Attachment C

Non-Codified Study Justifications

(2/10/2021)

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INTRODUCTION

This document presents a list of non-codified studies required or to be required by a data call-in (DCI) issued or expected to be issued by the EPA along with a rationale for requiring the data and an explanation of the practical utility of the data. The studies are grouped by scientific discipline.

TERRESTRIAL & AQUATIC NON-TARGET ORGANISMS

Insect & Pollinator Data

Pollinator Acute Oral Toxicity, Adult
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential acute effects to adult honeybees and other pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible effects of oral exposure on adult terrestrial insect survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute oral toxicity of this compound to adult honeybees and other insect pollinators. The Office of Pesticide Programs has made available a guidance regarding ecological testing for terrestrial invertebrates using the honeybee as a surrogate test species. The guidance discusses Tier I laboratory-based acute oral toxicity studies of individual adult bees as a critical component of the screening-level risk assessment process for examining potential adverse effects from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional guidance on the honeybee oral toxicity test design can be found in OECD Test Guideline 213 http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en .
Practical Utility of the Data
How will the data be used? The Tier I acute oral toxicity data on adult bees serve as a foundation for the screening-level assessment of potential risk to non-target organisms such as federally listed threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, from acute oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect effects on a broad range of taxa. This study will also provide information with which to compare whether oral toxicity estimates differ from contact toxicity estimates obtained from other Tier I studies. If acute oral effects data for adult honeybees and insect pollinators are not available, risks to terrestrial insects from acute oral exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Pollinator Acute Oral Toxicity, Larvae

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential adverse effects to developing bees and other insect pollinators could result from exposure to pesticide residues. Available toxicity studies do not address possible effects on brood (larvae and pupae) survival/development. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute oral toxicity of this compound to bee brood.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for terrestrial invertebrates using the honeybee as a surrogate test species. The guidance discusses Tier I laboratory-based acute toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional guidance on larval honeybee toxicity test design can be found in OECD Test Guideline 237 http://www.oecd-ilibrary.org/environment/test-no-237-honey-bee-apis-mellifera-larval-toxicity-test-single-exposure_9789264203723-en .

Practical Utility of the Data

How will the data be used?

The Tier I acute oral toxicity data on honeybee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms such as federally listed threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, and/or modify their designated critical habitat from acute oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential effects on terrestrial species and whether there is a differential sensitivity of larval bees relative to adult bees. If acute oral effects data for larvae are not available, risks to terrestrial insects from acute oral exposure will be assumed.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Pollinator Chronic Oral Toxicity, Adult

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential chronic effects to adult honeybees and other pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible lethal and sublethal effects of chronic oral exposure on adult terrestrial invertebrates and will assist in determining whether the sensitivity of adult bees differs from that of earlier life stages. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the chronic oral toxicity of this compound to adult honeybees and other pollinators.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance discusses Tier I laboratory-based chronic oral toxicity studies of individual adult honeybees as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Study design elements for the chronic 10-day oral toxicity test with honeybees are similar to the OECD Test Guideline 213 acute oral toxicity test http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en.

Practical Utility of the Data

How will the data be used?

The Tier I chronic oral toxicity data on adult bees serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered species and non-listed terrestrial invertebrate insects, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators and to determine whether adult toxicity differs substantially from other life stages evaluated in other Tier I tests. If chronic oral effects data for adults are not available, risks to terrestrial insects from chronic oral exposure will be assumed.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Pollinator Chronic Oral Toxicity, Larvae

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential effects to developing bees could result from chronic oral exposure to pesticide residues. Available toxicity studies do not address possible chronic effects on brood (larvae and pupae) survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine chronic larval/pupal toxicity and whether adult emergence is adversely affected. This study will provide information on whether honeybee larvae differ in sensitivity from adult bees following chronic exposure.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance discusses Tier 1 laboratory-based chronic oral toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance.

Additional information on larval honeybee toxicity repeat exposure test design can be found in the OECD draft guidance http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf .

Practical Utility of the Data

How will the data be used?

The Tier I chronic oral toxicity data on bee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed

threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators. These data will also assist in determining whether early life stages of the bee differ in their sensitivity to pesticides relative to adults. If chronic oral effects data for larvae are not available, risks to terrestrial insects from chronic oral exposure will be assumed.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Pollinator Tier II Semi-Field Toxicity Testing (tunnel/enclosure studies)

Rationale for Requiring the Data

Tier II studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates. Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Screening-level (Tier I) studies of individual bees do not address possible effects and/or exposure to pesticide residues at the colony-level. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine whether bee colonies may be negatively affected under relatively controlled exposure conditions of a semi-field study. In addition to providing effects data, these studies can provide data on exposure as pesticide residues in pollen/nectar of treated plants.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony studies under semi-field conditions can be found in the OECD Guidance 75 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%28 .

Practical Utility of the Data

How will the data be used?

Tier II colony-level data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species and to determine whether effects observed in the screening-level (Tier I) laboratory-based studies of individual bees are evident in colony-level studies under semi-field conditions. The Tier II semi-field test of whole colonies is a relatively controlled study, *i.e.*, bees are confined to a specific area, that is designed to represent potential field-level exposure and account for hive dynamics, which are not achievable from other pollinator studies. This study will be used to determine whether adverse effects to insect pollinators at the whole colony level, may result for the use of pesticides and will help to refine risk estimates derived in the screening-level risk assessment for beneficial terrestrial invertebrates. Measured residues in pollen/nectar can also be used to refine risk estimates derived from model-based or default values in the screening-level assessment.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Pollinator Tier II Semi-Field Toxicity Testing (feeding studies)

Rationale for Requiring the Data

Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive, and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Tier II feeding studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates based on Tier I studies of individual bees. Feeding studies utilize free foraging bee colonies that are "dosed" with specific quantities of test material and represent a means of ensuring exposure to the test material through spiked pollen and/or sugar solutions fed to the colony while still allowing the bees to forage freely. Since bee colonies are not confined to enclosures, colonies can be exposed for longer duration periods without subjecting the bees to stress that typically results from Tier II tunnel studies. Available toxicity studies of individual bees (Tier 1) conducted to support screening-level assessments do not address possible effects and/or exposure to pesticide residues at the colony-level. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine whether bee colonies may be negatively affected where bees are free foraging and have the option to collect/consume alternative forage items beyond the spiked food. Since multiple dose levels can be more readily tested, feeding studies can help to define dose-response relationships at the whole colony level.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony feeding studies can be found in the EPPO Guidance 170 at: http://www.nationalbeeunit.com/index.cfm?pageId=187 .

Practical Utility of the Data

How will the data be used?

Tier II colony feeding data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species. The colony feeding study is designed to represent potential field-level exposure and account for hive dynamics using longer duration exposure periods than are possible in Tier II tunnel studies. The study will be used to determine whether potential adverse effects to insect pollinators at the whole colony level when bees are able to forage naturally beyond the spiked food. Results from the feeding study will help to refine the screening-level risk assessment for beneficial terrestrial invertebrates that were based on Tier I studies on individual bees. Since feeding studies can help to define a dose-response relationship at the colony level, the studies can provide a means of determining exposure thresholds below which the likelihood of adverse effects on colonies may be low.

How could the data impact the Agency's future decision-making?

Tier II colony-level data will be used to refine screening-level risk estimates derived using Tier I laboratory-based data on individual bees. The Tier II data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Residues in Pollen and Nectar

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticide residues in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to hive where all life stages may be exposed. For some pesticides, the quantification of pollinator-relevant residues in treated flowering plants is needed, since pollinators will be exposed to residues from either current or prior season applications (due to the potential for residues to accumulate in plants and trees). Residues in edible/transportable-to-hive parts of treated trees and plants, including (where appropriate), but not limited to, guttation water, sap/resins, whole plant tissue (*e.g.*, leaves, stems), as well as blooming, pollen-shedding, and nectar producing parts (*i.e.*, flowers and, if present, extra-floral nectaries) of plants may

inform the potential for risk. Studies should be designed to provide residue data for crops and application methods of concern.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance.

Practical Utility of the Data

How will the data be used?

Measured residue data will be used to refine conservative estimates of pesticide exposure and reduce uncertainties associated with the Tier I exposure assessment by providing direct measurements of pesticide concentrations resulting from actual use settings. Measured residues may provide a more realistic understanding of exposure through contact or ingestion with which to calculate risk quotients for individual bees as well as to characterize exposure to the colony. If measured residue data are not available, risk estimates for terrestrial insects will be based on model-generated or default values used to support the screening-level assessment.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA will have to rely on conservative estimates of exposure which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Pollinator Acute Vapor Exposure Toxicity

Rationale for Requiring the Data

Pesticide chemicals can come in the form of solids, liquids or gases. Some pesticides are highly volatile or are gases (*e.g.*, fumigants). Conducting toxicity testing based on contact and ingestion routes such as might occur with liquid or solid pesticides is not appropriate for evaluating the toxicity of highly volatile compounds or gases. If environmentally-relevant concentrations are possible, such as may be the case for most pesticides used as fumigants, evaluation of the impact on non-target species, such as terrestrial invertebrates, including pollinators, provides valuable information for mitigating that risk in the use labeling. Therefore, to assess the toxicity of highly volatile pesticides and gases to terrestrial invertebrates, an acute vapor exposure toxicity study is appropriate *in lieu* of the toxicity testing through other delivery methods.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. These can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Design elements from Tier I laboratory-based studies of individual adult bees (OCSPP 850.3020, OECD Test Guideline 213, and OECD Test Guideline 214) and larval bees (OECD Test Guideline 237 as well as draft OECD guidance on chronic larval bee toxicity testing) may also provide useful information.

Practical Utility of the Data

How will the data be used?

Tier I data on individual bees serve as a foundation for the screening-level risk assessment process used to determine the potential for a pesticide (in the form of a gas/vapor) to affect non-target terrestrial invertebrate insects, including pollinators, in their environment. These data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential effects on terrestrial species. If inhalation toxicity data are not available, risks to terrestrial insects from vapor exposure will be assumed.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Beneficial Insects Toxicity

Rationale for Requiring the Data

Pesticides are intended, for example, to prevent, destroy, repel or mitigate pests. The physical and chemical properties of some pesticides may result in broad exposure and affect non-targeted species. It is important to determine if the use of some pesticides will affect other species that are beneficial to the environment. Beneficial insects are critical to maintaining environmental balance and in sufficient numbers, can often reduce pests and the need for pesticides. Knowing the impact of pesticides on beneficial and non-target insects is essential to mitigating risk to these organisms, informing the use labeling and parameters for pesticides.

Practical Utility of the Data

How will the data be used?

The data from this study will be used to determine the exposure and effects to assess the risk to beneficial non-target and ESA-listed species from a pesticide use. This information will also allow the Agency to refine the risk assessment and, if necessary, mitigate any risk identified.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Avian & Mammalian Testing

Avian Acute Inhalation Toxicity

Rationale for Requiring the Data

Pesticide chemicals can come in the form of solids, liquids or gases. Some pesticides are highly volatile or are gases. Conducting toxicity testing based on contact and ingestion routes such as might occur with liquid or solid pesticides is not appropriate for evaluating the toxicity of highly volatile compounds or gases. If environmentally relevant concentrations are possible, such as may be the case for most pesticides used as fumigants, evaluation of the impact on non-target species, such as birds, provides valuable information for mitigating that risk in the use labeling. Therefore, to assess the toxicity of highly volatile pesticides and gases to birds, an avian inhalation toxicity study is appropriate in lieu of the toxicity testing through other delivery methods.

Practical Utility of the Data

How will the data be used?

The results of this study will be used to determine the potential for a pesticide in the form of a gas to affect non-target birds, in their environment. This study is designed to quantify the toxicity endpoint in order to calculate the risk to birds. Should the study determine the risk is a concern, the Agency can use these data to inform the pesticide label to mitigate the risks.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Aquatic Organisms (Fish & Invertebrates)

Acute Freshwater Fish and/or Invertebrate Toxicity (Synergism)

Rationale for Requiring the Data

Pesticide synergists are incorporated into pesticide products to enhance their effectiveness (toxicity) to target organisms. Assessing potential ecological risks of pesticides may requires evaluation of potential exposure and toxicity of the active ingredient alone and evaluating the enhanced toxicity that results from the addition of synergists. The goal of obtaining this data is to determine the potential range of magnitudes of synergistic effects for pesticide active ingredients that are co-applied [or co-formulated] with synergists. Acute toxicity data for pesticide Typical End-use Products (TEPs) with synergists may be needed to evaluate exposure to water bodies which can potentially impact aquatic communities.

Practical Utility of the Data

How will the data be used?

EPA will use these data to determine the likelihood that acute risks can potentially impact aquatic communities. The data will be used to refine the screening-level ecological risk assessment to determine whether the synergistic effects of pesticides causes unreasonable adverse ecological effects to non-target species.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

NON-TARGET PLANTS (TERRESTRIAL & AQUATIC)

Non-Target Plant Reproductive Toxicity

Rationale for Requiring the Data

Plants exposed to some pesticides during their reproductive stages may exhibit adverse effects on reproduction. Plants provide food and habitat vital to ecological processes. In some cases, information may suggest that the plant reproductive effects are manifested at lower concentrations than the standard vegetative vigor effects. Therefore, a full understanding of the potential risks to non-target plants is essential in order to assess the potential environmental risks from the use of some pesticides.

Practical Utility of the Data

How will the data be used?

EPA will use the data to determine the concentration at which plants exposed to pesticides during their reproductive stages are likely to exhibit adverse effects. These data will be used to characterize the risk posed to plant reproductive processes in terrestrial ecosystems.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the

flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Terrestrial Plant Vapor Exposure Toxicity

Rationale for Requiring the Data

Pesticide chemicals can come in the form of solids, liquids or gases. Some pesticides are highly volatile or are gases. Conducting toxicity testing based on contact and ingestion routes such as might occur with liquid or solid pesticides, including the standard toxicity studies with terrestrial plants (*i.e.*, Tier I and tier II vegetative vigor), is not appropriate for evaluating the toxicity of highly volatile compounds or gases. If environmentally relevant concentrations are possible, such as may be the case for most pesticides used as fumigants, evaluation of the impact on non-target species, such as plant, provides valuable information for mitigating that risk in the use labeling. Therefore, to assess the toxicity of highly volatile pesticides and gases, a terrestrial plant vapor exposure toxicity study is appropriate in lieu of the toxicity testing through other delivery methods.

Practical Utility of the Data

How will the data be used?

The results of this study will be used to determine the potential for a pesticide in the form of a gas to affect non-target plants, in their environment. This study is designed to quantify the toxicity endpoint in order to calculate the risk to plants. Should the study determine the risk is a concern, the Agency can use these data to inform the pesticide label to mitigate the risks.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

WASTE WATER SYSTEMS (ENVIRONMENTAL FATE & TOXICITY)

Drinking Water Treatability

Rationale for Requiring the Data

The use of some pesticides may result in the presence of this chemical in the drinking water reservoirs and rivers by off-target spray drift and runoff. For drinking water exposure assessment, the Agency uses models to estimate exposures in the receiving water body to derive the estimated drinking water concentrations. Without drinking water treatment data to quantify the removal mechanism, the Agency will need to assume in the risk assessment that no removal occurs in water treatment.

Practical Utility of the Data

How will the data be used?

The data will be used to assess the removal efficiency of the pesticide in typical drinking water treatment facilities through the processes of chemical addition, coagulation and sedimentation. The removal efficiency derived from the water treatment test will be used to refine the expected drinking water exposure assessment.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency would have to assume that the pesticide is not removed or reduced in concentration in drinking water treatment facilities. This assumption would lead to high drinking water exposure values estimates. These values, if used in a dietary risk assessment, could yield risk estimates above the Agency's level of concern, which could necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and could result in significant use restrictions.

ENVIRONMENTAL FATE & TRANSPORT

Dissipation Study in Compost
Rationale for Requiring the Data
The application of pesticides to vegetative matter that is subsequently used as compost or animal feed has been found to retain pesticide residues and affect non-target plants. For example, this route of exposure is common across the picolinc acid herbicides (aminopyralid, clopyralid, and picloram), but may also apply to others. These data may be needed for some pesticides to demonstrate the rates of degradation and leaching in vegetative and manure composts.
Practical Utility of the Data
How will the data be used? A compost dissipation study would be instrumental in interpreting the monitoring data that will become available after this method is disseminated. This data, if received, could assist the Agency in understanding the degradation of some pesticides in compost, and thusly, enhance our knowledge on the time and type of environment needed to allow for safe use of contaminated compost. **How could the data impact the Agency's future decision-making?** The data will be used to characterize risk from pesticide residues in compost and may inform potential mitigation including compost holding times. The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Foliar Dissipation
Rationale for Requiring the Data
The Agency has a limited understanding of how some pesticides behave on crop foliage once applied. Depending on how quickly and to what extent the compound dissipates from foliage, residues may or may not pose potential exposure concern on and around foliage. Because dissipation on foliage and release rates are not well understood, foliar dissipation data is needed.
Practical Utility of the Data
How will the data be used? Understanding of the foliar dissipation of a pesticide informs the fate of the pesticide in terms of the rate of dissipation and identity of the residues at the site of application. These data permit refinement of the ecological animal risk assessment with chemical-specific information that will characterize the dietary exposure of mammals, birds, terrestrial-phase amphibians and reptiles to resultant residues. Furthermore, the data may also be used to characterize the exposure of non-target plants, resulting from its use on a treated field. In the absence of these data, default assumptions will be utilized in the risk assessment which may overestimate available residues. **How could the data impact the Agency's future decision-making?** The data will be used to characterize risk from pesticide residues in compost and may inform potential mitigation including compost holding times. The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA,

and could result in significant use restrictions.

Dissolution Kinetics Study in Aqueous Media

Rationale for Requiring the Data

Nanosized pesticides potentially have unusual or unique properties as compared to the dissolved or coarser particle and bulk pesticide forms, which may also affect its environmental fate and ecotoxicity. Some nanosized pesticides may pass through various protective barriers of living organisms (e.g., cell membranes, brain barrier) which would not occur or would not occur to the same degree as with the dissolved or coarser particle and bulk forms of the pesticide. Dissolution kinetics of a nanosized pesticide in aqueous media forms part of the foundation for understanding the environmental fate and ecotoxicity of the nanosized pesticide. The rate at which a nanosized pesticide dissolves after being released into water determines the length of time that the nanosized pesticide will potentially reside in the environment. Results of the dissolution kinetics study are used to help determine if exposure of the environment and non-target organisms to the nanosized pesticide and/or its aged particles is likely and to inform and refine environmental fate and ecotoxicity testing required with the nanosized pesticide and/or aged particles.

Practical Utility of the Data

How will the data be used?

This study will yield the rate and form of the transformation products released from the nanosized pesticide after mixing or immersion of the nanosized pesticide into aqueous media representing use and/or environmentally relevant conditions of temperature, pH, and hardness or salinity. This data will be used to determine the stability and persistence of the nanosized pesticide in the environment and the transformation products to which the environment is exposed.

Dissolution kinetics will be used by the Agency to determine if the environment is exposed to potentially nanosized pesticide particulates of concern and to provide input for exposure characterization and modeling. Additionally, results of the dissolution kinetics study are used to inform and refine environmental fate and ecotoxicity testing required with the nanosized pesticide and/or aged particles. For example, if the nanosized pesticide is found to completely dissolve after release before it reaches environments of concern, conducting higher tier ecotoxicity tests based specifically on exposure to the nanosized pesticide would not be required.

How could the data impact the Agency's future decision-making?

Without the dissolution study the Agency would have to assume that the nanosized pesticide is of sufficient stabilty in aqueous media to reach the environment and for non-target aquatic and terrestrial organisms to be exposed. This would trigger requiring both lower and higher tier environmental fate and ecotoxicity testing be conducted with the nanosized pesticide form. The lower and higher tier environmental fate and ecotoxicity data with the nanosized pesticide form will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat.

Rate of Deposition and Aggregation in Aqueous Media

Rationale for Requiring the Data

Nanosized pesticides potentially have unusual or unique properties as compared to the dissolved or coarser particle and bulk pesticide forms, which may also affect its environmental fate and ecotoxicity. Some nanosized pesticides may pass through various protective barriers of living organisms (e.g., cell membranes, brain barrier) which would not occur or would not occur to the same degree as with the dissolved or coarser particle and bulk forms of the pesticide. Aggregation (also referred to as coagulation) of particles which have been dispersed in aqueous media refers to the formation of clusters of the particles suspended in water. Over the course of aggregation, clusters can grow in size, from the nanoscale to much larger particles. As a consequence of this change in size, particles may settle to the bottom of the container. This process can occur

in a matter of seconds to hours. The rate at and the degree to which nanosized pesticides aggregate, agglomerate and precipitate from aqueous suspensions is required to determine if benthic and water column organisms are exposed to the nanosized pesticide or a nanosized aggregate, and to determine potential removal from to drinking water supplies.

Practical Utility of the Data

How will the data be used?

The study will yield aggregation rate coefficient(s) and/or stability ratios of a nanosized pesticide in aqueous media under environmentally relevant conditions of temperature, pH, conductivity, hardness or salinity, and concentrations of the nanosized pesticide. Information on the size of aggregates formed is also measured. This data will be used by the Agency to determine how long the nanosized pesticide will remain suspended in water or the rate of aggregation and sedimentation of the nanosized pesticide in the aquatic environment which is used to further inform and refine environmental fate, mammalian toxicity, and ecotoxicity data requirements. If the nanosized pesticide is found to rapidly form large aggregates and precipitate from water then its presence in drinking water is unlikely and toxicity testing required to support a drinking water assessment such as a chronic mammalian toxicity and a mammalian cancer study using the nanosized pesticide may not be needed, depending on if other exposure routes of concern for these exist. Benthic sediment toxicity testing may potentially be waived depending on the size of aggregates formed or if the nanosized pesticide is expected to stay suspended in the water column. If the nanosized pesticide or if nanosized aggregates are found to remain suspended in water then impacts to groundwater and exposure of water column species are expected and ecotoxicity data with the nanosized pesticide would be required.

How could the data impact the Agency's future decision-making?

Without these data, the Agency would have to assume that the nanosized pesticide is not removed or reduced in concentration in drinking water treatment facilities and would have to assume that both benthic organisms and water column organisms are exposed to the nanosized pesticide. Mammalian chronic and mammalian cancer data would be required to assess human health risks from drinking water exposure. This assumption would also potentially lead to high drinking water exposure value estimates. These values, if used in a dietary risk assessment, could yield risk estimates above the Agency's level of concern, which could necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Additionally, both lower and higher tier environmental fate and water column and sediment ecotoxicity testing be conducted with the nanosized pesticide form would be required. The lower and higher tier environmental fate and ecotoxicity data with the nanosized pesticide form will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat.

Zeta Potential in Aqueous Media

Rationale for Requiring the Data

Nanosized pesticides potentially have unusual or unique properties as compared to the dissolved or coarser particle and bulk pesticide forms, which may also affect its environmental fate and ecotoxicity. Zeta potential of a nanosized pesticide with and without associated product stabilization conditions, or protective coatings or capping material in aqueous media forms part of the foundation for characterization of the nanosized pesticide object itself and its surface chemistry, and for understanding its environmental fate and ecotoxicity. The zeta potential reflects the net surface charge of the nanosized pesticide object suspended in water and is used to predict if a nanosized pesticide object is expected to remain suspended or will agglomerate, aggregate or precipitate from water. This data is also used to predict if the nanosized

pesticide object will partition to sediments. For example, stable and positively charged particles are likely to partition to sediments while stable and negatively charged particles are likely to remain suspended in the water column.

Practical Utility of the Data

How will the data be used?

This study will yield the net surface charge of a nanosized pesticide in aqueous media under environmentally relevant conditions of temperature, pH, and conductivity and the impact to these in the presence of any associated protective coatings or capping material. From this information the iso-electric point(s) under relevant environmental conditions are established. This is a basic property of the nanosized pesticide which is used to characterize and define the nanosized pesticide. This data will be used by the Agency to determine if nanosized pesticide particles released into water will remain suspended in the water column or partition to the sediments. If the zeta potential indicates that under environmentally relevant conditions the nanosized pesticide objects are expected to partition to sediment then exposures to sediment dwelling species and plants will be expected. In this case, the Agency will require whole sediment tests with invertebrates and rooted vascular plant studies conducted using the nanosized pesticide.

How could the data impact the Agency's future decision-making?

Without the zeta potential study the Agency would have to assume that the nanosized pesticide released in aqueous media would partition to both sediment and stay suspended in the water column, resulting in exposure of both benthic organisms and organisms in the water column. This would trigger requiring benthic organism sediment toxicity testing, food chain transfer studies, and sediment fate studies. The benthic organisms sediment toxicity studies, food web chain transfer studies, and environmental fate studies will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat.

Water Chlorination Study

Rationale for Requiring the Data

It has been qualitatively demonstrated that the parent compounds of some pesticide active ingredients can be oxidized to the oxon form through chlorination during water treatment, and that this oxon may persist long enough to pass through the distribution system to the tap. The oxon may be more toxic to human health than the parent compound. Quantitative data on the formation and persistence of the oxon form in chlorinated water are necessary to estimate concentrations in treated drinking water and to evaluate human health risk from this exposure.

Practical Utility of the Data

How will the data be used?

Data on rates of transformation and on persistence of the oxon degradate will be used in estimating drinking water concentrations of the parent compound and the oxon form in order to evaluate risks to human health. In the absence of acceptable data, a quantitative assessment will be based on the assumption that all of the parent compound estimated to be present in raw water will be transformed to the oxon form during treatment, and that the oxon is persistent and will not dissipate prior to reaching the tap.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency would have to assume that all of the parent compound will be transformed to the oxon form during treatment and will not dissipate. This assumption would lead to high drinking water exposure values estimates. These values, if used in a dietary risk assessment, could yield risk estimates above the Agency's level of concern, which could necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and could result in significant use restrictions.

Measurement of Henry's Law Constant

Rationale for Requiring the Data

A measured Henry Law Constant value is needed to confirm the potential for a pesticide to dissolve in aquatic surfaces/bodies via atmospheric deposition. For pesticides that are persistent in the environment or with other fate properties, there may be the potential for aquatic exposure via atmospheric deposition for which this data is needed to assess potential exposures in aquative environments.

Practical Utility of the Data

How will the data be used?

These data will be used to determine the potential for exposure and unreasonable adverse effects in aquatic environments.

How could the data impact the Agency's future decision-making?

The data will be used to characterize risk from pesticide residues in compost and may inform potential mitigation including compost holding times. The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Outdoor Lysimeter Test For Toxicity of Leachate

Rationale for Requiring the Data

An outdoor lysimeter study on the toxicity of a compound's leachate to the ecological system is needed to determine the composition of the leachate and environmental exposure levels possible to inform the ecological risk assessment. This information is particularly useful with compounds having complex degradate profiles.

Practical Utility of the Data

How will the data be used?

The data may be used to further characterize the toxicity of this compound to non-target and endangered species, either by direct effects or by indirect effects, and to reduce uncertainties associated with the ecological risk assessment. By refining the assessment, the Agency will be able to determine whether current labeling is appropriate and whether further mitigation is necessary. In the absence of these data, uncertainty may remain related to the effects of this compound and its leachate and degradates to non-target and endangered species.

How could the data impact the Agency's future decision-making?

The data will be used to characterize risk from pesticide residues in compost and may inform potential mitigation including compost holding times. The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Leaching Study
Rationale for Requiring the Data
Determining if a pesticide or its degradate leaches is important in determining if that compound can migrate over time and result in exposures to the environment. EPA has already codified the requirement for a leaching study for antifoulant coating/paint and wood preservative uses (40 CFR 158.2280). A leaching study may also be needed for other use patterns without a codified requirement to assess potential exposures (such as, but not limited to, direct environmental contact to a materials preservative in plastics, adhesives, building materials, and textiles, or down-the-drain exposure, e.g., when a textile treated with a pesticide is laundered and wash water is sent down the drain). There are often no leaching studies available to assess these exposures.
Practical Utility of the Data
How will the data be used? EPA may need the data to conduct the ecological effects and environmental fate assessments to determine the rate at which a pesticide or its degradate leaches into the environment and whether the amount of pesticide in the leachate would be of toxicological concern. The use of actual empirical data for assessment inputs will address critical limitations of risk modeling (i.e., assumptions based on estimated inputs), resulting in more accurate risk assessments. **How could the data impact the Agency's future decision-making?** Conservative estimates of pesticide leaching, such as 100 percent leaching, will be used unless information on leaching is submitted or found from open literature to refine estimates of leaching. The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is not likely to jeopardize listed or endangered species or its critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

HUMAN HEALTH TOXICITY

Comparative Cholinesterase Assay (CCA)
Rationale for Requiring the Data
For some compounds, such as the organophosphate and N-methyl carbamate pesticides, acetylcholinesterase (AChE) inhibition is the most sensitive toxicological effect for either the parent compound or the environmental degradate, the oxon. In order to address the potential differences in potency of the oxon as well as life stage sensitivities to these compounds, the Agency needs AChE inhibition data for specific life stages in order to address the FQPA safety factor for infants and children. The CCA study is designed to provide specific AChE measurements at the compounds time to peak inhibition at different life stages and therefore provides a robust measurement of inhibition in young adult, juvenile, fetal and pregnant rats.
Practical Utility of the Data
How will the data be used? The new AChE data generated in the CCA study would be used to either confirm an existing FQPA factor or used to derive a data specific FQPA factor directly from the CCA study and be used in both the single chemical and cumulative risk assessments. The updated FQPA factor could therefore either reduce or increase risk estimates in the dietary assessments. If the dietary risk is increased based on information in the new CCA study, then additional mitigation may be needed to address potential risks of concern. If the dietary risk is decreased, then uses may be able to be expanded. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency is required to retain the 10x FQPA safety factor for a dietary risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and could result in significant use restrictions.

Comparative Thyroid/Developmental Assay (CTA)

Rationale for Requiring the Data

Chemicals that perturb thyroid homeostasis and result in hypothyroidism are known to be associated with neurological disorders and alterations in neurological development, both in animals and humans. Thyroid susceptibility may be suggested for some pesticides necessitating data to adequately characterize the potential of the pesticide to disrupt thyroid hormone homeostasis, growth and development, and neurodevelopment. Thus, if there is evidence that a pesticide produces effects on thyroid function or structure, the comparative thyroid/developmental assay would be required in lieu of the rat Developmental Neurotoxicity Study (DNT) in order to obtain specific data on thyroid function. The test substance would be administered to groups of pregnant rats during gestation and lactation with measurements made of triiodothyronine (T3), thyroxine (T4), and thyroid stimulating hormone (TSH) as well as histopathology of the thyroid gland. The EPA's *Guidance for Thyroid Assays in Pregnant Animals, Fetuses and Postnatal Animals and Adult Animals* addresses the issue of disruption of thyroid hormone homeostasis during development. The CTA is critical to addressing the potential sensitivity of infants and children under the FQPA safety factor in risk assessment.

Practical Utility of the Data

How will the data be used?

The Agency will use these data to confirm or revise the FQPA safety factor and/or dose used in the risk assessment. If the dietary risk is increased based on information in the new CTA study, then additional mitigation may be needed to address potential risks of concern. If the dietary risk is decreased, then uses may be able to be expanded.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency is required to retain the 10x FQPA safety factor for the dietary risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

An *in-vitro* micronucleus assay for mutations in genetic material

Rationale for Requiring the Data

Oxygen radical species generated by pesticide chemicals can interfere with cell division and disrupt spindle tubules and potentially lead to genotoxic effects such as DNA damage and/or chromosomal aberrations. An *in vitro* micronucleus assay may be more relevant for assessment of genotoxicity as compared to traditional *in vitro* assays. The data from this test can be used to determine if the pesticide chemical is a clastogenic or aneugenic chemical.

Practical Utility of the Data

How will the data be used?

Positive results from the *in vitro* micronucleus test indicate that the test substance induces chromosome damage, or damage to the cell division apparatus, in cultured mammalian somatic cells. Negative results indicate that, under the test conditions, the test substance does not induce chromosome structural and or numerical aberrations in cultured mammalian somatic cells. If this tests shows that the nanoparticle has the potential to cause genetic mutations, then the Agency would require additional testing.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply a 10x FQPA safety factor to the compound in a dietary risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Extended One-Generation Reproduction Study (Inhalation)
Rationale for Requiring the Data
A reproductive study provides critical scientific information needed to characterize potential hazards during *in utero* fetal development as well as development of infants and children. Exposure to pesticides that are highly volatile or are gases, such as fumigants, occurs via the inhalation route, and data evaluating the potential impact of these compounds on the reproductive system is not available, therefore an extended one- generation reproductive toxicity study via the inhalation route is needed. Given that there could be potential repeat inhalation exposure to subpopulations residing near fumigant application sites (i.e. women that could potentially become pregnant, infants and children), an inhalation reproductive toxicity study is needed to conduct a complete and comprehensive inhalation assessment of potential critical post-natal toxicological effects. The extended one-generation reproductive toxicity study (EOGRTS) would allow for the integrated evaluation of multiple organ systems (with an emphasis on the nervous, immune, and reproductive systems) across several periods of development from conception through adulthood.
Practical Utility of the Data
How will the data be used? The Agency will use these data to confirm or revise the FQPA safety factor used in the risk assessment. In the absence of inhalation data, significant uncertainties remain concerning pre- and post-natal exposures. The availability of an EOGRTS would be used by the Agency to address these uncertainties. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to retain the FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

OCCUPATIONAL & RESIDENTIAL EXPOSURE

Water Concentration Studies (Swimming Pools & Spas)
Rationale for Requiring the Data
The concentration in the water of the parent material itself is known based on the label application rate (i.e., most pool chemicals provide a rate to be maintained or rate for shock treatments). However, under certain conditions (e.g., U.V. light, oxidation, temperature, etc.), certain pesticides used to treat swimming pools & spas can break down to form degradates as toxic as or more toxic than the parent compound. Data on degradates are needed to determine potential exposure to those chemicals and to develop a conversion rate of the degradate, if applicable.
Practical Utility of the Data
How will the data be used? The data will be used to develop a risk assessment and make a safety finding. The available degradate concentrations in swimming pool & spa water will be used to determine the magnitude of incidental oral exposure and risk. Based on these data, the Agency can determine if labels need to be adjusted or refined. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Monitoring Data on Fumigated Commodities
Rationale for Requiring the Data
The potential post-application exposures associated with commodity fumigation were not quantitatively assessed when these uses were established. The Agency did not have monitoring data to directly measure emissions from fumigated commodities/materials. These data will ensure that the Agency has the most accurate information possible on exposure to evaluate emission rates from treated commodities. Post-application risks estimates will be calculated for workers and will be used to determine if the potential for occupational exposure due to those emissions (i.e., for post-application workers who must handle or receive treated commodities) is below the Agency's level of concern.
Practical Utility of the Data
How will the data be used? These data will be used to determine if the exposure from handling treated commodities/materials is below the Agency's level of concern. In addition, these data will be used to inform emissions factors and buffer zone estimates during the treatment and aeration phases of the fumigations of commodities. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Ambient Air Monitoring
Rationale for Requiring the Data
Exposure to pesticides that are highly volatile or are gases, such as fumigants, occurs via the inhalation route. Post-application inhalation exposure is predicted to occur for community populations near fumigated fields and fumigation (treatment) facilities. This study is to determine whether exposures in high use areas from ambient levels are a concern. This data will also help EPA consider the proximity of use to populations, the proximity of use to sensitive sites, and the proximity of use to minority populations to address environmental justice concerns when making risk management decisions.
Practical Utility of the Data
How will the data be used? These data will be used to in risk assessments to evaluate post-application inhalation exposure for communities near fumigation sites; potential maximum peak air concentrations in areas of high seasonal use; and potential community-level exposure to air concentrations. These data will ensure that the Agency has the most accurate information possible to protect communities near fumigation sites. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Small Air Chamber Emissions Study
Rationale for Requiring the Data
Inhalation exposures to pesticide vapors may be expected during and after application of liquids (e.g., paints, detergents, metalworking fluids, and gels) treated with certain pesticides. Exposures to both professional applicators and do-it-yourself consumer products could be anticipated. Chamber emission data may be needed to determine if these exposures exceed applicable toxicological points of departure (PODs) and are a risk to human health.
Practical Utility of the Data
How will the data be used? The chamber emission data will be used along with appropriate source models in the EPA's Indoor Air Quality Model (IAQX) to assess inhalation exposures. The results of the assessment will be compared to the toxicological POD for the pesticide to determine if the risk to human health is a concern. **How could the data impact the Agency's future decision-making?** The chamber emissions data will be used to decide if the exposure to the pesticide vapors from the use of that pesticide in liquid products generate a risk of concern that requires mitigation. This mitigation could include reduction of the application rate or elimination of the use. If chamber emissions data are not available, then default assumptions of the pesticide's emission rate will be used in the IAQX model which might overestimate the risk, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

RESIDUE DATA

Residue Dissipation
Rationale for Requiring the Data
When the currently registered uses of a pesticide or its degradate may result in post-application dermal and incidental exposure during uses (such as, but not limited to, a materials preservative in wood, textiles, leather, plastics, flooring, carpets, building materials, and finishes or coatings), EPA must evaluate potential exposure and risk. When residue data are unavailable on the leaching of the pesticide or its degradate, the Agency must conduct high-end deterministic screening-level assessments to estimate potential exposure. Risk assessment outputs based on estimated inputs are designed to be overestimations resulting from the numerous assumptions made in the absence of chemical-specific post-application dissipation and persistence rates. These assumptions need to be refined with the residue dissipation study.
Practical Utility of the Data
How will the data be used? Data collected will be used to establish rate of residue transfer or release to refine or confirm human exposure predictions. The new data generated in the residue dissipation study may be used to assess possible dermal and incidental oral human exposure to the residue and will provide a better understanding of the potential exposure and risk for individuals handling, contacting, and/or using items treated with chemicals and finishes preserved with a pesticide. For example, the data may be used to assess the risks to children mouthing and chewing treated textiles or plastic or children playing on play sets built from treated wood. The use of actual empirical data for assessment inputs will address critical limitations of risk modeling (i.e., assumptions based on estimated inputs). **How could the data impact the Agency's future decision-making?** These refined data will allow the Agency to conduct human-health risk assessments using real-world, chemical-specific inputs and thus, minimize the potential for underestimating or overestimating risk. The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Additionally, without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could

yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Attrition Study

Rationale for Requiring the Data

An attrition study is used to inform whether a solid material has the potential to break up into small particles (dust) or if a nano-sized pesticide is likely to become airborne. The study purpose is to define dust levels and may be used to determine human inhalation exposure potential or to bridge between different exposure datasets. Submitting a protocol to the Agency prior to conducting the study may be necessary. To determine the resistance to attrition of granular carriers and granular pesticides, using the latest version of the American Society of Testing Materials (ASTM) Test Method E728-91 (2009) "Standard Test Method for Resistance to Attrition of Granular Carriers and Granular Pesticides" may be used.

Practical Utility of the Data

How will the data be used?

Data collected will be used to establish attrition potential of the pesticide in order to refine or confirm human exposure predictions. The new data generated may be used to assess possible inhalation human exposure and will provide a better understanding of the potential exposure and risk for individuals handling, contacting, and/or using items treated with chemicals and finishes preserved with a pesticide. For example, the data may be used to assess the occupational exposure when pouring the pesticide or inhalation exposure during drying or cutting of articles treated with the pesticide. The use of actual empirical data for assessment inputs will address critical limitations of risk modeling (i.e., assumptions based on estimated inputs).

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Nature of the Residue in Paper

Rationale for Requiring the Data

The nature of residue in paper chemistry study will allow the Agency to conduct chemical-specific, quantitative dietary risk assessments that utilize measured quantities of pesticide and its metabolite(s) that will be available for dietary consumption when pesticide-containing products are used during production of paper and paperboard used for food packaging. The Nature of the Residue in Paper study will determine whether residues persist in treated paper, the identity of those residues, and a measured upper limit on the total residue level that could migrate to food. The Migration Studies are automatically required but may be waived depending on the outcome of the Nature of the Residue in Paper study. Migration Studies determine the concentrations of specific residues of toxicological concern transferred from treated food-contact paper packaging to various types of food coming in contact with treated paper/paperboard.

Practical Utility of the Data

How will the data be used?

The Nature of the Residue in Paper study will be used to determine whether a pesticide or its metabolite(s) remain in the paper/paperboard manufactured from pesticide-treated pulp, whether it degrades, to what it degrades, and the upper limit on residues of concern that are available to migrate to food. This study may negate the need for assessing the dietary risk due to use as a slimicide in the pulp slurry used to make food-contact packaging, may be used as an upper (yet refined) exposure limit, and may be used to either waive or provide direction for the Paper Migration Study. Migration Studies determine the concentrations of specific residues of toxicological concern transferred from treated food-contact paper and paperboard to various types of food coming in contact with these surfaces.

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

Pet Fur Residue Transfer

Rationale for Requiring the Data

These data are necessary in order to allow the Agency to refine dermal and incidental post-application exposure and risks from pesticide containing pet collars. The use of pesticidal pet collars can result in dermal exposure to adults and children and incidental oral exposure to children following contact with a treated pet.

Practical Utility of the Data

How will the data be used?

The data would be used with the toxicological endpoints of concern to evaluate the residential risks associated with dermal and incidental oral exposure to pesticidal pet collars. Without this data, risk estimates will be based on best professional default assumption for pet fur residue transfer. Based on these data, the Agency can determine if the estimated risk is valid and what additional risk mitigation measures, if any, would be necessary to result in acceptable residential post-application exposure/risk from pesticidal pet collars

How could the data impact the Agency's future decision-making?

The data will inform the determination required under FIFRA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. Without these data, the Agency may need to apply an FQPA safety factor to the compound in the risk assessment, which could yield risk estimates above the Agency's level of concern and necessitate the implementation of mitigation measures, such as reduced application rates and cancellation of some uses. Moreover, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and FQPA, and could result in significant use restrictions.

USE PATTERN ON PRODUCT LABEL

Use Summary Data

Rationale for Requiring the Data

Use summary data are needed to determine the uses registrants intend to support under the Registration Review process. Additionally, these data are needed clarify ambiguous or missing data on labels for supported uses such that human health and ecological risk assessments for those supported uses can be conducted as part of the Registration Review process. These data may include use sites, use pattern information, application methods, personal protective equipment, and any other use restrictions pertinent for consideration in conducting risk assessments to evaluate the safety of the use of the pesticide.

Practical Utility of the Data

How will the data be used?

Data will be used to assess potential risk to people and non-target organisms from exposures to pesticides. The data will be used to reduce uncertainties associated with the human health and ecological risk assessments and will improve EPA's understanding of the potential effects on people and non-target organisms. It is expected that this information will ultimately be incorporated into an electronic labeling system (Office of Pesticide Program Electronic Label (OPPEL)) currently under development by EPA to make label information more quickly available to the public in an easily searchable format.

How could the data impact the Agency's future decision making?

These data are necessary to inform the determination required under FIFRA, FQPA, and/or ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects. This information will improve the quality of the risk assessment by being more representative of the registrant supported use, which will

also reduce the need for unnecessary mitigation work. The lack of these data will limit the flexibility that the Agency and registrants have in complying with FIFRA, FQPA and ESA, and could result in significant use restrictions.

NANO STUDY JUSTIFICATION

Study Title: Particle size and Diameter (size) distribution (DLS)

Rationale for Requiring the Data

Nanosized pesticides potentially have unusual or unique properties as compared to the dissolved or coarser particle and bulk pesticide forms, which may also affect its environmental fate and ecotoxicity. Dynamic Light Scattering (DLS) measures the hydrodynamic diameter of a nanosized particle in suspension or solution as well as its size distribution. The hydrodynamic diameter is the size of a hypothetical hard sphere that diffuses at the same rate as the particle being measured. This diameter depends not only on the physical size of the particle "core" but also on surface chemistry and structure and the surrounding medium, which determine the thickness of the electrical double layer around the particle. For instance, if ionic strength increases or polymers adsorbed on the surface of the particle decrease in chain, the electrical double layer around the particles would compress, allowing for more particle-particle interactions and resulting in increased aggregation and potential settling. Particularly useful in biological systems, DLS gives information about the stability of nanoparticles and how they behave in/interact with the solvent medium (proteins, biological molecules, etc.). It also gives information about the particles' state of aggregation/agglomeration by comparing the size measurements taken before and after sonication, allowing for the determination of whether the particles exhibit enhanced stability compared to conventional (non-nano) products.

Practical Utility of the Data

How will the data be used?

This study will yield the hydrodynamic diameter and size distribution of a nanosized particle in relevant media under environmentally relevant conditions of temperature, pH, and conductivity. The study also assesses the impact to the size and size distribution in the presence of any associated protective coatings or capping material and any changes in the environment. DLS will be used by the Agency to compare with SEM and TEM to determine how surface coatings or changes in the environmental media may influence particle size and size distribution. The data could also potentially be used to determine if nanoparticles released into water will aggregate/agglomerate, which may be used to further inform and refine environmental fate, mammalian toxicity, and ecotoxicity data requirements.

How could the data impact the Agency's future decision making?

Physical characteristics of nanomaterials are integral to their properties. The correlation between physical properties (size, shape, geometry, etc.) and chemical/material properties (solubility, partitioning, dissolution kinetics, etc.) is still poorly understood in the scientific community. This means that there is no way to know what a worst-case conservative estimate might be.

Without the DLS study, the Agency would use alternative testing methods (e.g. SEM and TEM) to determine particle size and size distribution. However, these methods are not sufficient for examining particles in suspension and identifying how their hydrodynamic size may differ from their physical size. Without that data, the Agency cannot determine if changes in particle shape, structure, or surface coatings or changes in the environmental media have an impact on the particle size, stability, and behavior, which may, in turn, affect the toxicity.

Study Title: Particle size and Diameter (size) distribution (SEM)

Rationale for Requiring the Data

Nanosized pesticides potentially have unique properties (such as size, shape, surface area, structure, chemical reactivity, etc.) which significantly differ from their bulk material form. Distinct nanoscale properties require detailed characterization methods to validate their attributes. Scanning Electron Microscopy (SEM) allows for

analysis and observation at the nano-surface level while also measuring particle size distribution, shape, surface morphology, dispersion, particle agglomeration, and surface modification. SEM used in combination with Energy Dispersive Spectroscopy (EDS) is used as part of chemical characterization of a nanomaterial.

Practical Utility of the Data

How will the data be used?

SEM analysis will provide information about physical characteristics of particles produced in formulation as well as show particle transformation following chemical changes (i.e., particle dissolution, exposure to saline conditions, aqueous media, pH change, etc.). Changes that influence such properties may correlate with measured toxicity and particle fate.

To visualize a particle's surface, an SEM instrument utilizes a beam of electrons to scan across the surface of a sample. Interactions between the atoms in the sample and the electron beam result in electronic signals emitted at or near the sample's surface. While the sample is being scanned, various electronic signals are collected, processed, and translated into an image. The type of SEM microscopy known as Secondary Electron SEM produces a 3-dimensional image of the sample's surface structure. The type of SEM microscopy known as Backscatter Electron SEM produces an image of the sample which shows the structure but shows the distribution of different atomic weight elements rather than the surface structure. Samples may be coated with a thin film of materials such as gold or platinum to improve contrast and the signal-to-noise ratio prior to analysis. SEM can be integrated with EDS for chemical characterization. Mass fractions of elements are identified throughout the sample's regions.

EDS works in conjunction with SEM. Atoms in the sample are energized by the electron beam in the SEM instrument. The energy is then released by the atoms in characteristic wavelengths of energy. EDS collects these wavelengths and displays which wavelengths of energy were released by the sample. This allows qualitative Atomic Identification of the specific atoms present in a section of a sample.

How could the data impact the Agency's future decision making?

Physical characteristics of nanomaterials are integral to their properties. The correlation between physical properties (size, shape, geometry, etc.) and chemical/material properties (solubility, partitioning, dissolution kinetics, etc.) is still poorly understood in the scientific community. This means that there is no way to know what a worst-case scenario conservative estimate might be.

Without SEM characterization analysis, the Agency would use alternative testing methods (e.g. TEM, DLS, surface area determination measurements) to estimate size, shape, surface, and structure. However, these methods are not sufficient for examining particles with complex surfaces or surface coatings. Without appropriate characterization data, the Agency cannot definitively determine if the particle's surfaces, surface changes, or elemental composition have an impact on toxicity.

The consequence of poor basic characterization is the same for nanomaterials as non-nano materials: no arguments regarding data waivers based on structure or other properties could be made, nor data bridging arguments from literature or separate studies. *In silico* tests may be incapable of being run (even worst-case scenarios) without certain basic characteristics plugged into the algorithm. Registrants would need to conduct more tests, which would take longer and be significantly more expensive in terms of both money and lab animal lives.

Study Title: Particle size and Diameter (size) distribution (TEM)

Rationale for Requiring the Data

Because nanoparticles can have unique properties depending on differences in aspects such as size, shape, and surface chemistry, it is necessary for the nanoparticles to be thoroughly characterized. Transmission Electron Microscopy (TEM) can be used to measure orientation, aggregation, agglomeration, size, and shape.

Practical Utility of the Data

How will the data be used?

TEM is a form of microscopy in which electrons are utilized in place of light. Electrons pass through the sample and either are blocked or pass through, depending on the atomic mass of the atoms present. As such, the TEM method is not always appropriate, as it requires a sample thin enough to allow electrons to pass through. TEM

may also potentially be used as supporting data for crystallographic measurements (see Chemical Speciation for more information). TEM, as a result, can be used to examine aspects of higher atomic mass portions of samples without being obscured by lower atomic mass parts of the sample, e.g., a metal oxide nanoparticle with organic compounds attached to the surface.

How could the data impact the Agency's future decision making?

Physical characteristics of nanomaterials are integral to their properties. The correlation between physical properties (size, shape, geometry, etc.) and chemical/material properties (solubility, partitioning, dissolution kinetics, etc.) is still poorly understood in the scientific community. This means that there is no way to know what a worst-case conservative estimate might be.

Lacking accurate characterization data would result in the Agency being required to determine properties, such as size and shape, from alternate testing data, e.g., SEM. Potentially critical properties data, particularly for particles with complex geometries (such as core-shell, hollow-shell, and certain types of Janus), typically require data such as SEM and TEM in conjunction, neither of which can fully substitute for the other.

The consequence of poor basic characterization is the same for nanomaterials as non-nano materials: no arguments regarding data waivers based on structure or other properties could be made, nor data bridging arguments from literature or separate studies. *In silico* tests may be incapable of being run (even worst-case scenarios) without certain basic characteristics plugged into the algorithm. Registrants would need to conduct more tests, which would take longer and be significantly more expensive in terms of both money and lab animal lives.

Surface Area Determination

Rationale for Requiring the Data

Because nanoparticles can have unique properties depending on differences in aspects, such as size, shape, and surface chemistry, it is necessary for the nanoparticles to be thoroughly characterized. Surface area is inversely related to particle size and can inform on the particle’s size, shape, surface roughness, porosity, and interactions with other particles. Surface area is also correlated with reactivity, dissolution, and catalysis. As particle size decreases, specific surface area (surface area per mass or volume) increases; as a result of this increase in the surface area to volume ratio, reactivity is enhanced, and risk from exposure to the nanoparticles may increase. However, if the particles are tightly aggregated in large clumps, then the amount of exposed surface area would decrease, and reactivity would be lower. Surface area may also change with changes in surface coatings or capping agents, which could reduce aggregation and thus increase surface area.

Practical Utility of the Data

How will the data be used?

This study will yield the surface area of a nanosized particle in powder form. The Brunauer, Emmett and Teller (BET) theory is one common method that calculates surface area based on gas adsorption; the amount of an adsorbate gas required to form a monolayer on the surface of a sample (monolayer capacity) is measured, and along with the cross-section area of that gas molecule, is used to determine the specific surface area. Surface area may potentially be used by the Agency as supporting data for particle size, shape, dissolution kinetics, etc.

If the nanosized pesticide is applied to coatings, paints, and textiles, which are dry or allowed to dry, nanosized particles may be released/broken off/abraded during application or use. Data on surface area may be helpful to the Agency in determining dermal, oral, and inhalation exposures, which are used to further inform and refine occupational and residential exposure scenarios. Although the study may not accurately reflect the properties of nanoparticles in aqueous media under environmentally relevant conditions, it can inform on the amount of surface area that may be exposed and thus available for potential reactions. This data may potentially be used to provide input for exposure characterization and further inform and refine environmental fate, mammalian toxicity, and ecotoxicity data requirements.

How could the data impact the Agency's future decision making?

Characteristics of nanomaterials are integral to their properties. The correlation between physical properties (surface area, size, shape, etc.) and chemical/material

properties (solubility, partitioning, dissolution kinetics, etc.) is still poorly understood in the scientific community. This means that there is no way to know what a worst-case conservative estimate might be.

Without the surface area study, the Agency would use alternative testing methods (e.g. SEM, TEM, and DLS) to estimate size, shape, surface, and structure. However, these methods are not sufficient for examining particles with porous surfaces or different surface coatings/capping agents. Without appropriate characterization data, the Agency cannot definitively determine if a particle's surface or surface changes have an impact on toxicity.

The consequence of poor basic characterization is the same for nanomaterials as non-nano materials: no arguments regarding data waivers based on structure or other properties could be made, nor data bridging arguments from literature or separate studies. *In silico* tests may be incapable of being run (even worst-case scenarios) without certain basic characteristics plugged into the algorithm. Registrants would need to conduct more tests, which would take longer and be significantly more expensive in terms of both money and lab animal lives.

Study Title: Stability to Sunlight, Detergents, Temperatures and Salinity

Rationale for Requiring the Data

Nanoparticles, as nanosized pesticides, have unique properties as compared to their bulk material forms. Nanoparticles embedded into textile materials can potentially be released from fabrics, degrade, exhibit Ostwald ripening, or exhibit other physical and chemical alterations during exposure to different conditions (irradiation, washing, interaction with sweat, temperature change, etc.) over time. Textiles can also release nanosized particles, which become aggregates/agglomerates while under certain stresses. For example, some particles are susceptible to oxidation under direct sunlight exposure, while others exhibit a change in physical characteristics and form agglomerates/aggregates in sunlight. Saline conditions will influence chemical speciation of particles in fabrics or the rate of ions released into the surrounding environment. Because the stability of a nanomaterial depends on several factors (ligand or capping agent, oxidation potential, ion release potential, type of integration into textile etc.), it is necessary to inspect their physical and chemical integrity under relevant weathering conditions.

Practical Utility of the Data

How will the data be used?

The study will yield the release rate and/or stability ratios of a nanosized pesticide under relevant conditions of sunlight exposure, laundry surfactant interactions, change in temperature, hardness, or salinity. This study will provide information on concentrations changes, if any, of nanoparticles under those conditions. As part of this analysis, aggregate/agglomerate formation can also be measured. Although particle stability may be assessed by many methods, zeta potential and dynamic light scattering (DLS) are among the most widely used. Microscopy measurements by SEM/EDS or TEM may potentially provide supporting data to identify particle transformations under different scenarios over time. This data will be used by the Agency to estimate the influence of nanoparticles used in textiles and their impact on toxicity as well as their environmental fate.

How could the data impact the Agency's future decision making?

Nanomaterials incorporated into textiles may exhibit changes in their physical or chemical properties under different conditions. However, the correlation between changes of properties and their influence upon change of environmental conditions are still poorly understood in the scientific community.

Without nanoparticle stability studies, the Agency would assume nanoparticles used in textiles are released into the environment and are unchanged by exposure conditions. The consequence of such assumptions would mean that nanoparticles released from textiles during the laundry process enter the environment via drinking water, wastewater, and/or sediment and are taken up by aquatic life. Further, it is assumed that nanoparticles will affect human toxicity by ingestion and dermal contact. The lack of data may yield estimates above the Agency's concern for all exposure scenarios. Additionally, this would trigger requirement of lower and higher tiered testing to determine probable adverse effects of nanoparticles.

Study Title: Chemical Speciation

Rationale for Requiring the Data

Because nanoparticles can have unique properties depending on differences in aspects such as size, shape, and surface chemistry, it is necessary for the nanoparticles to be thoroughly characterized. Chemical speciation is a combination of different methods to allow the characterization of both the inorganic and the organic portions of the nanoparticle.

Practical Utility of the Data

How will the data be used?

The inorganic portion requires analysis of atomic makeup, which requires atomic identification and analysis of the crystal structure. Atomic Identification may be provided by one of many methods but has been assumed to be performed via Energy Dispersive Spectroscopy (EDS) as this may be performed at the same time as Scanning Electron Microscopy (SEM) measurements (see Particle size and diameter (size) distribution (SEM)). For the crystal structure, the Agency assumes the use of X-ray Diffraction Spectroscopy (XRD).

EDS works in conjunction with SEM. Atoms in the sample are energized by the electron beam in the SEM instrument. The energy is then released by the atoms in characteristic wavelengths of energy. EDS collects these wavelengths and displays which wavelengths of energy were released by the sample. This allows qualitative Atomic Identification of the specific atoms present in a section of a sample.

While EDS may confirm the atoms present in a sample, XRD is used to determine the arrangement of those atoms (i.e., the crystal structure). Crystal structure can potentially alter the properties of a nanoparticle. This is conceptually similar to isomers in organic chemistry, where changing the configuration of the same atoms in a molecule may lead to completely different properties, particularly in biological media.

Data similar to that of XRD may be gathered from the diffraction pattern produced during Transmission Electron Microscopy (TEM). This data can be useful for confirmation of changes or stability of crystal structure of nanoparticles in a sample, rather than running multiple XRDs. However, the diffraction pattern may not always be clear enough to allow for determination as opposed to confirmation. As such, it may not be able to take the place of an XRD analysis.

The organic portion requires additional analysis. The exact method to identify the organic portion will differ depending on the nature of the portion. The Agency conservatively estimates that Fourier Transform Infrared Spectroscopy (FTIR) may be suitable for sufficient identification of most organic portions. However, in addition to identification of the organic portion, it is necessary to identify the density of the organic portion on the inorganic portion (also known as the surface loading). To measure this, the Agency has estimated that Thermogravimetric Analysis (TGA) will serve to satisfy this need.

How could the data impact the Agency's future decision making?

Characteristics of nanomaterials are integral to their properties. The correlation between speciation properties (atomic formula, surface loading, surface chemistry, etc.) and chemical/material properties (solubility, dissolution kinetics, renal clearance, etc.) is still poorly understood in the scientific community. This means that there is no way to know what a worst-case conservative estimate might be.

The consequence of poor basic characterization is the same for nanomaterials as non-nano materials: no arguments regarding data waivers based on structure or other properties could be made, nor data bridging arguments from literature or separate studies. *In silico* tests may be incapable of being run (even worst-case scenarios) without certain basic characteristics plugged into the algorithm. Registrants would need to conduct more tests, which would take longer and be significantly more expensive in terms of both money and lab animal lives.

Study Title: Pool Water Residues
Rationale for Requiring the Data
Nanosized pesticides potentially have unusual or unique properties as compared to the dissolved or coarser particle and bulk pesticide forms, which may also affect its environmental fate, ecotoxicity, and possibly human health. In swimming pool water, nanoparticles may remain unchanged indefinitely, undergo chemical transformations, or result in dissolved species in the water, possibly ionic species. Also, oxidants present in pool water may increase the rate of particle or particle coating material degradation. Nanoparticles can also undergo sequential transformation steps, thereby causing dissolution in water and later precipitating and forming new unknown products. In these cases, unknown residues will remain in water. Pool water residue testing would identify residues or transformation products formed as a result of nanoparticle presence in chlorinated environments. Thus, results obtained from this study will provide insights into the risk and toxicity potential associated with nanoparticles used in pool treatment scenarios.
Practical Utility of the Data
How will the data be used? This study will detect, identify, and measure amounts of chemical residues in pool water. If available, agglomerated residues will also be detected and measured. Data from this study will be used by the Agency to determine if residues or degradation or transformation products found in water, along with nanoparticle/nanosized pesticides, influence environmental fate and toxicity **How could the data impact the Agency's future decision making?** Without the pool residue study, the Agency would have to assume that nanoparticles used in pool water scenarios remain as nanoparticles and do not dissociate or degrade to release ionic species. Also, without sufficient data, the remaining residues that result from nanoparticles reacting in pool water will remain unknown. This would force the Agency to rely on literature studies; however, literature studies may lack findings about new nanopesticides, potential residues, or new transformation products formed. Lack of data will also trigger supplemental environmental fate and mammalian toxicity tests with nanoparticles in pool water. Supplemental residue data with nanoparticles will inform the determination required under FIFRA or ESA as to whether registration of the nanosized pesticide is likely to result in unreasonable adverse effects.