Respiratory Experience of PROMETRIKA, LLC

Experience in Asthma, COPD, and AECB

- PROMETRIKA has recently submitted a full NDA in asthma: the PROMETRIKA team developed the ISS, ISE, and other summary sections of the NDA while conducting the data management, statistical analysis and medical writing tasks for two additional US studies for that dossier.
- Since it's founding, PROMETRIKA has been involved in design, analysis, and data management of 6 asthma studies.
- PROMETRIKA core team members were responsible for the statistical and data management activities for a European submission of a steroid metered-dose powder inhaler (MDPI) evaluated for the treatment of asthma. They also participated in protocol development and report writing. This dossier was approved by BfArM, the German regulatory authority, in 1999. The submission included a multi-center international Phase III study, which was designed to investigate the therapeutic equivalence of a glucocorticosteroid delivered by either the new MDPI or an approved device. As members of the US project team for this MDPI device, PROMETRIKA staff members had a pivotal role in devising the US strategy and development plan, as well as the pre-IND package and subsequent IND submitted to the FDA. These efforts included the design and development of a number of protocols and case report forms for Phase II and Phase III studies in asthma.
- In the area of COPD, the staff has worked on seven Phase I and Phase II studies from protocol design through finalization of the clinical study reports. Some of PROMETRIKA's team members had a pivotal role in the design of the development plans and studies for a long-acting anticholinergic agent used in the treatment of COPD. This compound was under development in both MDI and nebulized formulations.
- The PROMETRIKA core team was responsible for the Phase IV support of a marketed oral asthma medication and an oral antibiotic indicated for AECB. The team's activities in this respect included the design, data management and statistical analysis of Phase IV studies, as well as pharmacoeconomic analyses for formulary submission. One Phase IV trial in nocturnal asthmatics and another Phase IV trial in AECB patients were published in peer-reviewed journals with PROMETRIKA team members as co-authors.
- PROMETRIKA's data management staff has conducted a number of clinical trials with PFT data captured directly from medical equipment at investigational sites and has significant experience with management of data captured from electronic peak flow meters.
- PROMETRIKA's statistical and medical writing experience in asthma and COPD includes involvement in specialized studies such as serial PFT studies for determination of onset and duration of action and a complex methacholine challenge study. As a result of this experience, PROMETRIKA's biostatisticians have significant expertise in the application and interpretation of the statistical methods used in the analysis of data from these specialized studies.

Experience in Allergic Rhinitis and Allergic Conjunctivitis

- Members of the PROMETRIKA core team participated in the development and compilation of an NDA and a computerized new drug application (CANDA) that were submitted to the FDA for a nasal steroid used to treat allergic rhinitis. The submission included 13 clinical studies. In addition to performing the statistical tasks for many of the individual studies, our biostatisticians were responsible for the development of the Integrated Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE), writing the Statistical Methodology summary section, and interacting with the medical and statistical reviewers at the FDA. This NDA was approved in 2000.
- From 2001 to 2003, PROMETRIKA staff participated in the drug development process for a soft steroid administered intranasally for allergic rhinitis. The team members' responsibilities included study design, data management, statistical analyses, and medical writing for six studies (Phase I through Phase III). This project was conducted by a multidisciplinary global project team and Ms. Judith Harris (Head of Project Management and Quality Systems at PROMETRIKA) had overall project management responsibility.
- PROMETRIKA staff members were also responsible for the preparation of the ISS, ISE, Application Summary, pre-clinical sections, and individual study reports of an NDA for an ocular antihistamine to treat allergic conjunctivitis. This drug was previously approved in Europe; however, the analysis methods used for the European submission did not meet the requirements of the FDA for drug approval. Hence, a complete re-analysis of data and re-writing of most of the European study reports was required by the Agency. PROMETRIKA staff members conducted all statistical analyses and medical writing of the US dossier, which included 18 European studies and one Phase III US study. This NDA was approved in 2000 within six months following submission.
- PROMETRIKA personnel were also involved in the protocol development of two Phase IV studies. One study was designed to evaluate the effects of a nasal steroid for the treatment of allergic rhinitis on the growth velocity of prepubescent children, and the second study was designed to compare the efficacy and safety of an antihistamine with an active control in the treatment of allergic conjunctivitis. Our biostatisticians had key roles in planning these studies, each of which had unique design features.

Commercialization Support

- Since its founding, PROMETRIKA has been responsible for commercialization support of an oral medication for treatment of asthma. PROMETRIKA statisticians have conducted analyses for a number of publications and abstracts presented in respiratory and allergy meetings for that product.
- Prior to starting the company, PROMETRIKA personnel have participated in commercialization support of a number of respiratory and allergy products. Working

with marketing experts in a mid-sized pharmaceutical company, the PROMETRIKA team has acquired the skills and knowledge necessary to devise and implement design strategies for Phase III development that can be used to distinguish the brand in the marketplace, post approval.

- PROMETRIKA team members have also written abstracts and designed posters for presentation at several professional meetings. Dr. Miganush Stepanians (President & CEO of PROMETRIKA), at the request of the Marketing Department, presented at the American Academy of Asthma, Allergy, and Immunology annual meeting, results of a meta-analysis that demonstrated the efficacy of a product for treating allergic conjunctivitis.
- PROMETRIKA offers specialized expertise in pharmacoeconomics. Dr. Nicole LaVallee (Director of Biostatistics at PROMETRIKA) was responsible for designing and performing cost-effectiveness evaluations for detailed dossiers of several marketed products. For three drugs, indicated for AECB, allergic rhinitis, and allergic conjunctivitis, cost-effectiveness analyses against marketed competitors were conducted and presented to various managed healthcare organizations, including one of the largest healthcare service contractors in the northwestern US. These submissions helped secure formulary coverage on numerous healthcare plans for these products.
- The PROMETRIKA team members have developed and co-authored numerous publications including abstracts, posters, and peer-reviewed journal articles specific to respiratory and allergy indications.

Senior Consultant to PROMETRIKA/ Medical Advisor on Respiratory and Allergic Diseases

Elliot Ellis, MD

Dr. Ellis, former Medical Director at Muro Pharmaceutical and a nationally known allergist/clinical immunologist is Professor Emeritus at the State University of New York at Buffalo. He is the former President of the American Academy of Allergy, Asthma and Immunology and has served as Chairman of the American Board of Allergy and Immunology; Chief of Pediatric Allergy/Immunology at the National Jewish Hospital and Research Center, Denver, CO; and Chairman of the Department of Pediatrics at the Children's Hospital of Buffalo. Dr. Ellis is one of the three founding editors of the two-volume textbook, "Allergy: Principles and Practice" (now in its 6th edition), which is considered to be the definitive work in the field. He has published widely in the field of allergy and particularly on asthma. Currently, he is serving as a pharmaceutical company consultant and volunteers at the Free Medical Clinic in St. Petersburg, FL, where he lives.