Number 7 February 14, 1977

Citation Classics

Litchfield J T& Wilcoxon F A. A simplified method of evaluating dose-effect experiments. *J. Pharmacol.* Exp. Ther. 96:99-113, 1949.

Due to the widespread use of statistical methods for evaluating biological data, it was necessary to solve a dose-percent curve. This paper presents a rapid graphic method for approximating the median effective dose and the slope of dose-percent effect curves. This method is able to estimate the confidence limits for any conventional probability or for a dose other than the median effective dose. [The SCI® indicates that this paper was cited 2,238 times in the period 1961-1975.]

John T Litchfield, Jr., M.D.
Hardscrabble
P.O. Box 85
Heathsville, Virginia 22473

December 14, 1976

"Frank Wilcoxon, a complete stranger to me, learned early in 1945 that I had accepted a position with the same labora-tories where he was working. He had already concluded that the Litchfield-Fertig method for 'Graphic solution of the dosage-effect curve'[1] was logical and attractive but capable of improvement. His enthusiastic wish to collaborate with me on this project was such that he left explicit instructions with the reception desk that he was to be called there immediately upon my arrival. As a consequence, I met Frank and began discussing the method before I even saw my employer or went to the personnel department.

"I had spent many hours computing dose-per cent effect curves using a mechanical calculator in order to devise a 15-20 minute approximation to replace a 2-3 hour task. In view of Frank's intense interest in the method, my considerable ego was abruptly deflated when I learned that he considered the method too laborious, confusing, and time consuming. However, he rapidly convinced me that most biologists found logarithms and probits incomprehensible but were accustomed to dosages and per cent effects or responses. By using specially ruled graph paper (logarithmic-probability), the data could be plotted directly and a line fitted by eye without need to convert to logarithms and probits. In addition, he had devised a Chi^2 test to tell whether or not the trial line was a reasonable one. This included a nomograph which eliminated the calculations necessary for determining Chi^2 values.

"From that first meeting on we concentrated on the construction of the other nomographs needed to eliminate calculations and on the set of instructions for the revised and simplified test. As these were perfected we undertook 'clinical trials' with less and less sophisticated subjects in order to discover and clarify any points which were confusing. Our product was judged satisfactory when it was used successfully by our colleagues whose speciality was organic chemistry. It was then submitted for publication.

"Although formally trained as an organic chemist, Frank was also an expert in plant physiology, mathematics, and statistics. His intense interest in short, quick statistical methods led to his discovery and the opening up of the field on non-parametric statistics. Had it not been for his intense interest there might never have been the Litchfield-Wilcoxon method."

1. **Litchfield J T & Fertig J W.** Graphic solution of the dosage-effect curve. *Bull. J. Hopk. Hosp.* 69:276-86, 1941.