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Agency

Prevention, Pesticides
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1-Methyl-3,5,7-Triaza-1-Azoniatricyclodecane Chloride (Busan1024) Summary Document: Registration Review

1-Methyl-3,5,7-Triaza-1-Azoniatricyclodecane Chloride
(Busan 1024)
Summary Document
Registration Review: Initial Docket
June 2007

Approved By:

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I. PRELIMINARY WORK PLAN

Introduction

The Food Quality Protection Act (FQPA) of 1996 amended the Federal Fungicide Insecticide and Rodenticide Act (FIFRA) to mandate a new program: registration review. All pesticides distributed or sold in the United States generally must be registered by EPA, based on scientific data showing that they will not cause unreasonable risks to human health, workers, or the environment when used as directed on product labeling. The new registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the new registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can continue to be used safely. Information on this program is provided at http://www.epa.gov/oppsrrd1/registration_review/.

The Agency has begun to implement the new Registration Review program and will review each registered pesticide approximately every 15 years to determine whether it continues to meet the FIFRA standard for registration. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state clearly what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. 1-Methyl-3, 5, 7-triaza-1-azoniatricyclodecane chloride (Busan 1024) is an antimicrobial pesticide used in materials preservative applications and to prevent bacterial growth in specific industrial processes and water systems.

Risk Assessment Status & Anticipated Risk Assessment and Data Needs

Human Health Risk Assessment Status

No human health, dietary, residential, or occupational risk assessments have been performed for the active ingredient Busan 1024. Based on the registered uses of Busan 1024 as a materials preservative and in industrial processes and water systems, there is potential for residential and occupational exposure and risk. Therefore, the Agency anticipates conducting a complete occupational and residential human health exposure risk assessment for all Busan 1024 uses. For a detailed discussion of the anticipated human health exposure and risk assessment needs please refer to Section III, C. *Human Health Exposure and Risk Assessment.*

Dietary Exposure

Dietary exposure and risk will need to be assessed for Busan 1024 when used as a materials preservative in paper, paper coatings, pigment slurries, adhesives and detergents. Treated materials have the potential of contacting food, resulting in indirect food contact with busan 1024.

Residue Chemistry

For the dietary risk assessment, modeling can be used to estimate the dietary intake that results from the use of Busan 1024 as a materials preservative in adhesives, detergents, paper, papermaking coating and pigment slurries. For antimicrobial pesticides, a tier-I assessment is often sufficient to estimate dietary risk. For Tier-I dietary assessments, Estimated Daily Intakes (EDIs) are established using FDA methodologies. EDIs (mg/person/day) represent the migration of a pesticide into food from a treated surface. Examples of treated surfaces include paper and paper board. Tier-I assessments assume 100% of a pesticide migrates into food from treated surfaces. No residue chemistry data are needed at this time. However, if there are risks identified in the Tier 1 assessments, the Agency would then need additional residue chemistry guideline studies.

Drinking Water

It is possible that the Agency may need human drinking water exposure and risk assessments if analysis of initial Tier I screening for environmental fate and effects indicate that the magnitude of exposure to potential drinking water sources could be high.

Anticipated Human Health Data Needs

No human health toxicity endpoints for the active ingredient Busan 1024 have been selected. Consequently, toxicity endpoints need to be established. For further details regarding the anticipated human health toxicity data needs please refer to Section III, C. *Human Health Exposure and Risk Assessment* and Appendix B, *Exposure Guideline Study Justification*.

The Agency anticipates that the following data are needed to conduct a complete human health exposure and risk assessment for all Busan 1024 uses. Please refer to Appendix A for a detailed description of the anticipated toxicity database needs and Appendix B for a detailed description of the anticipated occupational and residential applicator and post-applicator exposure data needs.

Human Health Toxicity Data Needs for the AI:

- (GLN 870.3100) 90-Day Oral Toxicity-rodent
- (GLN 870.3150) 90-Day Oral Toxicity-non-rodent
- (GLN 870.3465) 90-Day Inhalation Toxicity-rat
- (GLN 870.4100) Chronic Toxicity- rodent
- (GLN 870.4200) Carcinogenicity-rat
- (GLN 870.4200) Carcinogenicity-mouse
- (GLN 870.3700) Prenatal Developmental Toxicity-rabbit
- (GLN 870.3800) Reproduction and Fertility Effects

Residential Applicator Exposure Data Needs:

- (GLN 875.1300) Inhalation Outdoor Exposure
- (GLN 875.1400) Inhalation Indoor Exposure
- (GLN 875.1600) Data Reporting and Calculations
- (GLN 875.1700) Product Use Information

Occupational Applicator Exposure Data Needs:

- (GLN 875.1300) Inhalation Outdoor Exposure
- (GLN 875.1400) Inhalation Indoor Exposure
- (GLN 875.1600) Data Reporting and Calculations
- (GLN 875.1700) Product Use Information

Residential Post-Application Exposure Data Needs:

- (GLN 875.2300) Indoor Surface Residue Dissipation[1]
- (GLN 875.2700) Product Use Information
- (GLN 875.2900) Data Reporting and Calculations
- (GLN 875.3000) Non-dietary Ingestion Exposure

Occupational Post-Application Exposure Data Needs:

- (GLN 875.2700) Product Use Information

Anticipated Physical/ Chemical Property Data Needs

Although physical/chemical property data have been provided by the registrant for some chemicals that are used to form the active ingredient, Busan 1024, no data on physical/chemical properties of the active ingredient have been submitted by the registrant. As a result, the Agency anticipates requiring the registrant to provide these data. The Agency also expects to need information on the physical form of the one currently registered end-use product. For a detailed discussion of the anticipated physical chemistry data needs please refer to Section III, D. *Physical/Chemical Properties and Environmental Fate.*

The anticipated physical chemistry data needs include the following:

- (GLN 830.1550) Product Identity and Composition
- (GLN 830.1600) Description of Materials Used to Produce the Product
- (GLN 830.1620) Description of Production Process
- (GLN 830.1670) Discussion of Formation of Impurities
- (GLN 830.1700) Preliminary Analysis
- (GLN 830.1750) Certified Limits
- (GLN 830.6302) Color
- (GLN 830.6303) Physical State
- (GLN 830.6304) Odor
- (GLN 830.3613) Stability to Sunlight, Normal and Elevated Tem. Metals/Metal Ions
- (GLN 830.6314) Oxidation/Reductions: Chemical Incompatibility
- (GLN 830.6315) Flammability
- (GLN 830.6317) Storage Stability
- (GLN 830.6319) Miscibility

[1] These studies may not be needed based on the outcome of other studies or 100% residue transfer assumptions in the risk assessment.

- (GLN 830.6320) Corrosion Characteristics
- (GLN 830.6321) Dielectric Breakdown
- (GLN 830.7000) pH of Water Solutions or Suspensions
- (GLN 830.7050) UV/VIS Absorption
- (GLN 830.7200) Melting Point/ Melting Range
- (GLN 830.7220) Boiling Point/ Boiling Range
- (GLN 830.7300) Density/Relative Density/Bulk Density
- (GLN 830.7370) Dissociation Constant in Water
- (GLN 830.7520) Particle Size, Fiber Length and Diameter Distribution
- (GLN 830.7550) Partition Coefficient (n-Octanol)/H_20), Shake Flask Method
- (GLN 830.7560) Partition Coefficient (n-Octanol/ H_20), Generator Column Method
- (GLN 830.7840) Water Solubility: Column Elution Method, Shake Flask Method
- (GLN 830.7860) Water Solubility, Generator Column Method
- (GLN 830.7950) Vapor Pressure

Anticipated Environmental Fate Data Needs

An environmental fate assessment has not been conducted for Busan 1024. The Agency believes that environmental fate data are needed because of potential exposures to waste water treatment plants (WWTPs); and discharges in WWTP effluents (biosolids and/or water) may be high. Data are needed to determine if there is a potential for exposure; and to ascertain if residues that may occur in effluents and environmental compartments (e.g., surface waters) will result in impacts to non-target organisms. Therefore, the Agency anticipates needing the proposed Tier I environmental fate data for the active ingredient and/or any of its major degradation products that are of potential concern for all registered uses of Busan 1024. The following data are needed to conduct an environmental fate assessment:

- (GLN 161-1) Hydrolysis Study
- (GLN 850.6800) Modified Activated Sludge, Respiration Inhibition
- (GLN 835.1110) Activated Sludge Sorption Isotherm
- (GLN 835.3110) Ready Biodegradability

It is possible that under specific conditions the Agency may need additional environmental fate studies. For a detailed discussion of the environmental fate status and anticipated data needs please refer to Section III, D. *Physical/ Chemical Properties and Environmental Fate,* and Appendix C, *Environmental Fate Guideline Study Justification.*

Ecological Exposure Risk Assessment Status

The Agency has not conducted ecological risk assessments for Busan 1024. The potential for Busan 1024 to be released into the environment at exposure levels of concern to ecological organisms is expected to be low for most registered use patterns. Busan 1024 uses that have potential for environmental exposure are industrial process water discharges/materials preservative discharges; and oil drilling waters & muds on land & in marine areas.

The Agency anticipates conducting a hazard assessment for the active ingredient and/or any of it metabolic and/or hydrolytic degradates identified to be of potential concern. The hazard assessment will be used to meet current labeling needs and to determine hazard endpoints for ecological organisms potentially exposed in the event of a spill or other potential environmental releases of Busan 1024.

Industrial process water discharges, preserved materials, starches and detergents containing Busan 1024 may contaminate waste water treatment plants (WWTPs) and release into the aquatic environment. The Agency anticipates conducting a waste water treatment plant (WWTP) risk assessment for industrial process water and materials preservative releases. Modeling will predict the amount of antimicrobial that passes through a standard WWTP and concentrations that will enter the aquatic environment. The WWTP model estimates will be used in a deterministic risk assessment. If analysis of initial Tier I screening tests indicate that ecological toxicity and magnitude of exposure exceed levels of concern for drinking water and ecological effects, the Agency may need additional data to refine the ecological risk assessment for the industrial processes and materials preservative use patterns for Busan 1024.

The planned ecological risk assessment will allow the Agency to determine whether Busan 1024 use has “no effect” or “may affect” federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that Busan 1024 “may affect” a listed species or its designated critical habitat, the assessment will be refined. The refined assessment will allow the Agency to determine whether use of Busan 1024 is “likely to adversely affect” the species or critical habitat or “not likely to adversely affect” the species or critical habitat. When an assessment concludes that a pesticide's use “may affect” a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and National Marine Fisheries Service (Services), as appropriate.

For a detailed discussion of the status of the ecological exposure and risk assessments for Busan 1024 refer to Section III, E. *Ecological Exposure and Risk* and Appendix D, *Ecological Guideline Study Justification*.

Anticipated Ecological Exposure Data Needs

Acute studies on non-target plant and estuarine/marine fish, shrimp and oysters are needed. These data will be used to conduct hazard and Tier I risk assessments to evaluate down-the-drain and oil drilling waste exposures to aquatic ecosystems and endangered species. The following is a summary of the needed ecotoxicity studies:

- (GLN 850.1035) Acute Marine Mysid Shrimp Toxicity
- (GLN 850.1055) Acute Marine Bivalve Embryo Larvae Toxicity
- (GLN 850.1075) Acute Toxicity to Marine Fish
- (GLN 850.5400) Tier II Green Algae using *Selenastrum capricornutum*

For a detailed discussion regarding the anticipated ecological data needs refer to Section III, E. *Ecological Exposure and Risk* and Appendix D, *Ecological Guideline Study Justification*.

Time-line

EPA has created the following estimated timeline for the completion of the Busan 1024 registration review.

Activities	**Estimated Month/Year**
Open Public Comment Period for Busan 1024 Docket	June 2007
Close Public Comment Period	September 2007
Develop Final Work Plan (FWP)	October 2007
Issue DCI	August 2008
Data Submission	August 2012[2]
Open Public Comment Period for Preliminary Risk Assessments	December 2013
Close Public Comment Period	February 2014
Open Public Comment Period for Proposed Reg. Review Decision	May 2014
Close Public Comment Period	July 2014
Final Decision and Begin Post-Decision Follow-up	November 2014

Guidance for Commenters

The public is invited to comment on EPA's preliminary registration review work-plan and rationale. The Agency will consider all comments as well as any additional information or data provided prior to issuing a final work plan for the Busan 1024 case.

In addition to any studies such as those outlined in this document, stakeholders are also specifically asked to provide available information and data in the following areas:

1. Confirmation on the following label information:
    a. Sites of application
    b. Formulations
    c. Application methods and equipment
    d. Maximum application rates
    e. Frequency of application, application intervals and maximum number of applications
    f. Geographic limitations on use
2. Use or potential use distribution

[2] Time-frames may change depending on the studies needed.

3. Use history
4. Usage/use information for non-agricultural uses (e.g., materials preservation)
5. Typical application interval
6. State or local use restrictions
7. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
8. Monitoring data

Busan 1024 is not identified as a cause of impairment for any water-bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at: http://oaspub.epa.gov/tmdl/waters_list.impairments?p_impid=3. The Agency invites submission of water quality data for these chemicals. To the extent possible, data should conform to the quality standards in Appendix A of the "OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process," (http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

Next Steps

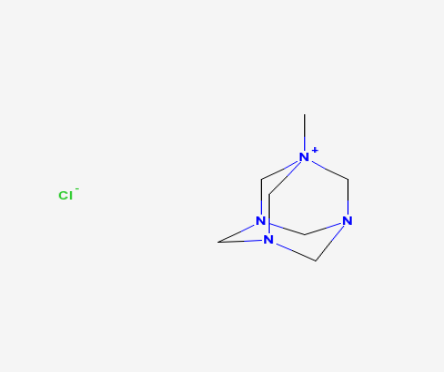
After the comment period closes, the Agency will prepare a Final Work Plan for this pesticide.

II. FACT SHEET

Background Information

- Busan1024 registration review case number: 5026
- Busan 1024 PC Code: 128889
- Busan 1024 CAS#: 76902-90-4
- Technical registrant: Buckman Laboratories
- First approved for use in a registered product: August 7, 1987
- Not subject to reregistration (no Reregistration Eligibility Decision [RED])
- Antimicrobials Division Chemical Review Manager (CRM): K. Avivah Jakob, jakob.kathryn@epa.gov
- Antimicrobials Division Product Manager (PM): Marshall Swindell, swindell.marshall@epa.gov

Chemical Structure of Busan 1024



Use & Usage Information

For additional usage information and details, please refer to Section III, Table 1 *Application Information for 1-methyl-3,5,7-Triaza-azoniatrycclodecane chloride (PC Code 12889).*

- Busan 1024 is a bacteriostat and microbiocide/microbistat that is used as a materials preservative (non-food use only) in emulsion paints, latex emulsions, adhesives, detergents, laundry starch, caulks, grouts, spackling compounds, textiles, inks, polishes, waxes, papermaking chemicals, papermaking coatings and metalworking fluids. Busan 1024 is also used for industrial processes and water systems in petroleum production and recovery and fountain wash systems.
- There is one registered product containing Busan 1024 as an active ingredient, formulated as a ready-to-use solution.
- Pests controlled include deterioration/spoilage bacteria and fungi (e.g., in metal working coolants).
- Application rates range from 0.05% to 1.0% Busan 1024 by weight of the formulation (500 ppm to 10,000 ppm).

Recent Regulatory Actions

- Ecological and human health risk assessments have not been conducted for Busan 1024.
- On March 18, 2004 the use of Busan 1024 for latex emulsion preservation (materials preservative incorporation) was granted by the Agency.

Ecological Risk Assessment Status

Ecological risk assessments have not been conducted for Busan 1024 and the existing data are not adequate for assessing the risk associated with Busan 1024 use. The potential for Busan 1024 to be released into the environment at exposure levels of concern to ecological organisms is expected to be low for most registered uses; however, the Agency anticipates conducting risk assessments for industrial waste water discharges and material preservatives that potentially pass through waste water treatment plants (WWTPs), and for oil drilling wastes discharged in terrestrial and aquatic environments. The final Busan 1024 registration review decision will include an endangered species effect determination. Please refer to Section III, *Status of Human Health and Ecological Risk Assessment for Busan 1024*, for a detailed discussion of the anticipated ecological risk assessment and data needs.

Human Health Risk Assessment Status

At this time, the Agency is unable to evaluate potential human health risks for Busan 1024 because of limited data and the lack of risk assessments currently available. For a detailed discussion of the anticipated risk assessment and data needs for human health please refer to Section III, *Status of Human Health and Ecological Risk Assessment for Busan 1024.*

Tolerances

- There are no tolerances listed under 40 CFR 180.448 for Busan 1024.
- The current label for Busan 1024 states, "Busan 1024 may not be used for preservation of materials which may contact food." Dietary exposure and risk will need to be assessed for Busan 1024 when used as a materials preservative in paper, paper coatings, pigment slurries, adhesives and detergents because these treated materials have the potential for indirect food contact and therefore a dietary assessment will be needed.

Data Call-In Status

- A data call-in has not been issued for Busan 1024, as it was registered in 1987 and is not subject to reregistration.

Labels

There is one registered product for the active ingredient 1-methyl-3,5,7-triaza-1-azoniatricyclodecane chloride (Busan 1024). Due to the limited amount of products associated with this active ingredient, the one product label has been included within the Busan 1024 docket. For future reference, during registration review a list of product registration numbers will be included in the docket. Product registration labels may be

obtained from the Pesticide Product Label System (PPLS) website at: http://oaspub.epa.gov/pestlabl/ppls.home.

III. STATUS OF HUMAN HEALTH AND ECOLOGICAL RISK ASSESSMENT FOR BUSAN 1024 (1-methyl-3,5,7-triaza-1-azoniatricyclodecane chloride) (PC Code 128889; CAS# 769-90-4) (Active Ingredient of Busan 1024–Registration Review Case Number 5026)

A. INTRODUCTION

The active ingredient, 1-methyl-3,5,7-triaza-1-azoniatricyclodecane chloride, present in the registered product, Busan 1024, is an antimicrobial pesticide used in materials preservative applications and to prevent bacterial growth in specific industrial processes and water systems. This active ingredient will be undergoing registration review to determine potential human and ecological exposures and risks from these uses. The Antimicrobial Division's Busan 1024 Registration Review Team has evaluated the human health and ecological assessments to determine the scope of work necessary to support the registration review. During registration review the AD team will examine potential human and ecological toxicity, physical/chemical properties, environmental fate, exposures, and risks as a result of registered uses. Data needs are determined largely by the potential human and ecological toxicity and exposures associated with these types of uses. Information on the use profile of Busan 1024 is presented in Section B of this status report. The status of human exposure and risk assessment is presented in Section C. The status of data on physical/chemical properties and environmental fate is presented in Section D of this report. Ecological exposure and risk assessment status for Busan 1024 is presented in Section E of this report. The purpose of reviewing the status of this registration review case is to determine whether sufficient data are available, whether new human health and ecological risk assessments are needed to support registration review, and to report why the Agency feels it may be necessary to either require new guideline studies and/or to conduct new risk assessments under the registration review process.

Structure Activity Relationships

EPA must rely upon information of appropriate quality and reliability for each decision made by the Agency. In the Office of Pesticide Programs (OPP), the evaluation process for a pesticide chemical traditionally begins with the applicant's submission of a set of studies conducted with the specific pesticide chemical of interest. The use of the results of such testing (measured data) is a logical, scientifically rigorous process that identifies the physical, chemical, and environmental fate properties of the pesticide, as well as the dose and endpoints at which an adverse effect can occur in various animal species.

Today, there is significant interest in alternative techniques, i.e. techniques other than data generation that could significantly inform the Agency's decision-making process. During the last 6-years, OPP has made increasing use of structure activity relationship (SAR) as part of its regulatory decision-making process. In the SAR process, a chemical's molecular structure is compared to that of other chemicals for which data are available. These structural similarities are then used to make predictive

judgments about a chemical's physical, chemical, and biological properties. Thus, the chemical's physical, chemical, and biological properties are a function of (or directly related to) the chemical's molecular structure. Quantitative SAR is referred to as QSAR. To develop a QSAR, a selected set of measured data on a single physical, chemical, or biological property is used to derive a model (an equation) to predict the value of that property.

Since SAR assessments and QSAR modeling are another set of tools that are available to Agency scientists, OPP has begun a process shift that envisions shifting from the current study-by-study approach to an approach in which the use of predicted data, generated using validated models, is considered along with information from open literature and studies specifically generated under Part 158 requirements. All relevant information would be considered as part of a weight-of-the-evidence evaluation.

At this time, EPA believes that for certain endpoints, especially physical/chemical and fate properties, that SAR and QSAR might be effectively utilized to fulfill these data requirements for many antimicrobial pesticide chemicals. When considering biological properties, at this time, EPA believes that SAR and QSAR can be most effectively utilized in the evaluation of chemicals that exhibit lower toxicity for human health and/or ecotoxicity parameters. This is appropriate because the risk assessment for lower toxicity chemicals can be stream-lined, i.e., a screening-level assessment procedure rather than multiple tiers of assessments with progressively more data requirements.

If stakeholders believe that submission of predicted data can fulfill one of the data needs for Busan 1024, then the Agency invites submission of this information. The submitter would be expected to supply a rationale describing the utility of the information and provide documentation on the scientific validity of the information. The determination that the predicted data fulfills the data requirement would be at the sole discretion of the Agency. Pre-submission consultation with the Agency is encouraged.

Data Requirements and Data Waivers

The Agency employs a step-wise process to assist the registrant in determining the data needed to support its particular product. The actual data and studies needed may be modified on an individual basis to fully characterize the use and properties of specific pesticide products under review. While EPA will assist the registrant in outlining data needs, it is important to emphasize that it is the registrant's obligation under FIFRA to demonstrate that an individual product meets the standard under FIFRA and/or FFDCA. Accordingly, registrants are encouraged to consult with the Agency on the appropriate data requirements, as outlined here, as related to their specific product during this registration review process.

Since there is much variety in pesticide chemistry, exposure, and hazard the Agency tries to be flexible. The Agency also recognizes, however, that due to the particular nature and risk of some pesticides, registrants may seek to obtain data waivers or may suggest alternative approaches to satisfying data needs. Some products may have unusual physical, chemical, or biological properties or atypical use patterns which would

make particular data requirements inappropriate, either because it would not be possible to generate the required data or because the data would not be useful in the Agency's evaluation of the risks or benefits of the product. The Agency will waive data needs it finds are inappropriate, but will ensure that sufficient data are available to make the determinations required by the applicable statutory standards.

Considering the above, registrants may request to use surrogate data or alternative methods to meet data needs or request a waiver of data based upon chemistry, exposure, or hazard rationales that support their position. Registrants are encouraged to discuss the request with the Agency before developing and submitting supporting data, information, or other materials. All waiver requests must be submitted to the Agency in writing. The request must clearly identify the data need(s) for which a waiver is sought along with an explanation and supporting rationale why the registrant believes the data requirement should be waived. In addition, the applicant must describe any unsuccessful attempts to generate the required data, furnish any other information that the registrant(s) believes would support the request, and when appropriate, suggest alternative means of obtaining data to address the concern that underlies the data requirement. The Agency will review each waiver request and subsequently inform the applicant in writing of its decision.

B. USE PROFILE

The uses of antimicrobial pesticide chemicals regulated under FIFRA are highly variable and complex and have been organized into twelve categories of use patterns based on similarity of use, pesticide function, method of incorporation into end-use products, method of application of end-use products, types of establishments in which products are used, environmental media to which antimicrobials are expected to be released, and types of receptors expected to come into contact with antimicrobial pesticides. The twelve general use patterns for antimicrobial pesticides include:

(1) Agricultural premises and equipment;
(2) Food handling/storage establishments, premises, and equipment;
(3) Commercial, institutional and industrial premises and equipment;
(4) Residential and public access premises;
(5) Medical premises and equipment;
(6) Human drinking water systems;
(7) Materials preservatives;
(8) Industrial processes and water systems;
(9) Antifoulants and ballast water;
(10) Wood preservatives;
(11) Swimming pools; and
(12) Aquatic areas.

Busan 1024, EPA Registration number 1448-92, is the only registered product for this active ingredient undergoing registration review. Of these 12 general use patterns for antimicrobial pesticides, two are applicable to Busan 1024: materials preservatives and industrial processes and water systems. Specific uses, general use patterns, and potential

for long-term exposure determine data needs for terrestrial and aquatic non-target organisms, environmental fate, human toxicity, and occupational and residential exposure for the active ingredient of Busan 1024. Table 1 presents information on each of the specific use sites for the general use patterns that are applicable to Busan 1024, including the method of application, application rate, and range of percent by weight of active ingredient to be added to each use site.

TABLE 1

Materials preservatives				
Emulsion paints	Ready-to-use: 1448-92	In-can preservative	Add 0.05 – 0.5% product by weight	May not be used for preservation of materials which may contact food
Latex emulsions	Ready-to-use: 1448-92	Open and closed loading	Add 0.05 – 0.5% product by weight	May not be used for preservation of materials which may contact food
Adhesives	Ready-to-use: 1448-92	Open and closed loading	Add 0.1 – 0.5% product by weight of formulation (1000 to 5000 ppm)	May not be used for preservation of materials which may contact food
Detergents, laundry starch	Ready-to-use: 1448-92	Open and closed loading	Add 0.1 to 0.3% product by weight of formulation (1000 – 3000 ppm)	May not be used for preservation of materials which may contact food
Caulks, grout, spackling compounds	Ready-to-use: 1448-92	Open and closed loading	Add 0.05% to 0.15% product by weight of formulation (500-1500 ppm)	May not be used for preservation of materials which may contact food
Textiles	Ready-to-use: 1448-92	Open and closed loading	Add 0.8 – 1% product by weight (8000 – 10000 ppm)	May not be used for preservation of materials which may contact food
Inks	Ready-to-use: 1448-92	Open and closed loading	Add 0.02 – 0.1% product by weight (200 – 1000 ppm)	May not be used for preservation of materials which may contact food
Polishes and waxes	Ready-to-use: 1448-92	Open and closed loading	Add 0.3 – 0.75% product by weight (3000 – 7500 ppm)	May not be used for preservation of materials which may contact food
Papermaking chemicals and coatings	Ready-to-use: 1448-92	Open and closed loading	Add 0.3 – 0.5% product by weight	May not be used for preservation of materials which may contact food

Table 1. Application Information for 1-methyl-3,5,7-Triaza-1-azoniatricyclodecane chloride (PC code 128889)				
Use Site	**Formulation**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Metalworking fluids	Ready-to-use: 1448-92	Open and closed loading	In soluble oils and semi-synthetic fluids: Add sufficient product to provide a concentration of 0.3 – 0.5% Synthetic metal working fluids: Add sufficient product to provide a concentration of 0.1 – 0.5%	May not be used for preservation of materials which may contact food
Industrial processes and water systems				
Petroleum production and recovery	Ready-to-use: 1448-92	Open and closed loading	Add O.2 – 0.3% product by weight (2000 – 3000 ppm)	May not be used for preservation of materials which may contact food
Fountain wash systems	Ready-to-use: 1448-92	Open and closed loading	Add 0.15 to 0.3% product by weight (1500 – 3000 ppm)	May not be used for preservation of materials which may contact food

C. HUMAN HEALTH EXPOSURE AND RISK ASSESSMENT

No human health dietary, occupational, or residential risk assessments have been performed for the active ingredient Busan 1024. The current label states, "Busan 1024 may not be used for preservation of materials which may contact food." The current label, however, lists several uses including a material preservative in adhesives, detergents, papermaking chemicals and coatings; all of which have potential food contact uses.

Toxicity

The registrant has submitted both a 90-day dermal toxicity study in rats (MRID 413071-01) and 21/28-day toxicity study (MRID 258510). The 90-day study has been reviewed by the Agency as acceptable. In this study, there were no dermal and systemic effects identified at the limit dose of 1000 mg/kg/day. The 21/28-day study is no longer acceptable with current guidelines (GDLN 870.3200). Since Busan 1024 is classified as Toxicity Category IV for skin irritation, not a sensitizer, and the 90-day dermal toxicity study indicates no dermal and systemic effects, a quantitative short- and intermediate-term dermal exposure assessment will not be needed.

The registrant has also submitted a prenatal developmental toxicity study in rats (MRIDs 150730 and 263286) that is guideline acceptable. However, based on a limited database that includes toxicity data gaps for a number of data needs, the Agency was not

able to select an oral and inhalation toxicological endpoint, and the determination of cancer potency was inconclusive. A more complete toxicity database will be needed to quantify risk for the dietary, incidental ingestion and inhalation exposure scenarios. No toxicity endpoint values for the active ingredient of Busan 1024 have been selected. Consequently, toxicity endpoints will need to be established. In general, the Agency generally requires a basic toxicity dataset to characterize the hazard and risks through all exposure routes (oral, inhalation, and dermal), and the Agency can characterize the dermal exposure route for Busan 1024 only at this point.

Refer to Appendix A for specific justifications on toxicity guideline studies. This appendix identifies, for example, why certain Busan 1024 use patterns may trigger specific toxicity data based on length of exposure and why the Agency needs studies to examine species sensitivity. It should be noted that although Busan 1024 has adequate acute data, the Agency cannot use LD_{50} (lethal dose – a single dose that kills half [50%] of the animals tested) from acute oral studies for hazard characterization and toxicity endpoints selection for risk assessment, as toxicity observed in a repeated exposure setting is much different and higher than toxicity observed in an one-time acute exposure setting.

Dietary Risk Assessment

Dietary exposure and risk will need to be assessed for Busan 1024 when used as a material preservative. Based on label language, use sites of Busan 1024 include: paper, paper coatings, pigment slurries, adhesives, and detergents.

Residue Chemistry

Modeling can be used to estimate dietary intake that results from the use of Busan 1024 as a material preservative in adhesives, detergents, paper making and coatings. Often, a Tier I assessment is sufficient to determine dietary risk. For a Tier I assessment, FDA methodologies are employed for determining Estimated Daily Intakes (EDIs). Estimation of EDIs are based on the premise that some pesticide is likely to migrate from treated surfaces into food from surfaces like counter tops, cutting boards, paper and paper boards, kitchen utensils, etc. EDIs (mg/person/day) represent the migration of a pesticide into food from a treated surface.

EDIs are then converted into Daily Dietary Doses (DDD) (mg/kg/day). % aPAD and % cPAD are estimated based on the acute and chronic dietary end points. If the Tier I assessments do not show any risk concerns, then no additional residue chemistry additional guideline studies would be needed. However, if there are risks identified in the Tier 1 assessments, the Agency would then need additional residue chemistry guideline studies.

Drinking Water

Note that it is possible that the Agency may need human drinking water exposure and risk assessments if analysis of initial Tier I screening for environmental fate and microbial effects indicate that the magnitude of exposure to potential drinking water sources could be high rather than negligible or low.

Occupational and Residential Risk Assessment

Based on the registered uses of Busan 1024 as materials preservatives and in industrial processes and water systems, there is potential for residential and occupational exposure and risk. No residential or occupational exposure and risk assessment has been performed for Busan 1024. Consequently, the Agency will need to perform an assessment of residential and occupational exposure and risk. Mixer/loader and applicator exposure scenarios include open and closed loading of Busan 1024 in industrial settings, such as the manufacturing process for paints, textiles, paper, metal working fluids, and petroleum production and recovery. In addition, there is the potential for applicator exposure during painting (residential and professional painters) and for metal working fluid machinists. Potential post-applicator exposures include exposures to treated products such as textiles.

For both the occupational and residential assessments, a 90-day inhalation study will be needed to set toxicity endpoints for this route of exposure. As mentioned earlier in the toxicity section a dermal exposure assessment will not be needed. If the Agency receives acceptable oral toxicity data, an oral endpoint value with 100% absorption factor could potentially be used in lieu of inhalation data. For a residential assessment, oral toxicity data are also needed to evaluate incidental oral exposures.

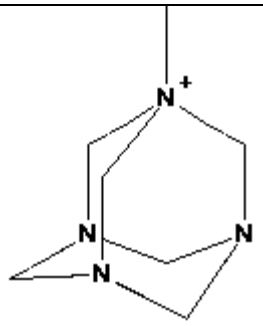
Inhalation occupational assessments will be needed during registration review for use in manufacturing settings (e.g. paper making), commercial painters, and metal working fluid machinists. Based on most of the currently supported uses, short-and intermediate-term inhalation scenarios will be needed for registration review. Evaluation of long-term exposures are only needed for the metal working fluid machinist scenario. Residential assessments will be needed for short- and intermediate-term inhalation (e.g. painting) and children's postapplication incidental oral exposures for textiles. The Agency will likely use task force submitted data for applicator to conduct these occupational or residential assessments. Refer to Appendix B for more specific on the exposure data needs and why this information is necessary.

D. PHYSICAL/CHEMICAL PROPERTIES AND ENVIRONMENTAL FATE[3]

Submission of physical/chemical property data is needed for registration of Busan 1024. The registrant has submitted no data on physical/chemical properties of the active ingredient. As a result, the Agency anticipates requiring the registrant to provide these data. The Agency also expects to need information on the physical form of the manufacturing and end-use products. The chemical structure of Busan 1024 is provided in table 2.

3 Including potential effects on wastewater treatment plants (WWTPs).

Physical/chemistry data help the Agency in evaluating hazard and exposure including acute toxicity (inhalation), workers' exposure (vapor pressure), and bioaccumulation (environmental fate). These studies also help in determining the disposal policy (ecological effects). Storage stability helps the Agency in determining if the product would remain stable in a formulation etc.

Chemical Name	1-Methyl-3,5,7-Triaza-1-Azoniatricyclodecane Chloride
Common/Trade Names	Busan 1024
CAS Number	76902-90-4
Structure	 Cl-

Additionally, the Agency is planning to determine (1) the potential of antimicrobial pesticides and/or their major transformation products to directly adversely affect biological treatment processes present in a wastewater treatment plant (WWTP); (2) the amount of an antimicrobial pesticide and/or its major transformation products present in influents to a WWTP and in effluents (water or bio-solids) that a WWTP releases to the environment; and (3) whether antimicrobial pesticides found in WWTP effluents or environmental compartments, such as surface water, exceed the Agency's Levels of Concern (LOCs) for nontarget organisms. One source of antimicrobials in surface water is disposal of consumer products such as soaps and detergents, into household wastewater. Also, if EPA determines that other use categories result in discharges to WWTPs, than the Agency will conduct any other assessments normally performed for these other use categories.

The environmental fate data expected to be needed for the technical grade of the active ingredient and/or any of its major transformation products that are identified to be of potential concern are: (1) hydrolysis study (OPP guideline number 161-1); (2) modified activated sludge respiration inhibition test (OPPTS guideline number 850.6800); (3) activated sludge sorption isotherm test (OPPTS guideline number 835.1110); and (4) ready biodegradability study (OPPTS guideline number 835.3110). Data from the hydrolysis study will enable the Agency to determine if the antimicrobial

pesticide hydrolyzes in water discharged to WWTPs, in aquatic effluents WWTPs discharge to surface waters, or in surface waters. The modified activated sludge respiration inhibition test will allow the Agency to identify antimicrobial pesticides which could harm microorganisms found in biological wastewater treatment systems and would also indicate suitable concentrations for use in the ready biodegradability study. The activated sludge adsorption isotherm test will allow EPA to assess the distribution of antimicrobials among the aqueous, solid, and vapor phases of WWTPs. In addition, this study will identify those chemicals that are likely to adsorb to sludge. Examination of the sludge compartment is necessary since humans and nontarget organisms may potentially be exposed to antimicrobials that adsorb strongly to sludge that are applied to land as a soil amendment. Finally, the activated sludge adsorption isotherm test results will help determine which ready biodegradability test method is most appropriate. The ready biodegradability study will enable the Agency to determine the likelihood that an antimicrobial will biodegrade during the wastewater treatment process. It is possible that under specific conditions the Agency may need additional environmental fate tests. Further description of the environmental fate guideline studies needed by the EPA is presented in Appendix C.

E. ECOLOGICAL EXPOSURE AND RISK ASSESSMENT

For most registered uses of Busan 1024, the potential for exposure to ecological organisms is expected to be low. Although the Agency has not performed label hazard or ecological risk assessments, the Agency expects to need ecological toxicity studies for the active ingredient and/or any of its metabolic and/or hydrolytic transformation products identified to be of potential concern. As a result, the Agency will likely need the following base set of ecological toxicity studies.

- algal toxicity (Tier II) using freshwater green alga, *Selenastrum capricornutum* using TGAI – (OPPTS 850-5400);

The Antimicrobial Division has no ecological risk assessment for Busan 1024 to date. All uses were previously considered “indoor” having no potential for environmental exposure. In response to concerns over persistent compounds in surface waters and disruptions to sewage treatment processes, the Agency has reevaluated the definition of “indoor” in regard to environmental exposure. In order to perform wastewater treatment plant (WWTP) and ecological risk assessments, the Agency must evaluate the toxicity of busan 1024 to nontarget and endangered or threatened terrestrial and aquatic animals and plants. Busan 1024 uses having potential for environmental exposure are industrial process water discharges/materials preservative discharges, and oil drilling waters and muds on land and in marine areas.

The justifications for guideline studies for ecological non-target organisms and plants are presented in Appendix D. As mentioned in Appendix D, these guideline studies will provide the Agency with endpoints to be used in wastewater treatment plant surface water exposures. It is possible that after further review and under specific conditions the Agency may need additional ecological toxicity tests.

The planned ecological risk assessment will allow the Agency to determine whether Busan 1024 use has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that Busan 1024 "may affect" a listed species or its designated critical habitat, the assessment will be refined. The refined assessment will allow the Agency to determine whether use of Busan 1024 is “likely to adversely affect” the species or critical habitat or "not likely to adversely affect" the species or critical habitat. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and National Marine Fisheries Service (Services), as appropriate.

IV. GLOSSARY of TERMS & ABBREVIATIONS

ai	Active Ingredient
AR	Anticipated Residue
ASTM	American Society for Testing and Materials
AWPA	American Wood Preserver's Association
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GENEEC	Tier I Surface Water Computer Model
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking submitted studies.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Ambient Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAIRA	Pure Active Ingredient Radiolabelled
PCA	Percent Crop Area

PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q_1*	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLN	Special Local Need (Registrations Under Section 24©) of FIFRA)
TGAI	Technical Grade Active Ingredient
TEP	Typical End-Use Product
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard

V. APPENDICES

Appendix A. Toxicity Guideline Study Justifications		
870.3100	90-Day Oral Toxicity Study (Rodent)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of exposure via the oral route. The needed study will provide insight into concerns regarding toxicity via the oral route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study would form the foundation for hazard characterization and toxicity endpoints selection for risk assessment through all exposure routes (oral, inhalation, and dermal). The data would allow the Agency to conclude more definitively whether or not there would be any concerns for oral toxicity in the rat. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population including infants and children as needed by the FQPA. **3) How could the data affect the risk assessment?** The study would form the foundation for hazard characterization and toxicity endpoints selection for risk assessment through all exposure routes (oral, inhalation, and dermal). It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human oral exposure (as well as inhalation and/or dermal) with limited data and no repeated-dose toxicity data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a 90-day (guideline) oral toxicity study, in order to adequately evaluate real world human exposure to Busan 1024 based on how it is used (e.g., food-use paper or paperboard, liquid detergents, treated textiles, etc.).

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
870.3150	90-Day Oral Toxicity Study (Non-rodent)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of exposure via the oral route. The needed study would provide insight into concerns regarding toxicity via the oral route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study would form the foundation for hazard characterization and toxicity endpoints selection for risk assessment through all exposure routes (oral, inhalation, and dermal). The data would allow the Agency to conclude more definitively whether or not there would be any concerns for oral toxicity in a non-rodent species. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population including infants and children as needed by the FQPA. **3) How could the data affect the risk assessment?** The study would form the foundation for hazard characterization and toxicity endpoints selection for risk assessment through all exposure routes (oral, inhalation, and dermal). It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human oral exposure (as well as inhalation and/or dermal) with limited data and no repeated-dose toxicity data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a 90-day (guideline) oral toxicity study, in order to adequately evaluate real world human exposure to Busan 1024 based on how it is used.

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
870.3465	90-Day Inhalation Toxicity Study (Rat)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of exposure via the inhalation route. The needed study would provide insight into concerns regarding toxicity via the inhalation route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study may result in a change in how risks are quantified. The data would allow the Agency to conclude more definitively whether or not there would be any concerns for inhalation toxicity in the rat. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human inhalation exposure with limited data and no inhalation data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a 90-day (guideline) Inhalation toxicity study, in order to adequately evaluate real world human exposure to Busan 1024 particles based on how it is used (The OPPTS Guidelines require an MMAD of 1-3 μm in inhalation toxicity studies of aerosols so that a portion of the test article will reach the lungs).

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
870.4100	Chronic Toxicity Study (Rodent)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of long-term exposure. The needed study would provide insight into concerns regarding toxicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study may result in a change in how risks are quantified. The data would allow the Agency to conclude more definitively whether or not there would be any concerns for chronic toxicity in the rat. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population including infants and children as needed by the FQPA. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human exposure via all routes (oral, inhalation or dermal) with limited data and no chronic data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a chronic (guideline) toxicity study, in order to adequately evaluate real world human exposure to Busan 1024 based on how it is used, particularly used as material preservative in Metal Working Fluids (MWF).
870.4200	Carcinogenicity Study (Rat)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of long-term exposure. The needed study would provide insight into concerns regarding carcinogenicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study may result in a change in how risks are quantified. The data would allow the Agency to conclude more definitively whether or not there would be any concerns for carcinogenicity in the rat. This would

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population including infants and children as needed by the FQPA. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The inconclusive results of the mutagenicity data, difficulty of predicting real world human exposure via oral routes with limited data and no carcinogenicity data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a carcinogenicity (guideline) study, in order to adequately evaluate real world human exposure to Busan 1024 based on how it is used, particularly used as material preservatives in Metal Working Fluids (MWF).
870.4200	Carcinogenicity Study (Mouse)	**1) What is the value of the study?** The Agency does not have a full picture of the potential effects which could occur as a result of long-term exposure. The needed study would provide insight into concerns regarding carcinogenicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study may result in a change in how risks are quantified. The data would allow the Agency to conclude more definitively whether or not there would be any concerns for carcinogenicity in the mouse. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks to the U.S. general population including infants and children as needed by the FQPA. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation.

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		4) What is triggering the need for this data? The inconclusive results of the mutagenicity data, difficulty of predicting real world human exposure via oral routes with limited data and no carcinogenicity data or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a carcinogenicity (guideline) study, in order to adequately evaluate real world human exposure to Busan 1024 based on how it is used, particularly used as material preservatives in Metal Working Fluids (MWF).
870.3700	Developmental Toxicity Study (Rabbit)	**1) What is the value of the study?** The needed study would provide insight into concerns regarding pre- and/or postnatal toxicity as needed by FQPA. It may also provide a toxicity endpoint applicable to risk assessment. **2) How would the data be used?** The study may result in a change in how risks are quantified. The data would allow the Agency to conclude more definitively whether or not there are any concerns for pre- and/or postnatal toxicity in the rabbit. This would provide a more complete hazard characterization of Busan 1024 in regards to the potential risks of developmental toxicity. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. It is possible that the database uncertainty factor be reduced or removed, resulting in different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human exposure via oral route with limited data and no developmental toxicity data in rabbit or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a developmental (guideline) toxicity study in the rabbit, in order to adequately evaluate real world human exposure to Busan 1024, particularly women in the 15-49 years of age and infants and children, based on how it is used.
870.3800	Reproduction and Fertility Effects (Rodent)	**1) What is the value of the study?** The needed study would provide insight into concerns regarding the potential risks of reproductive toxicity in the rat as well as potential neurotoxicity in developing offspring. It may also provide a toxicity endpoint

Appendix A. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		applicable to risk assessment. **2) How would the data be used?** The data would allow the Agency to conclude more definitively whether or not there are any concerns for potential reproductive toxicity in the rat. Since the reproductive toxicity study would also include neurotoxicity evaluations, it would also provide some information regarding potential neurotoxicity in developing offspring exposed to Busan 1024. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. The needed study may provide a toxicity endpoint applicable to risk assessment. It is possible that the database uncertainty factor be reduced or removed, resulting in a different magnitude of the value of the endpoint used for regulation. **4) What is triggering the need for this data?** The difficulty of predicting real world human exposure via oral route with limited data and no reproductive toxicity data in rat or other alternative information, such as SAR (structure-activity-relationship), surrogate data, and/or weight-of-evidence to the Agency **triggered** the need for a reproductive (guideline) toxicity study in the rat, in order to adequately evaluate real world human exposure to Busan 1024, particularly women in the 15-49 years of age and infants and children, based on how it is used.

Appendix B: Exposure Guideline Study Justifications

875.1300 and 875.1400 (Applicator)	Inhalation Outdoor Exposure and Inhalation Indoor Exposure	*Note: Inhalation exposure data are needed for both residential and occupational uses. The selection of an outdoor versus an indoor site is based on the high end exposure scenario (for inhalation the selection is typically indoors). In almost all cases, repeating an exposure study for the same scenario outdoors and indoors is not necessary.* **1) What is the value of the study?** The inhalation exposure route is very important for exposure scenarios such as paint rollers and airless sprayers where aerosols would be generated. In addition, inhalation exposures from liquid pouring are evident in exposure studies in the Pesticide Handlers Exposure Database (PHED). The significance of these exposures is directly affected by the severity of the inhalation toxicological endpoint of concern. At this point in time, no toxicological data are available to assess the inhalation risk. The existing Chemical Manufacturer Association (CMA) data base and PHED for these scenarios are limited in scope for QA/QC and number of monitoring units. EPA presented the need for additional handler exposure data to the January 2007 Science Advisory Panel (SAP) as well as to the April 2007 Human Studies Review Board (HSRB) and both groups agreed that additional data are warranted. **2) How would the data be used?** The inhalation exposure data would be used to assess the residential short-term duration of painting with a paint brush/roller and an airless sprayer. For occupational uses, the inhalation exposure data would be used to assess the short- and intermediate-term commercial painters (brush/roller and airless sprayer), machinists using metal working fluids (MWFs), as well as pouring Busan 1024 (e.g., poured into paint as a preservative in manufacturing settings, paper making, etc). **3) How could the data affect the risk assessment?** The inhalation exposure data would be used to determine the accuracy of the inhalation risks to both residence and occupational workers. If risks warrant mitigation, the inhalation exposure data would provide the types of mitigation necessary such as respiratory protection from respirators or closed systems for commercial uses to potential removal of uses from the label.

Appendix B: Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		4) What is triggering the need for this data? The criteria for the inhalation exposure data are based on the potential for respiratory exposure from the labeled uses (e.g., airless sprayers) and evidence of toxicity. If no toxicological endpoints of concern were identified, then the inhalation exposure data would not be needed.
875.1600 (Applicator)	Data Reporting and Calculations	**1) What is the value of the study?** For all exposure studies this data need is needed to facilitate the review of the data. **2) How would the data be used?** The study report and all raw data/calculations would be reviewed for the adequacy of the data. **3) How could the data affect the risk assessment?** The data are needed to interpret the inhalation exposure data collected. **4) What is triggering the need for this data?** This data need is triggered if an exposure study is conducted.
875.1700 (Applicator)	Product Use Information	**1) What is the value of the study?** Product use information is a description of how the product is actually applied; it is not a field study. A description of how this product is used would provide for a comprehensive realistic assessment of its potential applications. **2) How would the data be used?** The description of the application techniques would be used to define the exposure scenarios to be assessed in the risk assessment. **3) How could the data affect the risk assessment?** A complete description of product use would ensure that the risk assessment is inclusive of the types of exposures occurring during residential and occupational use.

Appendix B: Exposure Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		4) What is triggering the need for this data? The need for a risk assessment as needed under Registration Review would require that the risk assessor understands how the product is applied.
875.2300 (Post Application)	Indoor Surface Residue Dissipation	**1) What is the value of the study?** No data are currently available to determine the residues available for incidental oral exposure from treated textiles (dermal exposure is not considered as there are no dermal toxicological endpoints of concern). As a first tier to the risk assessment 100% residue transfer is assumed. If no risk concerns are evident, this study would not be needed. If risks of concern are indicated at 100% residue transfer, then this study is needed to refine the assessment. **2) How would the data be used?** This product is used as a material preservative in textiles. The available residues from clothing would be used to determine the magnitude of children's incidental exposure from treated clothing. **3) How could the data affect the risk assessment?** The data are needed to refine the risk estimates if risks of concern are identified assuming 100% residue transfer from treated clothing apparel. **4) What is triggering the need for this data?** The specific Busan 1024 use triggering the criteria for the surface residue data is the potential for incidental oral exposure from the material preservative use in textiles and evidence of toxicity. If no toxicological endpoints of concern were identified for the oral route, then the surface residue data would not be needed. Moreover, if risks of concern are not identified when 100% residue transfer is assumed, the data are not needed.
875.2700 (Post Application)	Product Use Information	**1) What is the value of the study?** Product use information for the post application data need is a description of what types of consumer products are treated; it is not a field study. A description of what types of consumer products are treated, specifically what types of textiles, would provide for a comprehensive realistic assessment of potential post application exposures.

Appendix B: Exposure Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		2) How would the data be used? The listing of the end use consumer products would be used to define the exposure scenarios to be assessed in the risk assessment. For example, if treated textiles include clothing, bedding, etc then a children's exposure scenario needs to be assessed. However, if the treated textiles are limited to awnings, doormats, etc., a post application assessment may not be needed. **3) How could the data affect the risk assessment?** A complete description of consumer products treated would ensure that the risk assessment is inclusive of the types of exposures occurring during residential use. **4) What is triggering the need for this data?** The need for a risk assessment as needed under Registration Review would require that the risk assessor understands how the product is applied.
875.2900 (Post Application)	Data Reporting and Calculations	**1) What is the value of the study?** For all exposure studies this data need is needed to facilitate the review of the data. **2) How would the data be used?** The study report and all raw data/calculations would be reviewed for the adequacy of the data. **3) How could the data affect the risk assessment?** The data are needed to interpret the residue data collected. **4) What is triggering the need for this data?** The data reporting need is triggered if a residue study is conducted.
875.3000 (Post Application)	Non-dietary Ingestion Exposure	**1) What is the value of the study?** The design of the non dietary ingestion exposure study can be combined with the Indoor Surface Residue Dissipation study (875.2300) to determine the available residue leaching from a child mouthing treated clothing articles.

Appendix B: Exposure Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		2) How would the data be used? This product is used as a material preservative in textiles. The available residues from clothing would be used to determine the magnitude of children's incidental exposure from treated clothing. **3) How could the data affect the risk assessment?** The data are needed to refine the risk estimates if risks of concern are identified assuming 100% residue transfer from treated clothing apparel. **4) What is triggering the need for this data?** The criteria for the surface residue data are the potential for incidental oral exposure from the material preservative use in textiles and evidence of toxicity. If no toxicological endpoints of concern are identified for the oral route, then the non-dietary ingestion exposure data would not be needed. Moreover, if there are no risks of concern when 100% residue transfer is assumed, the data are not needed.

Appendix C. Environmental Fate Guideline Study Justifications

OPP 161-1	Hydrolysis	**1) What is the value of the study?** Results from the hydrolysis study will indicate the stability and persistence of Busan 1024, indicating the potential for this chemical to contaminate water discharged to WWTPs. In aquatic effluents, WWTPs may discharge directly to surface waters. The Agency will address the risks of concern. **2) How would the data be used?** Data would show/help in establishing chemical hydrolysis as a route for degradation of a pesticide and to identify, if possible, the hydrolytic products formed which may adversely affect non-target organisms and may contaminate water and food source of aquatic organisms. **3) How could the data affect the risk assessment?** The results of hydrolysis data would indicate if Busan 1024 is persistent or it degrades into degradation products which may adversely affect nontarget organisms and may contaminate their food and water and possibly soil. **4) What is triggering the need for this data?** Hydrolysis data is needed to conduct the fate assessment to support indoor uses for Busan 1024.
850.6800	Modified Activated Sludge, Respiration Inhibition	**1) What is the value of the study?** The modified activated sludge, respiration inhibition test would allow EPA to identify antimicrobial pesticides which could harm microorganisms found in biological wastewater treatment systems and would also help establish correct concentrations for use in the ready biodegradability test. **2) How would the data be used?** The data would be used to determine the potential of Busan 1024 to directly harm the nontarget organisms and/or to microbial treatment processes present in a WWTP and to determine suitable noninhibitory concentrations of Busan 1024 to be used in biodegradability tests. **3) How could the data affect the risk assessment?** If the data shows that Busan 1024 is toxic to nontarget organisms and/or to microbial process found in WWTPs

Appendix C. Environmental Fate Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		then, the Agency may need Tier II environmental fate data to evaluate potential adverse effects on WWTPs. **4) What is triggering the need for this data?** Studies are needed to conduct environmental fate assessment and to determine the potential exposure of Busan 1024 to waste water treatment plants (WWTPs) (via effects on WWTP microbes).
835.1110	Activated Sludge Sorption Isotherm	**1) What is the value of the study?** The results from activated sludge sorption study would allow EPA to assess the distribution of the antimicrobial among the solid, aqueous, and vapor phases of WWTPs. Specifically, this study identifies those chemicals which sorb to sludge biomass. **2) How would the data be used?** The data would be used to determine the sorption potential of Busan 1024 to activated sludge biomass and in biological wastewater treatment systems. **3) How could the data affect the risk assessment?** If Busan 1024 is not sorbed or biodegraded then, it would pass through a biological treatment system unaffected and it would contaminate surface and drinking waters and also have potential adverse effects to nontarget organisms. **4) What is triggering the need for this data?** Studies are needed to conduct environmental fate assessment and to determine the sorption potential of activated sludge for the removal of specific chemical compounds in biological wastewater treatment systems.
835.3110	Ready Biodegradability	**1) What is the value of the study?** The ready biodegradability study would enable the Agency to determine the likelihood that the antimicrobial pesticide of biodegrading in aquatic environments under aerobic conditions. **2) How would the data be used?** The results from the data would be used to determine the rate and extent of aerobic biodegradation of Busan 1024

Appendix C. Environmental Fate Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		when it is released into aquatic environments and would help establish if Busan 1024 is stable or not stable under real environmental conditions. **3) How could the data affect the risk assessment?** If the results shows low biodegradability then, Busan 1024 would occur in significant quantities in WWTP effluents (water and biosolids) and in environmental compartments (e.g., surface waters) such that potential adverse effects to nontarget organisms, found in such environmental compartments, may occur. **4) What is triggering the need for this data?** Data are needed to conduct environmental fate assessment and to determine the ready biodegradability of Busan 1024.

Appendix D: Ecological Guideline Study Justifications		
850.5400	Tier II green algae using *Selenastrum capricornutum*	**1) What is the value of the study?** As part of a Tier I risk assessment, one indicator plant species is tested for phytotoxicity. This study would allow the Agency to categorize busan 1024 as toxic or non-toxic to plants. If toxic, additional higher tier plant tests would be needed. An endangered species assessment for endangered or threatened plants is not possible without this study. **2) How would the data be used?** This study would be used to evaluate the toxicity of busan 1024 to non-target plants in terrestrial and aquatic ecosystems. **3) How could the data affect the risk assessment?** Adverse effects to non-target plants in terrestrial and aquatic ecosystems may result in mitigation to protect species at risk. Mitigation might include reduced label dosages, neutralization of effluents prior to discharge into water, restrictions on use in sensitive ecosystems or where endangered species are present, or other mitigation measures. **4) What is triggering the need for this data?** Increased concern from state regulators and the public to evaluate impacts on WWTP operations, endangered species, and persistence in the environment, since initial registration, have triggered the need for this study. Green algae are critical to ecosystem health and productivity.

Appendix D: Ecological Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data:
850.1075 850.1035 850.1055	Acute marine fish toxicity Acute marine Mysid shrimp toxicity Acute marine bivalve embryo larvae toxicity	**1) What is the value of these studies?** As part of a Tier I risk assessment, three aquatic animal species are routinely tested by the agency as indicators of potential toxicity to aquatic life and ecosystem health. These studies allow the Agency to categorize busan 1024 as toxic or non-toxic to aquatic animal life and to perform ecological risk assessments. If toxic, additional higher tier tests would be needed to refine the risk assessment. An endangered species assessment for endangered or threatened estuarine and marine aquatic fish and invertebrates is not possible without these studies. Research bears out that data for a fish cannot serve as a surrogate for an invertebrate and that shrimp react differently to toxicants than bi-valves due to their physiology and location in the water column. Also, data for freshwater species cannot serve as surrogate data for estuarine/marine species due to differences in water pH, salt content, and other variables that may affect the test substance. **2) How would the data be used?** These studies would be used to evaluate the toxicity of busan 1024 to non-target and endangered/threatened aquatic animals in estuarine and marine aquatic ecosystems. **3) How could the data affect the risk assessment?** Adverse effects to aquatic animal species in estuarine and marine aquatic ecosystems may result in mitigation to protect species at risk. Mitigation might include reduced label dosages, neutralization of effluents prior to discharge into water, restrictions on use in sensitive ecosystems or where endangered species are present, or other mitigation measures. **4) What is triggering the need for this data?** Increased concern from state regulators and the public to evaluate impacts on endangered species and persistence in the environment, since initial registration, have triggered the need for these studies. Aquatic animals are critical to the food chain and ecosystem health and productivity.