INTRO AND HISTORY FOR LIFELINE

History and Issues Leading to the Development of LifeLine™

Prior to 1996, risk assessment practices used to regulate pesticides reflected the technology, data and the legislative mandates of the time. Each pesticide use was regulated independently; deterministic values were used in simple paradigms. Single databases were utilized to describe population characteristics and activity patterns. Dietary risk was the key focus for regulatory risk management.

In the mid 90's, several factors merged to change the fundamental approaches to risk assessment for pesticide regulation. The legislative mandate changed with the passage of the Food Quality Protection Act (FQPA). Technology changes with the easy access to fast and powerful computers permitting utilization of large databases and performing complex iterative calculations. Information sources expanded and quality of data has begun to improve. Before a model could be developed, these changes deserved a thorough consideration.

The Legislation

The FQPA required risk assessment entailing new considerations:

- All pesticidal uses of a given active ingredient (and other non-pesticidal sources of exposure) are to be considered together in an **aggregate assessment.** This requirement addresses the reality of exposure in our lives, but this is not a simple task. We cannot just "add up" all of the separate exposures. We must be able to consider together all exposure possibilities, but characterize them clearly. Which are concurrent, which are mutually exclusive. Some are exposures of long duration, some may be episodic, some are brief spurts or spikes. We must be able to delineate the different routes of exposure from these different sources. Our aggregation must preserve the information about dose by inhalation versus oral versus dermal, since the toxicological significance may be key. Also, different uses may yield exposures to different people or to the same people at different times of the year, or different phases of a life. (e.g. The applicator exposure cannot be added to the dietary exposure of an infant.)

  Thus, aggregation is not just a sum of exposures. Aggregation requires a spatial and temporal consideration -- a consideration of the exposure opportunities of different people at different places at different times. The implications of this are profound. It means that people's lifetime opportunities of exposure must be carefully defined. Exposure is now defined in more than terms of magnitude. It is defined also in terms of duration, route, personal characteristics (age, physiology) of the exposed person, etc. Implementation of aggregation of exposure carries with it the obligation to define exposure and risk in these new terms. They are essential for any meaningful aggregated assessment.

- All active ingredients having a similar mechanism of action must be considered together in a **cumulative assessment.** Thus, as a family of chemicals is considered together, the assessment procedure must preserve key characteristics of each individual chemical. Although there may be commonality in their mechanism of action, each may have different potencies and that may be related to the route of exposure. Each may have different abilities to cross dermal barriers, different excretion rates, different physical characteristics. The assessment must preserve the ability to recognize the relative contribution of each to the total exposure.

  Temporal and spatial and personal elements of exposure, as discussed under aggregate exposure, apply here as well. In addition, we recognize that any error, bias or uncertainty embodied in the assessment elements of ONE chemical contribute to the error, bias and uncertainty of the cumulative assessment. When many chemicals are considered together, these problems can magnify and skew the resulting assessment. Traditional practices of the past embraced utilization of extremes—in the name of prudent regulatory protection. Those laudable practices, born of technical necessity, threaten cumulative exposure assessments by magnifying conservative assumptions to the point where such assessments are a construction of bias rather than a reflection of data. New models must permit far more flexibility in viewing the full display of exposure possibilities in a menu of different perspectives. Only then can the regulatory risk manager consider reasonable mitigation options and their consequences.

- A special focus is required for potential risks to infants and children. Considering **age related risk** requires many of the same elements of assessment discussed above. This task underscores the need for new and enhanced data about the activities and exposure opportunities to each age group and the activity or physiological characteristics of each.

The Technology

New opportunities abound for utilizing today's (and tomorrow's) technology to aid in the tasks at hand. With present computer capacity, we can create, manage and manipulate large databases and utilize multiple databases simultaneously. We can perform complex iterative calculations involving probabilistic techniques. We have great flexibility in the format of assessment "outputs"—how the answers are presented. Indeed, the risk assessment is vastly more complex, but the answer can be viewed in new and extremely useful ways. The old conservative biases were the tool used because the full array of risk could not be viewed. To some degree, that challenge is being met and risk can be viewed over the life of individuals, over key periods of exposure opportunity, across general or specific populations, by unique routes or sources of exposure, and by a range of distributional options.

The Data

The new exposure and risk assessment questions demand definition of people and population characteristics (temporal, spatial, personal) to set up the foundation on which to hang the chemical-specific exposure information. Data are needed that define physiological characteristics of humans throughout their lifetime. Data are needed to define the activities undertaken by humans throughout their day, season, and lifetime. Activities are greatly influenced by geographical region, season, socioeconomic situation, age, education, urban/rural dwelling, and possibly ethnicity. Other factors may also play a role in characterizing opportunities for pesticide exposure.

Until recently, few databases played a significant role in pesticide risk assessment. The predominant databases have been the USDA dietary surveys, public and private data about food residues, and the specific physical/chemical characteristics about the specific chemicals. Data about the individual were gleaned from the USDA dietary surveys.

We have recognized new, powerful databases that meet some needs of the new assessment issues. The US Census is a powerful database that we will learn to utilize in better ways as we develop new tools. We also have information about the size and construction of homes throughout the United States, information about where people live, when they move, relocation frequencies and sequences. We know more about use of pesticides in the home, garden and on pets. We also have begun to define the areas where utilized data are sparse—transportation, public grounds, recreational areas, schools, institutions (hospitals, camps), commercial buildings, retail centers, and other places where we spend our time and where exposure opportunities exist. Relevant data may already be available and yet unidentified by those constructing the assessment models. Or, regrettably, relevant data may not yet exist at all and resources may be necessary to create the data. Good assessment models should characterize the potential utility of the data, so that the design and resources applied to data creation are appropriate for the possible improvement in the assessment.

Regulatory Needs and Public Interest

There has been a rising need for risk management that enhances integration of new pest management practices, safer alternatives and local particulars of risk management. There is an increasing need to recognize the global use of pesticides and the implications on our risk profile. There is a growing demand for the risk assessment practice to be transparent, and for the risk assessment tools to be available to any interested party. With that comes the necessity to audit the inputs to risk assessments and for a mechanism whereby all users have access to underlying sciences about the tools' data and algorithms.

Development of LifeLine™,

The architects of LifeLine™, Hampshire Research Institute, Christine Chaisson and Paul Price, undertook a mission to create risk assessment software that met the contemporary challenges and to make those tools available to all interested parties. Working together with other contributing scientists and technicians, the project team has produced Version 1.0 of LifeLine™, and prepared a user support program to aid all users, particularly the majority of users who have never previously had access to software used in the regulatory process. The experience gleaned from working with the databases, design concepts and computational displays are being prepared for presentation in various scientific venues.

We presented the fundamental design and principles of the LifeLine™ software to the Science Advisory Panel on September 22, 1999. A copy of that presentation material is available to this Panel.

The presentation of September 28th, 2000 is focused on the utility of the software in relation to the challenges outlined above. In particular, we wish to demonstrate the LifeLine™ architecture and application options in conducting aggregate and cumulative exposure/risk assessment We will present some of the profiles that can be produced to view characteristics of aggregate and cumulative exposure. These profiles visualize key areas of interest, in terms of age-specific exposure, influences of "safety factors", population differences, relative contribution to exposure by different uses of pesticides, different active ingredients, and the influence of seasonal variation, socioeconomic and regional differences. Inferences on the importance of missing data will be pointed out. Some of the options for graphical presentation of the full array of risk calculations are presented as examples of the new tools available to the risk assessor for considering risk mitigation scenarios.

We solicit your comments on future applications of LifeLine™ and advice on how best to interpret output reports derived from the model. To assist the SAP in this task, each panel member is provided the following documents:

- Description of the architecture and features of LifeLine™ Version 1.0

- Demonstration Exposure Assessment doing aggregate assessment and cumulative assessment, comparing, contrasting and profiling the exposure elements of interest. Paper entitled: "Assessing Aggregate and Cumulative Pesticide Risk Using a Probabilistic Model", by Paul S.Price, John F.Young, and Christine F. Chaisson.

  Abstract: Determining aggregate and cumulative risks from exposures to pesticides presents a number of challenges. The analysis must capture the correlations in residues that occur from both additive and exclusionary processes in the use of pesticides. The analysis also requires a quantitative mechanism for

evaluating risks associated with exposures to time-varying mixtures of pesticides. This paper presents an analysis of aggregate exposures and risks associated with exposures to a hypothetical pesticide, Alpha, and the cumulative exposure to and risk from three hypothetical pesticides, Alpha, Beta, and Gamma. The cumulative risks are evaluated by determining the systemic (absorbed) doses that result from inhalation, dermal, and oral exposures to the pesticides. A "toxicity equivalent" model of cumulative risk is used to quantitatively evaluate cumulative risks. The assessment of cumulative exposure was performed using the LifeLine™ Version 1.0. This model simulates pesticide exposure using an individual-based approach where daily exposures are evaluated for each person, season, and location.

- Background document for Sept 22, 1999 SAP entitled: Review of an Aggregate Exposure Assessment Tool.