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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: August 15, 2012

SUBJECT: Transmission of Background Materials and Charge to the Panel for the September 11 - 14, 2012 Session of the FIFRA Scientific Advisory Panel (SAP) entitled "*Pollinator Risk Assessment Framework*".

FROM: for Donald Brady, Ph.D., Director
Environmental Fate and Effects Division
Office of Pesticide Programs (7507P)

Please 8/15/12

TO: Fred Jenkins, Ph.D., Designated Federal Official
FIFRA Scientific Advisory Panel
Office of Science Coordination and Policy (7201M)

Please find attached one compact disc (CD) containing the documents for the September 11 - 14, 2012 Session of the FIFRA Scientific Advisory Panel (SAP) on "*Pollinator Risk Assessment Framework*". These documents include the White Paper, which is being provided for the Panel's review, along with reference materials; the documents have been electronically transmitted to you via email as well. Also included in this transmittal memo are the charge questions to the SAP.

The documents associated with the White Paper do not contain any information protected under the statute as Confidential Business Information (CBI) or information protected from disclosure to foreign and multi-national pesticide producers under FIFRA Section 10(g).

The CD attached contains the documents identified in the table below. Please feel free to call us if you have any questions.

White Paper (Review Document)	Source	Author(s)	Date	FIFRA 10(g) Protected
White Paper in Support of the Proposed Risk Assessment Process for Bees	CD Folder	U.S. EPA	August 2012	No
Appendix 1: Estimation of food consumption rates for worker larvae and adults	CD Folder	U.S. EPA	August 2012	No
Appendix 2: Discussion of Potential Pesticide Exposures through Consumption of Contaminated Drinking Water	CD Folder	U.S. EPA	August 2012	No
Appendix 3: Summaries of empirical studies from unpublished, registrant-submitted studies that were used to evaluate Tier I methods for estimating pesticide exposures	CD Folder	U.S. EPA	August 2012	No
Appendix 4: Summaries of empirical studies from the scientific literature that were used to evaluate Tier I methods for estimating pesticide exposures	CD Folder	U.S. EPA	August 2012	No
Appendix 5: Transpiration Stream Concentration Factors (TSCFs)	CD Folder	U.S. EPA	August 2012	No
Compendium of open literature citations used in support of the white paper	CD Binder	Open Literature	August 2012	No[1]

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Charge Questions for the FIFRA Scientific Advisory Panel
on
Pollinator Risk Assessment Format

September 11 – 14, 2012

Problem Formulation

1. **Section 2.2.1** of the white paper discusses the protection goals and associated assessment endpoints for assessing risks to honey bees (*Apis mellifera*). The protection goals are:
   - protection of pollination services;
   - protection of honey and hive product production; and,
   - protection of pollinator biodiversity.

   As described in the white paper, assessment endpoints are based on their ecological relevance, their susceptibility to known or potential stressors and their relevance to protection goals.
   a. Please comment on whether the assessment endpoints (*e.g.*, population size and stability of managed bees, quantity and quality of hive products, and species richness and abundance) identified in **Table 1** in **Section 2.2.1** of the white paper are consistent with the Agency's protection goals. Please include a discussion of any additional assessment endpoints that may be necessary to meet those protection goals
   b. Please comment on whether the measurement endpoints at the level of the colony (*e.g.*, colony strength and survival, contamination of pollen and nectar and species richness and abundance) identified in **Table 1** are consistent with the assessment endpoints identified in the table and any additional assessment endpoints discussed in Part "a" of this question. Please include a discussion of any additional measurement endpoints that may be necessary to represent those assessment endpoints.
   c. Please comment on whether the measurement endpoints at the level of the individual bee (*e.g.*, individual adult and larval [brood] survival, queen fecundity, brood emergence success, worker longevity) identified in **Table 1** are consistent with assessment endpoints identified in the table and any additional assessment endpoints discussed in Part "a" of this question. Please include a discussion of any additional measurement endpoints that may be necessary to represent those assessment endpoints.

2. **Section 2.2** of the white paper discusses a series of conceptual models for assessing risks of honey bees resulting from pesticide applications. These models depict the nature of the stressor (*i.e.*, nonsystemic and systemic pesticides that are applied as foliar treatments, soil and/or seed treatments, or trunk injection), its source (*e.g.*, direct deposition on bees or pollen), the exposure media (*e.g.*, residues on plants, residues in/on

pollen/nectar), receptors (*e.g.*, foraging bees, developing brood) and attribute changes (*e.g.*, reduced [bee] population, reductions in the quantity/quality of honey).

a. Please comment on whether the conceptual models depicted in **Figures 4** through **8** are consistent with the protection goals and assessment endpoints identified in **Table 1** and discussed in Question 1.

3. The focus of the white paper and proposed risk assessment process on the honey bee reflects two important factors: 1) honey bees are considered one of the most important pollinators globally from both a commercial and ecological perspective; and 2) standardized test methods for evaluating exposure and effects of chemicals in a regulatory context are more developed with the honey bee compared to non-*Apis* bees. Both the Introduction (**Section 1**) and the Problem Formulation sections (**Section 2**) of the white paper indicate that honey bees have historically served as a surrogate for other beneficial insects. As discussed in **Section 5.3** of the white paper, there is uncertainty regarding the extent to which honey bees serve as surrogates for native species, especially where life history strategies and differential sensitivity across species render native species more or less vulnerable to pesticides.

   a. Please comment on the extent to which the assessment of risks to the honey bee may serve to meet the protection goals identified in the white paper (*i.e.*, protection of pollination services; protection of honey and hive product production; and protection of pollinator biodiversity).

   b. Until guidelines are developed for testing non-*Apis* species of bees, please comment on the extent to which the honey bee may or may not serve as a reasonable surrogate for non-*Apis* bees, given the differences in life history strategies and potential different sensitivities to pesticide toxicants. Please include a discussion of which types of non-*Apis* bees may be particularly well represented by either the individual-level or colony level endpoints identified in Table 1 of the white paper; as well as which types of non-*Apis* bees may not be as well represented, and therefore, may be the focus of potential areas for future research.

Exposure Assessment

As discussed in Section 3 of the white paper, the magnitude of measured pesticide residues on bees and in plant matrices relevant to the diet of the bee vary considerably. At a screening level (Tier I), estimates of exposure are intended to be sufficiently conservative to account for the observed variability so that there is a low likelihood that actual exposure would be greater than the values used in the screen. To accomplish this, the proposed methods described in the white paper use upper-bound estimates that approximate an upper 95th percentile confidence limit based on the distribution of measured residue values in relevant matrices.

4. **Contact Exposure.** The exposure characterization of the white paper (specifically, **Section 3.1.1.2**) proposes a screening-level (Tier I) approach for quantifying contact

exposure to foraging bees for pesticides applied via foliar spray. This proposed method is based on the maximum of residue values on honey bees from a field study conducted by Koch and Weisser (1997). The white paper also discusses a method based on the T-REX upper-bound concentration for arthropods directly sprayed with pesticides while located directly on a treated field. Although the second method is not proposed for the Tier I exposure assessment for honey bees, it could be used to assess contact exposures to other insect pollinators.

a. Please comment on the strengths and limitations of the proposed approach for assessing contact exposures to honey bees in Tier I exposure assessments (*i.e.,* 2.7 µg a.i./bee per 1 lb a.i./A), which is based on the honey bee specific maximum concentration reported by Koch and Weisser (1997).
b. Please comment on the potential utility of the T-REX upper-bound residue value (*i.e.,* 12 µg a.i./bee per 1 lb a.i./A), for a broader number of arthropod species to represent contact exposures to honey bees and to other insect pollinators that are directly sprayed with pesticides.

5. **Dietary Exposure (Consumption Rates).** As discussed in the effects assessment section of the white paper (**Section 4.1**), acute oral toxicity data (LD_{50}) are necessary for adult and larval bees in order to characterize the potential risks of a pesticide. Because these toxicity data are expressed on a dose basis (*i.e.,* µg a.i./bee), it is necessary to convert estimated concentrations of pesticides in food (expressed as mg a.i./kg) into doses. Honey bees fulfill their nutritional requirements through consumption of nectar, honey, and bee bread (pollen/honey). In addition to requiring bee bread and nectar or honey, bees also require royal jelly and brood food (jelly) to fulfill their nutritional requirements. In the proposed approach, it is assumed that exposures through consumption of nectar and pollen are conservative representations of potential exposures through consumption of honey and bee bread, respectively. This approach is likely to be conservative because it assumes that pesticides do not degrade while honey and bee bread are stored in the hive and have undergone some degree of processing (*e.g.*, fermentation). For bees that consume honey, it is assumed that the estimated pesticide exposures can be related back to the original concentration in nectar by accounting for the amount of sugar consumed by bees. It is also assumed that pesticide exposures through consumption of pollen and nectar are protective of pesticide through consumption of royal jelly and brood food given that empirical data indicate that pesticide concentrations in royal jelly are a >100 times lower than concentrations in food consumed by nurse bees. In the proposed approach, pesticide doses received by bees are calculated using nectar and pollen consumption rates for larval and adult worker bees. As discussed in detail in **Appendix 1** of the white paper, the proposed values for larvae and adult workers are based on an analysis conducted by EPA, which built upon work published by Rortais *et al.* (2005), Crailshaim *et al.* (1992 and 1993) and others. For larvae, the proposed total food consumption rate is 120 mg/day, which is based on the total daily consumption of pollen and nectar (based on honey consumption) by larvae during day 5 of the uncapped larval life stage. For adult worker bees, the proposed food consumption rate is 292 mg/day,

based on food consumption rates of nectar foraging bees, which are expected to receive the greatest dietary exposures among different types of worker bees. In addition, as discussed in **Appendix 1**, it is likely that these food consumption rates are protective of drones and queens.

a. Although bee larvae typically consume processed foods in the form of royal jelly and brood food throughout much of their development, they also consume honey and pollen during the last two days of the uncapped period. Please comment on the proposed use of nectar and pollen consumption rates of larvae during the last day of the larval developmental stage. Please include a discussion of the conservatism, strengths and limitations of this approach as well as a discussion of how this value may or may not correspond to data generated from larval toxicity endpoints.
b. Please comment on the strengths and limitations of basing the Tier I screen for adult honey bees on food consumption rates of nectar foraging bees, including a discussion of the conservatism of this approach, and how it relates to other types of worker bees and castes.
c. Please comment on the assumption that exposures through consumption of nectar and pollen are conservative representations of potential exposures through consumption of honey, bee bread, brood food and royal jelly, all of which represent processed foods

6. **Dietary Exposure.** The dietary exposure methods described in **Section 3.1** of the white paper differ in the nature of the estimated concentrations in pollen and nectar consumed by bees. For foliar spray applications, the proposed approach involves the use of the tall grass residue value from the T-REX model (v. 1.5) as a surrogate for pesticide concentrations in nectar and pollen. For soil treatments, the white paper proposes the use of the Briggs model, which is designed to estimate pesticide concentrations in plant shoots resulting from plant uptake of pesticides from treated soil. Estimated pesticide concentrations in plant shoots are proposed as a surrogate for concentrations in pollen and nectar. For seed treatments, the white paper proposes the use of the International Commission for Plant-Bee Relationships' (ICP-BR) 1 mg a.i./kg concentration as an upper-bound concentration in nectar and pollen. The paper explores the strengths and limitations of each method relative to the ability to derive reasonably conservative estimates of pesticide exposures to bees, with a focus on how well the estimates relate to empirically based measures of pesticides in pollen and nectar from crops treated with pesticides.
    a. *Foliar spray:* Please comment on the analysis presented in Section 3.1.1.1, with a focus on the extent to which the T-REX tall grass upper-bound residue may serve as an adequate surrogate to represent upper-bound pesticide concentrations in pollen and nectar of flowers that are directly sprayed with pesticides.
    b. *Soil applications:* Please comment on the analysis presented in Section 3.1.2, with a focus on the extent to which the Briggs' model may generate estimates of pesticide exposure in plant stems that can represent upper bound pesticide concentrations in pollen and nectar of flowers.

c. *Soil applications:* Please discuss the relative strengths and limitations of the 1 mg a.i./kg value and the soil uptake model (the Briggs' model) proposed in the white paper as Tier 1 screens, including consideration of the extent to which this method may generate conservative Tier I estimates of dietary exposures to bees. Does the Panel conclude that the one approach may be better suited to specific types of assessment scenarios? If so, please elaborate. Alternatively, if both approaches are equally suited for a Tier I screen, please provide guidance on how to be capture variability and uncertainty in the exposure estimates using the two approaches.
d. *Seed Treatments:* Please comment on the analysis presented in Section 3.1.3, including a discussion of the strengths and limitations of the use of 1 mg a.i./kg value as an upper-bound concentration for pollen and nectar of seed-treated crops.
e. Please comment on other approaches or data that should be considered for estimating upper-bound estimates of pesticide residues in pollen and nectar as a Tier I screening-level assessment for pesticides applied via foliar spray, soil application or seed treatment.

7. **Consideration of other Exposure Pathways**. The proposed measures of exposure are based on what are believed to be the primary routes, *i.e.*, direct contact and ingestion of contaminated pollen and nectar. Additional routes of exposure are considered (*e.g.*, dust, drinking water), but not included in the proposed Tier I exposure assessment method. As discussed in **Section 3.1.4.1** of the white paper, effective quantitative screening methods for estimating exposures through contaminated dust are not discernible at this time. The most effective management of bees exposure to pesticides through dust appears to be through pesticide application (*e.g.*, stickers) and seed planting practices, especially since dust exposure is expected to be a concern for only a limited number of pesticides and application scenarios. In regards to pesticide exposures through drinking water, **Appendix 2** presents an analysis of potential exposures to bees through various sources of water to support the exclusion of drinking water exposure in the Tier I screen. The results of this analysis indicate that if bees consume the majority of their water from puddles or ponds, the exposures relative to dietary and direct spray are insignificant. The preliminary analysis indicates that if bees drink a substantial amount of water from guttation fluid or dew, conservative exposures may be similar to or even exceed pesticide exposures through the diet or direct spray. Further investigation concluded that pesticide exposures through dew and guttation fluid are not expected to be as significant when compared to diet, primarily because they are not likely to consistently drink a substantial amount of water from these sources.
    a. Please comment on the strengths and limitations of basing the Tier I exposure method on contact and diet. Does the Panel agree that for the majority of pesticide applications, the primary exposure routes for bees will be represented by contact and diet?
    b. *Dust:* If the Panel believes that this exposure route should be quantitatively included in the Tier I exposure method, for the relevant application type(s) (*i.e.*,

seed treatment), please discuss the data that may be needed to address the exposure route quantitatively.

c. *Drinking Water:* Please comment on the analyses, discussions provided in **Appendix 2** of the white paper and the conclusion that pesticide exposure to bees through drinking contaminated water is not expected to be a major route of exposure when compared to contact (following foliar spray applications) and diet. If the Panel believes that this exposure route should be quantitatively included in the Tier I exposure method, for the relevant application type(s) (*i.e.*, foliar spray, soil treatment, seed treatment, or trunk spray), please discuss why and what data may be needed to address the exposure route quantitatively.

d. *Other Routes:* Please identify and discuss additional exposure routes (if there are any besides contact with dust and consumption of drinking water) that would contribute significantly to pesticide exposure of bees and explain how and why such exposures could be considered quantitatively in establishing the Tier I exposure value.

Effects Assessment

8. **Tier I Effects Assessments.** As discussed in the Problem Formulation (**Section 2.2.1**), the assessment endpoints for the ecological risk assessment of bees involve maintaining honey bee population size, stability of managed bees, quality and quantity of hive products, species richness and abundance. In order to use the results of toxicity studies quantitatively in risk assessment, it is important to identify specific endpoints which will be measured in toxicity tests as these measurement endpoints must have clear linkages to assessment endpoints. As indicated in **Table 1** of **Section 2.2.1**, at the individual bee level (which is the focus of the Tier I assessment), measurement endpoints relevant to these assessment endpoints include: individual survival, adult bee longevity, brood size, brood success, and queen fecundity. The acute and chronic toxicity tests with larvae and adults can be used to quantify effects of pesticides on all of these endpoints, with the exception of queen fecundity (which would require an egg laying study involving the queen). The focus of the chronic toxicity tests with larvae and adults is on mortality that may occur during the tests. Potential impacts of a pesticide on brood size and success can be assessed by determining whether there is decrease in the number of brood (*i.e.*, larvae) following a chronic exposure of larvae to that pesticide. Potential impacts of a pesticide on adult survival and longevity can be assessed by determining the mortality and the decrease in the life spans of adult bees following chronic exposures to the pesticide. The notable limitation to the proposed chronic toxicity endpoints is that they do not include measures of queen fecundity.

   a. Please comment on the extent to which currently available bee toxicity tests, which focus primarily on mortality/survival, serve as an effective Tier 1 screen.

   b. Please comment on additional measurement endpoints (*e.g.*, growth) which should be considered in future modifications of Tier 1 test protocols and which are appropriately linked to the proposed assessment endpoints. Given that the

queen is the reproductive unit of the colony, please comment on methods to evaluate effects on individual queens, considering practical limitations of testing with queens.

9. **Tier 1 Larval Toxicity Testing. Section 4.1** of the white paper discusses new data requirements for the screening-level effects assessment and recommends obtaining and using larval toxicity data on individual bees. The paper specifically identifies the assay initially proposed by Aupinel *et al.* (2007) as one methodology for quantifying acute oral larval toxicity in the Tier I screen. These assays rely on feeding bees a sugar solution which has been spiked with the test material; however, this *in vitro* method of feeding larvae differs from the process by which the larvae would typically be fed within the colony environment, *i.e.* by nurse bees secreting either brood food or royal jelly.
    a. Please comment on the extent to which the Aupinel *et al.* (2007) *in-vitro* method serves as an appropriately conservative estimate of Tier 1 acute oral exposure of honey bee larvae to pesticides, given differences in this test design from actual in-hive exposure conditions (*e.g.*, during the first 3 days of the larval development stage larvae consume royal jelly and brood food) and the uncertainty regarding the extent to which larvae rely exclusively on pollen/nectar as opposed to royal jelly/brood food.
    b. Please comment on the extent to which pesticides would be more or less bioavailable using the synthetic matrix relied on for feeding developing bees in this *in vitro* method.
    c. Please comment on the extent to which the absence of trophallaxis (*i.e.*, the transfer of food/fluids between colony members) may render larvae more or less vulnerable to pesticides.
    d. Please comment on alternative methods for testing individual larvae that may be appropriate for quantitative use in a Tier I screening-level assessment.
    e. Typically acute toxicity tests are concluded between 48 – 96 hrs. Please comment on the appropriate duration of toxicity tests for assessing acute toxicity to individual larval and adult bees.

10. **Tier 1 Chronic Toxicity Testing Bees. Section 4.1.2** of the white paper discusses the status of chronic toxicity tests with individual adult and larval bees. At this time, no formal guidelines have been developed for conducting chronic toxicity tests with either adult or larval bees, although studies with individual bees of various ages are routinely reported in open literature.
    a. Please comment on the conclusion that adequate procedures have not been sufficiently developed and validated for assessing chronic toxicity to individual bees in a risk assessment context.
    b. Please comment on the potential use of the 10-d adult worker and 7-day *in vitro* larval toxicity tests discussed in the white paper for assessing chronic toxicity once these methods are fully vetted.

c. Although 10-day adult and 7-day larval toxicity tests have been proposed, please comment on whether alternative durations of pesticide exposure may be more appropriate for determining chronic toxicity for adult and larval bees at a Tier I screen.
d. The white paper identifies NOAEC as the chronic toxicity measurement endpoint. Please comment on the possible use of EC_x values as a measure of chronic toxicity for use in RQ calculations.
e. Please provide comments on what percent effect would be considered a relevant measure of chronic toxicity for individual bees given the potential compensatory effects which honeybee colonies may exhibit relative to the effects of pesticides.
f. Although the white paper identifies some measurement endpoints for assessing chronic toxicity to individual bees (*e.g.*, survival), please comment on other endpoints to consider in chronic toxicity studies which the Panel believes are important and the associated study design elements.
g. **Section 4.1.3** of the white paper discusses the uncertainties associated with developing risk assessments based on studies of sublethal effects when sufficient linkages have not been developed to understand how the sublethal endpoints may be quantitatively related to typical assessment endpoints (*i.e.*, growth, impaired survival, and reproduction) at the whole colony level. Please comment on the proposal to use data on sublethal endpoints to qualitatively (*i.e.*, no Risk Quotient is derived) characterize effects and risk until sufficient linkages between these endpoints and the defined assessment endpoints have been developed (*e.g.*, Adverse Outcome Pathways).

11. **Tier II Semi-field Effects Assessments (Whole Colony).** For Tier II assessments, **Section 4.2** of the white paper identifies two types of test methods that may be used to assess colony-level effects, *i.e.*, semi-field tunnel tests [OECD 75; EPPO 170]; and semi-field feeding studies. These studies are intended to help characterize risks identified in the Tier I level assessment that are based on exposures and toxicity data for individual bees and quantified using Risk Quotients.
    a. Although colonies are typically confined to enclosures for Tier II studies and these enclosures can limit the environmental realism of the study conditions, tunnel studies provide an opportunity to collect colony-level effects and potentially exposure information. Please comment on the relative strengths (*e.g.*, foraging activity by adult worker bees is limited to treated crop; trophyllaxis enabled) and limitations (*e.g.*, limited study duration, smaller colony sizes, reduced forage area) of these methods.
    b. Please comment on any other types of colony-level studies that should be considered as part of Tier II.
    c. Please comment on the most important endpoints that should be measured in the Tier II studies (*e.g.*, adult forage bee mortality, brood development, queen fecundity, overall colony strength) that are linked to assessment endpoints and their associated protection goals.

d. **Section 4.2.2** of the white paper discusses a full-field feeding design. This methodology is discussed under Tier II assessments since the colony is relatively confined to foraging on either spiked sucrose solutions or spikes pollen. The intent of this methodology is to ensure that colonies are exposed to known residue levels over longer durations than the semi-field tunnel study designs. A limitation to the study is that bees may simply store spiked food rather than consume it and that the reliance on a single source of food may introduce confounding effects (*e.g.*, nutritional deficits) into the study. Please comment on the environmental realism and utility of full-field feeding studies as a line of evidence in characterizing risk to honey bee colonies.

e. As discussed in **Section 4.3.4** of the white paper, it is important to consider the biological significance of a measured effect in addition to its statistical significance. Please comment on the nature and magnitude of effects that would be sufficient to conclude biologically significant effects on the colony and/or the need to transition to Tier III assessments.

12. **Tier III Effects Assessments**. **Section 4.3** of the white paper discusses the proposed risk assessment process in Tier III that relies on assessing effects at the colony level where colonies are not confined (*i.e.*, full field) and exposure is intended to represent environmentally realistic conditions. As discussed in the white paper, interpretation of the biological significance of colony-level effects can be challenging, regardless of their statistical significance. Conversely, high variability in field studies can limit the statistical power of the study to detect treatment effects. The paper identifies uncertainties associated with the extent to which bees forage on the treated crop, the size of treatment site, controlling for alternative forage/pesticide use area, and ensuring suitable controls; these factors combine to render these studies highly resource intensive.
    a. Please comment on the strengths and limitations of full field studies described in the white paper.
    b. Please comment on the proposed modifications to the field study design elements presented in **Section 4.3.2** of the white paper.
    c. Please comment on factors that should be considered in evaluating the biological significance of effects measured in full-field studies in relation to the proposed assessment endpoints and related protection goals.
    d. Please comment on factors and methods that should be considered when extrapolating observed effects at the colony level in semi-field and field studies to those expected to occur in the environment (*e.g.*, spatial and temporal scale of exposure, hive management practices, presence of multiple chemical and non-chemical stressors, *etc*).
    e. A number of study design elements are discussed in **Section 4.3.5** of the white paper; however, even in the best designed studies, there can be confounding effects which can limit the utility of these studies in risk assessment. Please comment on factors that should be considered in determining the utility of field studies for pesticide risk assessment, including a discussion of the

representativeness of a study for a National Level assessment (*i.e.*, the pesticide may be used anywhere in the United States and its territories).

Risk Characterization

13. **Risk Estimation. Sections 2** (Proposed Risk Assessment Process) and **5** (Risk Characterization) of the white paper indicate that the proposed risk assessment process is intended to be tiered and iterative. As part of the Tier I screen, a number of iterations can be conducted on exposure estimates that allow the risk quotient (RQ) values to be further refined and potentially pass the screen without requiring higher tier effects testing at the semi- or full-field level. However, while the proposed Tier I process for bees is quantitative and results in an RQ value which can in turn be compared to a Level of Concern (LOC), higher tier refinements are used to qualitatively (*i.e.*, no RQ derivation) determine whether whole hives will be adversely affected from the use of a pesticide based on the initial screening-level assessment.
    a. Please comment on the use of data on individual bees to transition to higher tier studies given that the Tier I studies focus on survival as the primary measurement endpoint although additional endpoints may be forthcoming as test designs continue to develop.
    b. Please comment on the derivation of the Level of Concern, *i.e.*, LOC=0.4) and the extent to which is serves as an appropriate screen to transition to higher tiers of testing/refinement.
    c. Please comment of the quantitative aspect of the screening-level (Tier I) assessment and the use of Tier II and Tier III whole hive studies to qualitatively characterize risk.
    d. Please comment on the assumption that the effects on individual bees measured in laboratory studies must be considered in the context of whole colony studies conducted under semi-field and full-field conditions.
    e. Please comment on the proposed use of a weight-of-evidence approach based on information obtained from multiple tiers of risk assessment for characterizing pesticide risks to honey bees.
    f. Please comment on how best to characterize overall uncertainty or weigh different areas of uncertainty in risk characterization.
    g. Please comment on how to focus/prioritize uncertainties when designing and interpreting Tier II and Tier III studies.

14. **Colony-level Modeling**. As part of the proposed risk assessment process, **Section 5.4** of the white paper discusses the concept of using colony-level models as a means of integrating exposure and effects information generated from the multiple risk assessment tiers and in turn linking this information quantitatively to the proposed assessment endpoints. Conceptually, such models could inform the need for transitioning from lower tiers to higher tiers in the risk assessment process. They could also be considered in identifying critical design elements of higher tier studies (*e.g.*, semi-filed or full field studies).

a. Please comment on the concept of using colony-level ecological models to inform the proposed risk assessment process for honey bees, as indicated above.
b. Please comment on the state of the science regarding available honey bee models discussed in **Section 5.4.2** of the white paper in relation to their potential application in a regulatory risk assessment context. In particular, please comment on the extent that such models have been evaluated using empirical data related to honey bee population dynamics and the availability of such data for their parameterization.
c. Please comment on the most important elements that should be considered in reviewing available honey bee colony ecological models for potential application in risk assessments.