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Questions for
FIFRA Scientific Advisory Panel Meeting:
CALENDEX Session

9/5/00

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QUESTION #1

A major requirement of the Food Quality Protection Act is that exposures to pesticides across various pathways and routes (e.g., dermal exposure through turf uses) be appropriately combined such that an "aggregate" exposure assessment can be performed. Calendex^{TM} software from Novigen Sciences is able to perform this aggregation. Calendex^{TM} permits a time-based integration of both residential and dietary (food and water) exposures to pesticides. This is performed probabilistically such that aggregation (or combining) of residues across multiple routes is accounted for in an appropriate and realistic manner.

> **Do the algorithms and methodologies used by Calendex^{TM} appropriately combine (or aggregate) exposures to pesticides in a way which incorporates important factors associated with multiple routes of exposures, including the probability of co-incident applications and/or exposures and the demographic, temporal, and spatial aspects of exposure? Can the Panel suggest any improvements in the way this aggregation is performed by Calendex^{TM} or see any significant limitations?**

QUESTION #2

OPP's Aggregate Risk Assessment guidance calls for making appropriate matches in the demographic, temporal, and spatial characteristics in the exposure scenarios encountered by each "representative individual." Consistency in the pertinent demographic, temporal, and spatial characteristics is necessary to obtain realistic estimates of potential exposures to individuals in groups of concern. It is possible, for some of the large sets of data used by OPP, to divide databases into smaller databases by establishing separate groups by variable. For example, the CSFII food consumption data base may be broken down by age, sex, ethnicity, season of the year, or combinations of these variables, e.g. Hispanic female teenagers.

OPP believes that it is valuable and appropriate to subdivide its databases using a number of these variables to ensure a more realistic aggregate analysis. For example, food consumption varies significantly by age, and therefore it is appropriate to match or stratify on food consumption values by age. Likewise, where possible, OPP favors stratification of data on residential exposure

by season or region of U.S. and data on water exposure by region/locality of U.S. Matching or stratifying on other factors, however, may be of lesser importance (e.g, food consumption by region of U.S., ethnicity, or urbanization; water exposure by ethnicity). Since the available data sources and information for an extensive analysis which fully incorporate all potential factors are limited, attempting to match all these factors may lead to parsing the data so finely that the robustness and validity of the analysis suffer. When data are not stratified according to a variable, OPP has a larger, presumably more robust database for characterizing exposure.

> **Does the Panel have any thoughts on available procedures or techniques which could be used to determine which databases, variables, or factors which it is most appropriate to stratify on so as to produce the most realistic, yet robust, characterization of the distribution of exposures?**

QUESTION #3

Most of current data on food consumption and activity patterns concentrate on relatively short periods of time. For example, USDA's CSFII consumption data cover a period of only two (non-consecutive) or three (consecutive) days. In order to perform aggregate analyses over *multiple* days, the algorithms in Calendex™ randomly repeat the two (or three) day reported consumption values for an individual over the time period of interest. For example, if the distribution of daily exposures averaged over a 4 week time period is desired, then Calendex™ will repeatedly sample for each individual from only the two or three-day consumptions recorded for that individual.

> **Given the absence of longitudinal data concerning food consumption, is the method by which Calendex™ incorporates and uses the available single day consumption data from USDA's CSFII reasonable? Are there any suggestions or improvements that Panel members recommend? Can any statements be made about whether this practice will tend to overestimate or underestimate exposures?**

QUESTION #4

As indicated in Question #4, the Calendex™ software permits the user to generate for use by Calendex™ his or her own equations describing exposure. In the case of residential exposures, these equations can, if desired, be based on OPP Standard Operating Procedures for Residential Exposures. Calendex™ software permits the exposure equations to include terms in the form of point estimates, distributional estimates, or a combination of both.

Does that panel see any difficulties in using input data expressed as both point estimates and distribution estimates in the same (single) exposure analysis? Are there any cautions the Panel may offer to OPP with respect to interpretation of results or performance of sensitivity analyses when inputs into an assessment are present as both point estimates and distributional estimates?

QUESTION #5

Calendex[TM] offers the potential for overlaying daily exposure through multiple scenarios. Since the Calendex[TM] software does not limit the user to specific pre-programmed or "canned" exposure scenarios, the program allows the user to incorporate any exposure scenarios that can be conceived of, created, and modeled by the user.

Are there any reasonable situations for which OPP can limit the number of scenarios considered or can otherwise limit the analysis to those scenarios which are considered non-negligible in terms of exposure? Does the Panel have any suggestions as to criteria should be considered to exclude a particular scenario?

QUESTION #6

Calendex[TM] expresses an aggregate risk in terms of an "MOE", or *margin of exposure*. When multiple routes are evaluated , each having a different NOAEL (No Observed Adverse Effect Level), Calendex[TM] first calculates route-specific MOEs for each individual in the assessed population, then calculates a "Total MOE" for each individual, and finally presents as output the *distribution* of "Total MOEs" for all assessed individuals.

Consistent with previous SAP advice, OPP has elected to use the "Total MOE approach" in the conduct of its aggregate risk assessment and Calendex[TM] has adopted this methodology when performing aggregate risk assessments. Does the SAP have any further cautionary notes or comments on this approach or on the way this approach is implemented in Calendex[TM]?

QUESTION #7

OPP in its initial evaluation of potential residential exposures conducts its assessments assuming that use occurs, i.e., OPP estimates exposures given the assumption of use as per maximum label directions. When performing aggregate exposure assessments in which food, water, and

residential exposures are combined, OPP intends to incorporate the probability of treatment in its assessments to account for co-occurrence. If this information is available, OPP would also intend to probabilistically incorporate the range of application rates in its assessments. This method of handling data is similar to that used for food where actual percent crop treated and range of application rates, if available, are fully incorporated into the probabilistic assessment.

Does the Panel have any comments, suggestions, or thoughts on this approach for incorporating residential use scenarios into OPP's aggregate exposure assessments?