



MARK T. BUTT, DVM, DACVP

Frederick, MD | 301-378-0505 | mbutt@toxpath.net

EDUCATION

- New York State College of Veterinary Medicine, Cornell University, Ithaca, New York* Oct 1988 – Sep 1991
Residency in Veterinary Anatomic Pathology
- New York State College of Veterinary Medicine, Cornell University, Ithaca, New York* June 1984
Doctor of Veterinary Medicine
- Virginia Tech, Blacksburg, VA* March 1980
Bachelor of Science in Forestry and Wildlife
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CERTIFICATIONS

- Diplomate, *American College of Veterinary Pathologists (Anatomic Pathology)* 1991
- Licensed to practice Veterinary Medicine in State of Maryland
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EXPERIENCE

Tox Path Specialists, LLC, Frederick, MD June 2007 - Present
President/Founder

- Neuropathology evaluations in support of preclinical development of neuroactive compounds, devices and drug delivery systems
- Specialized morphometric/stereologic procedures for the quantification of nervous system (and other system) structures including: neuron counts, neuron size, peripheral nerve morphometrics, intraepidermal nerve fiber density measurements, angiogenesis quantification
- Specialized and routine staining procedures for nervous system evaluations, including GFAP, Fluoro-Jade B, microglia cells, tyrosine hydroxylase, neuronal groups
- General toxicologic pathology in support of the preclinical development of pharmaceuticals with extensive experience evaluating primates, rodents, dogs, sheep/goats, rabbits and pigs
- Consultant for study design, study conduct and management of pathology resources
- Facilitate interactions between biotechnology/pharmaceutical companies and contract research organizations
- Extensive device experience including stimulation devices in the brain, spinal nerve root, vagus nerve and peripheral nerve
- Extensive experience with implanted drug delivery systems including bolus and continuous infusion via intracerebroventricular, intrathecal, and intraparenchymal catheters
- Frequent national/international speaker on the evaluation of the nervous system
- Invited speaker to multiple FDA sponsored events

Charles River Laboratories, Pathology Associates (PAI), Frederick, MD

Jan 2001 – June 2007

General Manager

- Scientific and financial management of all pathology operations within Pathology Associates (210 employees/35 board certified pathologists and other doctoral level professionals) including offices in Maryland, North Carolina, Missouri, Illinois, Ohio, Colorado and California
- Scientific management of Charles River pathology operations in Massachusetts, Ohio, Arkansas and Nevada (80 employees including 12 pathologists and other professionals)
- Preparation and management of an approximately \$30 million budget
- Project manager and pathology support for government and commercially sponsored toxicologic protocols with emphasis on studies involving drug development for neurologic disorders
- Neuropathology consultant for many of the major pharmaceutical firms, contract research organizations and biotechnology companies
- Evaluator of more than 200 neuropathology directed toxicity studies and peer reviews in monkeys, dogs, rodents, sheep and pigs
- Proposal preparation for commercial and government programs, including successful awards from the National Cancer Institute (7 year, \$2.8 million total contract value) and the National Toxicology Program (10 year, \$28.6 million total contract value)

Pathology Associates, Frederick, MD

Dec 1999 – Jan 2001

Director of Operations, Pathology Processes and Procedures

- Develop and maintain a support staff consisting of project coordinators, research associates, pathology assistants and archive technicians tasked to support the pathologists and improve the efficiency of the work flow
- Investigate and implement automation initiatives aimed at improving the overall efficiency of project management
- All duties associated with the role of staff pathologist and project manager as outlined below with emphasis on neuropathology

Pathology Associates, Frederick, MD

June 1994 – Dec 1999

Senior Staff Pathologist and Project Manager

- Project manager and study pathologist for government and commercially sponsored toxicologic and carcinogenesis protocols with emphasis on studies involving drug development pertinent to neurologic disorders
- Principal Investigator, National Cancer Institute Pathology and Veterinary Support for Preclinical Toxicology Studies program
- Database management, support and validation of pathology data systems

CIBA-GEIGY (now Novartis) Pharmaceuticals, Summit, New Jersey Dec 1991 – June 1994
Pathologist

- Gross and microscopic evaluation, organ weight interpretation and integration of clinical pathology and clinical data of GLP acute, 13-week and chronic (1 year) studies in all laboratory species with emphasis on neuropathology
- Member/head drug development teams
- Assist with IND submissions
- Supervision of the necropsy facility
- Completion of senior level GLP and Drug Development training programs

Department of Pathology, New York State College of Veterinary Medicine, Cornell University, Ithaca, New York July 1990 – Dec 1991
Diagnostic Pathologist/Instructor

- Direct supervision of nine residents and eighty senior veterinary students rotating through the diagnostic services of the College
- Final preparation of reports
- Direct communication with referring veterinarians and in-house clinicians
- Teaching: VM 536 Sophomore Pathology (faculty member responsible for gastrointestinal pathology), VM 638 Sophomore Pathology Seminar, VM 540 Necropsy Pathology

New York State College of Veterinary Medicine, Cornell University, Ithaca, New York Oct 1988 – July 1990
Resident in Anatomic Pathology

- All duties of a pathology resident, including student supervision, biopsy and necropsy service work and participation on in-house diagnostic programs

Franklin Veterinary Associates, Greencastle, Pennsylvania June 1985 – Oct 1988
Practicing Veterinarian

- All aspects of agricultural practice and small animal medicine and surgery

Pender Veterinary Clinic, LTD, Fairfax, Virginia June 1984 – June 1985
Practicing Veterinarian

- All aspects of companion animal medicine and surgery

PUBLICATIONS

Books

Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011.

Book Chapters

Butt M. Practical stereology in a preclinical toxicology setting: a pathologist's perspective. In: Mouton P. ed. *Neurostereology*. Hoboken, NJ: J Wiley and Sons. Expected date of publication: 2013.

Bolon B, Butt M, Garman R, Dorman D. Nervous System. In: Haschek W et al eds. *Handbook of Toxicologic Pathology* 3rd edition. Academic Press. Expected date of publication: July 2013.

- Butt M, Sills R, Bradley A. Nervous System. In: Sahota P, Popp J, Hardisty J and Gopinath C, eds. *Toxicologic Pathology in Preclinical Safety Assessment*. Boca Raton, FL: CRC Press/Taylor & Francis. 2013:895-930.
- Butt M. The neuropathology report and the neuropathology peer review report. In: Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011:505-511.
- Butt M, Alcaraz A. Diagnostic neuropathology. In: Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011:463-473.
- Butt M. Evaluation of the adult nervous system. In: Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011:321-338.
- Switzer B, Butt M. Histological markers of neurotoxicity (nonfluorescent). In: Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011:181-190.
- Salvo H, Butt M. Regulatory guide to the histopathological assessment of neurotoxicity studies. In: Bolon B, Butt M, eds. *Fundamental Neuropathology for Pathologists and Toxicologists: Principles and Techniques*. Hoboken, NJ: J Wiley and Sons; 2011:519-535.
- Journal Articles**
- Breckenridge C, Sturgess N, Butt M, Wolf J, et al. Pharmacokinetic, neurochemical, stereological and neuropathological studies on the potential effects of paraquat in the substantia nigra pars compacta and striatum of male C57BL/6J mice. *NeuroToxicology*. 2013;37:1-14.
- Beckman D, Yourenneff M, Butt M. Neurotoxicity assessment of artemether in juvenile rats. *Birth Defects Research (Part B)*. 2013;98:183-199.
- Bolon B, Garman R, Pardo I, Jensen K, Butt M, et al. STP position paper: Recommended practices for sampling and processing the nervous system (brain, spinal cord, nerve and eye) during nonclinical general toxicity studies. *Toxicologic Pathology*. 2012;00:1-21.
- Kaufmann W, Bolon B, Bradley A, Butt M, et al. Proliferative and nonproliferative lesions of the rat and mouse central and peripheral nervous systems. *Toxicologic Pathology*. 2012;40:87S-157S.
- Pfeifer R, Felice B, Boyd R, Butt M, et al. Safety evaluation of chronic intrathecal administration of heparan N-sulfatase in juvenile cynomolgus monkeys. *Drug Deliv. and Transl. Res.* 2012;2(3):187-200.
- Felice BR, Wright TL, Boyd RB, Butt M, Pfeifer RW, Pan J, Ruiz JA, Heartlein MW, Calias P. Safety evaluation of chronic intrathecal administration of idursulfase-IT in cynomolgus monkeys. *Toxicologic Pathology*. 2011;39(5):879-92. Epub 2011 May 31.
- Bolon B, Bradley A, Butt M, Jensen K, Krinke G, Mellon RD. Compilation of international regulatory guidance documents for neuropathology assessment during nonclinical general toxicity and specialized neurotoxicity studies. *Toxicologic Pathology*. 2011;39(1):92-96. Epub 2010 Nov 30.

- Zorbas M, Hurst S, Shelton D, Evans M, Finco D, Butt M. A multiple-dose toxicity study of tanezumab in cynomolgus monkeys. *Regulatory Toxicology and Pharmacology*. 2011;59(2):334-342. Epub 2010 Dec 3.
- Butt M. Morphologic changes associated with intrathecal catheters for direct delivery to the central nervous system in preclinical studies. *Toxicologic Pathology*. 2011;39(1):213-219. Epub 2010 Dec 8.
- Butt M. Vacuoles in dorsal root ganglia neurons: some questions. *Toxicologic Pathology*. 2010;38(6):999.
- Bolon B, Anthony D, Butt M, et al. "Current pathology techniques" symposium review: advances and issues in neuropathology. *Toxicologic Pathology*. 2008;36(6):871-889.
- Hovland DN, Boyd RB, Butt MT, et al. Six-month continuous intraputamenal infusion toxicity study of recombinant-methionyl human glial cell line-derived neurotrophic factor (r-metHuGDNF) in rhesus monkeys. *Toxicologic Pathology*. 2007;35(5):676-692.
- Moser VC, Phillips PM, Levine AB, Butt M et al. Neurotoxicity produced by dibromoacetic acid in drinking water of rats. *Toxicol Sci*. 2004;79(1):112-122. Epub 2004 Feb 19.
- Freeman C, Weiner M, Kotkoskie L, Borzelleca J, Butt M. Subchronic and developmental toxicity studies in rats with Ac-Di-Sol croscarmellose sodium. *Int J Toxicol*. 2003;22(3):149-57.
- Signorin J, Ulrich CE, Butt M, D'Amato EA. 13-week inhalation toxicity study (including 6- and 13-week recovery periods) with ammonium persulfate dust in albino rats. *Inhal Toxic*. 2001;13(11):1033-1045.
- Kotkoskie LA, Butt MT, Selinger E, Freeman C, Weiner ML. Qualitative investigation of uptake of fine particle size microcrystalline cellulose following oral administration in rats. *J Anat*. 1996;189(Pt 3):531-535.
- Butt MT, Papendick RE, Carbone LG, Quimby FW. A cytotoxicity assay for Clostridium spiroforme enterotoxin in cecal fluid of rabbits. *Lab Anim Sci*. 1994;44(1):52-54.
- Barr MC, Butt MT, Anderson KL, Lin DS, Kelleher TF, Scott FW. Spinal lymphosarcoma and disseminated mastocytoma associated with feline immunodeficiency virus infection in a cat. *J Amer Vet Med Assoc*. 1993;202(12):1978-1980.
- Haas L, Perdrizet J, Butt M, Posso M, Quimby F, Casey J. Engraftment of bovine leukemia virus infected lymphocytes into SCID mice. *Virology*. 1993;192:655-658.
- Bookbinder PF, Butt MT, Harvey HJ. Determination of the number of mast cells in lymph node, bone marrow, and buffy coat cytologic specimens from dogs. *J Amer Vet Med Assoc*. 1992;200(11):1648-1650.
- Butt M, Weldon A, Step D, deLahunta A, Huxtable C. Encephalitic listeriosis in two adult llamas (Lama glama): Clinical presentations, lesions, and immunofluorescence of Listeria monocytogenes in brainstem lesions. *Cornell Vet*. 1991;81(3):251-8.
- Prichard M, Ducharme N, Wilkins P, Butt M. Xanthine oxidase formation during experimental ischemia of the equine small intestines. *Canadian J Vet Res*. 1991;55:310-314.

Butt M, Bowman D, Barr M, Roelke M. Iatrogenic transmission of *Cytauxzoon felis* from a Florida panther (*Felis concolor coryi*) to a domestic cat (*Felis domesticus*). *J Wild Dis*. 1991;27(2):342-347.

Butt M. Diagnosing erythrocyte parasitic diseases in the cat. *Comp Cont Ed*. 1990;12:628-635, 638.

ABSTRACTS AND POSTERS

Grondin R, Ai Y, Hardy P, Butt M, Hokanson K, Gerhardt G, Gash D, Bumcrot D, Zhang Z. *Targeted drug delivery to the midbrain for Parkinson's disease treatment*. 7th Neurodegenerative Conditions Research & Development Conference, September 2013, Boston, MA. (Abstract)

Breckenridge C, Botham P, Butt M, Smith L, Sturgess N, Wolf J. *Dietary administration of paraquat for 13 weeks does not result in a loss of dopaminergic neurons from the substantia nigra of mice*. Society of Toxicology Annual Meeting, March 2013; San Antonio, TX. (Poster)

Butt M. *High i.p. doses of paraquat do not result in a loss of dopaminergic neurons in the substantia nigra of the mouse*. Society of Toxicology Annual Meeting, March 2013; San Antonio, TX. (Poster)

Korte S, Butt M, Rose C, Niehoff M. *12 week intrathecal administration study in port catheterized juvenile cynomolgus monkeys*. Society of Toxicology Annual Meeting, March 2013; San Antonio, TX. (Poster)

Wright TL, Lieb J, Pfeiffer R, Butt M. et al. *A 6-Month Toxicity Study of Idursulfase Administered via Monthly Intrathecal Lumbar Injections and Weekly Intravenous Injections in Cynomolgus Monkeys*. Society of Toxicology Annual Meeting, March 2009; Baltimore, MD. (Abstract)

Jabbour AJ, Lum RC, Weigele MS, Magowan JA, Sacaan AI, Bozigian H, Butt MT. *Neuropathological examinations of the brain after repeated dosing with tetrabenazine*. American College of Toxicology Annual Meeting, November 2008; Tucson, AZ. (Poster)

Tatalick L, Daifuku R, Butt M, Kessler D. *Reduced neurotoxicity of a novel vitamin E Paclitaxel emulsion compared to approved Paclitaxel and Docetaxel formulations in a rat model*. American Association of Cancer Research Annual Meeting, April 2001; Los Angeles, CA. (Abstract)

Vick A, Ten Hoor C, Lerner M, et al. *Recovery of immune response following administration of an anti-CD 154 monoclonal antibody (Hu5C8) to cynomolgus monkeys*. The Toxicologist (abstract issue of Toxicological Sciences) 39th Annual Meeting of the Society of Toxicology, Volume 54, Number 1, March 2000. (Abstract)

Chenegelis C, Elangham C, Butt M, Maccicchini M. *Subchronic toxic and neurotoxic effect of ACPC (1-aminocyclopropane-1-carboxylic acid) in rats*. 38th Annual Meeting of the Society of Toxicology, 1999; New Orleans, LA. (Poster)

Ulrich C, Signorin J, Henson J, Butt M. *A 13-week inhalation toxicity study (with recovery) of ammonium persulfate in albino rats*. 38th Annual Meeting of the Society of Toxicology, 1999; New Orleans, LA. (Poster)

Signorin J, Arquinaldo E, Butt M. *A 28-Day intranasal study in Sprague-Dawley rats with Avicel RC-591*. 38th Annual Meeting of the Society of Toxicology, 1999; New Orleans, LA. (Poster)

Smith A, Rodman L, Butt M, et al. *Neurotoxicity produced by Breflate (NSC-656202), a Brefeldin A prodrug in beagle dogs*. 36th Annual Meeting of the Society of Toxicology, 1997; Cincinnati, OH. (Poster)

Kotkoskie L, Freeman C, Butt M, Weiner M. *28-day repeated dose delayed neurotoxicity study in hens with reoflam PB-460 triaryl phosphate*. 35th Annual Meeting of the Society of Toxicology, 1996; Anaheim, CA. (Poster)

Orr J, Boyd R, LeBel C, Butt M. *Intracerebroventricular access to the rhesus monkey brain for specialized toxicity studies*. 35th Annual Meeting of the Society of Toxicology, 1996; Anaheim, CA. (Poster)

Kotkoskie L, Butt M, Selinger E, Freeman C, Weiner M. *Qualitative investigation of intestinal uptake in rats orally administered a fine particle size microcrystalline cellulose*. The Anatomical Society of Great Britain and Ireland, Summer Meeting, 1995; Belfast, Ireland. (Poster)

PRESENTATIONS

Evaluation of the adult nervous system in preclinical toxicity studies

British Society of Toxicologic Pathology, Modular Education Programme in Toxicological Pathology, Module 11 Nervous System and Special Senses, Department of Pathology, Cambridge University, March 2013; Cambridge, UK.

Pathology associated with direct drug delivery to the CNS

British Society of Toxicologic Pathology, Modular Education Programme in Toxicological Pathology, Module 11 Nervous System and Special Senses, Department of Pathology, Cambridge University, March 2013; Cambridge, UK.

Regulatory guidelines for adult and developmental neurotoxicity testing

British Society of Toxicologic Pathology, Modular Education Programme in Toxicological Pathology, Module 11 Nervous System and Special Senses, Department of Pathology, Cambridge University, March 2013; Cambridge, UK.

Application of lesion quantification to dedicated neuropathology studies

British Society of Toxicologic Pathology, Modular Education Programme in Toxicological Pathology, Module 11 Nervous System and Special Senses, Department of Pathology, Cambridge University, March 2013; Cambridge, UK.

Evaluation of immunosuppressive effects on the central nervous system

Toxicology Forum 38th Annual Winter Meeting, March 2013; Washington, DC.

Application of lesion quantification to dedicated neuropathology studies.

National Toxicology Program Symposium on Neuropathology, April 2012; Research Triangle Park, NC.

Neuroscience: From Fundamentals to Pharma: The Toxicologic Pathology Perspective

C.L. Davis Pathology Group Meeting, East Hanover, NJ.

Morphologic assessment of preclinical safety studies involving direct delivery to the central nervous system

From proof of concept to clinical readiness workshop, Controlled Release Society 38th annual meeting and exposition, July 2011; National Harbor, MD.

The pathology of direct central nervous system delivery in preclinical studies

Society of Toxicologic Pathologists Annual Meeting, June 2010; Chicago, IL. (Platform Presentation)

FDA-CFSAN Toxicologic Pathology Seminar Series: Invited Speaker

Four hour seminar to members of the FDA regarding the pathology aspects of studies supporting the regulatory submission of neuroactive test articles and devices. Sep 2010.

Evaluation of the Adult Nervous System in Preclinical Studies. Workshop on Determining the Need and Developing a Strategy for a Neurotoxicity Testing

Sponsored by the ASTM Committee F04 on Medical and Surgical Implants and Materials and U.S. Food and Drug Administration. May 2009.

Evaluation of the Adult Nervous System

Society of Toxicology 48th Annual Meeting, March 2009; Baltimore, MD.

Getting the most out of your pathologist

Roundtable of Toxicology Consultants, American College of Toxicology Annual Meeting, November 2008; Tucson, AZ.

Toxicologic pathology of the central nervous system

Lecture to graduate students in the School of Public Health, Johns Hopkins University, May 9, 2008; Baltimore, MD.

Getting the most out of your pathologist Parts I and II

Presentations for the Preclinical Training Institutes first annual Study Director Training Course, June 8-11, 2008; Lake Tahoe, NV.

Neuropathology for non-pathologists

American College of Toxicology Mid-Atlantic Division Annual Satellite Meeting, May 7-8, 2008; Falls Church, VA.

Toxicologic pathology of the central nervous system.

Lecture to graduate students in the School of Public Health, Johns Hopkins University, May 9, 2008; Baltimore, MD.

Neuropathology of CNS implants and infusions

CNS Drug Delivery Satellite Symposium, Society for Neuroscience, November 2, 2007; San Diego, CA.

Special procedures in neuropathology: Case studies in laboratory animals

Presentation to the residents and faculty of the College of Veterinary Medicine, University of Florida, May 2, 2007; Gainesville, FL.

Toxicologic pathology of the central nervous system

Lecture to graduate students in the School of Public Health, Johns Hopkins University, May 11, 2006; Baltimore, MD.

Beginning with the end in mind: Designing (or salvaging) a study to obtain useful neuropathology endpoints

Mid Atlantic Society of Toxicology Symposium Neurotoxicology: Basics and Beyond, Rutgers EcoComplex Environmental and Research Center, October 31, 2006; Bordentown, NJ.

Neuropathology for the toxicologist

Society of Toxicology Annual Meeting (Continuing Education Session), March 5, 2006; San Diego, CA.

The preclinical assessment of neuroactive compounds with emphasis on bypassing the blood brain barrier
Cornell College of Veterinary Medicine, April 6, 2006; Ithaca, NY.

Seminar on Advanced Pathologic Techniques: Current Issues in Neuropathology
American College of Veterinary Pathologists Annual Meeting (Sponsored by the ILSI Health and Environmental Sciences Institute), December 3, 2005; Boston, MA.

Practical methodology in rodent neuropathology for the over-worked pathologist
2nd Research Triangle Park Rodent Pathology Course, September 12-14, 2004; Research Triangle Park, NC.

The pathology of delivering drugs directly to the central nervous system
Department of Biomedical Sciences Visiting Scientist Lecture Series: Mice and Molecules, Cornell University College of Veterinary Medicine, September 2003; Ithaca, NY.

The preclinical assessment of neuroactive compounds with emphasis on bypassing the blood brain barrier
British Society of Toxicologic Pathology, Modular Education Programme in Toxicological Pathology, Module 10 Nervous System and Special Senses, Department of Pathology, Cambridge University, July 2003; Cambridge, UK.

The pathology of direct central nervous system drug delivery
Annual Meeting of the American College of Veterinary Pathologists, November 2002; New Orleans, LA.

Neuropathological approach in CNS delivery studies
Safety Evaluation of Drugs for Central Nervous System Delivery (satellite symposium following the Annual Meeting of the Society of Toxicology), November 1999; New Orleans, LA.