THREAT AGENT DEFEAT MODELING AND TESTING USING WMD SIMULANTS

Understanding Mixtures

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Human history contains many examples of combining chemical compounds to produce new and improved tools for our survival i.e. medicine, dyes, soaps, and metal alloys. The discovery of novel chemical mixtures has continued to modern times with beneficial drug combinations to combat cancer and deleterious combinations used for military or law enforcement purposes. Mixtures of chemical compounds and their combined effects on the human body present an extraordinarily complex problem that requires a reliable characterization method. Typically, the chemical compounds being mixed will manifest similar effects in the human body i.e. cytotoxicity, sedation, etc. The method of characterization for mixtures needs to address whether the two chemical compounds, acting together produce a combined effect that is consistent with their individual potencies, termed additive, an effect greater than additive, termed synergistic or an effect that is less than additive, termed sub-additive. There have been many methods developed to determine if a drug combination departs from additivity however the Loewe methodologies graphical representation of an isobole is the original method. For this project an isobole was established for a well-known drug combination that causes hepatoxicity, acetaminophen and amoxicillin with clavulanate, to build the foundation for the characterization of the innumerable potential chemical combinations that present a threat to the warfighter.