Supplemental Material for:
February 5-8, 2002 SAP
25 January 2002

Background Paper

Rolling Time Frame Approach

One important aspect of the preliminary cumulative risk assessment for the organophosphate pesticides (OPs) is the manner in which estimated exposure is compared with toxicity endpoints. This paper briefly describes and compares two different "modes" of analysis in DEEM/Calendex which are available and permit consideration of either a single day or varying time frames of analysis. It is hoped that this document will provide sufficient background material for the Panelists to address the various questions and concepts relating to rolling time frames during the February 5-8, 2002 FIFRA Scientific Advisory Panel Meeting. The concepts discussed here have specific applicability to Question #2 of the Food Exposure session and Question #1 of the Risk Characterization session.

DEEM/Calendex Time Frames of Analysis

The DEEM/Calendex program can perform analyses by either of these two options.

- Under the first option (termed the single consecutive day option), separate, independent estimates are made for each day of the year (January 1, January 2, etc.). These can be arrayed into an exposure timeline for any selected percentile and graphed. That is, for example, the estimated 99th (or any other percentile) percentile exposure value is calculated by DEEM/Calendex for each day of the year from January 1 through December 31. These represent independent daily estimates of the 99th percentile exposures on each day of the year and do not necessarily represent the same individual on consecutive days. Thus, it is NOT possible (with this mode of analysis) to interpret an extended period (or series) of elevated exposures over time as necessarily representing extended exposures to the *same* individual, and comparison of any estimated exposure to multi-day endpoints (e.g., a multi-day BMD_{10}) would be expected to provide a very conservative estimate of risk to the extent that exposures on consecutive days at any given percentile are unlikely to be the same individual.

- Under the second option (termed the multiple sequential day option), a rolling (or sliding) time frame is used and multi-day average exposures are calculated for each

individual (e.g, average exposures for each individual for January 1 through January 7, January 2 through January 8, etc.). Under this mode, average exposures over multiple consecutive days (e.g., January 1 through 7, January 2 through 8, etc.) are assessed for the same individual. It is then this distribution of multi-day average exposures at any given percentile which serves as a basis of comparison with the (multi-day) BMD_{10}. DEEM/Calendex permits rolling time frames of 7-, 14-, 21-, and 28-days duration.

In the Preliminary Cumulative Risk Assessment, exposures were estimated on a single-day basis (the first option) and a comparison made of each independent DEEM-estimated single-day exposure with the steady-state (21 day) equilibrium BMD_{10} value (see the exposure profile plots presented in the Preliminary Cumulative Risk Assessment in Figures III.I.2-1 to III.U.2-20). That is, separate exposure estimates were made for January 1, January 2, etc. for each individual in the CSFII survey *for each (single) day of the year* with exposure at a given percentile (e.g., 99^{th}) calculated and compared to a multi-day BMD_{10}. In viewing these figures, and despite their one-day exposure basis, OPP is NOT concerned with exposure spikes lasting only one or perhaps a few days since the MOE's associated with these "spikes" are based on multi-day toxicity endpoints. Rather, OPP is interested in extended periods of high exposure (or, equivalently, low MOEs) which indicate not that an *individual* is being exposed to high levels of OP pesticides over a multi-day time period, but instead that the overall level of exposure to the sub-population in the tails of the distribution has increased. This is an important distinction which brings up two issues:

- comparing a series of elevated single-day exposures to multi-day endpoint may have less relevance than comparing a multi-day average exposure (at any given percentile) to a multi-day endpoint.

- Consecutive single-day estimates of exposure are likely to significantly overestimate multi-day exposures to an individual (at the higher percentiles) i.e., the individuals at or around the 99^{th} percentile are unlikely to appear there on consecutive days.

The alternative option is to estimate multi-day rolling average exposures in which average exposures over multiple consecutive days (e.g., January 1 through 7, January 2 through 8, etc.) are assessed for the same individual. It is this multi-day average exposure which then serves as a basis of comparison with the (multi-day) BMD_{10}. There are a number of advantages to this alternative. In addition to providing a means of estimating exposure which is more directly comparable to a multi-day endpoint, the multiple sequential day mode of analysis better incorporates variability in exposure for an individual across multiple days and is likely to provide a more realistic estimate of exposures for individuals across multiple days. It is also flexible with

respect to matching time-frame associated with BMD_{10} in that multi-day averages can be calculated over 7, 14, 21, or 28 days.

Importantly, however, the USDA's Continuing Survey of Food (CSFII) does not provide consumption data across the multiple consecutive days which would be of interest. That is, the USDA food consumption survey does not provide *longitudinal* data in which the consumption of the same individual is followed and traced for any extended period of time. The CSFII consumption data which serves as a basis of DEEM/Calendex exposure estimates is limited to two non-consecutive days of data (i.e., two days separated by 3-10 days) for each interviewed individual. This means that any multi-day average exposure for any given individual (as calculated by DEEM/Calendex's multiple sequential day rolling time frame approach) repeats, for each individual on each day of the time frame of interest, one of that individuals' two reported diets (randomly) in a sequential series (e.g., Day 1 diet, followed by Day 2 diet, then Day 2 diet again, Day 1 diet, etc.)[1]. Two issues become apparent with the use of CSFII data in this way:

(1) The DEEM/Calendex method assumes that the food contribution to exposure is the result of eating an ongoing diet that, for each individual, corresponds only to one of the two, non-sequential, daily diets reported for a person in the USDA Continuing Survey of Food Intake by Individuals (CSFII). This assumption does not correspond to reality in that a person will likely have greater variability in his or her eating habits than would be reflected by randomly selecting from two days of food choices. Thus, any consecutive day period of interest will contain in Calendex a series of repeated diets which do not reflect the true variability that likely exists in any given individual's diet.

(2) Since residue values are drawn at random (and anew) for each day's selected diet during the time frame of interest, true correlations that may exist between residues on subsequent days may not be accurately reflected in the DEEM/Calendex analysis. Specifically, the DEEM/Calendex method also cannot account for either the "leftover" phenomenon, i.e. the fact that there is likely to be some correlation between foods consumed by an individual on consecutive days, or the fact that there is likely to be some correlation between the residue levels found on fresh foods consumed on consecutive days. For example, left-overs eaten on subsequent days might be expected to contain similar or equivalent residues to those eaten on a previous day. The DEEM/Calendex program would draw residues anew from its residue distribution file for the food commodity of interest which would thereby not be reflective of actual residues to which individuals consuming leftovers would be exposed. In addition, as another example,

[1] Note that while each individual's two days or reported diet is repeated for the time frame of interest, residues for each commodity comprising that diet are randomly drawn so that each day's exposure is different.

individuals for many commodities might be assumed to consume on subsequent days foods obtained from the same source and the DEEM/Calendex calculations instead assume that the residues contained in these foods are independent. For example, if oranges were eaten on two consecutive days, the OP pesticide residues would be assumed in the DEEM/Calendex program to be independent. In reality, if these oranges were purchased at the same time (or selected from the same bag), it is not likely that these residues are entirely independent as both oranges likely share a common treatment history.