UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

December 16, 2009

MEMORANDUM

SUBJECT: Transmittal of Meeting Minutes of the FIFRA Scientific Advisory Panel Meeting on the Evaluation of Updated Standard Operating Procedures for Residential Exposure Assessment

TO: Debbie Edwards, Ph.D.
Director
Office of Pesticide Programs

FROM: Myrta R. Christian
Designated Federal Official
FIFRA Scientific Advisory Panel
Office of Science Coordination and Policy

THRU: Laura Bailey
Executive Secretary
FIFRA Scientific Advisory Panel
Office of Science Coordination and Policy

Frank Sanders
Director
Office of Science Coordination and Policy

Please find attached to this memorandum the meeting minutes of the FIFRA Scientific Advisory Panel open meeting held in Arlington, Virginia on October 6 – 9, 2009. This report addresses a set of scientific issues being considered by the Environmental Protection Agency pertaining to the "Evaluation of Updated Standard Operating Procedures for Residential Exposure Assessment."

Attachment

cc:

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Vickie Dellarco
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Donald Brady
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OPP Docket

FIFRA Scientific Advisory Panel Members

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SAP Minutes No. 2009-10

A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding:

Evaluation of Updated Standard Operating Procedures for Residential Exposure Assessment

October 6 – 9, 2009
FIFRA Scientific Advisory Panel Meeting,
Held at the
Environmental Protection Agency Conference Center
Arlington, Virginia

NOTICE

These meeting minutes have been written as part of the activities of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP). The meeting minutes represent the views and recommendations of the FIFRA SAP, not the United States Environmental Protection Agency (Agency). The content of the meeting minutes does not represent information approved or disseminated by the Agency. The meeting minutes have not been reviewed for approval by the Agency and, hence, the contents of these meeting minutes do not necessarily represent the views and policies of the Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

The FIFRA SAP is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act and established under the provisions of FIFRA as amended by the Food Quality Protection Act (FQPA) of 1996. The FIFRA SAP provides advice, information, and recommendations to the Agency Administrator on pesticides and pesticide-related issues regarding the impact of regulatory actions on health and the environment. The Panel serves as the primary scientific peer review mechanism of the EPA, Office of Pesticide Programs (OPP), and is structured to provide balanced expert assessment of pesticide and pesticide-related matters facing the Agency. FQPA Science Review Board members serve the FIFRA SAP on an *ad hoc* basis to assist in reviews conducted by the FIFRA SAP. Further information about FIFRA SAP reports and activities can be obtained from its website at http://www.epa.gov/scipoly/sap/ or the OPP Docket at (703) 305-5805. Interested persons are invited to contact Myrta R. Christian, SAP Designated Federal Official, via e-mail at christian.myrta@epa.gov.

In preparing the meeting minutes, the Panel carefully considered all information provided and presented by EPA, as well as information presented by public commenters. This document addresses the information provided and presented by these groups within the structure of the charge.

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Evaluation of Updated Standard Operating Procedures for Residential Exposure Assessment

October 6 – 9, 2009
FIFRA Scientific Advisory Panel Meeting,
Held at the
Environmental Protection Agency Conference Center
Arlington, Virginia

Steven G. Heeringa, Ph.D.
FIFRA SAP Chair
FIFRA Scientific Advisory Panel
Date: December 16, 2009

Myrta R. Christian, M.S.
Designated Federal Official
FIFRA Scientific Advisory Panel
Date: December 16, 2009

Federal Insecticide, Fungicide, and Rodenticide Act
Scientific Advisory Panel Meeting
October 6 – 9, 2009

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Chensheng Lu, Ph.D., Mark and Catherine Winkler Assistant Professor of Environmental Exposure Biology, Exposure, Epidemiology, and Risk Program, Department of Environmental Health, Harvard School of Public Health, Boston, MA

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INTRODUCTION

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) has completed its review of Scientific Issues Associated with the "Evaluation of Updated Standard Operating Procedures for Residential Exposure Assessment." Advance notice of the meeting was published in the *Federal Register* on July 24, 2009. The review was conducted in an open Panel meeting held in Arlington, Virginia, from October 6 – 9, 2009. Dr. Steven G. Heeringa chaired the meeting. Myrta R. Christian served as the Designated Federal Official.

The *Standard Operating Procedures for Residential Exposure Assessment* (i.e., Residential SOPs) is a set of standard instructions for estimating exposure resulting from various non-occupational pesticide uses including lawn and garden care, foggers, and pet treatments. Developed by the Health Effects Division of EPA's Office of Pesticide Programs (EPA/OPP/HED) in the 1990s pursuant to the Food Quality Protection Act (FQPA) requiring consideration of non-dietary non-occupational exposures for the purposes of aggregate pesticide exposure estimates, they were first presented to the FIFRA SAP in 1997 (http://www.epa.gov/scipoly/sap/meetings/1997/september/finalsep.htm#2) with additional SAP review in 1999 (http://www.epa.gov/scipoly/sap/meetings/1999/092199_mtg.htm), and have since been utilized with various updates to data sources and methodologies, including a supplemental document in 2001 [Science Advisory Council for Exposure Policy #12: Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessment. February 22, 2001 (EPA/OPP/HED)].

Recently, the Agency has undertaken a substantial revision to the Residential SOPs to:

> Incorporate interim updates and revisions since their inception;
> Research, incorporate, and statistically analyze more current and reliable data for the purposes of informing standard algorithm inputs (i.e., point estimates and distributions for deterministic and probabilistic exposure assessments, respectively); and,
> Update and/or revise standard exposure assessment methodologies.

EPA's goal is to have a set of instructions that include transparent methodologies and data inputs and guide, in a straightforward and user-friendly fashion, the assessment of non-occupational pesticide exposure. The Agency was seeking comment from the Panel on the adequacy of the exposure assessment methodologies and algorithms; the applicability, analysis, and use of available pesticide use information, activity pattern information, and pesticide exposure data; the process by which inputs are selected for use in residential pesticide exposure assessments; and the overall clarity, transparency, and utility of the SOPs.

Drs. Steven Bradbury, Deputy Director, Office of Pesticide Programs, EPA, and Tina Levine, Director, HED, OPP, provided opening remarks at the meeting.

The agenda for this SAP meeting included presentations from the Health Effects Division (HED) in the OPP and public comments.

PUBLIC COMMENTERS

Written statements were provided by:

James TerBush, BioSpotVictims.org

Tim Creger, Pesticide Program Manager, and Craig Romary, Environmental Programs Coordinator, Nebraska Department of Agriculture

Gary Adamkiewicz, Ph.D., M.P.H., Research Scientist, Harvard School of Public Health

Nicholas Halbach, D.V.M., Director, PESP Hesperian Group

Oral statements were provided by:

Jeffrey H. Driver, Dr.P.H., D.A.B.T., M.T., C.L.S., Consultant to a group of Task Forces (listed below)

John H. Ross, Ph.D., D.A.B.T., Consultant to a group of Task Forces listed below

Nasser Assaf, Ph.D., Valent BioSciences Corporation

Dennis Klonne, M.S., Ph.D., D.A.B.T., Toxicology & Exposure Assessment Services, Inc.

Task Forces: Outdoor Residential Exposure Task Force (ORETF); Non-Dietary Exposure Task Force (NDETF); Residential Exposure Joint Venture (REJV); Antimicrobial Exposure Joint Venture (AEJV); Antimicrobial Exposure Assessment Task Force II (AEATFII); Quat Residue Group (QRG)

SUMMARY OF PANEL DISCUSSION AND RECOMMENDATIONS

Provision of Standard Operating Procedures (SOPs) for Residential Exposure Assessment (REA) is an essential component of the pesticide registration process EPA has established in accordance with FIFRA. The SAP commends EPA for its efforts in producing and assembling the updated REA SOPs.

Issue 1 **Exposure Sources, Routes, and Populations of Concern**

The SAP agrees that the exposure pathways that EPA has included are worthy of examination. The Panel easily identified additional pathways that are not currently included in the SOPs. For purposes of transparency, the SAP would like to see more explicit explanation for exclusion of potential pathways. Sources and routes of exposure for which the Panel would like to see at least screening level calculations include indoor and outdoor residues, adult hand-to-mouth activity, post-market and home garden food contamination, inhalation of re-suspended house dust and soil particles, and inhalation of vapors in some specific situations. For scenarios that are ultimately excluded as relatively unimportant, provision of supporting information in the form of screening level calculations in an appendix is recommended.

The SAP agrees that a sentinel population approach is reasonable, but finds that it is not always well implemented in the SOPs. The Panel finds the proposed SOPs to be inadequate regarding delineation and naming of child populations. For instance, children aged 3-6 should not be designated "toddlers." The Panel is also not satisfied that the SOPs are sufficiently transparent with respect to protection of pregnant women and fetuses. Suggested remedies varied from explicit listing of both pregnant women and fetuses as sentinel populations to merely further explanation of the reasons the Agency believes the draft SOPs are adequately protective. More detailed explanation of motivation and criteria for designation of all sentinel populations is strongly recommended.

Issue 2 **Utility and Transparency of the Residential SOPs**

The Panel finds that EPA's current stance with respect to deterministic versus probabilistic analyses is ambiguous. While multiple references to probabilistic analysis can be found in the revised SOPs, treatment of the topic is very incomplete. Potential users are left without true guidance. EPA must first clarify what the SOPs are intended to achieve. Traditionally the SOPs have employed point estimates of key parameters that were expected to be individually conservative, leading to an overall conservative result. This approach is relatively easy to implement, but the degree of conservatism of the resulting exposure estimates is a source of contention. In contrast, true probabilistic analysis is not intrinsically conservative. It can inform post-hoc implementation of conservatism if outcomes at high population percentiles are selected as decision points. However, true probabilistic analysis is likely to be hindered by lack of adequate data for many of the pathways currently included and is unlikely to be justifiable as a Tier 1 approach. Therefore EPA should clarify the hierarchy of deterministic and probabilistic techniques in the context of the REA SOPs.

Most members of the Panel favor amendment of the REA SOPs to calculate absorbed rather than potential dose within REA. This would facilitate both comparison of the relative importance of individual routes and pathways within a particular scenario, since fractional absorption will not be constant, and comparison of SOP-generated predictions to relevant biomonitoring data where available.

For purposes of improved stakeholder accessibility, the SAP believes that provision of additional example calculations throughout the document would improve the SOPs. Current examples are limited and tersely presented.

The Panel recommends that a glossary and acronym list be added. References should be provided in a single section in alphabetical order. Web links to other relevant Agency documents should also be provided whenever possible.

With respect to specific exposure factors, the Panel is particularly concerned that current treatment of transfer coefficients is not transparent. Dependence of transfer coefficients on the residue measurement technique used in the experiments in which the transfer coefficients were derived is not explicitly stated.

Issue 3 **Consideration of Data Sources**

(The following recommendations also apply to Issue 2.) The document needs a general statement regarding acceptability of data. This should include criteria for rejection on either scientific or ethical grounds. Criteria for assuming that data fit particular distributions should also be included and general approaches to weighting and aggregating data from multiple sources should be described. Within particular scenarios, exclusion of data that would appear to be relevant, but that have been judged unacceptable, should be explicitly noted.

The Panel recommends that the Agency, if it has not already done so, investigate state agencies, professional associations and their European Union counterparts as possible sources of new and relevant data.

Issue 4 **Analysis and Utilization of Available Data**

The Panel finds that EPA has not fully revealed the manner in which data are selected or analyzed.

SAP comments were specifically requested on five subtopics. With respect to exposure data for developing pet activity dermal transfer coefficients, the Panel finds the difference in transfer coefficients estimated for solid and liquid formulations to be questionable.

With respect to scenario-specific data used to estimate surface-to-hand residue transfer for non-dietary ingestion exposure assessments, the Panel notes that surface transfer efficiency is an example of an exposure factor described by a distribution that is compiled using data from multiple prior studies of widely varying methodology and size. In the absence of stated criteria for aggregation of disparate data, the Panel is unable to endorse EPA's assumption.

With respect to repellent application data to establish formulation-specific rates, the Panel finds the approach acceptable, but notes that actual values are not yet provided.

With respect to use of occupational re-entry exposure data to establish dermal transfer coefficients for home gardening and ornamental maintenance, the SAP is generally supportive. One Panelist believes that additional introductory material on the underlying data should be provided, as it may be unfamiliar to persons working in the residential exposure arena.

With respect to data supporting differentiation between potential exposures following indoor broadcast treatments and localized "crack-and-crevice" treatments, the SAP agrees that lower residues are probable from crack-and-crevice treatments. At least one Panelist cautions that the available data, while consistent with EPA's approach, are limited and should not be viewed as definitive.

Issue 5 **Residential Exposure Assessment Methodologies and Algorithms**

The Panel finds that most of the methodologies and algorithms employed in the proposed SOPs are conventional and acceptable. Many have appeared in prior Agency documents and/or been vetted by prior SAPs. The Panel recommends that the Agency revisit and clarify its approach to estimation and use of transferable residues and transfer coefficients.

SAP comments were specifically requested on three subtopics. With respect to hand-to-mouth and object-to-mouth related non-dietary ingestion, the Panel expressed mixed opinions. Most members are generally satisfied with the Agency's approach, pending correction of the misnamed variables representing frequency of mouth touches. One Panelist believes that the Stochastic Human Exposure and Dose Simulation (SHEDS) hand-to-mouth and object-to-mouth protocols are more complex than currently available data can justify and suggested that a simpler protocol would be more defensible.

With respect to use of the well-mixed box model for estimating inhalation exposure, most members of the Panel agreed that the approach is a common simplification and is acceptable. One Panelist objected to application of the well-mixed box model to outdoor scenarios. Several Panelists expressed concern that associated settling and flushing rate assumptions lead to too rapid cessation of exposure in light of observations that pesticide residues can linger indoors for years. These concerns are linked to concerns regarding failure to account for chronic exposure to residues, which were also expressed in the response to Issue 1.

With respect to ingestion of dust, the Panel agrees with the Agency that it is a potentially important exposure pathway. However, the Panel notes that many parameters required for estimation of dust ingestion dose have not yet been specified and is concerned that prediction of pesticide levels in dust will not be straightforward. The Panel therefore declines to endorse the dust ingestion paradigm as currently constituted.

PANEL DISCUSSION AND RECOMMENDATIONS

Agency Charge

1. Exposure Sources, Routes, and Populations of Concern

The scope of this effort by the Agency has been to focus on revising its methods for conducting exposure assessments for the most commonly available products which, through various routes, i.e., dermal, inhalation, etc., may lead to exposure in the home or otherwise in the general population. For example, pet uses, lawn care, insect repellents, and indoor pest control are common exposure sources and dermal, inhalation, and non-dietary ingestion through mouthing behavior are common exposure routes. A constant challenge in the completion of exposure assessments associated with the residential uses of pesticides is ensuring that they are reflective of the current marketplace which rapidly evolves to provide the latest conveniences to consumers. The advent of monthly flea control spot application products is one example of market forces and technology altering the way pesticides are used in and around the home. These revisions have been primarily based on the availability of recent data received from various pesticide registrants as well as other public and private data. The Agency is aware that there are other residential exposure sources for which assessments have been conducted in the past, e.g., field volatilization and mosquito control applications, but which have not been included in this current effort. While future revisions will focus on methodologies for the aforementioned exposure sources, the use patterns included in the document are the focus of this FIFRA SAP meeting.

Additionally, as a standard routine pesticide exposure assessment practice, the Agency uses select age-based life stages (referred to as "sentinel populations") considered the most highly exposed for each scenario as a means to encompass exposures and risks for all potentially exposed age groups. This is done mainly to streamline the exposure and risk assessment process and save time and resources, but also as a reflection of the limitations of our data. For example, though based on limited data, observational studies appear to indicate that infants exhibit higher mouthing behavior than toddlers. However, toddlers may be the chosen sentinel population for non-dietary exposure assessments in certain scenarios because they spend a longer amount of time doing certain activities that contribute to greater overall exposure levels. This behavioral difference results in a greater potential to contact surface residues and thus a greater potential for exposure.

- **1-1. Please comment on the completeness of both the exposure sources and exposure routes identified for each scenario. If a type of product or a potential source of exposure has not been identified, please identify them and suggest modifications to ensure that they are reflected in the SOP document.**

- **1-2. Please comment on whether the sentinel population approach is reasonable for exposure assessment purposes and on the age-based choices for each scenario.**

Panel Response 1-1

The revised and updated REA SOPs represent an extensive effort and reflect consideration of multiple exposure sources and routes. The SAP agrees that the sources and routes of exposure covered by the proposed SOPs are worthy of examination. Nevertheless, the Panel has questions regarding additional sources or routes of exposure that are not currently included. The Panel agrees that it is reasonable for the Agency to attempt to focus on more important sources and routes of exposure and give less attention to less important sources and routes. However, the manner by which such distinctions have been made is often unclear. Generally, the Panel believes that the REA SOPs would be strengthened if EPA were to explicitly state criteria for inclusion or exclusion of specific exposure scenarios. The Panel recommends that the Agency provide screening level calculations for additional pathways not currently addressed (and possibly for currently included pathways where needed for comparison). If these calculations indicate that a pathway is not important, it would not need to be considered further. These calculations could be included in an appendix.

Comments on particular sources of exposure that one or more Panelist viewed as warranting at least screening level examination are provided below.

Indoor Residues

Multiple Panelists believe the SOPs should address the potential for chronic exposure from residues that remain long after various kinds of pesticide applications. Persistence is of particular interest in the indoor environment due to lack of direct sunlight and rainfall. Indoor pesticide residues may accumulate as a result of track-in or drift of materials applied outdoors or from indoor applications. Accumulation may be further exacerbated by multiple applications.

Many pesticides can be classified as semi-volatile organic chemicals (SVOCs). Behavior of these compounds indoors has recently been reviewed (Lioy, 2006; Weschler and Nazaroff, 2008). Some prior literature describes relevant pesticide-specific case studies (e.g., Gurunathan et al., 1998). Despite low vapor pressures SVOCs do migrate within the indoor environment. SVOCs tend to partition to indoor surfaces such as furniture, walls and particulate matter. This process appears to be facilitated by organic films found on those same surfaces. These pesticide residues have the potential to be a source of chronic exposure to persons occupying the space through inhalation (as vapors or re-suspended particulates), dermal contact, or non-dietary ingestion. These phenomena can be expected to occur in child care centers, schools and businesses as well as in residences.

For horse barns, the SOP states that dermal exposure and non-dietary ingestion need not be considered. People will come into contact with the horses, equipment such as saddles, and other impacted surfaces. It is easy to imagine that both dermal and hand-to-mouth exposures are possible under these conditions. Additional justification is needed for not considering these potential exposures.

Outdoor Residues

Pesticide drift off site and into neighborhoods can result from using various devices in specific outdoor situations. This is especially apparent for the residential mosquito misters. The current mister scenarios do not consider that residential misters can be located on decks as a virtual screen or next to a swimming pool. Periodic and systematic applications could lead to deposition onto eating surfaces, playground equipment, sandboxes, vegetable gardens, etc. Pesticide can also drift into neighbors' yards, and through open windows and doors. Residues might also ultimately penetrate buildings via passive or mechanically assisted infiltration. Similar concerns were expressed for scenarios developed for garden and tree application, use of outdoor candles and coils, and hornet and wasp sprays.

The Panel notes that EPA has scheduled another SAP meeting on *Scientific Issues Associated with Field Volatilization of Conventional Pesticides* for December 1-4, 2009. That meeting targets migration from treated agricultural fields. The Panel suggests that analogous processes are relevant to the REA SOPs.

Inhalation of Vapors and Aerosols

The inhalation route is not considered in some of the scenarios and one of the reasons given is that pesticides generally have low vapor pressures. Some Panelists are not satisfied that this justification is always sufficient. For example, application of a herbicide on a warm, still day (consistent with labeling directions) on weeds between patio stones might lead to inhalation exposure. Justification should be provided when inhalation exposures seem possible, but are not considered.

The Panel is aware of a new product, a battery-powered clip-on mosquito repellent dispenser, designed to control outdoor mosquito problems at the individual level. It does not appear to fall into either the fogging or misting system due to the close proximity of the source to the user's breathing zone and the continuous operation of the product while the wearer is outdoors.

At least one Panelist believes that the Agency should consider inhalation exposure of a child sleeping next to a dog or cat treated with flea-repellent or wearing a flea collar given potential exposure over multiple hours of sleep within the influence zone of the animal's fur.

Particle Re-suspension

The mister, garden and tree application, and residential turf scenarios do not consider re-suspension of pesticide-bearing particles from surfaces by wind and/or human activities. Inhalation of re-suspended particles may be an important exposure pathway under some conditions. Particles that are too large to reach the alveoli may still be ingested after clearance from the upper airways. Shalat (2009) recently reported on re-suspension as a consequence of activities on artificial turf. In the indoor environment, re-suspended house dust may contribute to chronic exposures discussed above.

Post-Market and Home Garden Dietary Contamination

Exposure to pesticides in food is not considered in REA as it is managed via tolerance limits on pesticides in commercial food as sold. However, this control mechanism does not account for some additional exposures related to diet. Commercial food can be contaminated in the residential setting post-purchase. For example, a child may consume food dropped on the floor, or transfer residues from hands to food while eating. Produce from home gardens may be contaminated by local pesticide application (e.g. outdoor misters or foggers). Nursing mothers may apply lanolin to sore nipples and lanolin may be contaminated with pesticide (Copeland et al., 1989).

Adult Hand-to-mouth Contact

Hand-to-mouth activity in adults may also be important in some settings. Behaviors associated with hand-to-mouth movements such as smoking, eating, use of smokeless tobacco, etc. could contribute to exposure in scenarios included in the current SOPs. The golf and pick-your-own farm scenarios are two particular examples in which people are likely to spend a number of hours in an activity without convenient access to hand washing facilities. In considering inadvertent oral exposure in adults, a review published by Cherrie et al. (2006) is a starting point. Those authors compiled previously reported incidences of face touching/mouthing among students (Woods and Miltenberger, 1996), nail-biting (Long and Miltenberger, 1998) and hand-to-face contacts among adults, lab workers, manufacturing and engineering workers, and office workers (Zainudin, 2004).

Panel Response 1-2

The Panel agrees that use of sentinel populations to describe likely high-end exposures is reasonable. However, the justification for selection of sentinel populations is not always clear in the REA SOPs. For example, the background section of the charge question stated that "based on limited data, toddlers may be chosen because they spend a longer time doing certain activities that contribute to greater exposures", but little information is provided in support of that conclusion driving the selection of the sentinel population. More explicit rationale for sentinel populations would be helpful throughout the document.

Definitions of children's age categories

In the updated SOPs, "toddlers" are defined as children aged 3–6. The Panel finds that this definition is not consistent with common usage. Toddlers are young children starting to walk. They "toddle" meaning that they have an unsteady gait. By the time most children are 2, they have been walking well for months and are not considered toddlers. In the American Academy of Pediatrics *Pediatric Environmental Health Handbook,* toddler age is defined as ending at 2. The *Handbook* defines a child who is 2–6 as a pre-schooler. Although EPA's (2005) *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures for Environmental Contaminants* is cited as justification for the "infant" and "toddler" SOP categories, those categories don't actually appear there (except in a summary of prior EPA documents that includes the original version of the REA SOPs). Instead, the 2005 document provides a

categorization that includes birth through age 1 (broken down into 4 finer categories) and from 1 year onwards, also broken down into finer categories.

Given this labeling problem, the Panel has several concerns. One is that using the toddler label for ages 3–6 is simply misleading and confusing. In addition, exposure factor data collected from 3–6 year olds might lead to underestimation of exposures to 2-3 year olds since hand-mouth and object-to-mouth behavior generally decline with age. Children with developmental delays, such as those with intellectual disabilities and/or autism, may still exhibit mouthing behavior at age 6. Finally, at least one Panelist is concerned that the Agency's questionable "toddler" age selection is an indication that actual infant and toddler exposures have not been adequately examined. Infants and toddlers are at peak ages for hand-to-mouth and object-to-mouth behavior. Medicaid laws reflect this reality by requiring health providers to test all Medicaid-eligible 1– and 2–year olds for lead poisoning (AAP, 2003). Pesticide exposure could similarly be high. EPA should assume that infants and young children are put on the floor, crawl around and put hands and objects in their mouths. EPA should also consider foot-to-mouth behavior since infants often engage in this activity and their feet may be contaminated with pesticide. These issues reinforce the Panel's concern that decisions regarding selection of sentinel age groups are not fully explained.

Other Issues Related to Limits of Age Ranges

Several members of the SAP raised concerns about assumed age ranges within the sentinel populations. For instance, neither children of ages 2-3 nor premature infants are currently considered and women of child-bearing age are defined as being over 18. In the gardening scenario, only adults are considered. Some Panelists felt that even young children might participate in gardening or pick-your-own farm activities and that teenagers be considered as possible applicators, especially for foggers and sprays.

Pregnant Women and Fetuses

The Panel believes that the Agency should more clearly address pregnant women and fetuses. The justification is two-fold. Some of the universal exposure factors, such as inhalation rate and body weight for the adult population, may not be suitable for pregnant women. Application of exposure factors applicable to adults generally could potentially lead to poor estimation of exposures to pregnant women. Secondly, from a toxicity perspective, pregnant women (and more specifically their fetuses) as a group are not only a sensitive but also a high-risk population. Recent results from animal studies have strongly suggested trans-generational epigenetic changes in responding to many chemicals, including a fungicide (Vinclozolin) commonly used in vineyards (Skinner and Anway, 2007). In the scope of epigenetic research, maternal exposure to environmental chemicals has been cited as a trigger for epigenetic changes in their offspring. The recent literature also reveals potential effects of prenatal exposure to organophosphate pesticides on neurological development (Young et al., 2005); head circumference (Berkowitz et al., 2004); and birth weight and birth length (Perera et al., 2003; Whyatt et al., 2004).

Several Panelists recommended that pregnant women and/or fetuses be explicitly designated sentinel populations. Other Panelists felt the Agency should consider treating pregnant women

as a sub-population within the adult population with provision of a limited set of modified exposure factors where appropriate. Still other Panelists suggested that the Agency's approach was adequate, just not well explained. Whatever the ultimate outcome, the Panel is in strong agreement that Agency must provide information in the SOPs (or an appendix) that explains and justifies its determination with respect to sentinel status of pregnant women and fetuses.

Other Special Populations

Several Panelists expressed concern that the current SOPs do not address some specific populations that have lifestyles that might lead to higher exposures or vulnerabilities that place them at greater risk of adverse impacts. These populations include senior citizens, members of certain ethnic and minority groups, and the socio-economically disadvantaged. Exposure estimates produced using the SOPs are highly dependent upon the type of application, the frequency of application, and the duration of contact. Exposures of senior citizens and the socio-economically disadvantaged may be affected by housing type/quality and/or mobility issues. As above, if EPA determines that these groups should not be considered as sentinel populations, it should justify this determination either in one of the beginning sections of the document or an appendix.

Agency Charge

2. Utility and Transparency of the Residential SOPs

Two primary goals of the Residential SOPs are to 1) serve as an instruction manual for residential pesticide exposure assessors, and 2) provide transparency to stakeholders who wish to understand how the Agency conducts residential pesticide exposure assessments.

- **2-1. Please comment on whether the Residential SOPs meet these goals, and if not, identify where improvements are needed.**

Panel Response 2-1

Given limitations in available data and the assumptions the Agency was required to make in constructing the various scenarios, the REA SOPs provide a reasonable framework for assessing exposure to a number of populations at risk for a number of scenarios and pesticide products. However the utility and transparency of the revised document cannot be addressed in the absence of discussion of the intended audience. The SAP acknowledges that the range of possible stakeholders is broad and that preparation of a document that is accessible to diverse stakeholders, technically adequate, and of reasonable length is a substantial task. However, the Panel would like to emphasize that it is very important for the document to be clearly written as it is likely to be widely used. For example, the previous version was embedded in guidance used in Europe.

The Agency has not made entirely clear whether the intended users ("exposure assessors") are limited to experienced professionals. In current form, the document is likely to be generally usable by such persons (i.e., EPA and other governmental agency staff, pesticide industry employees, and interested academics), but much less accessible to others. The document is very unlikely to be understood by much of the general population, who might reasonably be considered stakeholders. For benefit of the general public, the Panel strongly suggests that the Agency prepare additional information either as a frontispiece to the document or in a separate "fact sheet" that is written in plain English to explain the general information in the document.

Clarity of Goals

First and foremost, the Agency needs to fully explain how the SOPs fit into a tiered exposure assessment process. The Panel assumes that the SOPs are meant to facilitate a Tier 1 exposure assessment and that the predicted exposures are meant to be conservative. Discussion of how a Tier 2 analysis would be triggered and would proceed if Tier 1 results constitute unacceptable exposures should be added to the document.

However, any such discussion will be greatly hindered by the fact that the SOP does not provide sufficient information regarding conversion of potential doses predicted by the SOPs to absorbed doses required in the next step of the risk assessment process. (Although there are many repetitions in the SOPs of a basic equation in which potential dose is multiplied by an absorption factor to give absorbed dose, no discussion of appropriate values of the absorption factor, how they might vary, or limitations of this approach are provided.) Failure to include calculation of absorbed dose in the exposure assessment presents problems with respect both to technical quality and transparency.

With respect to transparency, a significant shortcoming is that potential exposures by different routes cannot be added because absorption efficiency is unlikely to be constant across routes. This means that in some cases, dominant exposure routes cannot even be identified at the exposure assessment stage.

With respect to impact on technical quality, dermal exposure provides a good example of potential difficulty. Dermal absorption efficiency varies depending on loading conditions, duration of exposure (which is itself often difficult to assess), age, area of the body and skin condition. The skin of infants, particularly premature infants, and toddlers is more permeable than adult skin (Giusti et al., 2001; Mancini, 2004; Nikolovski et al., 2008). Backs and genital areas are more permeable to many chemicals than are palms. Skin that is abraded or otherwise damaged (as in the case of common conditions such as eczema) is typically more permeable than skin that is intact. Occlusion of the skin, which is common, typically increases permeability. Dermal absorption is also subject to vehicle/mixture effects. Pesticides are often encountered as formulations containing carriers and inert ingredients. Some insect repellent products also contain sunscreen chemicals that can promote absorption of the repellent's active ingredient. Because of these issues, information about exposure conditions as well as potential dose is required to properly estimate internal dose. The more distant the evaluation of absorbed dose from evaluation of gross exposure, the less likely that exposure conditions will be appropriately considered.

Relationship to Reality

The Panel is generally interested in understanding how exposure predictions generated by the REA protocols compare to actual exposures experienced by relevant populations. This is especially important given arguments about the relative conservatism of SOP-generated predictions.

Ideally predictions based on the SOPs would be compared to biomonitoring data from representative populations. (Note that this would require estimation of absorbed dose.) However, the Panel is aware that directly applicable biomonitoring data are generally not available (i.e., large population trials of specific pesticide exposure scenarios are not available). In addition, many of the biomarkers of pesticide exposure are excreted relatively rapidly. Given the low likelihood of observing a response to an application event in a biomonitoring protocol not specifically designed for that purpose, general population data will mostly reflect chronic exposure to pesticides. Nevertheless, general population data such as the National Health and Nutrition Examination Survey (NHANES) and its European analogs do provide perspective on pesticide exposure predictions. At a minimum, predicted exposures for specific scenarios could be evaluated for their potential to cause individuals to deviate from background levels. A residential scenario prediction three orders of magnitude higher than the maximum observation in NHANES (or than upper tails in occupational studies such as those found in the Pesticide Handler Exposure Database (PHED)), for instance, would raise an immediate flag regarding quality of the estimate. NHANES data are relevant to examination of the chronic exposure scenario suggested for consideration by the Panel in response to Question 1-1, as are data from the Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants Study (CTEPP). A few small population trials of particular application techniques that entail biomonitoring have also been published (some of which are already cited in the REA SOPs).

In the absence of direct comparison of predicted exposures to empirical results, EPA can still provide qualitative discussion of uncertainty. Currently each section of the SOPs has a discussion of limitations. Expansion to a more systematic discussion (but still qualitative) of the uncertainties for each scenario is recommended. The European Food Safety Authority has set out such a format (EFSA, 2006; see in particular Table 3 on p. 13). In this approach, there is a brief list of all uncertainties in a table and they are scored with plus or minus symbols if a particular uncertainty is expected to lead to over- or under-estimation of exposure. In addition, one can scale the scoring by using from one to three symbols where the greater the uncertainty, the more symbols are included. The scale will depend on the overall level of uncertainty but one symbol might mean a factor of two, two symbols a factor of five, and three symbols an order of magnitude or more. Finally the overall level of uncertainty can be plotted on the same scale. This approach is admittedly subjective, but does formalize the exposure assessors or model developers' views and provides a more transparent basis for discussions by risk managers and stakeholders.

One member of the Panel suggested that EPA should also consider evaluating FIFRA (6)(a)(2) notices, Poison Control Center reports or other pesticide poisoning data bases for possible sources of insight into scenario selection and exposure estimates.

Clarity of Procedures

Many data sources familiar to persons engaged in pesticide exposure work are referenced in the document. However, other data known to the Panel are not mentioned (in some cases for defensible reasons also known to members of the Panel, but not explicitly stated). The current document lacks a discussion of criteria for selection and use of data sources. A general statement of principles regarding data acceptability should be added. Such a discussion is necessary for transparency and should extend to issues of both scientific and ethical quality. At least one Panelist suggested that brief descriptions of the effect of excluding particular data sets on predictions should also be included, perhaps in an appendix.

Data used in deriving estimates of exposure are often provided by the pesticide industry. As major beneficiaries of pesticide registration, it is entirely appropriate that pesticide manufacturers supply the bulk of the data needed to assess the safety of their pesticide products. However, this relationship often leads to misinterpretation of the motives of the Agency with respect to some of its exposure and risk assessment decisions, especially if the tiered exposure assessment and risk assessment processes are not well explained. Given this situation, a general statement of principles regarding the selection and use of data sources would be very helpful to stakeholders.

Definitions of some age groups are confusing in the current version of the SOPs. (See also the response to Question 1-2.) All age groups should be presented in a summary table and explanations regarding age groups dropped from consideration should be included. The Agency could include some example calculations in an appendix explaining why these age groups should not be the sentinel populations. Consistency with other Agency guidance should also be addressed.

In cases in which data are described in parametric terms, a statement should be included regarding the rigor with which the chosen distribution was selected. If the Agency actually performed goodness-of-fit testing or if such results are available from an original source, the relevant details should be provided. If implicit distributions are merely assumed, that fact should be revealed. These points are particularly important if the Agency does fully pursue a probabilistic approach. In cases in which no suitable empirical basis for parameter estimation exists, and estimation is ultimately based on "professional judgment", that fact should be clearly stated.

Procedures for combining data from multiple sources to produce distributions should be discussed. Panel members expressed particular concern regarding distributions for transferable residue and fraction transferred to hands. At least one Panelist felt that data from studies of multiple chemicals could not be reasonably combined in a single distribution.

Detailed examples of estimating exposure for the scenarios might be useful to stakeholders who are not entirely familiar with the SOPs. These could be included in the appendix. Some Panelists felt that the examples given in the text were not adequate. For example, on page 3-19, the source of the values in the calculations was not readily apparent.

The Panel finds the overall treatment of both transferable residues and transfer coefficients to be inadequate. Estimates of both factors vary markedly depending on multiple factors including chemical, formulation, method of sampling, and activity. More systematic discussion of dependencies and uncertainties is needed. Limitations of selection of values from individual studies should be explored.

At least one Panelist felt that estimation of handler exposures in the gardening scenario requires additional explanatory material. That scenario utilizes data obtained from studies of professional handlers not previously employed in the REA SOPs. Some related issues raised by Panel members included inadequate explanation of EPA's use of data from handler studies in which gloves were worn within the context of scenarios which do not presume glove use and inadequate explanation of weighting of data from patch dosimeters to estimate whole body exposures.

At least one Panelist found that estimation of overall exposure given time spent in treated and untreated areas was not clear.

Clarity of Terminology

The document needs a single glossary (rather than provision of definitions in scattered locations), a list of acronyms, and a list of all the variables used in the formulas. No variable names should be used twice (i.e., should not have different meanings in different equations). The glossary should define terms such as "sentinel population" and "probabilistic," and include brief descriptions of application methods such as "belly grinder" and "top spot."

Some of the SOPs are defined with an odd mixture of English and metric units. The document is written by and for scientists and the SOPs will be used internationally. The Panel encourages the Agency to consider revising the document to express all SOPs consistently in metric units. If the Agency feels that some parameters should be expressed in English units, those could be provided parenthetically.

In some cases, a conservative estimate of a particular exposure factor will be the 5^{th} percentile rather than the 95^{th} percentile. For example, for air exchange rates and dissipation rates lower values are more conservative and should be applied. The document should be checked for use of appropriate terminology and listing of appropriate values.

The Panel finds the terminology related to "replenishment" phenomena to be confusing. The variable Freq_Replen is misnamed. It is actually frequency of contact with the mouth (i.e., frequency of unloading, not loading). Versions for hand-to-mouth and object-to-mouth pathways should be distinguished by subscript as they have different numerical values. A single variable name, N_Replen, is also used for the rate of replenishment of loads on both hands and objects, which is similarly confusing.

At least one Panelist found the name "Outdoor Aerosol Spray Area Foggers" unsatisfactory. A shorter title for this scenario is suggested.

Proofreading and Additional Materials Requested

The document needs further proofreading as numerous typographical mistakes were found. A few examples are provided in the Appendix A of this report.

References should be compiled in a single location organized in alphabetical order, not segregated by chapter/appendix. The current reference lists do not appear to include all studies cited in the document, in particular missing references cited in tables in the appendices. Table and figure titles and legends should be reviewed for clarity.

Because some stakeholders may not have access to published materials, the Agency should, where feasible, consider adding cited Agency documents or key tables from Agency documents as appendices. Alternatively links to Agency web sites could be provided.

Agency Charge

3. Consideration of Data Sources

The Agency has attempted to comprehensively identify sources of applicable data for use in revising the Residential SOPs by evaluating exposure assessment literature, studies generated by pesticide registrants, survey research, and data provided in peer reviewed Agency publications such as the *Exposure Factors Handbook*, the *Child-Specific Exposure Factors Handbook*, and *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants*.

- **3-1. Please comment on the strengths and limitations of the data sources identified by the Agency, including the implications of associated study designs, and how these factors might impact their use in exposure assessment.**

- **3-2. Please comment on whether additional data are available and how they might be incorporated into the document.**

Panel Response 3-1

In general, the Panel agreed that the Agency has done a reasonable job of identifying data sources and in presenting them to the Panel, but other papers and data sources exist that could potentially enhance the REA SOPs. The Panel encourages the Agency to actively seek data that might be available from state agencies, professional societies or authorities within the European Union.

The Panel notes that inhalation exposures, including inhalation exposures from particle re-suspension, were not considered as an important source of exposure in the residential scenario. Therefore either data sources relevant to that pathway were not considered or they were dismissed, perhaps justifiably, but without explanation. Sources of data related to that topic and to behavioral differences in children and adults, surface-to-hand transfers, volatilization, and

aerosols suggested by various members of the Panel can be found in the References. Additionally, it was unclear to what extent industry-generated data had been included or excluded. Per the response to Question 2-1, the Agency should discuss its criteria for inclusion and exclusion of data and note all exclusions including those based on findings of EPA's Human Studies Review Board.

Exclusion of potential exposure pathways due to lack of descriptive data should be distinguished from exclusion due to documented relative lack of importance.

A lack of acceptable behavior and activity data in children is consistently identified as a gap in many sections of the SOPs. The Panel believes that the Agency should specifically identify and justify use of data obtained in studies using adults as surrogates for children. Several Panelists pointed out that it is generally well accepted in the fields of psychology and kinesiology that adults cannot adequately mimic a young child's behavior, either in terms of type of activity or duration and intensity of activity.

The Agency should continue its efforts to employ the results from videotaping studies of children to test the performance of any of the adult profiles in mimicking children's activity and behavior patterns. Information gaps need to be filled by well designed research projects, but in the interim a sensitivity analysis approach should also be used to understand the effect of information gaps on exposure estimates. This is a different type of analysis than one performed to examine 'known' variability found in weak or inadequate data bases. Not taking into account the uncertainties related to information gaps can give assessors a false sense of security about the estimate and its associated level of uncertainty.

It is clear from the data sources cited in the SOPs that some information is derived from controlled experiments and other information is from observational studies or studies that employed little control. While experiments can provide precise estimates (of exposure or effect) for the specific scenarios examined, they may not relate easily to realistic situations. Observational studies typically have high relevance to realistic situations but estimates are much less precise, depending to a large extent on sample size. Reviewers need to understand the underlying study type to properly understand the nature of the uncertainty estimates reported. That is, an estimated parameter with low reported uncertainty may not necessarily be the best estimate to describe a realistic scenario (or say median response) if the original estimate was derived from a controlled experiment performed in an unrealistic or extremely low-probability (distributional tail) scenario. See also the answer to Question 2-1 regarding *Relationship to Reality* for suggestions on reporting data source/quality.

Panel Response 3-2

The Panel suggests that the EPA should search for additional information describing air exchange rates in buildings. The 1997 Exposure Factor Handbook is being used as a basis for those numbers. However, the recent emphasis on energy conservation may lead to revisions in the distribution of ventilation rates (i.e., air-change-per-hour (ACH)) values in homes, apartments, and commercial buildings. Suggestions for sources for newer information are the National Institute of Standards and Technology, the American Society of Heating, Refrigerating

and Air-Conditioning Engineers, EPA's own Indoor Environments Division, and the Industrial Codes Council, Inc.

The Panel has raised the issue of chronic exposure to indoor residues. An aspect of that issue involves track-in of pesticides applied outdoors. One Panelist suggested that EPA consider a methodology found in a New York State Department of Environmental Conservation (NYSDEC) technical support document for calculating soil clean-up objectives available at http://www.dec.ny.gov/chemical/34189.html (document and all appendices) or http://www.dec.ny.gov/docs/remediation_hudson_pdf/techsuppdoc.pdf (main body of report). A very recent paper by Layton and Beamer (2009) is also relevant.

Some additional references not specifically cited here but deemed relevant by individual members of the Panel are included in the References. Some of these are new and therefore may have escaped Agency attention (e.g., Shalat, 2009).

Agency Charge

4. Analysis and Utilization of Available Data

The Agency has summarized and presented the data analysis for all exposure factors. Examples include the analysis of transferable residues indoors, and on lawns, garden plants, and pets; analysis of post-application exposure studies for the purposes of developing transfer coefficients for children playing on lawns, homeowner gardening, and contacting pets; and analysis of insect repellent efficacy studies to establish formulation-specific application rates. Additionally, where data are lacking and surrogate data have been proposed or data are unavailable and expert judgment is applied, the Agency has attempted to explain the rationale behind its choices. Examples include "time spent outdoors playing" as a surrogate for time spent on lawns, "time spent outdoors at a farm" as a surrogate for time spent at a "pick-your-own" farm, and assumptions for spray volumes for residential handlers.

- **4-1. Please comment on whether the various data analyses and data choices for each scenario are scientifically sound and reasonable for the purposes of residential pesticide exposure assessment. Please include commentary on the analysis and use of:**

  a. **exposure data for developing pet activity dermal transfer coefficients;**
  b. **scenario-specific data used to estimate surface-to-hand residue transfer for non-dietary ingestion exposure assessments;**
  c. **repellent application data to establish formulation-specific rates;**
  d. **occupational re-entry exposure data to establish dermal transfer coefficients for home gardening and ornamental maintenance; and,**
  e. **data supporting differentiation between potential exposures following indoor broadcast treatments and localized "crack-and-crevice" treatments.**

- **4-2. Please identify specific examples and recommendations for analytical**

modifications or any additional data that may enhance or supplement those presented in the SOPs.

Panel Response 4-1

The Panel commends the Agency's effort in compiling data relevant to a wide range of exposure scenarios. However, soundness of data analyses cannot be evaluated in the absence of full disclosure of procedures. (See comments under ***Clarity of Procedures*** regarding assignment of distributions and aggregation of multiple data sets in response to Question 2-1.)

Regarding the specific questions posed to Panel:

(a) ***Exposure data for developing pet activity dermal transfer coefficients:***

Several Panelists expressed concern regarding the order of magnitude difference between the transfer coefficients (TCs) for solid and liquid formulations in the pet activity dermal exposure scenario. This disparity may be attributable to alternative methodologies used in the different studies from which those TC values were derived, but questions still arise regarding uncertainty and transferability of these estimates (and of other transfer coefficients used in the SOPs).

(b) ***Scenario-specific data used to estimate surface-to-hand residue transfer for non-dietary ingestion exposure assessments:***

The surface-to-hand transfer efficiency distribution employed in the SOPs is taken from Beamer et al. (2008). As noted previously, rules for aggregation of data from multiple sources are not clear. Transfer efficiency can reasonably be expected to vary with time since deposition and with loading. The data compiled by Beamer et al. are derived from disparate sources that did not control for these variables.

(c) ***Repellent application data to establish formulation-specific rates:***

Methods for determining repellent application rates used in the non-dietary ingestion exposure protocol are generally acceptable. However, the actual distribution is not yet provided. This is also a case in which higher risk occurs at lower interval length between applications, so careful specification of the "conservative" percentile is necessary.

(d) ***Occupational re-entry exposure data to establish dermal transfer coefficients for home gardening and ornamental maintenance:***

The Panel generally found use of occupational exposure data for the home gardener scenarios to be reasonable. As noted in the Panel's response to Question 2-1 regarding clarity of procedures, one member of the Panel expressed a desire for a more detailed introduction to the professional handler data.

(e) ***Data supporting differentiation between potential exposures following indoor broadcast treatments and localized "crack-and-crevice" treatments:***

Per the text in section C.5.1 and Table C-5, assumption that the deposited residue from crack-and-crevice application is equivalent to 10% of the deposited residue from broadcast application is based primarily on a single recent study that reported residues resulting from both treatments. Additional support for this estimate should be sought. One member of the Panel pointed out that crack-and-crevice treatment can logically be expected to produce lower exposure than broadcast application due to typically lower mass applied and less accessible initial placement. However that individual also argued that the existing crack-and-crevice literature should not be viewed as definitive as it consists of a limited number of small studies with some questionable methodological features.

Additional comments on various aspects of the residential pesticide exposure assessments offered by members of the Panel include the following:

Given that many of pesticides can remain in the indoor environment for periods of months or years, several members of the Panel are concerned that values of the dissipation rates used in the post-application dermal exposure equation might be too high. It may also be that a first-order approach only provides a reasonable approximation in the initial period after application. This concern is tied to the reservations of several Panelists regarding use of data presented by Chinn (1981) to estimate evaporative loss following spray applications. Chinn's experiments represent evaporation from a glass plate under conditions of mechanical ventilation. The indoor environment features numerous surfaces to which pesticides can partition, leading to lowered thermodynamic activity and retarded evaporation.

In regard to "time spent at a farm", if a Monte Carlo analysis is to be conducted, the distribution should be truncated at the lower end as there is likely a minimum time that people will stay at the farm given the driving times likely necessary to get to the farm.

At least one member of the Panel questions the distinction drawn between the "cup" and "spoon" methods of granule application. Observed median dermal exposures were over an order of magnitude lower for the "cup" method (Merricks, 2001). The studies represent very different conditions and the labor performed in the spoon study (Pontal, 1996), which was conducted outside the U.S., was much more strenuous. Dosimetry data were collected and analyzed by different methods. It is not reasonable to attribute the observed differences simply to use of a spoon or a cup to apply granules. Provision of separate parameters on the basis of choice of cup vs. spoon is therefore questionable as is subsequent use of the cup result as a surrogate for "shaker can" powder application.

Panel Response 4-2

Several Panel members expressed concern regarding the Agency's definition and use of transfer coefficients (TCs) throughout the SOPs. See also the response to Question 2-1. The Agency's explanation of TCs is inadequate, and in need of further clarification. In particular the dependence of dislodgeable residues and transfer coefficients on chemical, formulation, sampling method and activity should be reviewed and summarized.

One Panel member suggested that TCs are methodologically specific and should be used only with data obtained using the matched method. This should be explicitly stated in the SOP document. This stems in part from disparate approaches to residue determination. Traditional agricultural TCs were derived using a method intended to recover all the material not inextricably bound to leaves. Because the modified California roller is intended to mimic human dermal transfer, it is much less efficient than chemical extraction methods used traditionally in agriculture. TCs estimated using inefficiently collected residue data can be very large and cannot be coupled with residue data obtained by relatively efficient methods.

Confusion over the use of TCs was highlighted in the public comment in which turf reentry data were presented by the Joint Ventures and Task Forces (JVTF). Based on their own analysis of turf reentry data, JVTF representatives criticized Agency practice with respect to TCs. Because members of Panel have not had access to the data underlying the JVTF presentation, the Panel cannot confirm or refute the JVTF arguments. A nonlinear relationship between dermal exposure and turf transferable residue (TTR) could be explained by the use of different residue and exposure sampling methods over the range of application rates tested. This episode simply highlights a general need for more transparent presentation of TC-related data in the context of REA.

Agency Charge

5. Residential Exposure Assessment Methodologies and Algorithms

Most of the residential exposure scenarios use algorithms that employ chemical- and scenario-specific exposure monitoring data coupled with applicable exposure factors to predict exposures. They are common approaches for pesticide exposure assessment and consistent with the Agency's *Guidelines for Exposure Assessment* with some being included in recent SAP discussions. Examples include the use of applicator exposure monitoring data for various chemicals and scenarios to derive the unit exposure-based residential handler exposure algorithm (January 2007 SAP), the use of post-application exposure monitoring data for various chemicals and scenarios to derive the transfer coefficient-based post-application dermal exposure assessment (December 2008 SAP), and the non-dietary ingestion exposure model (August 2005 and August 2007 SAP). Other scenarios, like post-application inhalation exposure following indoor and outdoor fogger applications, now rely more heavily on standard 1st principles modeling to predict exposures, which tend to require less case-specific data. There are also some scenarios, like insect repellents and dust ingestion indoors, that are new additions to the Residential SOPs whose methodologies will benefit from SAP review.

- **5-1. Please comment on whether the methodologies and algorithms for each scenario used are scientifically sound and reasonable for the purposes of these SOPs. Please include commentary on:**

  a. scenario-specific approaches for both hand-to-mouth and object-to-mouth non-dietary ingestion exposure;

b. post-application inhalation exposure (e.g., the well-mixed box model); and,
c. considerations for assessing exposure via ingestion of dust.

- **5-2. Please identify specific examples and provide recommendations for improvement or alternative approaches.**

Panel Response 5-1

The SAP believes that the methodologies and algorithms for each scenario used are scientifically reasonable. The Panel is less confident as to whether the methodologies and algorithms are scientifically sound. For several exposure pathways scientifically sound algorithms do not currently exist.

Most of the residential exposure scenarios use algorithms that employ chemical- and scenario-specific exposure monitoring data coupled with applicable exposure factors to predict exposures. They represent common approaches for pesticide exposure assessment and are consistent with the Agency's *Guidelines for Exposure Assessment.* Many have been vetted by prior SAPs. Examples include the use of applicator exposure monitoring data for various chemicals and scenarios to derive the unit exposure-based residential handler exposure algorithm (January 2007 SAP), the use of post-application exposure monitoring data for various chemicals and scenarios to derive the transfer coefficient-based post-application dermal exposure assessment (December 2008 SAP), and the non-dietary ingestion exposure model (August 2005 and August 2007 SAP). Other scenarios, such as post-application inhalation exposure following indoor and outdoor fogger applications, now rely more heavily on modeling from first principles to predict exposures, which tends to require less case-specific data. There are also some scenarios, such as insect repellents and dust ingestion indoors that are new additions to the Residential SOPs.

General Recommendations:

The members of the SAP have not reviewed every algorithm in detail for mathematical correctness. The differential equations have to correspond to the physical model and the solution has to be mathematically correct. From what we have been able to see, there is no reason to doubt the overall quality of the work. However, given that these SOPs will be used for many years and in many countries, the Agency would do well to obtain an independent review of all equations and formulae. Also, there are implicit references to software for implementing the SOPs but no code is shown. The code will need an audit to ensure that it implements the algorithms correctly. A code audit will be essential if the code is to be released for use outside the Agency.

The Panel believes that the Agency should address chronic exposures to pesticide residues indoors. This issue is addressed in Question 1-1 regarding completeness of the SOPs. EPA already has a tool suitable for this purpose. Chronic exposure can be addressed via SHEDS with implementation of the proposed indoor fate and transport submodel (Bennett and Canales, 2005) adapted from Bennett and Furtaw (2004). Use of this approach was endorsed by a prior SAP in 2007.

Per the Panel's response to Question 2-1, the SOP does not provide sufficient information as to how the exposure information developed using the SOP will be used to develop doses in the next step of the risk assessment process. This can be remedied by amending the SOPs to calculate absorbed dose and providing relevant examples for each route of exposure.

Regarding the specific questions posed to Panel:

(a) ***Scenario-specific approaches for both hand-to-mouth and object-to-mouth non-dietary ingestion exposure:***

Opinions were mixed on this issue. Most Panelists were satisfied with the general approach taken, although confusion regarding the variable Freq_Replen must be addressed. One Panelist suggested that the Agency consider replenishment of hands by touching body areas to which insect repellent had been applied. At least one other member of the Panel believes that the hand-to-mouth scenario, which is adapted from SHEDS, is more complex than can be justified by currently available data since some of the parameters required (e.g., hand replenishment at 15 minute intervals) have no clear empirical basis.

(b) ***Post-application inhalation exposure (e.g., the well-mixed box model)***

Assumption of a well-mixed box outdoors is probably conservative, but has the desirable feature of mathematical simplicity, and is therefore an acceptable approach. Members of the SAP expressed concerns about related matters. Under the proposed protocol, if the estimated amount applied to the room results in a concentration exceeding the vapor pressure of the compound, the concentration is assumed equal to the vapor pressure initially and then declines from that point. However in reality total air concentration can exceed vapor saturation since aerosols can be present. Air samples collected by polyurethane foam (PUF) filter or by lungs can contain chemical mass in excess of the amount in saturated air. Therefore the saturation adjustment is not conservative. In addition fogger-generated aerosols are assumed to settle in 2.5 hours, but potential chronic exposures to residues remaining on surfaces due to aerosol or vapor deposition are not considered.

(c) ***Considerations for assessing exposure via ingestion of dust:***

The approach shown in Eq. 7.22, multiplication of a dust ingestion rate by a pesticide concentration on dust, is conventional and acceptable. There is some potential for double counting if both a hand-to-mouth protocol and a dust ingestion protocol are implemented, but this is acceptable in the context of a conservative approach. Selection of values of the dust ingestion rate based on data in the Exposure Factors Handbook is proposed. However no values are cited, so the Panel cannot fully assess use of Eq. 7.22.

Panel members expressed additional uncertainty regarding estimation of dust concentration and the link between dust concentration and discreet pesticide applications. Parameter values for dust concentration estimation (Eq. 7.23) are not provided (Table 7-19 is a placeholder). Since pesticide residues in house dust can be derived from either recent or historical applications either indoors or outdoors, estimation of pesticide content based on a single application is unlikely to

be fruitful. (This issue is linked to the Panel's interest in chronic exposure assessment as expressed in the response to Question 1-1.) Panel members also note that if measured values, rather than estimated values, are used, results obtained by various dust collection methods may be highly variable and, in the case of aggressively extracted deep carpet dust, of questionable relevance to exposure.

Panel Response 5-2

The Panel expressed some confusion over the Agency's approach to probabilistic versus deterministic analysis. (See the Panel's response to Question 2-1.) One member suggested that approximate standard errors be estimated for each of the point estimates. Approximate standard errors of point estimates can be obtained by using the Delta method, which is described in many standard references (see also Appendix B). This leads to a probabilistic approach that the agency may find useful.

Since many of the predictive equations used in the SOP involve products and ratios of input variables, the approach demonstrated in Appendix B can be used to compute approximate standard errors for many exposure scenarios. Delta methods can also be used to obtain standard errors for exposure scenarios that involve power and exponential functions such as those found in Equation 8.3 of the draft SOP. Alternatively, when one has probability distributions associated with the input variables in an exposure estimate, one could approximate a standard error for an exposure estimate by simulating input variables from their respective distributions. For example, one could simulate values for the input variables from their respective probability distributions, and then compute an exposure estimate from the simulated values. One could repeat this 10,000 times, and then calculate the standard deviation of these 10,000 simulated exposure estimates to get a standard error to associate with an exposure estimate.

The Panel agrees that a Tier 1 deterministic approach should produce a conservative result. However, there are competing approaches that one could use to be conservative. While it is not stated explicitly, the Agency's approach appears to be to achieve a conservative result by choosing a conservative value of each of the input variables, typically a nominal 95^{th} percentile value (or 5^{th} percentile where appropriate). An alternative approach would involve use of the estimated 95^{th} (or other appropriate) percentile of the calculated exposure. An example that illustrates the difference between these approaches in a 2-variable case is presented as Appendix B.

It should be noted that criticism of deterministic approaches as excessively conservative typically starts from the assumption that nominal 95^{th} percentiles used in deterministic analyses actually are 95^{th} percentiles. However, if distributions were actually known, a full probabilistic analysis could be conducted and a known level of conservatism imposed after the fact. In practice the actual percentiles that the selected point estimates represent are not known. Guesstimated 95^{th} percentiles may be much more or much less conservative than intended.

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APPENDIX

Appendix A – Miscellaneous Errors in the Draft Technical Guidelines, Standard Operating Procedures for Residential Pesticide Exposure Assessment

- Page 1-3. The parenthetical in the definition of EF should be e.g. not i.e. as frequency of product use and frequency of exposure are not always the same.
- Page 2-3, Table 2-2. The data in Table 2-2 appear to be specifically for males, but that information is not provided in the title.
- Page 2-8; bullet points. "Partial palm [without] fingers" is defined incorrectly (to include fingers).
- Page 3-7; For trigger sprayers, one bottle (volume not given) is assumed. Herbicides are routinely found in 1.33 gallon containers with a trigger sprayer and this volume should be considered for Tier 1 calculations.
- Page 3-13; last full paragraph. Reference should be to Appendix C.7.1 (turf/transfer coefficients) rather than C.6.1 (turf/transferable residues).
- Page 3-14; Table 3-5. Why are toddler values (liquid vs. granular TC) different at the median if each is 42% of the adult value and the adult values are not different at the median?
- Page 3-16; Equation 3.7. "Hands" is not subscripted in the numerator.
- Page 3-27. A quantity with units of volume/mass cannot be density. It is specific volume.
- Page 7-40. D is defined both as daily dissipation (Eq. 7-23; should be lowercase?) and as dose (Eq. 7-24).
- Pages B-110, 111. Citations of Knarr (1998) are probably in error. Elsewhere there are references to Knarr (1988) and Knarr (1991), which have different MRID nos, but the same title.

Appendix B – Conservatism of Estimation

Consider an outcome that is the product of two variables:

$$E = X \cdot Y$$

Assuming X and Y are normally distributed, the variance of E can be estimated as:

$$\sigma_E^2 = \mu_Y^2 \cdot \sigma_X^2 + \mu_X^2 \cdot \sigma_Y^2 + 2 \cdot \mu_X \cdot \mu_Y \cdot \rho_{XY} \cdot \sigma_X \cdot \sigma_Y$$

If X and Y are uncorrelated or weakly correlated, this result simplifies to:

$$\sigma_E^2 \approx \mu_Y^2 \cdot \sigma_X^2 + \mu_X^2 \cdot \sigma_Y^2$$

Two (of many) possible conservative estimates of E can be calculated as 1) the product of the estimated 97.5th percentiles of X and Y:

$$E_1 = (\mu_X + 2 \cdot \sigma_X) \cdot (\mu_Y + 2 \cdot \sigma_Y)$$
$$= \mu_X \cdot \mu_Y + 2 \cdot (\mu_X \cdot \sigma_Y + \mu_Y \cdot \sigma_X) + 4 \cdot \sigma_X \cdot \sigma_Y$$

or 2) as the estimated 97.5th percentile of the product of X and Y:

$$E_2 = \mu_X \cdot \mu_Y + 2 \cdot \sqrt{\mu_Y^2 \cdot \sigma_X^2 + \mu_X^2 \cdot \sigma_Y^2}$$

The first term to the right of the equals sign is the same for E_1 and E_2. The relative conservatism of each estimate is dependent upon the additional terms in each equation. Example calculations are presented in Table B-1. In each case the value of E_1 is greater than that of E_2. This illustrates the effect of "compounded conservatism" and the merits of an approach in which the initial analysis is probabilistic and conservatism is imposed after the fact. Application to scenarios involving more than two variables is more difficult, but possible.

Table B-1.

Scenario	μ_X	σ_X	μ_Y	σ_Y	E_1	$\sqrt{\mu_Y^2 \cdot \sigma_X^2 + \mu_X^2 \cdot \sigma_Y^2}$	E_2
1	2.00	1.00	2.0	1.0	16.00	2.83	9.66
2	0.12	0.06	8.5	10.7	7.18	1.38	3.78
3	0.66	1.89	8.5	10.7	132.76	17.55	40.71
4	0.12	0.06	1800.0	310.0	580.80	114.23	444.45