Appendix A3

Pyrogenicity Peer Review Panel Biographies

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Karen Brown, Ph.D. (Panel Chair)

Dr. Brown received her Ph.D. in Microbiology and Biochemistry at Oklahoma State University in Stillwater. She is President, Pair O' Docs Enterprises, consulting with companies and with the U.S. Department of Agriculture Animal and Plant Health Inspection Service (APHIS) Center of Veterinary Biology on development of *in vitro* assays to replace animal tests for release of veterinary vaccines and is a Consultant, sharing the CEO position for MVP Laboratories. Dr. Brown's resume indicates her broad expertise in *in vitro* and *in vivo* pyrogen testing and thorough knowledge of regulatory requirements for drug and product development. Early in her career, Dr. Brown developed bench and supervisory experience working in Quality Control conducting animal testing, including the rabbit pyrogen test and *in vitro* Limu endotoxin testing. She initiated an *in vitro* development group at Bayer as Head of Biological Research and Development that specialized in developing and validating ELISAs for Limulus Amebocyte Lysate (LAL) testing and antigen quantitation for release of biological products. Dr. Brown remains involved in endotoxin testing by consulting with various companies to determine correlations in endotoxin levels in various veterinary products to reactions produced by some of these products when used to vaccinate animals. She has expertise in microbiology, veterinary medicine, vaccine and biologicals development and safety testing, *in vitro* methods development, and technical government relations (European Union [EU] and United States [U.S.]). Dr. Brown was Chairman of the *In Vitro* Working Group of the Veterinary Biologics Section of the Animal Health Institute (AHI) and APHIS liaison (regulatory) for registration of new vaccine and diagnostic products. Dr. Brown has conducted or managed research and development to register 44 new drug products, pharmaceuticals, vaccines, or diagnostic products or technologies and she has 44 publications and presentations and 23 U.S. patents. She is a member of the AHI, Veterinary Biologics Section, the Association of Veterinary Biological Companies, the American Society for Microbiology, and the U.S. Animal Health Association.

Brian Crowe, Ph.D.

Dr. Crowe received his Ph.D. in Microbiology from Trinity College in Dublin, Ireland. He is the Director of Immunology (Vaccines) at Baxter Vaccine AG in Austria and has responsibility for two research departments (Molecular Immunology and Humoral Immunology) and a quality control department (Biological Control) comprised of three quality control laboratories (Bacteriology, *in vitro* and *in vivo* testing). Dr. Crowe's resume demonstrates a significant and broad level of expertise in pyrogen test methodology and knowledge of laboratory, manufacturing, and validation procedures. Dr. Crowe has responsibility for general safety and toxicity testing and heads the Rabbit Pyrogen Testing and Endotoxin (LAL) Testing Units for Baxter Bioscience in Austria with testing rates of 3,000 to 26,000 samples per year. Dr. Crowe has extensive experience with high throughput screening, cytokine response assays, cytotoxicity testing, inflammatory response assays, complement testing, and other molecular, cellular, and humoral immunological response testing. He is also well versed in Good Manufacturing Practice and Good Laboratory Practice (GLP) standards and in issues of validation and audit requirements and procedures. Dr. Crowe has authored or coauthored 25 publications and 4 patents. His research interests are focused on bacterial and viral vaccines.

Nancy Flournoy, M.S., Ph.D.

Dr. Flournoy received a M.S. degree in Biostatistics from the University of California at Los Angeles, and a Ph.D. in Biomathematics from the University of Washington. She is Professor and Chair of the Department of Statistics at the University of Missouri-Columbia. Her research interests include adaptive designs, bioinformatics, chemometrics, clinical trials, and environmetrics. She has an extensive list of edited volumes and papers on statistical theory, statistical genetics and immunology, epidemiology in immune suppressed subjects, clinical trials for prevention and treatment of viral infection, transplantation biology and its effects on digestion, lungs, eyes, mouth, and central nervous system, optimization of statistical processing, and additional papers, interviews, and technical reports. She has editorial responsibilities for numerous statistical journals, serves on numerous advisory boards, and nominating committees. She is a member and past Chair of the Council of Sections of the American Statistical Association, and served in various other statistical, medical and toxicological societies or programs as Chair or as a member of the Board of Directors. She is a former member of the Scientific Advisory Committee on Alternative Toxicological Methods. She also served on the Expert Panels for the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) that evaluated the Revised Up-and-Down Procedure; the Current Validation Status of *In Vitro* Test Methods for Identifying Ocular Corrosives and Severe Irritants; and Five *In Vitro* Pyrogen Test Methods.

Ihsan Gursel, MSc, Ph.D.

Dr. Gursel received his MSc. and Ph.D. degrees from the Middle East Technical University, Department of Biological Sciences in Ankara, Turkey. He is an Assistant Professor in the Department of Molecular Biology and Genetics at Bilkent University in Ankara. Dr. Gursels' resume indicates that he has significant experience studying the receptor family believed to mediate pyrogenic responses (i.e., Toll-like receptors [TLR]). Dr. Gursel's research interests include studies on the roll of TLR and TLR-ligand interactions in an innate immune response, gene expression and transcriptional profiling of immune cells via high throughput screening methods, design of controlled release systems for oligodeoxynucleotide targeting and delivery, and application of biodegradable natural polymers for biomaterials, tissue engineering, and drug delivery. Dr. Gursel has received numerous awards and grants to support his work and has authored or coauthored more than 45 publications, 7 patents, and has given 28 formal presentations related to his research. He has also refereed papers for the Journal of Leukocyte Biology, Immunopharmacology and Immunotoxicology, and Vaccine.

Ken Ishii, M.D., Ph.D.

Dr. Ishii received his M.D. and Ph.D. degrees from the School of Medicine at Yokohama City University in Kanagawa, Japan. He is a Group Leader for the Akira Innate Immunity Project at the Exploratory Research for Advanced Technology, Japan Science and Technology Agency, Osaka University. Dr. Ishii's resume indicates that he has extensive regulatory experience that includes pyrogen testing requirements for pharmaceuticals. Dr. Ishii was formerly a Staff Scientist at the Food and Drug Administration (FDA) Center for Biologics and Evaluation Research (CBER). His work experience includes regulation of Investigational New Drug applications related to DNA-based vaccines and immunotherapy

using DNA vaccine and immunostimulatory DNA (CpG DNA). Dr. Ishii also has regulatory experience related to vaccines and immunotherapies against infectious diseases and allergy. He has authored or coauthored 58 publications in peer-reviewed journals and holds 17 patents.

Jack Levin, M.D.

Dr. Levin received an M.D. from the Yale University School of Medicine in New Haven, CT. He is an Independent Investigator at the Marine Biological Laboratory at Woods Hole, MA. Dr. Levin is also a Professor of Laboratory Medicine and Professor of Medicine at the University of California School of Medicine in San Francisco. He previously held various academic positions (e.g., Professor of Medicine) at Johns Hopkins Hospital in Baltimore and holds additional positions (e.g., Associate Member of the Cancer Research Institute at University of California at Santa Cruz, attending physician and Director of the Anticoagulation Clinic at the Veterans' Administration Medical Center in San Francisco). Dr. Levin is board-certified in Internal Medicine by the American Board of Internal Medicine. Dr. Levin's resume indicates that he has extensive experience studying the pyrogenic response and pyrogen testing (e.g., research in hemoglobin-lipopolysaccharide interactions and pioneered gel-clot LAL technology). Dr. Levin is a former editor-in-chief of the Journal of Endotoxin Research, a member of the American Society of Hematology (serving on various committees), a member of the Corporation, Marine Biological Laboratory, a Fellow of the American College of Physicians, a member of the American Society for Experimental Pathology, American Society for Clinical Investigation, the California Academy of Medicine, the International Endotoxin Society, and numerous other societies. Dr. Levin has co-organized nine international conferences and has 246 publications in peer-reviewed journals, book chapters, or edited series.

Albert Li, Ph.D., MBA

Dr. Li received his Ph.D. in Biomedical Sciences from the University of Tennessee, Oak Ridge and an Executive MBA from the University of Maryland University College in College Park. Dr. Li co-founded three companies to advance drug development. He is Chairman and CSO of ADMET Group, LLC; Founding Chairman, President, and CEO of *In Vitro* ADMET Laboratories in Rockville, MD; and Founding Chairman, President, and CEO of Advanced Pharmaceutical Sciences in Baltimore, MD. Dr. Li's resume indicates that he has a broad level of experience in validation of *in vitro* and alternative methods. Dr. Li has secured multiple research grants to advance a drug candidates from the preclinical laboratory through clinical trials, developed proprietary technology of interest to the pharmaceutical industry, and established a GLP laboratory for *in vitro* efficacy, metabolism, and toxicity testing. Dr. Li has published over 130 scientific papers, numerous books/special journal issues, and is frequently invited to speak in national and international conferences.

David Lovell, Ph.D., FIBiol, CBiol, F.S.S., CStat

Dr. Lovell received a Ph.D. from the Department of Human Genetics and Biometry, University College, London. He is currently Reader in Medical Statistics at the Postgraduate Medical School at the University of Surrey. Previously, he was Associate Director and Head of Biostatistics support to Clinical Pharmacogenomics at Pfizer Global Research and Development in Sandwich, Kent providing data management and statistical support to pharmacogenetics and genomics. He joined Pfizer in 1999 as the Biometrics Head of Clinical

Pharmacogenetics. Before joining Pfizer, Dr. Lovell was the Head of the Science Division at BIBRA International, Carshalton, which included Molecular Biology, Genetic Toxicology, Biostatistics and Computer Services. At BIBRA, Dr. Lovell managed the statistical and computing group providing specialized statistical support to BIBRA's Clinical Unit and contract research work. He conducted and managed research programs on genetics, statistics and quantitative risk assessment for the EU and United Kingdom (U.K.) Government Departments. His research interests at BIBRA were in the use of mathematical and statistical methods together with genetic models in the understanding of toxicological mechanisms and risk assessment problems. Dr. Lovell had previously been a Senior Research Officer with the U.K. Medical Research Council (MRC) Experimental Embryology and Teratology Unit, a visiting Postdoctoral Fellow at the National Institute of Environmental Health Sciences in North Carolina, U.S., a Geneticist at the MRC Laboratories, Carshalton and a Research Assistant in Cytogenetics at Birmingham University. He has acted as a consultant to a number of organizations, has considerable experience of working with Regulatory Authorities, has many publications related to his work and has wide experience of making presentations to a wide range of audiences. He is a member of the U.K. Government's advisory Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment and the Independent Scientific Advisory Committee for Medicines and Healthcare Products Regulatory Agency database research. He served on the NICEATM-ICCVAM Expert Panels that evaluated the Frog Embryo Teratogenesis Assay - Xenopus, *In Vitro* Test Methods for Identifying Ocular Corrosives and Severe Irritants, and Five *In Vitro* Pyrogen Test Methods.

Melvyn Lynn, M.S., Ph.D.

Dr. Lynn received M.S. and Ph.D. degrees in Microbiology from Rutgers University in New Brunswick, New Jersey. He is currently Senior Director and Global Head, Sepsis and Anti-Infectives Therapeutic Area at Eisai Inc. Dr. Lynn's expertise in the area of pyrogenicity is evidenced from his involvement in the clinical development of TLR4 antagonists and antimicrobials. Dr. Lynn directs global clinical development of a TLR-4 antagonist and antimicrobials and is head of a multifunctional, international project team, for which he regularly interacts with FDA and international regulatory agencies. Dr. Lynn has participated in global Standard Operating Procedure process development teams and served on the Eisai Global Clinical Development Global Development Board to address globalization of clinical development of drugs and clinical processes. Dr. Lynn has authored or coauthored 24 peer-reviewed publications, a review, two book chapters, a research letter, and 28 abstracts. Dr. Lynn has additional drug development experience during his tenure at the Bristol-Myers Squibb Company.

Anthony Mire-Sluis, Ph.D.

Dr. Mire-Sluis received his Ph.D. in Cell Biology and Biochemistry from the Department of Haematology at the Royal Free Hospital Medical School. He is Senior Director – Product Quality and External Affairs at AMGEN, Inc. with former positions as Head of the Cytokine Group at the National Institute for Biological Standards and Control, Director of Bioanalytical Sciences at Genentech, Inc., Head of Analytical Science and Standards in the Center for Biologics Evaluation and Research (CBER) at the FDA and Principal Advisor for Regulatory Science and Review in the Office of Biotechnology Products and Office of Pharmaceutical Sciences in the Center for Drug Evaluation and Research at the FDA. Dr. Mire-Sluis's resume demonstrates his expertise in regulatory science associated with pyrogen

testing with experience in product quality and development of biologicals, in immunology, and prior experience with the FDA. Dr. Mire-Sluis has managerial and product development experience including management of analytical and product quality departments of up to 75 staff (postdoctoral and technical levels). He is involved in strategic planning of development of biotechnology-derived products, including toxicology, assay development, and quality control. Dr. Mire-Sluis has expertise in the detection, measurement, and characterization of biological materials using immunological, molecular biological, and cell biological technology (cytokines, growth factors, enzymes, monoclonal antibodies). He is involved in high throughput screening technology, bioassay and immunoassay designs, risk assessment and process validation. He is a member of the World Health Organization consultative committee for therapeutic drug standardization, Chairman of the International Union of Immunological Societies Standardization Committee and of the human therapeutics committee of the International Association for Biologicals, a board member for the Journal of Immunological Methods, a member of the U.S. Pharmacopeia Biological Assay Statistical Analysis Expert Working Group and the Biological Assay Validation Expert Working Group. Dr. Mire-Sluis has authored almost 100 peer-reviewed publications.

Jonathan Richmond, BSc (Hons) Med.Sci., MB ChB, FRCSEd, FRMS

Dr. Richmond received a Bachelor of Science in Medical Science with Honors (B.Sc. [Hons] Med.Sci.) and Bachelor of Medicine and Bachelor of Surgery (MB ChB) degrees with Distinction in Medicine and Therapeutics from Edinburgh University. Presently, he is head of the Animals Scientific Procedures Division at the Home Office. He is a Fellow of the Royal College of Surgeons of Edinburgh (FRCSEd) and a Fellow of the Royal Society of Medicine (FRMS). Other appointments include convener of the U.K. interdepartmental group on the 3Rs, board member U.K. National Centre for the 3Rs, convener of the International Standards Organization Technical Corrigendum 194/Working Group 3 (*Biocompatibility of Medical Device Materials*), and member of related expert working groups. He is a former member of the EU Committee on Scientific and Technical Progress and past Chairman of the European Commission Technical Expert Working Group on ethical review. He served as chair of the peer review panel for the reduced murine local lymph node assay (LLNA) test protocol and prediction model for ESAC in 2007 and has been designated as an ESAC peer reviewer for ECVAM's performance standards for the standard LLNA. He served on the NICEATM-ICCVAM Expert Panel that evaluated Five *In Vitro* Pyrogen Test Methods. He has a variety of publications in peer-reviewed journals and national and international meetings, on the principles and practice of surgery, regulation of biomedical research, principles of humane research, bioethics, and public policy.

Peter Theran, V.M.D.

Dr. Theran holds a Doctor of Veterinary Medicine degree from the University of Pennsylvania. He has had many years of experience both as a veterinary internal medicine specialist at the Massachusetts Society for Prevention of Cruelty to Animals' Angell Memorial Animal Hospital in Boston, and as the director of Boston University Medical Center's Laboratory Animal Science Center. He presently serves on a number of government committees as an animal welfare member, and is a member of the Board of Directors of the Institute for *In Vitro* Sciences in Gaithersburg, MD and Chimp Haven in Shreveport, Louisiana. He served on the NICEATM-ICCVAM Expert Panels that evaluated the *In Vitro* Test Methods for Identifying Ocular Corrosives and Severe Irritants, and Five *In Vitro*

Pyrogen Test Methods. He is a former member of the Advisory Committee on Alternative Toxicological Methods and SACATM. He is presently working as a consultant.

Kevin Williams

Mr. Williams received a B.S. degree in Microbiology from Texas A&M University. He is a Microbiologist in the Quality Control Laboratory at Eli Lilly & Company. Mr. Williams' resume indicates that he is a well-noted expert in pyrogen testing (Bacterial Endotoxin Test [BET] and LAL) and validation and he has authored several books on endotoxins. His responsibilities include bacterial endotoxin testing and validation, automation of BET, depyrogenation validation, automated microbial identification system validation, validation of sterility tests, preservative effectiveness testing, microbial purity testing and validation, and bioburden testing and validation. Mr. Williams is a member of the LAL User Steering Committee, the Parenteral Drug Association, and the American Society for Microbiology. He has developed a method to calculate tolerance limits for excipients based on unit formula content of finished drug and developed novel methods of recovering endotoxin from parenteral drug packaging components. Mr. Williams served as editor of the textbook, "Microbial Contamination Control in Parenteral Manufacturing," and contributed a chapter on "Historical and Emerging Themes in Parenteral Manufacturing Control." He also edited the textbook "Endotoxins," and contributed chapters on endotoxin and contamination control.