Time 2005-2009, percentage point differences.....	145
Fig 7.11:	Most Common Mistakes Biopharmaceutical Sponsors Make with their CMOs.....	148
Fig 7.12:	Country Selections as Destination for International Outsourcing of BioManufacturing (All Respondents).....	150
Fig 7.13:	Percent U.S. Respondents Considering Country as 'Possible' Outsourcing Destination.....	152
Fig 7.14:	Percent Western European Respondents Considering Country as 'Possible' Outsourcing Destination.....	155
Fig 8.1:	Usage of Disposables in Biopharmaceutical manufacturing, any Stage of R&D or Manufacture	162
Fig 8.2:	Usage of Disposables in Biopharmaceutical manufacturing, any Stage of R&D or Manufacture; 2005-2009	164
Fig 8.3:	Average Annual Growth Rate, Disposables, 2005-2009	167
Fig 8.4:	Percentage-Point Increase in Usage of Disposables, 2005-2009.....	168
Fig 8.5:	Usage of Disposables in Biopharmaceutical manufacturing, by Stage of Manufacture (R&D through Commercial Manufacture)	171
Fig 8.6:	Newly Introduced Disposables, Past 12 Months	173
Fig 8.7:	Percent of Downstream Operations 100% Disposable, by Application	176
Fig 8.8:	Current Issues: Leachables and Extractables in Disposable Devices.....	179
Fig 8.9:	Usage of Disposables in Biopharmaceutical Manufacturing; Biotherapeutic Developer vs CMO	181
Fig 8.10:	Reasons for Increasing Use of Disposable System Components in 2010.....	184

Fig 8.11:	Reasons for Increasing Use of Disposables 2005-2009.....	186
Fig 8.12:	Reasons for Increasing Use of Disposable System Components, Biotherapeutic Developers vs CMOs.....	189
Fig 8.13:	Most Critical Reason for Increasing Use of Disposables.....	192
Fig 8.14:	Reasons for Restricting Use of Disposables	194
Fig 8.15:	Factors Restricting Use of Disposables, 2005-2009	196
Fig 8.16:	Factors Restricting Use of Disposables in Biotherapeutic Developer vs CMO.....	198
Fig 8.17:	Top Reasons for Not Increasing Use of Disposables, 2009	201
Fig 8.18:	Top Reasons for Not Increasing Use of Disposables, 2007-2009	203
Fig 8.19:	Top Reasons for Not Increasing Use of Disposables, U.S. vs Western Europe	205
Fig 8.20:	Top Reasons for Not Increasing Use of Disposables, Biotherapeutic Developer vs CMO.....	208
Fig 8.21:	Average Budget Per Facility, Single-use Disposable System Components.....	210
Fig 8.22:	Average Budget, Single-use Disposable System Components, 2007 vs 2010.....	212
Fig 8.23:	CAGR: Growth Rate in Budget on Single-use / Disposable System Components 2007-2010 (by device)	214
Fig 8.24:	1-Year Percent Change in Budget for Single-use / Disposable System Components; 2010 Budgets	215
Fig 8.25:	Average Disposables Budget Per Facility, Disposable Systems; Biotherapeutic Developers vs CMOs	217
Fig 8.26:	Disposable Bioreactor Attributes Considered “Very Important”	221
Fig 8.27:	Disposable Bioreactor Attributes Considered “Very Important”, 2008 vs 2009.....	222
Fig 8.28:	Impact of Waste Disposal for Disposables	225
Fig 8.29:	Select Comments Regarding Waste Disposal for Disposables; U.S. vs Western Europe	226
Fig 8.30:	Single-Use Product Vendor Satisfaction Factors	229
Fig 9.1:	Impact of Downstream Processing on Overall Capacity	234
Fig 9.2:	Impact of Downstream Processing on Overall Capacity; Biotherapeutic Developers vs CMOs	236
Fig 9.3:	Impact of Downstream Processing on Overall Capacity; U.S. vs Western Europe	237
Fig 9.4:	Impact on Capacity of Depth, Chromatography and UF Purification Steps.....	238
Fig 9.5:	Impact on Capacity of Purification Steps: Experiencing at “Significant” or “Severe” Constraints, 2007 - 2009.....	239
Fig 9.6:	Impact on Capacity of Purification Steps, U.S., vs Western Europe.....	240
Fig 9.7:	Issues Regarding Protein A Usage	242
Fig 9.8:	Issues Regarding Protein A Usage, 2008 vs 2009	243

Fig 9.9:	Issues Regarding Protein A Usage; US vs. Western Europe.....	245
Fig 9.10:	Problem Areas in Downstream Operations, 2007 vs 2009	247
Fig 9.11:	New Downstream Processing Solutions in 2010.....	250
Fig 9.12:	New Downstream Processing Solutions in 2010; Biotherapeutic Dev. vs CMO	253
Fig 9.13:	New Downstream Processing Solutions in 2010; US vs Western Europe .	255
Fig 10.1:	Implementation of Process Analytical Technology (PAT): New vs Existing Biomanufacturing Processes.....	258
Fig 10.2:	Implementation of Process Analytical Technology (PAT) for New Biomanufacturing Processes, 2008 vs 2009	259
Fig 10.3:	Hurdles Hindering Implementation of PAT	261
Fig 10.4:	Batch Failure Frequency	263
Fig 10.5:	Average Rates of Failure, by Primary Cause, and Phase of Manufacture, 2009	265
Fig 10.6:	Average Rates of Failure, by Primary Cause, and Phase of Manufacture, 2008	266
Fig 10.7:	Quality problems traced to vendors.....	269
Fig 10.8:	Automation Technologies Implemented, or to be I mplemented in 2010	271
Fig 10.9:	Automation Technologies to be Implemented; Comparing 2008 vs 2009.....	272
Fig 10.10:	Automation technologies, once fully implemented, that will have greatest impact on production efficiency.....	273
Fig 10.11:	Quality Initiative Implementation Problems	277
Fig 10.12:	Quality Initiative to be Implemented in Next 12 Months	280
Fig 10.13:	Quality Initiative to be Implemented in Next 12 Months, Comparing 2008 vs 2009.....	281
Fig 10.14:	Factors Used to Measure Quality of Suppliers	283
Fig 11.1:	New Hires in Biopharmaceutical Manufacturing (2010)	286
Fig 11.2:	New Hires in Biopharmaceutical Manufacturing (2014)	287
Fig 11.3:	Areas Where Hiring Difficulties Exist in Biopharmaceutical Operations....	289
Fig 11.4:	Areas Where Hiring Difficulties Exist in Biopharmaceutical Operations, US vs Western Europe	292
Fig 11.5:	Comparison of Percent of Workforce with Specific Education Levels (2006 Data)	294
Fig 11.6:	Training for New Operations/Manufacturing Employees	296
Fig 11.7:	Changes in Training for New Operations/Manufacturing Employees	296
Fig 12.1:	Area of Biopharmaceutical Involvement, Vendor.....	300
Fig 12.2:	Vendors' Years in Business Supplying Biopharmaceutical Industry	301
Fig 12.3:	Geographic Locations in which Vendors Currently Actively Sell Products or Services.....	302
Fig 12.4:	Geographic Sales Regions, US Respondents.....	303

Fig 12.5: Geographic Sales Regions, W. European Respondents	304
Fig 12.6: Respondents' Primary Job Function	305
Fig 12.7: Biopharmaceutical Supply Market Segment Sales Growth Distribution	306
Fig 12.8: Average Annual Vendor Segment Sales Growth Rates, 2009	307
Fig 12.9: Average Annual Vendor Sales Growth Rate, 2006 – 2009, by Segment ...	308
Fig 12.10: Average Annual, Vendor Sales Growth Rate, 2006 – 2009.....	309
Fig 12.11: Vendors' Approx Annual Sales to Biopharmaceutical Segment %.....	310
Fig 12.12: Vendors' Average Budget Change for 2010	312
Fig 12.13: Vendors' Average Budget Change for 2010 vs 2009, Summary	313
Fig 12.14: Vendors' Average Pricing Changes in 2009	314
Fig 12.15: Vendors' Average Pricing Changes, 2009 Actual, 2010 Projected	315
Fig 12.16: CMOs Service Price Shifts in 2010, Distribution	317
Fig 12.17: Average CMOs Service Price Shifts in 2010.....	318
Fig 12.18: Problems Faced by All Suppliers	319
Fig 12.19: Problems Faced: Sales Reps Only	320
Fig 12.20: Problems Faced by Suppliers; U.S. vs Western Europe.....	321
(Fig 10.7 Recap): Biomanufacturers' and CMOs Quality Problems Traced to Vendors	322
Fig 12.21: Overall Quality Measures for Business Relationships.....	323
Fig 12.22: Vendor Expansion Activities in 2010 within biopharmaceutical manufacturing	325
Fig 12.23: Days of Sales Staff Training Provided	328
FIG 12.24: Areas Where Training May Help Sales Staff Perform Better	329

TABLES

Table 1.1 Biologics (Large Molecule), Worldwide, through March 2010.....	2
Table 1.2 Summary All Therapeutics vs Biologics (Large Molecule), Worldwide, through March 2010 (Comparing 2008-2010)	4
Table 1.3 Worldwide Pipeline, Large Molecules, 2010.....	4
Table 1.4 Worldwide Biopharmaceutical Revenue by Product Class, 2007 and 2009 estimates.....	7
Table 1.5 Biopharmaceutical Blockbusters: >\$1 billion revenue, and Expression Systems/Host Cells.....	7
Table 1.6 Biopharmaceutical Markets, U.S. & EU – Products and Revenue by Class, 2009	10
Table 1.7 Expression Systems/Hosts for U.S./EU Marketed Recombinant Proteins/mAbs.....	13
Table 7.1 Percent of US-based Respondents Indicating Country as Likely Outsourcing Destination	153

OVERVIEW

Market Trends

The biotech industry is starting the new decade with good reason for cautious optimism. Based on results from this study of biomanufacturing, most companies are more confident, but also more realistic: Even as 2010 brings good results, managers are continuing to expect better performance from their staff, and are implementing strategies for reducing costs, improving management of outsourcing relationships, and managing costs more closely. Some of last year's budgetary shifts are becoming solid trends that are defining how biopharma will evolve over the coming years. Key developments in 2010 will include advances in science, technology, the economy and regulations:

- **Biopharmaceuticals:** Biologics are recognized as increasingly important to the pharmaceutical industry. The number and percentage of biopharmaceuticals and the contributions of these to the profits of the pharmaceutical industry will continue to increase. Increased investment in biopharmaceutical R&D makes sense, with these products the source for profits, especially as loss of patent protecting and generic competition erode mainstream pharmaceutical industry profits.
- **Biopharma Approvals:** 2010 will see an increased number of biopharmaceuticals entering major markets. FDA approvals of biopharmaceuticals increased in 2009, reversing a trend of low and decreasing numbers. Over 60 biopharmaceutical products currently have applications either pending or expected to be filed in 2010, joining over 335 currently approved by FDA¹. Many of these will receive prompt approvals.
- **Biosimilars are coming!** Legislation enabling abbreviated, comparisons-based, FDA approvals pathway for biologics will be enacted. Although it will take several years for FDA to fully implement related regulations, with the U.S. market more receptive to biosimilars and other me-too products, there will be a significant increase in the number of biosimilars in development and companies entering this field. Biosimilars will expand the number of companies active in R&D and manufacture. This will include an increasing number of foreign companies, many based in developing countries, seeking to develop biosimilars for the U.S. market.
- **Cost-containment:** Governments in the U.S. and other major pharmaceutical markets will continue efforts to reduce costs. This will increasingly involve integration of cost-effectiveness assessments in approval and insurance coverage decisions, including U.S. health care delivery regulators (CMS) increasingly getting involved. Therapeutics will increasingly need to show improvement and cost-savings relative to competing products.

¹ Source: www.biopharma.com/approvals_2009.html

- **Bioprocessing:** Many recent trends in bioprocessing, particularly biopharmaceutical manufacturing, will continue. Companies will continue to invest in expansion of manufacturing capacity, with increasing attention and investments being made to resolve bottlenecks in downstream purification. Experienced bioprocessing professionals will be in increasing demand in 2010, as senior staff (baby boomers) start to retire.
- **Bioprocessing technologies:** Cost-containment will continue to drive progress, led by the increasing adoption of new technologies, improved yields from upstream processing, and better expression systems, host cells and genetic engineering technologies for large-scale manufacture that will improve not only manufacturing processes, but quality, and even clinical performance. Upstream expression yields will continue to increase, along with the concurrent problems with downstream purification as it struggles to keep up.
- **Industry consolidation:** Merging and purging among companies will likely increase. Larger companies, particularly Big Pharma with ailing R&D pipelines, will continue to acquire smaller firms and merge among themselves, along with consolidation, post-merger downsizing and layoffs. This has been a short-term fix or distraction for many companies' experiencing problems with internal innovation, particularly the failure to develop new blockbusters needed to replace the many products coming off patent.
- **R&D independence:** While organizational consolidation continues, the trend of large companies seeking to repackage their R&D programs as more independent, entrepreneurial-type efforts will continue. There will be increased questioning of whether consolidation, particularly among large companies, is actually a prudent strategy.
- **Internationalization:** The growth in biotechnology, particularly biopharmaceutical, markets will continue worldwide, with much expansion in China, India, and other rapidly developing countries where middle classes are expanding, and exerting demand through their increasing affluence. Manufacturing capacity and R&D will continue to increase rapidly worldwide, including in developing countries.
- **Economy, spending and outsourcing:** The world economy will continue its slow recovery, while investments in biopharmaceutical manufacturing capacity and R&D continue and increase. Despite this, companies will continue to cut back internally, including outsourcing wherever they can. More, non-critical R&D and manufacturing will be outsourced and offshored or transferred to other countries offering lower labor and other costs. However, we are already seeing a slowing of this trend, as worldwide demand for experienced professionals and increasing growth and affluence in many foreign countries reduce the cost savings from offshoring.

-
- *New technologies in the market:* 2010-2011 could well see the first U.S. and other major market approvals of therapeutic technologies that have been stalled in development, including gene therapy and cancer vaccines. Personalized medicine will continue to advance slowly, with more diagnostics being used to guide selective use of biopharmaceuticals, increasing efficacy for qualifying patients and decreasing overall health care costs.
 - Influenza vaccines: Recent experience with the H1N1 influenza epidemic and vaccines may adversely affect the growth of the market for influenza and, to a lesser extent, other vaccines. With the press, governments and public health establishment having over-stressed (as it may have turned out) the threat from H1N1 influenza and with vaccines arriving late, many will continue to ignore getting vaccinated, and future large-scale public vaccination programs may be more difficult to mount.

Overall, 2010 will be a good year for the biotechnology and biopharmaceutical industries, with these remaining viable, relatively insulated, and in a position for solid future growth.

Market Potential

There are currently nearly 12,000 large molecule biopharmaceuticals in preclinical discovery or clinical trials around the world today. Over 4,600 of these are in clinical development². These biotherapeutics target nearly 150 disease states and promise to bring better treatments to patients. However, new biotherapeutics must increasingly be affordable and cost-effective, with even the U.S. and other affluent countries facing severe problems financing health care delivery. As confirmed by our survey data, the industry clearly recognizes that continual improvements in performance and optimization of manufacturing processes are necessary to achieve this. Besides a more competitive biopharmaceuticals market, with ever more products entering the market, including many biosimilars in coming years, insurers, governments and the public have come to expect streamlining of biopharmaceutical operations. These drugs tend to be the most expensive and also often the most critically-needed of all pharmaceutical products. As the global demand for production of biotherapeutics grows, the question of whether current manufacturing capacity and production performance are sufficient to deal with the challenge and how the industry will adapt and evolve become important strategic issues.

Despite a recent upturn in industry R&D- and manufacturing-related expenditures, including new technologies that are coming online (much of it disposables-based), the global economic situation still poses problems for those involved in biomanufacturing. Financing remains tight, and in the U.S. it is unclear how recently-enacted health care reform will affect the biopharmaceutical industry, whether sales will increase due to wider insurance reimbursement or whether government- and payer-imposed cost constraints and money-saving efforts could lead to decreased sales.

² 2009 Biopharm Insights Data (www.biopharminsight.com)

The continued addition of new capacity and improvements in bioprocessing, including updated and totally new processes, whether through in-house manufacturing or outsourced contract manufacturing, have long-term cost implications. Designing new production facilities, bringing new capacity on line, and establishing new support services continue to become technically more accessible and simpler. However, success increasingly requires more complete and accurate knowledge of the market, along with adequate lead-times, large capital expenditures, and careful planning. This makes accurate market and manufacturing situation assessments and planning all the more essential.

Both biopharmaceutical producers and contract manufacturers need to keep on top of the current status and future trends in industry capacity. This report summarizes information obtained from biopharmaceutical manufacturers worldwide in late 2009 and early 2010. Its intent is to provide a quantitative assessment of industry capacity, production trends, and benchmarks. As an on-going benchmarking effort, this study offers a view into current and future potential global industry bottlenecks and opportunities.

METHODOLOGY

This report is the seventh in our annual evaluations of the state of the biopharmaceutical manufacturing industry. The strength of the methodology remains in its breadth of coverage, which yields a composite view from the respondents closest to the industry. This year, BioPlan Associates, Inc. surveyed 326 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations in 35 countries worldwide; plus 125 industry vendors and direct suppliers of materials, services and equipment to this industry segment. Using a web-based survey tool, we obtained and evaluated information regarding respondents' current capacity, production, novel technology adoption, human resources, quality, and outsourcing issues. We assessed respondents' projected reasons for bottlenecks, and their perception of how these bottlenecks might be resolved.

We brought in experts from the industry to provide in-depth analysis of the events shaping the past year, and the trends that will shape biopharmaceutical manufacturing in 2010-2014. Our subject matter experts include:

- E. Faye Coggins, Founder and Principal of BioTraction Associates, LLC
- Alfred C Dadson Jr, Sr Director, Manufacturing Operations, XOMA LLC
- Geoff Hodge, VP, Process Development & Technology, Xcellerex, Inc.
- David G. Jensen, Managing Director, Kincannon & Reed Global Executive Search
- Vladimir Kostyukovsky, Sr. Technical Manager, Kymanox
- Stephen M. Perry, President, Kymanox
- John L. Quick, Founder & Principal, Quick & Associates, Inc.
- Ronald A. Rader, President, Biotechnology Information Institute
- Rowena L. Roberts, PhD, Founder and Principal Biotraction Associates, LLC
- Abdul Wajid, Ph.D., Sr. Director, Process Sciences XOMA LLC
- Scott Wheelwright, President, Strategic Manufacturing Worldwide

Our partner organizations contributed their time and effort to ensure accurate coverage of the worldwide biopharmaceutical industry:

- BioProcess International, (Westborough, MA)
- Bioprocessing Journal (Williamsburg, VA)
- Biopharm Insight (Norwood, MA)
- Biopharm International (Iselin NJ)
- Contract Pharma, (Ramsey, NJ)
- CanBiotech (Mississauga, Canada)
- Genetic Engineering News (New Rochelle, NY)
- Media Gen

- Pharmaceutical Manufacturing (Itasca, IL)
- Pharmaceutical Technology (Iselin, NJ)

In addition, to ensure our coverage, we include this year our media partners, without whose assistance we would not have as been able to reach the high quality of respondents

- ABO – Alliance of Bio-Box Outsourcing (China)
- AIBA (India)
- Ausbiotech (Australia)
- BayBio (San Francisco, CA)
- Beijing Pharma and Biotech Center (Beijing)
- BioForward (Madison, WI)
- BioMelbourne Network (Melbourne, Australia)
- BioProcessUK (London, United Kingdom)
- Massachusetts Biotechnology Council (Cambridge, MA)
- NC Biotechnology Center (RTP, NC)
- Bio-Process Systems Alliance (BPSA, Washington, DC)
- Strategic Manufacturing Worldwide, Inc. (CA)

The detailed benchmarking information and industry analysis contained here was prepared based on these data, and information from earlier studies. Additional information on methodology, breakouts on specific segments, and data from earlier surveys may be obtained by contacting us at the address below.

Eric S. Langer
President
BioPlan Associates, Inc.
2275 Research Blvd., Suite 500
Rockville, MD 20850
301-921-5979
elanger@bioplanassociates.com
www.bioplanassociates.com

SEVENTH ANNUAL

Report and Survey of Biopharmaceutical Manufacturing Capacity and Production

Another report in the BioPlan Associates, Inc.'s biopharmaceutical series:

- Biopharmaceutical Expression Systems and Genetic Engineering Technologies
- Advances in Biopharmaceutical Manufacturing and Scale-up Production, 2nd Ed, American Society for Microbiology
- Biopharmaceutical Products in the US and European Markets, 6th Ed
- Advances in Biopharmaceutical Technology in China
- Advances in Biopharmaceutical Technology in India
- Top 60 Biopharmaceutical Organizations in China
- Top 60 Biopharmaceutical Organizations in India
- Quick Guide to Clinical Trials
- Quick Guide to Biotechnology in the Middle East
- Quick Guide to Biofuels

The 7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production is the most recent study of biotherapeutic developers and contract manufacturing organizations' current and projected future capacity and production. The survey includes responses from 326 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations from 35 countries. The survey methodology includes input from an additional 125 direct suppliers of raw materials, services, and equipment to this industry. In addition to current capacity issues, this study covers downstream processing problems, new technologies, expression systems, quality initiatives, human resources and training needs of biopharmaceutical manufacturers, growth rates of suppliers to this industry, and many other areas.

April 2010

