

**STATEMENT OF  
FRED N. ESHELMAN, Pharm.D  
CEO, PHARMACEUTICAL PRODUCT DEVELOPMENT, INC.  
FOR  
THE HOUSE ENERGY AND COMMERCE  
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS  
FEBRUARY 12, 2008**

**Introduction**

Good morning Chairman Stupak, Congressman Shimkus, and Members of the Subcommittee. I am Fred N. Eshelman - the founder of Pharmaceutical Product Development, Inc. ("PPD"). Since July 1990, I have served as its Chief Executive Officer. It is my pleasure to be here today as a representative of PPD. Attached to this statement is a copy of my *curriculum vitae*.

**PPD**

PPD is a global Contract Research Organization ("CRO"). We provide drug development services to pharmaceutical, biotechnology, and medical device companies and government organizations – all of which are referred to as sponsors.

As a CRO, PPD is hired by sponsors of clinical trials to perform obligations of the sponsors arising under the Federal Food, Drug and Cosmetic Act and FDA's clinical study related regulations, principally 21 CFR Parts 50, 56 and 312 and/or 812. Under FDA regulations, a sponsor may transfer the legal obligation for compliance with regulatory requirements to a CRO.

Sponsors may contract with CROs to perform a wide variety of tasks. Often, a CRO is asked to monitor a study's investigation sites in order to confirm that a site's conduct is consistent with the protocol, applicable regulations, and Good Clinical Practices ("GCPs"). In

addition, a CRO may also be asked to take part in the selection and training of investigators, provide data management services, perform biostatistical analysis of study data, conduct quality assurance, prepare / submit regulatory filings, or provide medical writing services in support of a new drug application or final study report. In some cases, a sponsor may simply delegate full responsibility for the administration of a study to a CRO.

Regardless of the scope of the delegation, the FDA regulations require that any delegation of authority be set forth in a written agreement. Under FDA regulations, any obligation that is not specifically transferred to the CRO is *retained* by the sponsor. These requirements are set forth in 21 CFR section 312.52.

#### **Ketek (Study 3014)**

In the Fall of 2001, PPD contracted with Aventis to perform specified services in connection with the study of Ketek (Study 3014). Study 3014 was designed by Aventis as a large clinical trial and involved 24,000 patients and 1,800 investigative sites across the United States. Under the terms of our agreement, the following tasks were delegated to PPD:

1. Recruit and select physicians to serve as site investigators, negotiate site agreements, and make site payments;
2. Assist a third-party vendor in training investigators on study policies and procedures;
3. Create an Interactive Voice Response System to randomize patients and manage the supply of the study drug to sites;
4. Monitor study sites;

5. Track site documentation and communications;
6. Facilitate the transfer of case report forms submitted from the sites to Aventis's data management vendor and assist in resolving queries; and
7. Notify Aventis of serious adverse events and adverse events of special interest among patients.

Other than these obligations, Aventis did not contract with PPD to perform additional services. For instance, PPD did not provide any data management, medical writing, quality assurance, or biostatistics services.

With regard to addressing investigator misconduct, federal regulations require that the sponsor either secure compliance or end the investigator's participation in the study. If an investigator is terminated, then the FDA must be notified. This requirement is set forth in 21 CFR section 312.56(b). Under our contract with Aventis, PPD was to report any investigator that did not comply with the study plan to Aventis. We did *not*, however, have the authority to end an investigator's participation in the study or to report an investigator's conduct to the FDA.

#### **Kirkman-Campbell Site**

During the course of its monitoring activities in Study 3014, PPD's staff uncovered compliance concerns at the site of an investigator now familiar to this Subcommittee, Dr. Anne Kirkman-Campbell. In October 2001, Dr. Kirkman-Campbell was engaged as an investigator for Study 3014. She managed a medical practice in Gadsden, Alabama. As this Subcommittee knows, Dr. Kirkman-Campbell ultimately enrolled 407 patients over a 3 month span, which established her site as Study 3014's highest enroller.

PPD's monitoring team made its first visit to the Kirkman-Campbell site in late November 2001. In February 2002, PPD's monitoring team visited the Kirkman-Campbell team for a second time. During the visit, PPD personnel determined that the site failed to document critical source information. PPD staff also found many inconsistencies and modifications regarding patient signatures on Informed Consent forms. Further, subjects appeared to have been randomized for the study in extremely high volumes during short time intervals. In some circumstances, 20 or more patients were randomized approximately 1 minute apart from each other. Additionally, PPD monitors found staff at the Kirkman-Campbell site uncooperative.

At the same time of the February visit, PPD also analyzed data from the Kirkman-Campbell site regarding patient blood samples due to concerns raised by our staff. Based upon PPD's review, there appeared to be a lack of variability among blood samples shared by many patients. The data suggested that the Kirkman-Campbell site engaged in "blood sample-splitting," which is assigning a patient's blood sample to one or more patients in order to maximize enrollment totals.

#### **March 4, 2002 Conference Call**

In light of these concerns, PPD staff asked for a conference call with Aventis. We were concerned about the information we had acquired and wanted to ensure that we brought this information to Aventis's attention. During a March 4, 2002, conference call with employees at Aventis, PPD personnel set forth in detail their concerns about the Kirkman-Campbell site.

At the conclusion of that call, Aventis said that it would look into Kirkman-Campbell's compliance issues and devised an action plan. First, Aventis said it would initiate its own analysis of the Kirkman-Campbell lab data to determine the probability that the site had engaged

in blood sample-splitting. Ultimately, Aventis informed PPD that it had analyzed the lab data and that the data was not indicative of scientific misconduct. Second, the Aventis study manager was tasked with contacting Dr. Kirkman-Campbell about the site's informed consent and randomization problems raised by PPD. Ultimately, Aventis and PPD sent a follow-up letter to Dr. Kirkman-Campbell, raising these issues. Aventis did not ask PPD to terminate Dr. Kirkman-Campbell as an investigator or to report her conduct to the FDA.

### **Conclusion**

Mr. Chairman, on behalf of PPD, I would like to thank you for the opportunity to testify before this Subcommittee. I hope that my testimony provides the Subcommittee with a better understanding of PPD, the regulatory and contractual framework that governs our conduct, and our role in the Kirkman-Campbell matter. I welcome any questions that you have.

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## **CHIEF EXECUTIVE OFFICER**

**Fred N. Eshelman**

### **EXPERIENCE**

#### **PPD, INC., WILMINGTON, NC (PPDI, NASDAQ)**

Chief Executive Officer and Vice Chairman

July 1990 - Present

#### **GLAXO INCORPORATED, RESEARCH TRIANGLE PARK, NC**

Senior Vice-President, Development Division

January 1989- June 1990

Responsible for Metabolism, Toxicology and Project Planning, Pharmaceutical Development, Regulatory Affairs, Biostatistics/Data Management, and Phase III Clinical. Co-Chairman, US-UK Joint Development Committee, Member of Executive Committee and Board of Directors, Glaxo Inc. and Glaxo International Research Limited.

Vice-President, Clinical Operations

September 1988 - December 1988

Responsible for all Glaxo Inc. clinical research (Phases I-V) and Biostatistics/Data Management. Member of Operations Committee.

#### **PHARMACEUTICAL PRODUCT DEVELOPMENT, WILMINGTON, NC**

President and Founder

June 1985 - August 1988

Clinical research management company involved in all phases of product development in a variety of therapeutic areas.

#### **BOEHRINGER-MANNHEIM CORPORATION, ROCKVILLE, MD**

Director of Clinical Research

October 1984 - June 1985

**GLAXO INCORPORATED, RESEARCH TRIANGLE PARK, NC**

Group Director, Clinical Research

May 1983 - September 1984

Associate Director, Clinical Research

August 1979 - April 1983

**BEECHAM LABORATORIES, BRISTOL, TN**

Associate Director, Clinical Research

December 1977 - August 1979

Director of Professional Relations

August 1977 - May 1978

**BIO/BASICS INTERNATIONAL, NEW YORK CITY, NY**

Assistant Director, Clinical Operations

1976 - 1977

**EDUCATION**

- Harvard Business School  
OPM Class 22  
1993 - 1995
- University of Cincinnati, Division of Graduate Studies  
Doctor of Pharmacy  
1974
- Cincinnati General Hospital, Rotation to Cincinnati V.A. Hospital  
Clinical Pharmacy Residency  
1972 - 1974
- Duke University, Durham, NC  
Academic portion, Physicians' Associate Program  
1971 - 1972
- University of North Carolina, Chapel Hill, NC  
Bachelor of Science (Pharmacy)  
1972

- High Point University, High Point, NC  
Chemistry  
1966 - 1969

## **ACADEMIC EXPERIENCE**

### **UNIVERSITY OF NORTH CAROLINA, SCHOOL OF PHARMACY, CHAPEL HILL, NC**

Adjunct Professor & Board of Visitors

Present

### **UNIVERSITY OF ILLINOIS MEDICAL CENTER, COLLEGE OF PHARMACY**

Clinical Assistant Professor

1974 - 1976

## **PUBLICATIONS**

Available upon request.