

CURRICULUM VITAE

R. BARRY HOLTZ, Ph.D

DATE OF BIRTH: August 31, 1946

EDUCATION: Westminster College
New Wilmington, PA
B.S. in Biology, 1968

Pennsylvania State University
University Park, PA
Ph.D. in Biochemistry/Food Science, 1972

PROFESSIONAL HISTORY AND ACADEMIC POSITIONS:

Present

President/CEO
InterveXion Therapeutics, LLC
Little Rock, Arkansas

2000 – Feb. 2004 Senior Vice President, Biopharmaceutical Development
Large Scale Biology Corporation
Vacaville, California

1995 – 2000 Senior Vice President, Bioprocess Development and Biopharmaceutical
Manufacturing
Large Scale Biology Corporation (Formerly Biosource Technologies),
Vacaville, California

1989 – 1995 Vice President Bioengineering
Biosource Technologies, Vacaville, California
(Holtz Bioengineering acquired by Biosource January, 1989)

1980-1989 President and Director of Research
Holtz Bio-Engineering, Inc.
Morgan Hill, California

1973-1980 Founder and Director, Research and Engineering
MFI, Inc.
San Jose, California

1975-1979 Group Leader, Fundamental Research and
Group Leader, Environmental Research
Foremost Foods Company
Dublin, California

1974-1975 Assistant Professor
Department of Food Science and Nutrition
Ohio State University
Columbus, Ohio

1972-1974 NSF Post-Doctoral Research Biochemist
Scripps Institution of Oceanography
La Jolla, California

1968-1972 National Science Foundation Fellow
and Graduate Research Assistant
Pennsylvania State University

ACADEMIC HONORS AND AWARDS:

Honor Student, Westminster College, 1967-68
Sigma Xi Award for Excellence in Undergraduate Research, 1968
NSF Graduate Fellowship, Pennsylvania State University, 1968-72
NSF Post-Doctoral Research Fellowship, 1972-1974
Gamma Sigma Delta, Agricultural Honorary
Sigma Xi, Science Honorary
Beta Beta Beta, Biological Honorary
The Pennsylvania State University, Award for Outstanding Research, 1972
The Pennsylvania State University Outstanding Alumnus Award 2003
The Armsby Honor Society, Pennsylvania State University, 2004

PROFESSIONAL ORGANIZATIONS:

AAAS
Society for Industrial Microbiology and Biotechnology
Parenteral Drug Association
International Society of Pharmaceutical Engineering

JOB RESPONSIBILITIES:

Holtz Biopharma Consulting

Principal – is responsible for development and execution of consulting projects. Recent projects have been focused in several areas including , patient specific medicine (cancer therapies), metabolic diseases, and global scale vaccine development for emerging countries. The firm and its industry collaborators have recently assisted in the design, construction, validation, and development of quality plans for two patient specific cancer therapy manufacturing facilities. Holtz Biopharma Consulting serves a number of clients in process development, facility design and regulatory issues.

Large Scale Biology Corporation

Senior Vice President, Biopharmaceutical Development – was responsible for the product development of all proprietary biopharmaceutical products. Responsibilities included product development, clinical development, IND management and business development of five major internal drug candidates. Dr. Holtz was responsible for coordinating clinical sites, CRO's, and regulatory consultants and was the primary company fiduciary with regulatory agencies including the FDA and USDA/APHIS. Dr. Holtz

was also a key member of the product development effort and was charged with scientific, business and market analyses of new target therapies and opportunities for the company.

Dr. Holtz managed a group of over 50 scientists and manufacturing personnel and had two vice presidents of the company as direct reports. The company, during this period, completed a successful IPO valued at \$100M. Dr. Holtz was a member of the executive committee and was involved with senior management in the transition of the company from a private entity to a publically held company.

Dr. Holtz was the program director for the development, manufacturing and human clinical testing of a patient specific vaccine for Non-Hodgkin's B-cell lymphoma. This was a collaborative project with Dr. Ron Levy at the Stanford University Medical Center, Department of Oncology. This product was in clinical trials and had advanced to the beginning of a Phase III clinical trial after a successful clinical and CMC review by FDA in a pre-Phase III meeting.

Dr. Holtz was also the program director for the development of therapeutic alpha-galactosidase A, an enzyme replacement therapy. This drug was granted orphan drug designation by FDA and a successful pre-IND meeting was completed. A CRADA with NIH-NINDS and Dr. Roscoe Brady has resulted in the successful pre-clinical evaluation of the drug produced in the Kentucky facility.

Senior Vice President-Bioprocess Development – was responsible for all bioprocess development of products including biopolymers, pharmaceuticals and other complex biomolecules. Included in this responsibility is the successful scale-up of a fermentation process using recombinant DNA to produce melanin biopolymers for topical pharmaceutical use. the design and construction of a GMP-biopharmaceutical for the production of melanin, including the design of the facilities, control systems, bioreactors and downstream processing equipment for Rorer-Rhone Poulenc.

Dr. Holtz was responsible for the group that completed bioprocess development of the Geneware process for extraction and purification of recombinantly produced biomolecules from plants.

Dr. Holtz was also responsible for leading the design team and the construction and validation of the LSBC's 50,000 sq. ft. biopharmaceutical production facility for producing parenteral therapeutics from plants. This is the first facility of its kind ever built and has the capability of producing patient specific vaccines for B cell lymphoma. The large scale extraction capabilities of this facility can process 3000 kg of plant biomass per hour.

Other major projects included the design and construction of a large biopharmaceutical production plant for a major pharmaceutical partner. A state of the art, natural flavor production facility was also designed, constructed and brought into production in a partnership with RJR-Nabisco.

Holtz Bio-Engineering Inc.

President and Director of Research of a consulting bio-technology research laboratory and engineering group whose projects range from fermentation biochemistry, fermentation process control, cell culture bioreactor development and process control, Downstream recovery of biopharmaceuticals and other biochemicals. Food process biochemistry and engineering, removal of toxic chemicals from water, and environmental engineering.

Holtz Bio-Engineering also developed and marketed its own products including the Proteus 2000™ series of fermentation controllers and fermentation equipment. Projects have included the process development for the recombinant DNA production of proprietary CHO cell derived proteins that are currently marketed and production of recombinant enzymes and biopolymers by fermentation and downstream purification to a pharmaceutical raw material by physical and biochemical processes including ultrafiltration. Notable projects included the primary pilot plant for EPO clinical production at Amgen in 1986.

MFI Inc.

Founder and Director of Research and Engineering. Was responsible for basic research on the nutrition of edible fungi. Also responsible for all product and process development in the marketing of a delayed release nutrient for mushroom culture reduced to practice from a Pennsylvania State University patent. Designed and constructed one of the largest microencapsulation facilities in the world. Included was development of fluid systems, particle sizing, design and construction of fluid bed dryers. The microencapsulated product sales returned the highest value royalties in the history of Pennsylvania State University.

Foremost McKesson Inc., Foods Company-Group Leader

Group Leader of Fundamental Research and Group Leader, Water Research. Was responsible for the management of basic food research projects including the modification and production of new food proteins using biochemical modification and isolation by reverse osmosis, ultrafiltration and electro dialysis. As Group leader of Water Research Group was responsible for the Trace Organics Analysis Mass Spectrometry Laboratory and Water Research Engineering Laboratory. This group was later spun off as the McKesson Environmental Division. Was also Technical Manager for the Foremost-McKesson Water division, including Sparkletts and Alhambra bottled water companies. These divisions produced over 50 million gallons of purified water by reverse osmosis-deionization per year. Was responsible for the research and engineering of the Aqua Vend RO system to deionize drinking water and to remove organic compounds on the EPA Priority Pollutant list.

As Group Leader of fundamental research, studies were conducted in to the basic structure of lipase enzymes in casien micelles.

Was also responsible for the research and development efforts of MFI, Inc. whose research and engineering efforts were contracted to Foremost Research Center.

Ohio State University-Assistant Professor

Was responsible for developing and teaching an undergraduate university wide core curriculum course in basic food science and nutrition and conducting competitive grant sponsored research in the areas of marine biochemistry and fungal lipid metabolism. Served as a consultant to the Ralston Purina Co. and Foremost-McKesson Inc.

Scripps Institution of Oceanography-Postdoctoral Fellow-Research Biochemist

Was responsible for conducting independent research in the areas of phytoplankton lipid biochemistry, lipoprotein metabolism of salmonids, analytical biochemistry and electron microscopy of chloroplast membranes. Extensive shipboard studies were conducted.

Pennsylvania State University-Graduate Assistant

Was responsible for directing the activities of the Mass Spectrometry Laboratory in the Department of Food Science, including maintenance, modification, and operation of a GLC-Mass Spectrometer, sample preparation, food and natural products chemistry, and interpretation and publication of spectra.

PATENTS:

Dr. Holtz has been awarded twenty one United States patents in areas of bioprocess development, biosynthesis of small molecules, and biopharmaceutical product and process development.

SELECTED PUBLICATIONS AND INVITED SYMPOSIA:

1. R. Barry Holtz and L.C. Schisler. Lipid Metabolism of *Agaricus bisporus* (Lange) Sing.: I. Analyses of Mycelial and Sporophore and Mycelial Lipids. *Lipids*, 6:176 (1971).
2. R. B. Holtz, P. Swenson, M. Abel, and T. A. Walters. A Sebacate Contaminant Appearing in Chloroform. *Lipids*, 6:523 (1971).
3. R. B. Holtz. Qualitative and Quantitative Analyses of Free Neutral Carbohydrates in Mushroom Tissue by GLC-MS. *J. Agr. Food Chem.*, 19:1272 (1971).
4. R. Barry Holtz and Lee C. Schisler. Lipid Metabolism of *Agaricus bisporus* (Lange) Sing.: II. Biosynthesis of Sporophore Lipids. *Lipids*, 7:251 (1972).
5. R. B. Holtz, P. S. Stewart, S. Patton, and L. C. Schisler. Isolation and Characterization of Plasma Membranes from the Cultivated Mushroom. *J. Plant Physiol.*, 50:541 (1972).
6. R. Barry Holtz, E. D. Marquez, and A. A. Benson. Wax Ester Biosynthesis by Isolated Membrane Fractions from Calanoid Copepods. *Comp. Bioch. Physiol.*, 45B:585 (1973).
7. R. Barry Holtz and C. F. Phleger. The Membranous Lining of the Swimbladders of Deep Sea Fishes.: I. Morphology and Chemical Composition. *Comp. Bioch. Physiol.*, 45B:867 (1973).
8. R. Douce, R. B. Holtz, and A. A. Benson. Isolation and Properties of the Envelope of Spinach Chloroplasts. *J. Biol. Chem.*, 248:7215 (1973).
9. R. V. Josephson, R. B. Holtz, J. P. Misock, and C. F. Phleger. Composition and Partial Protein Characterizations of Swimbladder Foam from Deep Sea Fishes, *Coryphenoides acrolepis* and *Antimora rostrata*. *Comp. Bioch. Physiol.*, 52B:25 (1977).
10. R. B. Holtz and D. E. Smith. Lipid Analyses of Mushroom Compost. *The Mushroom Journal*, Sept. 1975, pp 13-16.
11. R. B. Holtz, R. F. Lee, and A. A. Benson. Fatty acid compositions of *Calanus pacificus* and *Calanus Hyperboreus*. Presented at the American Oil Chemist Society meeting, October, 1974.
12. R. B. Holtz, C. F. Phleger, and P. W. Grimes. Membrane Biosynthesis in Deep Sea Fishes. *Comp. Bioch. Physiol.*, 56B:25 (1977).
13. R. Barry Holtz. Lipids in Fungi, Book Review, *Science*, 189:629-30 (1975).

14. D. Beggs and R. Barry Holtz, Automated Analysis of Organic Pollutants in Water Via GC-MS. Pittsburg Conference 1978, Cleveland , Ohio.
15. R. B. Holtz and D. E. Smith. Environmental Trace Organic Analysis by GC-MS: Lab Management Considerations. Presented at Pacific Conference on Chemistry and Spectroscopy, Anaheim, CA., 1977.
16. R. Barry Holtz. Quality Assurance for the Modern Instrumental Analysis Facility. Food Product Development, October 1976, p. 90.
17. R. B. Holtz. Assuring Water Quality. Food Product Development, Dec. 1976, p. 70.
18. R. B. Holtz. Some Considerations For Quality Assurance Planning in Product Development. Food Product Development, June 1977.
19. C. F. Phleger, R. B. Holtz, P. W. Grimes, and D. L. Leighton. Chemical and Sensory Analysis of the Purple Hinged Rock Scallop (*Himitea multirugosus*). J. Comp. Bioch. Physiol 57A:342, 1978
20. R. B. Holtz and V. Miroyan. Use of Response Surface Methodology (RSM) for Experimentation in Mushroom Culture.: I. Development of a Delayed Release Nutrient. Mushroom Science, X. Proceedings of the 10th International Congress on Edible Fungi, Bordeaux, France, 1978.
21. R. B. Holtz and D. E. Smith. Lipid Metabolism of Mushroom Mycelia. Mushroom Science, X. Proceedings of the 10th International Congress on Edible Fungi, Bordeaux, France, 1978.
22. R. B. Holtz. Delayed Release Substances. 1st Northern American Mushroom Congress, San Francisco, CA, 1979.
23. R. B. Holtz, N. Markowitz and B. Spruce. Development of an Effective Delayed Release Pesticide for Control of Sciarid Flies. Mushroom Science, XI. Proceedings of the 11th International Congress on Edible Fungi, Sydney, Australia, 1981.
24. R. B. Holtz, Bioenergetic Considerations of Composting, 1st Spawn Mate Symposium, Palm Springs, CA, 1981.
25. R. B. Holtz, Increases in Yield, The R & D Perspective. 4th North American Mushroom Conference, Vancouver, Canada, 1983
26. R. B. Holtz, Research in Edible Fungi:Future Directions. 4th Spawn Mate Symposium, Scottsdale, AZ, 1985
27. R. B. Holtz, Cell Energy Metabolism in Agaricus as it relates to osmotic pressure. International Symposium on Edible Fungi, Colloquium Speaker. University Park, PA, 1985.
28. R. B. Holtz, and Lee C. Schisler, Utilization of Fatty Acids by *Agaricus Bisporus* in commercial Culture, Mycologia, 78(5), 1986 p.722.
29. R. B. Holtz, A System for Computer Process Control of Fermentation, Am. Biotech. Lab. Nov., 1986.
30. R. B. Holtz, Distributed Logic Control Sytems for Fermentation and Downstream Processing. Advances in Instrumentation, Vol. 42, Part 3, 1987.

31. R. B. Holtz and L. Grill, Commercial Production of Melanin with Tyrosinase Using Recombinant DNA Technology. American Society for Microbiology, Conference on Biotechnology, 1990
32. R. B. Holtz and Michael McCulloch, Preparation of Commercial Mushroom Inoculum Using Submerged Culture. Society for Industrial Microbiology, Bioprocess Symposium. 1995.
33. R. B. Holtz. Formation of Savory Flavor Products from Commercial Mushroom Production and Processing. Society for Industrial Microbiology, Bioproducts Symposium. 1995.
34. White, E. L. Reinl, S. J., Holtz, R. B. and Turpen, T. H. 1996. Matrix Assisted Laser Desorption Time of Flight (MALDI-TOF) Mass Spectrometry Analysis of Fusion Proteins Expressed by Recombinant Tobacco Mosaic Virus. Connectivity: The Winston-Salem Research & Technology Vision, Winston-Salem, North Carolina.
35. Turpen, T., Cameron, T.I., Reinl, S. J., Pogue, G. P., Garger, S. J., McCulloch, M. J., Holtz, R. B., Grill, L. K., Production of Recombinant proteins in Plants: Pharmaceutical Applications. The Soc. Exper. Biol., Canterbury, UK *J. Exp Botany* 48(Suppl), 12. 1997.
36. Turpen, T. H., Cameron, T., Reinl, S., Pogue, G. P., Garger, S. J., McCulloch, M. J., Holtz, R. B., and Grill, L. K., 1997 Phytopathology and the production of pharmaceuticals based on recombinant proteins. The American Phytopathology Society, Rochester, New York
37. G.P. Pogue, S. Garger, M. McCulloch, S. Reinl, B. Holtz, T. Turpen, J. Hildalgo, T. Cameron, L. Kreitzer, C. Gross, K. Hanley, L. K. Grill 1998. From Dirt to Drugs: The Use of Viral Vectors to Make Pharmaceutical Grade Recombinant Proteins, Fifth International Symposium on Positive Strand RNA Viruses.
38. R. Barry Holtz and Steven Garger, Commercialization of Recombinantly Derived Therapeutics from Tobacco Plants in a cGMP facility. Division of Biological Chemistry, American Chemical Society National Meeting, 1999
39. R. Barry Holtz. Purification Systems for Plant Derived Biologics. Invited Paper. Plant Derived Biologics Seminar. Sponsored by FDA/CBER and USDA/APHIS . Ames, Iowa, 2000
40. Gelderman, M. P., Oliver, K. L., Cameron, T.I., Garger, S. J., Holtz, R. B. and Brady, R.O. Humoral and Immune Responses to Alpha-Galactosidase A in the Murine Analog of Fabry Disease, FASEB, Experimental Biology 2001, Orlando, Florida.
41. Holtz, R. B. Vaccine Production Using Plants as Bioreactors : Regulatory Issues and Opportunities. Invited Paper. BIOPHEX. October, 2002, San Jose, California
42. Holtz, R. B. Forging Alliances between the Private Sector, Universities and Government, Key note speech, Arkansas Biosciences Institute. October 2002
43. Holtz, R. B. Rapid Scale-Up of Vaccine Production in Plants: Two Case Studies. Invited Speaker, World Vaccine Conference. Lyon, France. 2002
44. Reddy, S., Czerwinski, D., Rajapaksa, R., Reinl, S., Garger, S., Cameron, T., Barrett, J., Novak, J., Holtz, R. B., Levy, R. Plant Derived Single-Chain Fv Idiotype Vaccines are Safe and Immunogenic in Patients With Follicular Lymphoma: Results of a Phase I Study. American Society of Hematology, invited paper, December, 2002.

45. Holtz, R. B. Synchronizing cGMP manufacturing of biopharmaceuticals with clinical requirements. BioLogic, Geneva, 2003
46. Holtz, R. B. Economic assessment of biopharmaceutical processes: Use of modeling tools BioLogic , Boston, 2003
47. Gelderman, M. P., Oliver, K. L., Cameron, T.I., Garger, S. J., Holtz, R. B. and Brady, R.O. Pre-Clinical Studies of a Plant Derived Alpha-Galactosidase for Enzyme Replacement Therapy, Preclinica, January, 2004
48. G. Pogue, T. Cameron, L. Hamm, S. Rienl, A. McCormick, K. Hanley, E. White, R. O. Brady, M. Gelderman, G. Grabowskit, H. Du, L. Grill, D. Tuse, B. Holtz, and S. Garger. Rapid Optimization of Human Therapeutic Glycoprotein Expression Using a Transient Plant Expression system. CPMP Meeting, Montreal, 2005
49. R. B. Holtz, Quality Assurance of Downstream Processes: Considerations for PAT. R. B. Holtz. CPMP Meeting, Montreal, 2005
51. Blueprint for the Development of Plant Derived Vaccines for the Poor in Developing Countries. A Program of the Center for Infectious Diseases and Vaccinology, The BioDesign Institute at Arizona State University, Blue Ribbon Panel, 2005.
52. Plant-Derived Vaccines:Cost of Production. A Program of the Center for Infectious Diseases and Vaccinology, The BioDesign Institute at Arizona State University, Blue Ribbon Panel, 2005.
53. R. B. Holtz. Session Chairman, Case Studies in Alternate Biotech Manufacturing Process Development. PDA Annual Meeting, Anahiem, CA 2006
54. WHO Informal Consultation on Scientific Basis for Regulatory Evaluation of Candidate Human Vaccines from Plants, Geneva, Switzerland, 2005, Vaccine 24:4271-8. 2006
54. R. B. Holtz. Cancer Vaccine Development on the Fast Track: A case study in facilities planning for clinical support and Scale-up” BioLogic Europe, Amsterdam , 2006
55. R. B. Holtz. Session Chairman, Manufacturing and Quality Control section, New Cells for New Vaccines Conference, Internation Association for Biologicals, September, 2006, Miami.
57. R. B. Holtz, Making Real Medicines, Cross Disciplinary Science, Engineering and Management at its Best. Keynote Speech, INBRE Conference, November, 2006
58. R. B. Holtz, Cancer Vaccines: Strategic Planning of Manufacturing Development. Invited speaker. 14th Internation Conference on Gene Therapy, September, 2006, Dallas
59. R. B. Holtz, Mulitsite Collaborations for the Institutional Sponsor, Invited Speaker, Navigating Through the Sponsor-Investigator IND Minefield Conference, University of Arkansas for Medical Sciences, April, 2007, Little Rock.
60. R. B. Holtz, Validating Vaccine Facilities : Focus on Early Stage Companies and Institutions. Cambridge Healthcare Institute Conference, Immunotherapeutics & Vaccines Summitt. August, 2007,Boston
61. R. B. Holtz, Manufacturing Patient Specific Therapies: Strategic, Regulatory, and Scale-up Issues. Cell and Tissue Bioprocessing Meeting, October, 2007 Austin, TX

62. McCormick, A.A., Reddy, S., Reinl, S.J., Cameron, T.I., Czerwinski, D.K., Vojdani, F., Hanley, K., Garger, S.J., White, E.L., Novak, J., Barrett, J., Holtz, R.B., Tusé, D., and Levy, R. Plant-produced Idiotypic Vaccines for the Treatment of Non-Hodgkin's Lymphoma: Safety and Immunogenicity in a Phase I Clinical Study. PNAS, Vol. 105, 10131 -10136, 2008
63. R. B. Holtz, An Aggressive Facilities and Quality Systems Approach for Developing Biopharmaceutical Manufacturers. Cambridge Healthcare Institute Protein Conference, San Diego CA, January, 2008
64. R. B. Holtz, Phillip B. Maples, Biaoru Li, Courtney Haddock, Eli Gutierrez, Padmsini Kumar, Lori Debetaz, Neil Senzer, John Nemunaitis. Integration of LC Maldi-TOF/TOF Mass Spectrometry to Provide Proteogenomic Information for the Manufacture of Patient Specific Cancer Therapies. American Society for Gene Therapy, Boston, 2008

OTHER

Dr. Holtz serves on the technical advisory board of the NIH Program Project Grant for Drug Abuse Therapy Development, University of Arkansas Medical School, Little Rock, Arkansas and serves on the business advisory board to the Arkansas Biosciences Institute.

Dr. Holtz has served on the Board of Directors of the Owensboro, KY Chamber of Commerce and has served on two of the Kentucky Governor's advisory committees on high-technology economic development and development of the rural economy. He has also recently served on the National Institutes of Health, National Institute on Drug Abuse, Medications Development Scientific Workgroup.

Internet Links