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13 ABSTRACT (Maximum 200 words) The project was initiated October 1, 1991. Major accomplishments during the first year of the project were: 1) refinement of data analysis software; 2) conduct of a literature review of binary and multicomponent toxic response data; 3) analysis of a sample of data sets using the developed software; and 4) refinement of the theory of copulas with respect to multicomponent dose-response relationships. Papers relating to the work have been submitted and/or presented in the following locations: International Association on Water Pollution Research and Control, Water Science and Technology, Eastern North American Regional Meeting of the Biometric Society, Environmental Toxicology and Chemistry. One M.S. thesis related to this project has also been completed (Bruce A. Stirling).			
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Development of Novel Models for Describing Multiple Toxicity Effects

AFOSR 91-0428

Summary of First Year Progress

The project was initiated October 1, 1991. An M.S. student at Drexel was assigned to assist this project, Mr. Bruce Stirling. Mr. Stirling was supported by funds external to the AFOSR Project, however his thesis research is directly related to the project.

Tasks Performed and Accomplishments

During the period October 1, 1991 - September 30, 1992 (months 1-12), the following major activities were conducted:

- refine computer program to run on both DOS and Macintosh platforms
- modify computer program to include normal and Poisson data types (as well as binomial)
- perform a literature review of binary and multicomponent data
- test the program with representative data sets among those obtained
- refine theory of copula analysis of multicomponent dose-response relationships

Based on this work, the following major accomplishments can be reported:

1. We now have a fairly robust computer tool for the reduction of binary toxicant data using the interaction models summarized in the original proposal. This has been tested on data of the binomial, normal and poisson types, so that we have good confidence in the flexibility and reliability of the computations.
2. Using extensive manual and computer literature searches, we have a bibliography of approximately 300 references containing dose-response studies involving multiple compounds. Of these, approximately 100 contain numerical data amenable to further study. Of the 300 references, about half are concerned with one or more compounds of specific interest to the Air Force.
3. We have placed the results of our computer literature search in a summary computer data base file which contains, in addition to bibliographic data, descriptors about the nature of the study.
4. We have obtained hard copies of each of the english-language sources described in (3).
5. Quantitative analyses of six data sets have been performed.
6. Theoretical analysis of the modified isobole approach of Berenbaum has been commenced.
7. We have developed a method for fitting the various data sets to modified isobole models using Microsoft® EXCEL on a Macintosh.

On May 18-20, Professor J. Frank visited Drexel University, and presented a seminar on the early stages of his theoretical analysis of binary dose-response relationships. Professor's Haas and Frank discussed future activities with respect to this project.

On May 25-29, Professor Haas attended the Biennial Conference of the International Association

on Water Pollution Research and Control (IAWPRC). During this conference, he presented a poster on work leading up to the development of this project.

Bruce Stirling completed his thesis describing much of the above work in August 1992. This described much of the above work. Based on his thesis, we have prepared three papers. One paper, which is a formal version of the work presented at the IAWPRC meeting has already been published:

Haas, C.N. 1992. A New Approach for the Analysis of Mixture Toxicity Data. Water Sci. Technol. 26: 9-11: 2345-48.

A second paper was presented after the reporting period (March, 1993, at the Eastern North American Regional Meeting of the Biometric Society). The third paper is currently under review for publication in *Environmental Toxicology and Chemistry*.

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