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Prevention, Pesticides
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2,4 Imidazolidinedione (Hydroxymethyldimethyl Hydantoins) Summary Document Registration Review

2,4 Imidazolidinedione (Hydroxymethyldimethyl Hydantoins) Summary Document Registration Review: Initial Docket June 2007

Approved By:

6/21/07

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I. Preliminary Work Plan - 2,4 Imidazolidinedione (Hydroxymethyldimethyl Hydantoins)

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 intends to 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. 2,4 Imidazolidinedione (hydroxymethyldimethyl hydantoin) is an antimicrobial pesticide used in adhesives; air fresheners; caulking compounds; cleansers; fabric softeners; hydraulic fluids; inks; liquid detergents; metal working cutting fluids; paints, stains and coatings; paper/paperboard coatings; polishes; synthetic polymers; powdered detergents; sealants; carpet shampoos; soap; starch solutions; textiles; and wax.

- 2,4 Imidazolidinedione is comprised of two compounds: 1,3-Bis(hydroxymethyl)-5,5-dimethyl hydantoin (also referred to as DMDM Hydantoin) and Hydroxymethyl-5,5-dimethyl hydantoin (also referred to as MDM Hydantoin. Both of these active ingredients are formaldehyde releasing compounds. In this document these compounds may be referenced as the hydroxymethyldimethyl hydantoins.

Risk Assessment Status &Anticipated Risk Assessment and Data Needs:

Human Health Risk:

- Occupational and residential risk assessments will be needed to determine potential risks from hydroxymethyldimethyl hydantoin uses, including the potential inhalation exposure from the release of formaldehyde.
- The two active ingredients in this case are hydroxymethyldimethyl hydantoins; these chemicals are formaldehyde releasers. The Reregistration Eligibility Decision for formaldehyde will be completed in 2008.
- The Agency believes the hydroxymethyldimethyl hydantoins may degrade to 5,5-dimethylhydantoin (DMH). The halohydantoins are known to hydrolyze/degrade to DMH. A reregistration decision for the halohydantoins was issued in 2004, based on the DMH data.
- The Agency needs product chemistry and environmental fate data on the hydroxymethyldimethyl hydantoins. These data will enable the Agency to determine how quickly and completely hydroxymethyldimethyl hydantoins break down to DMH.
- Depending on how quickly hydroxymethyldimethyl hydantoins hydrolyze/degrade to 5,5-dimethylhydantoin (DMH), we may need data on the parent compounds, and/or other possible metabolites.
- If the degradation to DMH occurs rapidly and completely, data from DMH will be used to conduct the human health risk assessment for hydroxymethyldimethyl hydantoins.
- The Agency anticipates needing the following data in order to conduct a complete human health risk assessment for all uses. The toxicity data base for formaldehyde will be evaluated during the reregistration process, scheduled for completion in 2008. Some studies listed below may not be needed if the Agency determines that data from DMH may be used for this risk assessment. These studies are noted below.

DMDM Hydantoin & MDM Hydantoin

For Human Health Effects/Toxicity

- (GLN 870.2600) dermal sensitization [1]
- (GLN 870.3150) 90-day oral toxicity – non-rodent[1]
- (GLN 870.3250) 90-day dermal toxicity – rodent[1]
- (GLN 870.3465) 90-day inhalation toxicity – rat[1]
- (GLN 870.3700) prenatal developmental toxicity- rat[1]
- (GLN 870.3800) reproduction and fertility effects – rodent[1]
- (GLN 870.4100) chronic toxicity – rodent[1]
- (GLN 870.4200) carcinogenicity – rat and mouse[1]

1 These studies may not be needed based on the outcome of the environmental fate studies conducted with hydroxymethyldimethyl hydantoins.

5,5-DMH

- (GLN 870.3465) 90-day inhalation toxicity – rat
- (GLN 870.7600) dermal penetration – rat

DMDM Hydantoin & MDM Hydantoin

For Occupational and Residential Exposure

- (GLN 875.1100) dermal outdoor exposure
- (GLN 875.1200) dermal indoor exposure
- (GLN 875.1300) inhalation outdoor exposure
- (GLN 875.1400) inhalation indoor exposure
- (GLN 875.1600 & 875.2900) data reporting and calculations
- (GLNs 875.1700 & 875.2700) product use information
- (GLN 875.2300) indoor surface residue dissipation[2]
- (GLN 875.2500) inhalation exposure[2]
- (GLN 875.2700) product use information
- (GLN 875.2900) data reporting[2]
- (GLN 875.3000) non-dietary ingestion[2]

Environmental Fate and Ecological Risk:

- An environmental fate and ecological effects risk assessment has not been conducted for the hydroxymethyldimethyl hydantoins. Please refer to Section III, Ecological Effects Scoping Document for a detailed discussion of the anticipated risk assessment needs.

- The Agency anticipates needing the following data in order to conduct a complete environmental fate assessment:

  - (GLN 161.1) hydrolysis;
  - (GLN 850.6800) modified activated sludge respiration inhibition;
  - (GLN 835.1110) activated sludge sorption isotherm; and
  - (GLN 835.3110) ready biodegradability.

- The Agency anticipates needing the following data in order to conduct a complete ecological risk assessment, including an endangered species assessment for all uses:

  - (GLN 850.1010) acute toxicity to freshwater invertebrates;
  - (GLN 850.1075) acute toxicity to freshwater fish;

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

- (GLN 850.2100) acute avian oral toxicity; and
  (GLNs 850.4400 & 850.5400) algal toxicity (Tier II) using freshwater green alga, *Selenastrum capricornutum.*

The planned ecological risk assessment will allow the Agency to determine whether use of the hydroxymethyldimethyl hydantoins has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that the hydroxymethyldimethyl hydantoins "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 the hydroxymethyldimethyl hydantoins 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.

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Timeline:

EPA has created the following estimated timeline for the completion of the 2,4 Imidazolidinedione (hydroxymethyldimethyl hydantoins) registration review.

Activities	Estimated Month/Year
Phase 1: Opening the docket	
Open Public Comment Period for 2,4 Imidazolidinedione (Hydroxymethyldimethyl Hydantoins)Docket	June 2007
Close Public Comment Period	September 2007
Phase 2: Case Development	
Develop Final Work Plan (FWP)	October 2007
Issue DCI	August 2008
Data Submission	August 2012[3]
Open Public Comment Period for Preliminary Risk Assessments	December 2013
Close Public Comment Period	February 2013
Phase 3: Registration Review Decision	
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
Total (years)	7.5[3]

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

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 hydroxymethyldimethyl hydantoin case.

Stakeholders are also specifically asked to provide 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 per season
    f. geographic limitations on use
2. Use or potential use distribution (*e.g.*, geographical distribution of relevant uses).
3. Use history.
4. Application timing (application intervals) by use – national, state, and county.
5. Usage/use information for non-agricultural uses (*e.g.*, materials preservation).
6. Typical application interval.
7. State or local use restrictions.
8. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency.
9. Monitoring data.

Water Quality Information

The Agency invites submission of water quality data for this chemical. 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.

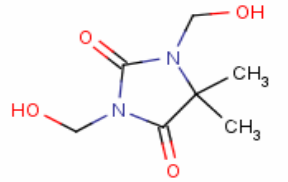
Next Steps

After the comment period closes in September 2007, the Agency will prepare a Final Work Plan for this pesticide.

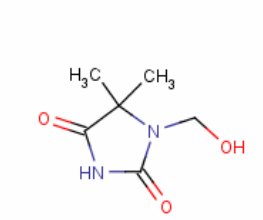
II. FACT SHEET

Background Information:

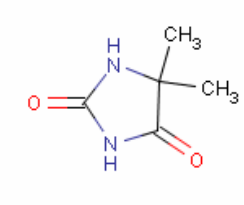
- 2,4 Imidazolidinedione (hydroxymethyldimethyl hydantoin) registration review case number: 5020
- 2,4 Imidazolidinedione; 1,3-bis (hydroxymethyl)-5,5-Dimethyl Hydantoin; DMDM Hydantoin is PC Code 115501 (CAS # 6440-58-0)



- 2,4 Imidazolidinedione; 1-(Hydroxymethyl)-5,5-Dimethyl Hydantoin; MDM Hydantoin is PC Code 115502 (CAS # 116-25-6)



- 5,5-Dimehtyhydantoin (DMH) (CAS No. 77-71-4)



- 2,4 Imidazolidinedione; inert PC Code: 815502 (CAS # 27636-82-4) & 715501 (CAS#: 6440-58-0)

- Technical registrant: Lonza
- First approved for use in a registered product: 1987
- Not subject to reregistration (no Reregistration Eligibility Decision [RED])
- Synonyms for 2,4-Imidazolidinedione, 1,3-bis(hydroxymethyl)-5,5-dimethyl- include: *1,3-Bis(hydroxymethyl)-5,5-dimethyl-2,4-imidazolidinedione, 1,3-Bis(hydroxymethyl)-5,5-dimethylhydantoin, 1,3-Di(hydroxymethyl)-5,5-dimethylhydantoin, 1,3-Dimethylol-5,5-dimethylhydantoin, 2,4-Imidazolidinedione, 1,3-bis(hydroxymethyl)-5,5-dimethyl-, 2,4-Imidazolidinedione, 1,3-bis(hydroxymethyl)-5,5-dimethyl-, DMDM Hydantoin, DMDMH, Hydantoin, 1,3-bis(hydroxymethyl)-5,5-dimethyl-, Hydantoin, 1,3-*

bis(hydroxymethyl)-5,5-dimethyl-, Hydantoin, 1,3-bis(hydroxymethyl)-5,5-dimethyl-, N,N'-Dimethylol-5,5-dimethylhydantoin

- Synonyms for 2,4 Imidazolidinedione, 1-(Hydroxymethyl)-5,5-Dimethyl include: *1-(Hydroxymethyl)-5,5-dimethyl-2,4-imidazolinedione, 1-(Hydroxymethyl)-5,5-dimethylhydantoin, 2,4-Imidazolidinedione, 1-(hydroxymethyl)-5,5-dimethyl-, 2,4-Imidazolidinedione, 1-(hydroxymethyl)-5,5-dimethyl-, Hydantoin, 1-(hydroxymethyl)-5,5-dimethyl-, Hydantoin, 1-(hydroxymethyl)-5,5-dimethyl-, Hydantoin, 1-(hydroxymethyl)-5,5-dimethyl-, MDM Hydantoin, Monomethylol dimethyl hydantoin, Monomethylol-5,5-dimethylhydantoin*
- PM: Adam Heyward: heyward.adam@epa.gov
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- Antimicrobials Division Product Manager (PM): Adam Heyward, heyward.adam@epa.gov

Use & Usage Information:

For additional usage information and details, please refer to the Appendix A.

- The hydroxymethyldimethyl hydantoins are an antimicrobial used in adhesives, air fresheners, caulking compounds, clay slurries, cleansers, coatings, dispersed colors, resin emulsions, fabric softeners, hydraulic fluids, inks, latex, liquid detergents, metal working cutting fluids, paints (emulsion, latex, water-based), paper/paperboard coatings, polishes, polymers (synthetic), powdered detergents, sealants, carpet shampoos, soap, stains (preservative incorporation), starch solutions, textiles, and wax.
- Pests controlled include algae, animal pathogenic bacteria, deterioration/spoilage bacteria, fungi, mold/mildew, slime-forming bacteria, slime-forming fungi, and yeasts.
- There are 16 registered products containing the hydroxymethyldimethyl hydantoins as an active ingredient; these formulations are also formaldehyde releasers.
- Application rates for the active ingredient range from 10 % to 96 % for 1,3-bis (hydroxymethyl)-5,5-dimethyl; and 0.4 % to 32 % for 1-(Hydroxymethyl)-5,5-Dimethyl Hydantoin.

Recent Actions:

No recent registration actions have occurred for the hydroxymethyldimethyl hydantoins.

Human Health Risk Assessment Status

Please refer to Section IV of this document for a detailed discussion of the anticipated risk assessment needs for human health. A summary is provided below.

Dietary (Food and Water):

- Several dietary assessments were conducted in 2001- 2003 for various indirect food contact uses on paper and other materials.

Residential:

- Residential uses of the hydroxymethyldimethyl hydantoins include: liquid detergents, fabric softeners, household cleaning products, soft soaps, water-based paints, room deodorizers, air fresheners, water-based gels and polymer emulsions for household products, textiles, water-based adhesives, sealants and caulks, latex for paper coatings, food and non-food contact paper and paperboard, carpet shampoos, polishes, waxes. The Agency will conduct a residential risk assessment as part of registration review.

Occupational:

- No occupational exposure assessment was performed for these hydroxymethyldimethyl hydantoin products being considered for registration review. The Agency will complete an occupational risk assessment for registration review of the hydroxymethyldimethyl hydantoins.

- An occupational assessment was conducted in 2001 for the primary uses of 1,3-dichloro-5,5-dimethylhydantoin, as the active ingredient in Dantochlor RW (81.1% a.i.), during batch mixing for introduction into industrial cooling water systems and pulp and paper process water.

Ecological Risk Assessment Status:

Ecological exposure and risk assessments have not been conducted for the hydroxymethyldimethyl hydantoins. Very limited ecological data on the hydroxymethyldimethyl hydantoins have been submitted to the Agency. Due to the lack of risk assessments and data, the Agency is unable to determine what types of ecological risks and hazards are expected as a result of the uses of the hydroxymethyldimethyl hydantoins. Please refer to Section III of this document, Status of Human Health and Ecological Risk Assessment for the Hydroxymethyldimethyl Hydantoins, for a detailed discussion of the anticipated ecological risk assessment and data needs.

The planned ecological risk assessment will allow the Agency to determine whether use of the hydroxymethyldimethyl hydantoins has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that the hydroxymethyldimethyl hydantoins "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 the hydroxymethyldimethyl hydantoins 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.

Tolerances

The hydroxymethyldimethyl hydantoins are registered as an indirect food-contact use as a slimicide in the manufacture of paper and paperboard. In addition the hydroxymethyldimethyl hydantoins are registered as a preservative/coating preservative in food contact paper and paperboard. The hydroxymethyldimethyl hydantoin uses on paper and paperboard are considered indirect food contact. There are no uses where hydroxymethyldimethyl hydantoins are applied directly to food. Currently there are no tolerances for this chemical.

Data Call-In Status

A data call-in has not been issued for the hydroxymethyldimethyl hydantoins since it was not subject to reregistration.

Labels

There are 16 registered products for the hydroxymethyldimethyl hydantoins. A list of registration numbers is included below. Product registration labels may be obtained from the Pesticide Product Label System (PPLS) website at: http://oaspub.epa.gov/pestlabl/ppls.home.

2,4 Imidazolidinedione (Hydroxymethyldimethyl Hydantoin) Registration Numbers

Registration Number	Product Name	Company Name
5383-111	Troysan 680	Troy Chemical Company
5383-123	Troysan 2063	Troy Chemical Company
6836-111	---	Lonza Inc.
6836-112	---	Lonza Inc.
6836-119	---	Lonza Inc.
6836-199	Dantogard XL-1000	Lonza Inc.
6836-200	Dantogard Plus Industrial Preservative	Lonza Inc.
6836-207	Dantogard II Preservative	Lonza Inc.
6836-208	Glycoserve II Preservative	Lonza Inc.
6836-271	Dantogard Plus Liquid	Lonza Inc.
6836-306	Dantoserve SG	Lonza Inc.
6836-307	Dantoserve MS	Lonza Inc.
6836-322	Dantogard 2000 Preservative	Lonza Inc.
47371-188	Dantocil IG	H & S Chemicals Division
47371-189	Dantocil HG	H & S Chemicals Division
47371-190	Dantocil SG	H & S Chemicals Division

Incidents:

No incidents related to the hydroxymethyldimethyl hydantoins use were found during a search of the following databases: the OPP Incident Data System (IDS); Poison Control Center data; California Department of Pesticide Regulation data; and National Pesticide Information Center data.

III. STATUS OF HUMAN HEALTH AND ECOLOGICAL RISK ASSESSMENT FOR 2,4 IMIDAZOLIDINEDIONE [DMDM HYDANTOIN (PC CODE 115501; CAS# 6440-58-0) AND MDM HYDANTOIN (PC CODE 115502; CAS# 116-25-6)] – REGISTRATION REVIEW CASE NUMBER 5020

A. Introduction

Two active ingredients 1,3-Bis(hydroxymethyl)-5,5-dimethyl hydantoin (also referred to as DMDM Hydantoin or DMDH) and Hydroxymethyl-5,5-dimethyl hydantoin (also referred to as MDM Hydantoin or MDMH) are included in the 2,4-Imidazolindinedione registration review case. These two active ingredients, hereinafter referred to as hydroxymethyldimethyl hydantoins, are antimicrobial pesticides' that are used in numerous materials preservatives applications. The Antimicrobial Division Hydroxymethyldimethyl Hydantoins 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. The team considered the uses of the hydroxymethyldimethyl hydantoins, which is presented in Section B of this report. The status of human exposure and risk assessment of these hydroxymethyldimethyl hydantoins is presented in Section C along with the corresponding chemical structures (see Table 1). The status of data on the physical/chemical properties and environmental fate of these hydroxymethyldimethyl hydantoins is presented in Section D of this report. Ecological exposure and risk assessment status for these two active ingredients 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 new data may be needed to support the registration review process.

Although on September 30, 2004, the Agency issued a decision regarding reregistration of halohydantoins, the Agency has not issued a decision regarding reregistration of hydroxymethyldimethyl hydantoins. In the late 1980s, the Agency has determined that halohydantoins are rapidly metabolized by mammals to 5,5-dimethyl hydantoin (DMH); however, no data are available to support the conclusion that hydroxymethyldimethyl hydantoins behave similarly to halohydantoins with regard to metabolic half-life and moieties of concern. Based on the chemical structure, hydroxymethyldimethyl hydantoins are likely to hydrolyze/degrade to DMH. Unlike halohydantoins, hydroxymethyldimethyl hydantoins break down to also form formaldehyde and therefore, are referred to as formaldehyde-releasing hydantoins. Consequently, the assessment of risks for hydroxymethyldimethyl hydantoins must also include an assessment of risks from exposure to formaldehyde.

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 registrant'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 hydroxymethyldimethyl hydantoins, 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 needs, as outlined here, as related to their specific product during this registration review process.

Since each pesticide is unique and there is much variety in pesticide chemistry, exposure, and hazard, the Agency tries to be flexible with regard to data needs. 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 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 that 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 need should be waived. In addition, the registrant must describe any unsuccessful attempts to generate the needed 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 which underlies the data need. The Agency will review each waiver request and subsequently inform the registrant 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.

Although halohydantoins and hydroxymethyldimethyl hydantoins have some similar uses, some uses for these two groups of hydantoins are different. Halohydantoins are used as disinfectants in commercial and residential swimming pools, spas, and hot tubs and as sanitizers for treatment of toilet bowl water in homes whereas the hydroxymethyldimethyl hydantoins are not. The only potential food-contact use for the halohydantoins is an indirect food-contact use as a slimicide in the manufacture of food contact paper and paperboard. In addition to use as a slimicide in the manufacture of food contact paper and paperboard, two additional indirect food-contact uses for hydroxymethyldimethyl hydantoins include filler preservative in food contact paper and paperboard and coating preservative for food contact paper and paperboard. There are no tolerances established for the hydroxymethyldimethyl hydantoins. Information on the use profile for the hydroxymethyldimethyl hydantoins follows.

DMDM hydantoin and MDM hydantoin are both present as active ingredients in 16 products. Of the 12 general use patterns for antimicrobial pesticides, two are applicable to the hydroxymethyldimethyl hydantoins: materials preservatives and residential and public access premises. Appendix A presents specific uses for general antimicrobial use patterns applicable to the hydroxymethyldimethyl hydantoins. 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 hydroxymethyldimethyl hydantoins. Appendix A presents information on each of the specific use sites for the general use patterns that are applicable to the hydroxymethyldimethyl hydantoins, including the method of application, application rate, and range of percent by weight of active ingredient to be added to each use site.

C. Human Health Exposure and Risk Assessment

No human health, occupational, or residential risk assessments have been performed for these hydroxymethyldimethyl hydantoins. When used as a material preservative in adhesives, liquid detergents, papermaking chemicals and coatings, hydroxymethyldimethyl hydantoins have potential indirect food contact uses. As a result, dietary exposure and risk assessments are needed.

Toxicity

In the late 1980s, the Agency determined 5,5-dimethylhydantoin (DMH) to be the moiety of mammalian toxicological concern for halohydantoins and selected this chemical to represent human health effects for this class of chemicals. Although the Agency has determined that halohydantoins are rapidly metabolized by mammals to DMH, no data are available to support the conclusion that hydroxymethyldimethyl hydantoins behave similarly to halohydantoins with regard to metabolic half-life and moieties of concern. Based on the chemical structure, hydroxymethyldimethyl hydantoins are likely to hydrolyze/degrade to DMH. Unlike halohydantoins, hydroxymethyldimethyl hydantoins break down to also form formaldehyde and therefore, are referred to as formaldehyde-releasing hydantoins. The chemical structures of the hydroxymethyldimethyl hydantoins are provided in table 1 and the metabolite DMH is in table 2.

In general, the Agency needs a basic toxicity dataset to characterize the hazard and risks through all exposure routes (oral, inhalation, and dermal). 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, dermal and/or inhalation toxicological endpoint for the hydroxymethyldimethyl hydantoins, and the determination of cancer potency was inconclusive. A more complete toxicity database will be needed to quantify risk for the dietary, incidental ingestion, dermal and inhalation exposure scenarios and toxicity endpoints will need to be established

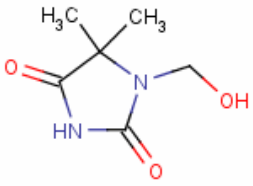
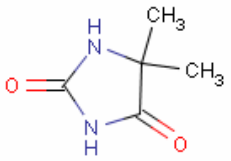
Table 1. Chemical Structures of the Hydroxymethyldimethyl Hydantoins	
Chemical Name	1,3-Dimethyl-5,5-Dimethyl Hydantoin
Common/Trade Names	DMDM Hydantoin, DMDMH
CAS Number(s)	6440-58-0
Structure	
Chemical Name	Hydroxymethyl-5,5-Dimethyl Hydantoin
Common/Trade Names	MDM Hydantoin, MDMH
CAS Number(s)	116-25-6
Structure	

Table 2. Chemical Structure of the DMH Metabolite	
Chemical Name	5,5-Dimethylhydantoin
Common/Trade Names	DMH
CAS Number(s)	77-71-4
Structure	

For the hydroxymethyldimethyl hydantoins, the registrant has submitted a 90-day oral toxicity study in rats (MRID 250311/132103) and 21/28-day toxicity study (MRID 138830/29025). The 90-day oral study has been reviewed by the Agency as core-minimum, but the 21/28-day study was determined to be a supplementary study. Only two doses tested (8 and 800 mg/kg/day); the LOAEL was determined to be 800 mg/kg/day based on the well defined erythema, moderate edema, subdermal hemorrhages and pustules with histopathological findings.

The registrant has also submitted a prenatal developmental toxicity study in rabbits (MRID 258269/149559) for the hydroxymethyldimethyl hydantoins that is core-minimum. No fetal toxicity and/or developmental toxicity were found at the highest dose tested (750 mg/kg/day). It should be noted that the Agency needs both rodent and non-rodent studies to examine species sensitivity for both developmental and 90-day oral toxicity studies.

Without the physical chemistry and fate data especially hydrolysis data (OPP guideline number 161-1) (see also Section D) for the hydroxymethyldimethyl hydantoins, it is difficult to predict how fast or slow the breakdown process is and whether the process is a relatively complete or partial breakdown. In addition, information on the metabolic half-life in mammals (guideline 870.7485) is also needed to determine whether humans are likely to be exposed primarily to the parent chemicals or to their metabolites. If the hydroxymethyldimethyl hydantoins are not rapidly metabolized in humans and humans are likely to be exposed to the parent chemicals for an extended period, the Agency will need extensive mammalian toxicity tests on both DMDM and MDM Hydantoins. The needed guideline (GLN) studies include:

- (GLN 870.2600) dermal sensitization *
- (GLN 870.3150) 90-day oral toxicity – non-rodent *
- (GLN 870.3250) 90-day dermal toxicity – rodent *
- (GLN 870.3465) 90-day inhalation toxicity – rodent *
- (GLN 870.4100) chronic toxicity – rodent *
- (GLN 870.4200) carcinogenicity – rat and mouse *
- (GLN 870.3700) prenatal developmental toxicity- rat *
- (GLN 870.3800) reproduction and fertility effects – rodent *

* These studies may not be needed based on the outcome of the environmental fate studies conducted using hydroxymethyldimethyl hydantoins.

In the event that the hydroxymethyldimethyl hydantoins degrade relatively quickly to the metabolite DMH, the Agency would not need as much data since the metabolite (DMH) has a relatively complete toxicity database. In addition, the Agency already has evaluated most of the mammalian toxicity data for DMH in the course of assessing dietary exposure and risk to the halohydantoins, reevaluated in 2004. If DMH is the metabolite of concern for the hydroxymethyldimethyl hydantoins, fewer toxicity studies would be needed. These needed studies are listed below.

- (GLN 870.3465) 90-day inhalation toxicity – rat
- (GLN 870.7600) dermal penetration – rat

The Agency anticipates needing this data in order to conduct a complete human health risk assessment for all uses. The toxicity database for formaldehyde will be evaluated during the reregistration process, scheduled for completion in 2008.

Refer to Appendix B for specific justifications on toxicity guideline studies. This appendix identifies, for example, why certain hydroxymethyldimethyl hydantoin use patterns may trigger the need for specific toxicity studies, based on the length of exposure. In addition, Appendix B provides a rationale for examining species sensitivity. If the Agency identifies metabolites other than DMH and formaldehyde, the Agency would also need mammalian toxicity data for these metabolites.

It should be noted that although hydroxymethyldimethyl hydantoins 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

As a result of the hydroxymethyldimethyl hydantoins indirect food uses, including paper and papermaking, adhesives, and liquid detergents, a dietary risk assessment will be needed for these chemicals.

Residue Chemistry

Modeling can be used to estimate dietary intake that results from the use of hydroxylmethyldimethyl hydantoins as a material preservative in adhesives, detergents, paper making and coatings. Often, a Tier I assessment is sufficient to determine dietary risk for antimicrobial pesticides. 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 guideline studies would be needed. However, if risks of concern are identified in the Tier 1 assessments, the Agency would then need additional residue chemistry guideline studies.

Drinking Water

In addition, if analysis of initial Tier I screening tests 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, it is possible that the Agency may need a human drinking water risk assessments.

Occupational and Residential Risk Assessment

The hydroxymethyldimethyl hydantoins break down to form formaldehyde. Therefore the hydroxymethyldimethyl hydantoins, are referred to as formaldehyde-releasing hydantoins. As mentioned previously, no data have been submitted indicating the half-life of environmental fate processes and/or identifying resulting degradates of these hydroxymethyldimethyl hydantoins. Consequently, it is not clear whether humans will be exposed primarily to hydroxymethyldimethyl hydantoins or to the metabolite via inhalation or dermal exposure in occupational and residential settings in which products containing these hydroxymethyldimethyl hydantoins as active ingredients are used. The chemicals for which the Agency needs data for the occupational and residential risk assessments, depends upon the how quickly the parent hydroxymethyldimethyl hydantoins, degrades and what degradates that result. If studies indicate that the hydroxymethyldimethyl hydantoins degrade to DMH, the common moiety with the halohydantoins, then it may be possible to use existing data from the halohydantoins rather than new studies conducted using the hydroxymethyldimethyl hydantoins.

In summary, a risk assessment for these hydroxymethyldimethyl hydantoins must consider potential risks associated with the active ingredients and the metabolites of concern, including formaldehyde.

Based on the registered uses of hydroxymethyldimethyl hydantoins for use as material preservatives and in residential and public access premises, there is potential for occupational and residential exposure. Although an occupational exposure assessment was performed for DMH, no occupational exposure assessment was performed for the hydroxymethyldimethyl hydantoins. Consequently, the Agency may perform an occupational exposure and risk assessment for registration review of the parent compound, the metabolite, and also examine the release of formaldehyde hydroxymethyldimethyl hydantoins depending largely on the fate and persistence of the parent compound. In addition, the Agency will need to conduct a residential exposure and risk assessment. For occupational exposures, mixer/loader and applicator exposure scenarios include open and closed loading of in industrial settings, such as the manufacturing process for paints, textiles, paper, and metal working fluids for hydroxymethyldimethyl hydantoins. In addition, there is the potential for applicator exposure during painting (residential and professional painters) and for metal working fluid machinists. Occupational postapplication exposure is expected to be minimal. However, potential residential post-applicator exposures are likely to include exposures to treated products such as textiles.

To assess both the occupational and residential assessments, additional toxicity data are needed. For example, a 90-day inhalation toxicity endpoint is needed in order to conduct an inhalation assessment and a 90-day dermal toxicity endpoint is also needed to perform a dermal assessment. For screening purposes, an oral endpoint with a default assumption of 100% absorption could potentially be used in lieu of inhalation data. However, this all depends on the toxicological database. For dermal exposure, it is also possible that oral toxicity data could also be used. However, the Agency may also need a dermal penetration study. The need for this study would likely be conditional, depending on the completion of the toxicity database. For a residential incidental ingestion exposure assessment, oral toxicity data are also needed.

Dermal and inhalation occupational assessments are 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 dermal and inhalation scenarios are needed for registration review. Long-term exposure estimates are only needed for estimating risks to machinists using metal working fluid. Residential assessments are needed for short- and intermediate-term inhalation (e.g. painting) and children's postapplication incidental oral exposures for textiles and carpets. The Agency will likely use task force submitted data for applicator to conduct these occupational or residential assessments. Refer to Appendix C for more details on the exposure data needed and a rationale for why this information is necessary.

D. Physical/Chemical Properties and Environmental Fate

Submission of physical/chemical property data is needed for registration of hydroxymethyldimethyl hydantoins. No product chemistry data have been submitted for either of the hydroxymethyldimethyl hydantoins. As a result, the Agency anticipates

needing these data. Physical/chemistry data help the Agency in evaluating hazard and exposure including acute toxicity (inhalation), workers' exposure (vapor pressure), and bioaccumulation (environmental fate). Storage stability data helps the Agency in determining if the product would remain stable in a formulation. Hydrolysis data (GLN 161-1) is needed in order to predict how fast or slow the breakdown process of hydroxymethyldimethyl hydantoins is to DMH and formaldehyde, and whether the degradation process is relatively complete or a partial breakdown.

The Agency has limited data on the physical form of the hydroxymethyldimethyl hydantoin products. However, a product chemistry review of Dantogard XL-1000, a manufacturing use product containing the highest percentage of a single hydantoin as the active ingredient was completed in the early 1990s. The label indicates that the physical form of this manufacturing use product is a solid. Because melting points of the active ingredients and the manufacturing use product exceed 30 degrees centigrade, no vapor pressure data were provided. Labels for several other products containing the hydroxymethyldimethyl hydantoins, indicate that they are liquids. Although the percentage of the two active ingredients is always indicated on the product labels, the physical form of the registered products is not. The physical form of the manufacturing use products and end use products can influence the potential for exposure to the two active ingredients. Given the absence of product chemistry data for either of the hydroxymethyldimethyl hydantoins, the Agency needs product chemistry data for both. In addition, the Agency needs information on the physical form of each registered product.

Additionally, the Agency is planning to determine (1) the potential of antimicrobial pesticides and/or their major degradates 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 degradates 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, such as surface water, exceed the Agency's Levels of Concern (LOCs) for non-target 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, the Agency will conduct any other assessments normally performed for these other use categories.

The anticipated environmental fate data needs for the hydroxymethyldimethyl hydantoins or any of its major degradates that are identified to be of potential concern are listed below.

- (GLN 161-1) hydrolysis study
- (GLN 850.6800) modified activated sludge respiration inhibition test
- (GLN 835.1110) activated sludge sorption isotherm test
- (GLN 835.3110) ready biodegradability study

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 non-target 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 studies. Further description of the environmental fate guideline studies needed by the EPA is presented in Appendix D.

E. Ecological Exposure and Risk Assessment

Based on the hydroxymethyldimethyl hydantoins uses as material preservatives and in residential and public access premises, the potential for exposure to ecological organisms is expected to be low. Although the Agency has not conducted an ecological exposure and risk assessment, the Agency expects to need ecological toxicity studies for the active ingredient and/or any of its metabolic and/or hydrolytic degradate products identified to be of potential concern. Potential exists for environmental exposure to ecological organisms in the event of a spill or other environmental release of hydroxymethyldimethyl hydantoins or hydroxymethydimethyl hydantoin-containing products. Although ecological toxicity studies conducted by Industrial Biotest Laboratories, Inc. were previously submitted, the Agency classified these studies as invalid. Consequently, the Agency needs new test data to be submitted. Potential for environmental exposure exists for material preservative uses of hydroxymethyldimethyl hydantoins in down the drain exposures, such as disposal of consumer products such as soaps and detergents into household wastewater. An endangered species risk assessment will also be performed. Studies that the Agency needs to conduct a risk assessment include the following:

- (GLN 850.1010) acute toxicity to freshwater invertebrates using the technical grade of the active ingredient using the TGAI;
- (GLN 850.1075) acute toxicity to freshwater fish using the TGAI;
- (GLN 850.2100) acute avian oral toxicity using the TGAI; and (GLN 850.5400).algal toxicity (Tier II) using freshwater green alga, *Selenastrum capricornutum.*

The Agency has no ecological risk assessment for hydroxymethyldimethyl hydantoins 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 uses” with regard to environmental exposure.

In order to perform wastewater treatment plant (WWTP) and ecological risk assessments, the Agency must evaluate the toxicity of hydroxymethyldimethyl hydantoins to non-target and endangered or threatened terrestrial and aquatic animals and plants. Hydroxymethyldimethyl hydantoins uses having potential for environmental exposure are industrial or consumer materials preservative discharges on land and in marine areas.

The justifications for guideline studies for ecological non-target organisms and plants are presented in Appendix E. As mentioned in Appendix E, 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 use of the hydroxymethyldimethyl hydantoins has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that the hydroxymethyldimethyl hydantoins "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 the hydroxymethyldimethyl hydantoins 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.

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

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Materials preservatives				
Water based stains, sealants, adhesives, caulks, joint cements, resin emulsions, inks, textile processing chemicals, liquid detergents, fabric softeners, soft soaps, household cleaners, room deodorizers, air fresheners, and water based surfactants, polymer emulsions, protective or decorative coatings, water based gels for household and industrial products, textiles, water-based adhesives, sealants, caulks, latex for paper coatings, water based paints for industrial and household use.	Soluble concentrate 6836-199 6836-200 5383-111 5383-123 6836-207 _____ Soluble concentrate 6836-111 Soluble concentrate	Incorporation	Product should be added to the formulation to be preserved at a rate of 0.1% to 1.0% or 1,000 to 10,000ppm, based upon the total weight of the product to be protected To ensure uniform distribution, slowly disperse product into product with agitation. Mix thoroughly until evenly dispersed throughout product. _____ Product should be added to the liquid detergent or soft soap formulation at the rate of 2.5 to 10 pounds per 1000 lbs. or to 2,500 to 10,000 ppm based upon the total weight of the formulation _____ Product should be added to the formulation to be preserved at a rate of 2.0 to 20.0 lbs. per 1000 lbs or 0.2% to 2.0% or 2,000 to 20,000 ppm based upon the total weight of the	This product is not to be used for food-contact packaging (6836-199), (6836-200), (6836-207), (6836-271)

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
	6836-271 _____ Soluble concentrate 6836-322 _____ Formulation intermediate 6836-208		product to be protected _____ Add to formulation to be preserved at the rate of 2.3 to 9.4 lbs per 1000 lbs or 2300 to 9400 ppm based upon the total weight of the formulation to be protected _____	

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Liquid detergents, soft soaps, room deodorizers/air fresheners, water-based surfactants, polymer emulsions, water-based gels for household/industrial products and textiles	47371-189	Incorporation	Should be added to the formulation to be preserved at a rate of 0.2% (2,000 ppm) based upon the total weight of the product to be protected	

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Non-food contact water-based adhesives, latex products, titanium dioxide and calcium carbonate dispersions typically used for paper coatings	47371-190	Incorporation	Use at levels of 4.0 lbs per ton of material being treated (2000 ppm)	

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Aqueous mineral slurry used in the manufacture of paper and paperboard	Soluble concentrate 47371-190 6836-119		4.0 pounds per ton of material being treated (2000ppm) To ensure uniform distribution, slowly disperse product into product with agitation. Mix thoroughly until evenly dispersed throughout product	This product is not to be used for food-contact packaging (6836-119)
Aqueous dispersions of inorganic mineral slurries such as clay, kaolin clay, calcium carbonate and titanium dioxide used in the manufacture of food contact and non-food contact paper and paperboard for both filler and paper coatings applications	6836-307	Incorporation	Should be added to the mineral slurry to be preserved at a rate of 0.05% to 0.30% (500 to 3,000 ppm) based on the total weight of the product to be protected; to ensure uniform distribution, slowly disperse product into product with agitation. Mix thoroughly until evenly dispersed throughout product	

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Metalworking fluids: Electroplating, electro deposition, phosphatizing, galvanizing, and general metal cleaning operations	Soluble concentrate 6836-199 6836-200 6836-271 6836-306 6836-119 _____ 47371-188	Incorporation	To control bacterial and fungal growth in metalworking fluids add at a concentration of 0.05% to 1.00% (500 to 10,000ppm) Re-dose as necessary depending upon the rate of preservation, dilution with makeup fluid, the nature and severity of contamination, level of microbial control required, filtration effectiveness, system design, etc. _____ Should be added to the cleaning fluid to be preserved at a rate of 0.2% (2,000 ppm) based upon the total weight of the solution	None stated _____ Not to be used to preserve fluids that will be used for food-contact packaging
High water-based hydraulic fluids and invert emulsion hydraulic fluids	47371-188	Incorporation	Should be added to the hydraulic fluid to be preserved at a rate of 0.2% (2,000 ppm) based upon the total weight of the solution	

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
Polymer emulsions and natural latex, surfactant solutions, tackifiers derived from rosin and hydrocarbon resins, water-based paints, paint components, stains and coatings for household and industrial use, protective and decorative coatings, water-based adhesives, sealants, joint cements and caulks, latex for paper coatings, water-based gels for industrial products and textiles; and water-based inks	6836-306 47371-188	Incorporation	Product should be added at a rate of 0.05% to 1.00% (500 to 10,000 ppm) based on the total weight of the product to be protected. Should be added to formulation to be preserved at a rate of 0.2% (2,000 ppm) based upon the total weight of the product to be protected	This product is not to be used for food-contact packaging.
Residential and public access premises				

Appendix A. Application and Specific Use Information for DMDM Hydantoin (PC Code 115501) and MDM Hydantoin (PC Code 115502)				
Use Site	**Formulation Type and Reg. No.**	**Method of Application**	**Application Rate/ No. of applications**	**Use Limitations**
(Materials preservative) Liquid detergent, fabric softener, soft soap	Soluble concentrate 47371-189 6836-199 6836-200 5383-111 5383-123 6836-207 _____ Soluble concentrate 6836-111 6836-322	Incorporation	Product should be added to the formulation to be preserved at a rate of 0.1% to 1.0% or 1,000 to 10,000ppm, based upon the total weight of the product to be protected To ensure uniform distribution, slowly disperse product into product with agitation. Mix thoroughly until Evenly dispersed _____ Product should be added to the liquid detergent or soft soap formulation at the rate of 2.5 to 10 pounds per 1000 lbs. or to 2,500 to 10,000ppm based upon the total weight of the formulation	None stated
	Formulation intermediate 6836-112 6836-208			

Appendix B. 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 will provide insight into concerns regarding toxicity via the oral route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study will form the foundation for hazard characterization and toxicity endpoints selection for risk assessment through all exposure routes (oral, inhalation, and dermal). These data will allow the Agency to conclude more definitively whether or not there would be any concerns for oral toxicity in a non-rodent species. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione with regard to the potential risks to the U.S. general population including infants and children as required by the FQPA. **3) How could the data affect the risk assessment?** The study will 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

Appendix B. Toxicity Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		(guideline) oral toxicity study, in order to adequately evaluate real world human exposure to 2,4 Imidazolidinedione based on how it is used.
870.2500	90-Day Dermal 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 dermal route. The needed study will provide insight into concerns regarding toxicity via the dermal route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The data will allow the Agency to conclude more definitively whether or not there would be any concerns for dermal toxicity. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione in regards to the potential risks to the U.S. general population. **3) How could the data affect the risk assessment?** 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 dermal exposure with limited 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) dermal toxicity study, in order to adequately evaluate real world human exposure to 2,4 Imidazolidinedione based on how it is used.

Appendix B. 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 will provide insight into concerns regarding toxicity via the inhalation route. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study may result in a change in how risks are quantified. The data will allow the Agency to conclude more definitively whether or not there would be any concerns for inhalation toxicity in the rat. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione 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 2,4 Imidazolidinedione particles based on how it is used. (The OPPTS Guidelines specify 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 B. 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 study will provide insight into concerns regarding toxicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study may result in a change in how risks are quantified. The data will allow the Agency to conclude more definitively whether or not there would be any concerns for chronic toxicity in the rat. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione in regards to the potential risks to the U.S. general population including infants and children as required 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 2,4 Imidazolidinedione 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 study will provide insight into concerns regarding carcinogenicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study may result in a change in how risks are quantified. The data will allow the Agency to conclude more definitively whether or not there would be any concerns for carcinogenicity in the rat. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione in regards to the potential risks to the U.S. general population including infants and children as required 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 2,4 Imidazolidinedione based on how it is used, particularly used as material preservatives in Metal Working Fluids (MWF) and the fact of releasing formaldehyde, a known carcinogen.

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 study will provide insight into concerns regarding carcinogenicity through long-term exposure. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study may result in a change in how risks are quantified. The data will allow the Agency to conclude more definitively whether or not there would be any concerns for carcinogenicity in the mouse. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione in regards to the potential risks to the U.S. general population including infants and children as required 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 2,4 Imidazolidinedione based on how it is used, particularly used as material preservatives in Metal Working Fluids (MWF) and the fact of releasing formaldehyde, a known carcinogen.

870.3700	Developmental Toxicity Study (Rat)	**1) What is the value of the study?** The study will provide insight into concerns regarding pre- and/or postnatal toxicity as required by FQPA. It may also provide a toxicity endpoint applicable to risk assessment. **2) How will the data be used?** The study may result in a change in how risks are quantified. The data will allow the Agency to conclude more definitively whether or not there are any concerns for pre- and/or postnatal toxicity in the rat. This will provide a more complete hazard characterization of 2,4 Imidazolidinedione 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 rabbit, in order to adequately evaluate real world human exposure to 2,4 Imidazolidinedione, 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 study will 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 applicable to risk assessment. **2) How will the data be used?** The data will 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 will also include neurotoxicity evaluations, it will also provide some information regarding potential neurotoxicity in developing offspring exposed to 2,4 Imidazolidinedione. **3) How could the data affect the risk assessment?** The study may result in a change in how risks are quantified. The 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 reproducitve (guideline) toxicity study in rat, in order to adequately evaluate real world human exposure to 2,4 Imidazolidinedione, particularly women in the 15-49 years of age and infants and children, based on how it is used.

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
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 will be generated. In addition, inhalation exposures from liquid pouring are evident in exposure studies in the Pesticide Handlers Exposure Database (PHED). Finally, there is also the potential for inhalation exposure for machinist using treated metal working fluids (MWF). The potential for the release of and exposure to formaldehyde during the product use also needs to be determined. The existing 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 will the data be used?** The inhalation exposure data will 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 will be used to assess the short- and intermediate-term commercial painters (brush/roller and airless sprayer), up to a long-term duration for machinists using metal working fluids (MWFs), as well as open pouring of the product (e.g., poured into paint as a preservative in manufacturing settings, paper making, etc).

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		The data will also be used to determine if the release of formaldehyde occurs and to what extent. **3) How could the data affect the risk assessment?** The inhalation exposure data will be used to determine the accuracy of the inhalation risks to both residence and occupational workers. If risks warrant mitigation, the inhalation exposure data will 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. **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, machinists, etc.) and evidence of toxicity. If the toxicological endpoints from 5,5-dimethylhydantoin are used to assess the risks, there is an endpoint of concern for the oral route. Note: No inhalation route specific toxicology data are available.
875.1100 and 875.1200 (Applicator)	Dermal Outdoor Exposure and Dermal Indoor Exposure	*Note: Dermal 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. 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 potential for dermal exposure is very likely for exposure scenarios such as paint rollers, airless sprayers, liquid pouring, and for machinist using treated metal working fluids (MWF). The existing 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

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		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 will the data be used?** The dermal exposure data will be used to assess the residential short-term duration of painting with a paint brush/roller and an airless sprayer. For occupational uses, the dermal exposure data will be used to assess the short- and intermediate-term commercial painters (brush/roller and airless sprayer), up to a long-term duration for machinists using metal working fluids (MWFs), as well as open pouring of the product (e.g., poured into paint as a preservative in manufacturing settings, paper making, etc). **3) How could the data affect the risk assessment?** The dermal exposure data will be used to determine the accuracy of the dermal risks to both residence and occupational workers. If risks warrant mitigation, the dermal exposure data will provide the types of mitigation necessary such as chemical resistant gloves or closed systems for commercial uses to potential removal of uses from the label. **4) What is triggering the need for this data?** The criteria for the dermal exposure data are based on the potential for dermal exposure from the labeled uses (e.g., airless sprayers, machinists, etc.) and evidence of toxicity. If the toxicological endpoints from 5,5-dimethylhydantoin are used to assess the risks, there is an endpoint selected for the dermal route.
875.1600	Data Reporting and	**1) What is the value of the study?**

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
(Applicator)	Calculations	For all exposure studies these data are needed to facilitate the review of the data. **2) How will the data be used?** The study report and all raw data/calculations will be reviewed for the adequacy of the data. **3) How could the data affect the risk assessment?** The data are needed to interpret the dermal 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 will provide for a comprehensive realistic assessment of its potential applications. **2) How will the data be used?** The description of the application techniques will be used to define the exposure scenarios to be assessed in the risk assessment. **3) How could the data affect the risk assessment?**

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		A complete description of product use will ensure that the risk assessment is inclusive of the types of exposures occurring during residential and occupational use. **4) What is triggering the need for this data?** The need for a risk assessment as required under Registration Review, will require that the risk assessor understands how the products are applied. These data will provide information on how these products are actually applied.
875.2500 (Post Application)	Inhalation Exposure	**1) What is the value of the study?** The post application inhalation exposure may be needed if it is determined that the use of these products have the potential to release formaldehyde during the product use conditions (e.g., open systems). **2) How will the data be used?** The post application inhalation exposure data will be used to assess the residential and/or occupational inhalation risks to formaldehyde if released based on product use. **3) How could the data affect the risk assessment?** The inhalation exposure data will be used to determine the accuracy of the post application inhalation risks to formaldehyde to both residence and occupational bystanders. If risks warrant mitigation, the inhalation exposure data will 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 C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		4) What is triggering the need for this data? The potential for these products to release formaldehyde is triggering the need for post application exposure data specifically to monitor for formaldehyde.
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 dermal and incidental oral exposure from treated textiles and carpets. Specific data needs for post application dermal exposure can be fulfilled using these residue data. As a first tier to the risk assessment 100% residue transfer is assumed. If no risk concerns are evident, this study will not be needed. If risks of concern are indicated at 100% residue transfer, then this study is needed to refine the assessment. **2) How will the data be used?** This product is used as a material preservative in textiles and as a carpet shampoo. The available residues from clothing and carpets will be used to determine the magnitude of children's dermal and incidental exposure from treated clothing and from treated carpets. **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 and carpets. **4) What is triggering the need for this data?** The specific 2,4 imidazolidinedione uses triggering the criteria for the surface residue data are the potential for dermal incidental oral exposure from the material preservative use in textiles along with the carpet shampoo and evidence of toxicity. If risks of concern are not identified when 100% residue transfer is assumed, the data are

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		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, will provide for a comprehensive realistic assessment of potential post application exposures. **2) How will the data be used?** The listing of the end use consumer products will 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 for textiles may not be needed. **3) How could the data affect the risk assessment?** A complete description of consumer products treated will 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 required under Registration Review will require that the risk assessor understands how the product is applied. These data will enable the risk assessor to understand how the products are applied.

Appendix C: Occupational and Residential Exposure Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
875.2900 (Post Application)	Data Reporting and Calculations	**1) What is the value of the study?** For all exposure studies these data are needed to facilitate the review of the data. **2) How will the data be used?** The study report and all raw data/calculations will 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 as well as hand-to-mouth behavior on treated carpets. **2) How will the data be used?** This product is used as a material preservative in textiles and as a carpet shampoo. The available residues from clothing and carpets will be used to determine the magnitude of children's incidental exposure from treated clothing and carpets.

Appendix C: Occupational and Residential Exposure Guideline Study Justifications		
Guideline	Study Title	Practical Utility of the Data
		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 and carpets. **4)What is triggering the need for this data?** The criteria for the surface residue data is the potential for incidental oral exposure from the material preservative use in textiles/carpets and evidence of toxicity. If risks of concern are not identified when 100% residue transfer is assumed, the data are not needed.

Appendix D: Environmental Fate Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
OPP 161-1	Hydrolysis	**1) What is the value of the study?** Results from the hydrolysis study will indicate the stability and persistence of 2,4 Imidazolidinedione, 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 will the data be used?** Data will 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 2,4 Imidazolidinedione 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 are needed to conduct the fate assessment to support indoor uses for 2,4 Imidazolidinedione.
850.6800	Modified Activated Sludge, Respiration Inhibition	**1) What is the value of the study?** The modified activated sludge respiration inhibition test will 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 will the data be used?** These data will be used to determine the potential of 2,4 Imidazolidinedione to directly harm the nontarget organisms and/or to microbial treatment processes present in a WWTP and to determine suitable noninhibitory concentrations of 2,4 Imidazolidinedione to be used in biodegradability tests.

Appendix D: Environmental Fate Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data
		3) How could the data affect the risk assessment? If the data shows that 2,4 Imidazolidinedione is toxic to nontarget organisms and/or to microbial process found in WWTPs, 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 2,4 Imidazolidinedione 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 will 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 will the data be used?** These data will be used to determine the sorption potential of 2,4 Imidazolidinedione to activated sludge biomass and in biological wastewater treatment systems. **3) How could the data affect the risk assessment?** If 2,4 Imidazolidinedione is not sorbed or biodegraded then, it will pass through a biological treatment system unaffected and it will 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 will enable the Agency to determine the likelihood that the antimicrobial pesticide of biodegrading in aquatic environments under aerobic conditions. **2) How will the data be used?** The results from the data will be used to determine the rate and extent of aerobic biodegradation of 2,4 Imidazolidinedione when it is released into aquatic environments and will help establish if 2,4 Imidazolidinedione is stable or not stable under real environmental conditions. **3) How could the data affect the risk assessment?** If the study results shows low biodegradability then, 2,4 Imidazolidinedione will 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 2,4 Imidazolidinedione.

Appendix E: Ecological Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data:
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 will allow the Agency to categorize formaldehyde releasing hydantoins as toxic or non-toxic to plants. If toxic, additional higher tier plant tests will be needed. An endangered species assessment for endangered or threatened plants is not possible without this study. **2) How will the data be used?** This study will be used to generate a plant toxicity endpoint so the Agency can evaluate the toxicity of formaldehyde releasing hydantoins 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. A plant toxicity endpoint will allow the Agency to determine if endangered or threatened species are at risk or if aquatic non-target plants are impacted before and after passing through WWTP into surface waters. **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. Data are needed to conduct ecological and endangered species assessments for down the drain uses as described above.
850.2100*	Acute avian oral LD50 toxicity	**1) What is the value of the study?** This study will allow the Agency to determine the toxicity of technical formaldehyde releasing hydantoins to birds. Conducting an endangered species assessment for birds is not possible without this endpoint. **2) How will the data be used?** This study will be used for hazard labeling in the event a spill of manufacturing use product occurs.

Appendix E: Ecological Guideline Study Justifications

Guideline	Study Title	Practical Utility of the Data:
		3) How could the data affect the risk assessment? If avian acute oral toxicity is 100 mg/Kg or less, in accordance with 40 CFR 156.85, the label must state: "This pesticide is toxic to birds." An avian toxicity endpoint will allow the Agency to determine if endangered or threatened species are at risk in the terrestrial and aquatic environments. **4) What is triggering the need for this data?** The Agency must determine if formaldehyde releasing hydantoins are toxic to birds. This is a Tier I screening level study representative of all birds. Data are needed to conduct ecological and endangered species assessments for down the drain uses as described above.
850.1075*	Acute freshwater fish toxicity	**1) What is the value of the study?** This study will allow the Agency to determine the toxicity of technical formaldehyde releasing hydantoins to freshwater fish. An endangered species assessment for fish is not possible without this endpoint. **2) How will the data be used?** This study will be used for hazard labeling in the event a spill of manufacturing use product occurs. **3) How could the data affect the risk assessment?** If the acute freshwater fish toxicity is 1.0 ppm or less, in accordance with 40 CFR 156.85, the label must state: "This pesticide is toxic to fish." A fish toxicity endpoint will allow the Agency to determine if endangered or threatened species are at risk in the terrestrial and aquatic environments. . **4) What is triggering the need for this data?** The Agency must determine if formaldehyde releasing hydantoin technical grade is toxic to fish. This is a Tier I screening level study representative of all freshwater fish. Data are needed to conduct ecological and endangered species assessments for down the drain uses as described above. .

850.1010*	Acute freshwater invertebrate toxicity using *Daphnia magna*	**1) What is the value of the study?** This study will allow the Agency to determine the toxicity of formaldehyde releasing hydantoins to freshwater aquatic invertebrate. An endangered species assessment for freshwater invertebrates is not possible without this endpoint. **2) How will the data be used?** This study will be used for hazard labeling in the event a spill of manufacturing use product occurs. **3) How could the data affect the risk assessment?** If the acute freshwater invertebrate toxicity is 1.0 ppm or less, in accordance with 40 CFR 156.85, the label must state: "This pesticide is toxic to aquatic invertebrates." A freshwater invertebrate toxicity endpoint will allow the Agency to determine if endangered or threatened species are at risk in the terrestrial and aquatic environments. **4) What is triggering the need for this data?** The Agency must determine if formaldehyde releasing hydantoins are toxic to freshwater aquatic invertebrates. This is a Tier I screening level study representative of all freshwater aquatic invertebrates. Data are needed to conduct ecological and endangered species assessments for down the drain uses as described above.