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August 29, 2011

Ms. Susan Bartow
Pesticide Re-evaluation Division (PRD)
OPP Regulatory Public Docket (7502P)
U.S. Environmental Protection Agency
Room S-4400, One Potomac Yard (South Bldg.)
2777 S. Crystal Drive
Arlington, VA 22202

Subject: EPA Docket ID: EPA-HQ-OPP-2011-0464
Comments on the Registration Review of Fipronil (Case #7423)

Dear Ms. Bartow:

BASF Corporation ("BASF") submits the below comments to the U.S. Environmental Protection Agency ("EPA") related to the Registration Review of fipronil, which opened under EPA Docket ID: EPA-HQ-OPP-2011-0464 ("Docket") on June 29, 2011.

NOTE: throughout these comments the following should be remembered with regard to nomenclature:

- "Fipronil" refers to the parent molecule *and* any metabolites and degradates. In addition, the code MB46030 and Fipronil Technical are synonymous.
- "Fipronil (parent)" refers only to the parent molecule. Most occurrences list it as such; however, when restating from other sources, only the term "parent" is used.
- "Fipronil sulfide (MB45950)" is a metabolite. Most occurrences list it as such; however, when restating from other sources, the naming convention used by the source is preserved.
- "Fipronil sulfone (MB46136)" is a metabolite. Most occurrences list it as such; however, when restating from other sources, the naming convention used by the source is preserved.
- "MB46513" refers to the photolysis degradate.

BASF appreciates the opportunity to both review and make comments related to the Docket. The availability of information electronically on regulations.gov is an important

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tool to registrants and the general public. If EPA has any questions regarding these comments, please contact me directly at (919) 547-2282, or by e-mail at: amy.s.dugger-ronyak@basf.com.

Best regards,

BASF Corporation – Agricultural Solutions

Amy Dugger-Ronyak, Product Registration Manager

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I. Overall Comments Related to EPA's Preliminary Work Plan for Fipronil

BASF manufactures fipronil for use in numerous EPA-registered end-use formulations. BASF is committed to the continued registration of products containing fipronil for all currently approved use sites and pests. BASF products containing fipronil are registered in the United States ("U.S.") to control termites and a wide variety of insect pests, both in crop and non-crop applications. These registrations are supported by an extensive human health, safety and environmental database. Since its first U.S. registration, products containing fipronil have had a long history of safe use and provide some of the best insecticide tools in the market today. This is particularly important for termite control and management throughout the U.S.

In its entirety, these comments should provide EPA the needed clarification of the current BASF-registered products and uses and highlight the supporting data that have previously been submitted to the Agency but that have not been reviewed and considered with the Preliminary Work Plan. Using the information provided herein, EPA should be able to more accurately assess, prior to the issuance of the Final Work Plan and/or Data Call-In, what data are truly required. Please note that also provided are comments related to specific EPA reviews.

Given the extent of BASF's comments, the errors within the Docket's supporting documents, and the studies that have been previously submitted to the Agency but that have not been reviewed and thus were not considered when drafting the Docket's supporting documents, BASF requests that EPA take the time to address all comments submitted to the docket, including requests to review previously submitted data before issuing the Final Work Plan and subsequent Data Call-In. Without such steps the Final Work Plan issued by the Agency will not accurately reflect what is already known about fipronil and thus not reflect what additional data may be required. **Given the magnitude of the changes that will need to occur, BASF respectfully requests that a 2nd comment period should be issued before the Final Work Plan.**

II. Overall Comments Related to EPA's Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Fipronil ("Preliminary Problem")

It is of importance to note that the Preliminary Problem is extremely general in nature and therefore does not accurately address the varied specific use patterns of currently

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registered fipronil end-use formulations. Several use patterns EPA has listed in the Problem Formulation are not applicable to the U.S. (e.g., aerial foliar spray application by airplane or helicopter for foliar sprays of crops or, likewise, direct foliar application of any kind) as there are no currently registered fipronil end-use products with these use patterns.

Given the diversity of fipronil use patterns, a Problem Formulation that is specific to each use pattern and the end-use products that fall within that use pattern should be prepared by EPA to accurately reflect what is currently understood about the molecule and what additional data may need to be generated. Without this separation by use pattern of the Problem Formulation, it is extremely difficult to understand why EPA is considering requiring certain data.

That said, BASF understands that EPA's data requirements have evolved since the initial registration of fipronil. Consequently, there may be some data requirements that need to be filled. EPA should acknowledge, however, that many higher tiered studies in the areas of environmental fate and ecotoxicology have already been conducted and submitted to the Agency. Extensive high-quality environmental monitoring data exists both in industry studies and in the open literature. Therefore, before finalizing any data requirements to be fulfilled during Registration Review and the subsequent Data Call-In, the data from these "real world" environmentally relevant studies should be fully considered. Many have already been submitted to EPA and are discussed further in later sections of this submission.

Regulatory data requirements to support EPA pesticide registrations are conducted according to a tiered system. Several of the data requirements listed by EPA in the Problem Formulation are indoor laboratory studies (almost exclusively Tiers I and II). BASF argues that many of the outdoor field "real world" studies (Tier III and Tier IV), that could potentially be triggered by laboratory studies, have been conducted and have either already been or can be submitted to the Agency. Therefore, it is unclear what the value of the additional laboratory data would be. Likewise, these types of studies do not seem appropriate (1) for an active ingredient that has been registered and studied since the mid-1980s or (2) in terms of animal welfare issues.

<u>In determining ecotoxicological data gaps, it should be noted that:</u>

- Generally speaking, if an organism is sensitive to fipronil (parent), it is sensitive to its metabolites and degradates (e.g., aquatic invertebrates). Conversely, if an organism is not sensitive to fipronil (parent), it is not sensitive to its metabolites or degradates (e.g., terrestrial non-target plants).
- Not all organisms are sensitive to fipronil (parent) or its metabolites and degradates (e.g., terrestrial non-target plants).

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III. Identification of Errors in Documents Listed in the Public Docket

Fipronil Summary Document Registration Review: Initial Docket, June 2011 [Docket ID: EPA-HQ-OPP-2011-0448-0003]

The below errors or comments should be noted.

- *EPA Statement:* Page 4, paragraph 3, last sentence: "Fipronil degrades to form persistent and immobile degradates—fipronil sulfide (MB45950), fipronil sulfone (MB46136), and MB46513."
    - *BASF Response:* Fipronil sulfide (MB45950) and fipronil sulfone (MB46136) are animal metabolites, while MB46513 is a photolysis degradate.

- *EPA Statement:* Page 4, paragraph 4, last sentence [and all other Docket occurrences]: "Fipronil was first registered in 1985…"
    - *BASF Response:* While there were Experimental Use Permits (EUPs) for fipronil in the mid-to-late 1980s, EPA did not grant the first registrations until May 1996 (technical and end-use products).

- *EPA Statement*: Page 10-11, *Request for Additional Information:*
    - *BASF Response:* BASF is reviewing and compiling information related to our registered products. This will be provided to EPA in a separate submission.

- *EPA Statement:* Page 12, *Use & Usage Information*, last bullet [and all other Docket occurrences]: "Application equipment includes low pressure…airplane, and helicopter."
    - *BASF Response:* No currently registered fipronil products permit aerial foliar spray application by airplane or helicopter for foliar use on crops.

- *EPA Statement:* Page 13, *Ecological Risk Assessment Status*, second bullet:
    - *BASF Response:* Many of the "risk concerns" relate to a specific product or use pattern. Therefore, it is inaccurate to infer (as the bullets do) that these "risk concerns" pertain to the molecule as a whole or to all uses. As with any pesticide, certain products or use patterns have more "risk concern" than others. As such, EPA should specify which "risk concern(s)" go with which products and use

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patterns. Only then can registrants and the public understand the reasoning behind potential data requirements.

- *EPA Statement:* Page 16-17, Incidents:
    - *BASF Response:* EPA indicated that between 2000 and 2010 4,243 incidents involving fipronil were reported. As EPA states in the **Fipronil: Review of Human Incidents dated March 1, 2011 [Docket ID: EPA-HQ-OPP-2011-0448-0005]** "Reports of adverse health effects allegedly due to a specific pesticide exposure (i.e., an "incident") are largely self-reported and therefore, generally speaking, neither exposure to a pesticide or reported symptom (or the connection between the two) is validated. Typically, causation cannot be determined based on incident data." And while BASF agrees with EPA that incident information can be an important feedback loop, it is equally important for EPA to acknowledge that reported incidents are just that, reported incidents and not confirmed. Additionally, in all likelihood, many incidents probably occurred from off-label use and/or misuse of the product, not due to the toxicity of fipronil to humans, animals or the environment.

      While usage data is typically proprietary, in a press release in 2009, a company stated in response to an EPA advisory for products containing fipronil that are used as pet spot-on treatments that since 1996, when the product was first registered, **over 1 billion** doses have been sold. That is approximately 80 million per year for this one use site.

Fipronil. Human Health Risk Assessment Scoping Document in Support of Registration Review (dated May 24, 2011) [Docket ID: EPA-HQ-OPP-2011-0448-0004]

- *EPA Statement:* Page 7 (last two paragraphs) and page 28 (Table 2) [and all other Docket occurrences]:
    - *BASF Response:* The term "neuromuscular toxicity" is used, while a more appropriate term to describe the effects of fipronil would be "neurological toxicity" or "neurotoxicity".

- *EPA Statement:* Page 25 (Table 2) [and all other Docket occurrences]:
    - *BASF Response:* The body weight gain changes in the 90-day oral toxicity studies in the mouse and dog are described as "increased", while they were actually "decreased" in the studies.

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Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Fipronil (PC Code 129121; DP 387319) *(dated May 4, 2011)* *[Docket ID: EPA-HQ-OPP-2011-0448-0006]*

- *EPA Statement:* Page 5, paragraph 1: "Current outdoor uses include…in-furrow treatment for control of corn root worm on corn…"
    - *BASF Response:* There are no currently registered products that permit in-furrow treatment for control of corn root worm on corn. Likewise for bait treatments for Texas leaf-cutter ants.

- *EPA Statement:* Page 6, *Conclusions from Previous Risk Assessments*: "Fipronil was first registered in 1993."
    - *BASF Response:* While there were EUPs for fipronil in the mid-to-late 1980s, EPA did not grant the first registrations for fipronil until May 1996 (technical and end-use products).

- *EPA Statement:* Pages 7-8, *Drinking Water Exposure Assessments*: "From the registered and proposed uses for fipronil, the highest concentration… The proposed use on in-furrow corn and rutabagas…."
    - *BASF Response:* There are no pending proposed or current fipronil registrations that permit application to onion seed or in-furrow corn treatments. The registration for rutabaga/turnip use is a Section 18 Emergency Exemption requested by the state of Oregon, and subsequently granted by EPA under FIFRA, to control cabbage maggot. Only currently approved uses should be taken into account when calculating the ground water exposure concentrations.

- *EPA Statement:* Page 8, *Stressor Source and Distribution*, paragraph 1 [as well as occurrences on page 10 in Figure 1 and page 11], "The current and proposed new uses..." and "The use pattern includes…"
    - *BASF Response:* Soil injection for termite control is missing. Also, there is no direct foliar corn use, only treated corn seed that is exported from the U.S. Therefore, direct application to corn should not be considered in any risk assessment.

- *EPA Statement:* Page 10: "Proposed uses of fipronil on sweet potato…"
    - *BASF Response:* There is no proposed or currently approved use on sweet potato.

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- *EPA Statement:* Page 11, paragraph 1: "The proposed pine seedling use…" and "The proposed perimeter house treatment…"
    - *BASF Response:* This pine seedling use was approved and is on the label of a currently registered end-use product. Likewise, perimeter house treatments using fipronil were approved.

- *EPA Statement:* Page 11, paragraph 2: "The screening level use assessment…"
    - *BASF Response:* There are no currently registered products that permit in-furrow treatment of corn, only seed treatment of corn that is exported from the U.S. Based on BASF-known amounts of fipronil used to manufacture formulations for seed treatment of corn that is exported, the screening-level assessment data is incorrect.

- *EPA Statement:* Page 12, *Environmental Fate and Transport*
    - *BASF Response:*
        - For paragraph 1, the Problem Formulation needs corrected to read, "Fipronil degrades to form the…metabolites fipronil sulfide (MB45950) and fipronil sulfone (MB46136) and the photolytic degradate MB46513.
        - As stated by EPA on page 16 of the Problem Formulation, a previously submitted soil column leaching study (a higher tier study) confirmed the immobility of fipronil. As such, EPA should remove the statement "However, fipronil residue may…" from the Problem Formulation.
        - A higher tier study was conducted to characterize the degradation of fipronil in an outdoor sediment-water system using kinetics models, and to estimate simple first-order degradation rates of fipronil and its metabolites fipronil sulfide (MB45950) and fipronil sulfone (MB46136) and the photolytic degradate MB46513. Concentrations of all four in water and sediment were measured over time in a simulated pond study and were used to derive parameters describing the fate of the compounds in sediment-water systems under outdoor conditions. Based on the fipronil degradation pathway in the environment and the results of the simulated pond study, simple first-order kinetic models were developed to describe the degradation of fipronil and its metabolites in the sediment-water system. The kinetic models, and thus the study, show that the two metabolites and the photolytic degradate degraded significantly faster in the environment

than in the laboratory. *(MRID No. 46936101: Tang, Z.; Ramanarayanan, T. (2006) Degradation of Fipronil and Its Major Metabolites Following Application of Chipco TopChoice Leachate to Outdoor Simulated Ponds: Kinetics Modeling. Project Number: MEFIX003/1, 2006/7010025. Unpublished study prepared by Bayer Corp. 25p.)*

- *EPA Statement:* Page 13, *Table 2*:
  - *BASF Response:* EPA needs to include the "real world" data from MRID No. 47245001 in Table 2. *(Burton, G.; LaPoint, T.; Kennedy, J.; *et. al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems: Final Report. Project Number: 2007/7009480, 47152301, 46936104. Unpublished study prepared by BASF Corporation, University of North Texas and Wright State University. 1013p.*)

- *EPA Statement:* Page 17, *Aquatic Field Dissipation*:
  - *BASF Response:* The stated information includes data related to use on rice. There is no direct application to rice registered in the U.S. As such, EPA needs to acknowledge that these uses are no longer relevant.

- *EPA Statement:* Page 20, *Effects on Terrestrial Organisms*, paragraph 2, last sentence, "Only the parent has been tested for reproductive effects in mammals…"
  - *BASF Response:* This statement is incorrect. Both animal metabolites MB45950 and MB46136 would have been evaluated in all animal studies (including reproductive studies) in which fipronil was tested as they are both significant animal metabolites.

- *EPA Statement:* Page 21, *Ecological Incidents*, paragraph 1, last sentence, "The degree to which the low number of years of outdoor use…"
  - *BASF Response:* Fipronil has been registered in the U.S. since 1996 with EUP trials dating further back. Thus, at a minimum, there is 15 years worth of data, which is not a low number of years.

- *EPA Statement:* Page 23, *Risk Hypothesis*, 2nd paragraph, "Application to foliar surfaces may serve…"
  - *BASF Response:* There are no products registered in the U.S. that permit foliar application of fipronil.

- *EPA Statement:* Pages 23-25, *Conceptual Diagram*:
  - *BASF Response:* The conceptual models need substantial revision as they do not reflect the exposure pathways for fipronil. Routes that

may not significantly contribute to risk are spray drift, leaching to groundwater, atmospheric transport, wet/dry deposition from atmospheric transport, ingestion. There may need to be conceptual models by specific use patterns.

- *EPA Statement:* Page 27, paragraph 3:
  - *BASF Response:* EFAST, the model referenced by EPA, is not one of EPA's standard water models used for exposure assessment. As such, EPA needs to provide further information to justify the appropriate use of the model for exposure assessment (e.g. has the model been reviewed by SAP, for what fipronil uses is the model suitable).

- *EPA Statement:* Page 28, paragraph 2: *"Available monitoring data will be used* to qualitatively characterize exposure and compare with modeling results … monitoring conducted by water management agencies…""
  - *BASF Response*: BASF agrees that available monitoring data should be considered in characterizing fipronil exposure. The following monitoring studies already been submitted by registrants, MRID Nos. 4743830, 46733902, 46733903, 46733904, 46733905)

- *EPA Statement:* Page 28, paragraph 3: "Two spray drift models…will be used to assess exposure…"
  - *BASF Response:* There are no registered foliar applications of fipronil; therefore, using these models does not make sense.

- *EPA Statement:* Page 29, *Integration of Exposure and Effects*:
  - *BASF Response:* There are no registered terrestrial non-food crop field corn uses.

- *EPA Statement:* Page 32, Table 4, 158 Guideline 162-2:
  - *BASF Response:* EPA's note in the comment column is not a correct statement. Anaerobic soil degradation rates are not required for exposure modeling, thus conducting a study will not provide relevant data for exposure and risk assessment purposes.

- *EPA Statement:* Pages 43-50, Appendix 1 of the Problem Formulation, *Currently Registered Uses for Fipronil*:
  - *BASF Comment:* Page 47 lists corn, field as terrestrial non-food + residential. This is incorrect. As a seed treatment, it should be terrestrial food + feed crop.

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- *EPA Statement:* Appendix 3 of the Problem Formulation. *Available effects data from most recent ecological risk assessment in 2007:*
    - *BASF Response:* Appendix 3 does not make reference to or include any of the data from MRID No. 46619103 *(Fipronil - Life-Cycle Toxicity Test with Mysids (Americamysis bahia) Under Static Conditions in a Water Sediment System. Project Number: 986/6163, 198247, 2005/5000047. Unpublished study prepared by Springborn Smithers Laboratories. 68p*), a higher tier study ran under more environmentally realistic conditions. The resulting NOEC is twelve times higher than that generated in MRID No. 43681201 *(Machado, M. (1995) Fipronil--Chronic Toxicity to Mysids (Mysidopsis bahia) Under Flow-Through Conditions: Final Report: Lab Project Number: 95-4-5820: 10566.1294.6353.530. Unpublished study prepared by Springborn Labs, Inc. 107p.)*
    - *BASF Response:* On page 68, EPA states that no NOEC was achieved in the chronic mysid toxicity study. This is incorrect. After an extensive review of this study, as stated in several EPA Memoranda, it was determined that a NOEC of 0.005 ug/L was reached.
    - *BASF Response:* On page 70, in the 2nd paragraph, EPA states that only an interim report has been submitted for the sediment recolinization study. This is incorrect. The final report for the sediment recolinization study was submitted to EPA on October 2, 2007 as MRID No. 47245001. *(Burton, G.; LaPoint, T.; Kennedy, J.; *et. al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems: Final Report. Project Number: 2007/7009480, 47152301, 46936104. Unpublished study prepared by BASF Corporation, University of North Texas and Wright State University. 1013p.)* Also, in the last sentence EPA refers to "…the drafting of this risk assessment." This is a typo and should be Problem Formulation.

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IV. BASF Response to EPA-Anticipated Data Requirements as Listed in the Fipronil Summary Document [DocketID: EPA-HQ-OPP-2011-0448-0003]

Guideline Number: 835.4400
Study Type: Anaerobic Aquatic Metabolism
Test Substance: Fipronil sulfide (MB45950)
BASF Response: The environmental monitoring database for fipronil (and its metabolites and degradates) is extensive. As, such there is little to be gained by gathering additional anaerobic aquatic metabolism laboratory data since anaerobic data are not used for risk assessment purposes and, thus, have no impact on risk decisions. Consequently, BASF requests that this EPA-anticipated data requirement be waived.

EPA can review specific relevant data found in the following article from the open literature: Lin K, Haver D, Oki L, and Gan J 2009. Persistence and Sorption of Fipronil Degradates in Urban Stream Sediments. *Environmental Toxicology and Chemistry* Vol. 28, No. 7, pp. 1462-1468. BASF is submitting this report for EPA to review and consider. See Appendix 1.

Guideline Number: 835.4400
Study Type: Anaerobic Aquatic Metabolism
Test Substance: Fipronil sulfone (MB46136)
BASF Response: The environmental monitoring database for fipronil (and its metabolites and degradates) is extensive. As, such there is little to be gained by gathering additional anaerobic aquatic metabolism laboratory data since anaerobic data are not used for risk assessment purposes and, thus, have no impact on risk decisions. Consequently, BASF requests that this EPA-anticipated data requirement be waived.

EPA can review specific relevant data found in the following article from the open literature: Lin K, Haver D, Oki L, and Gan J 2009. Persistence and Sorption of Fipronil Degradates in Urban Stream Sediments. *Environmental Toxicology and Chemistry* Vol. 28, No. 7, pp. 1462-1468. BASF is submitting this report for EPA to review and consider. See Appendix 1.

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Guideline Number: 835.4400
Study Type: Anaerobic Aquatic Metabolism
Test Substance: MB46513 (photolytic degradate)
BASF Response: The environmental monitoring database for fipronil (and its metabolites and degradates) is extensive. As, such there is little to be gained by gathering additional anaerobic aquatic metabolism laboratory data since anaerobic data are not used for risk assessment purposes and, thus, have no impact on risk decisions. Consequently, BASF requests that this EPA-anticipated data requirement be waived.

EPA can review specific relevant data found in the following article from the open literature: Lin K, Haver D, Oki L, and Gan J 2009. Persistence and Sorption of Fipronil Degradates in Urban Stream Sediments. *Environmental Toxicology and Chemistry* Vol. 28, No. 7, pp. 1462-1468. BASF is submitting this report for EPA to review and consider. See Appendix 1.

Guideline Number: 850.1010
Study Type: Freshwater Invertebrate Acute
Test Substance: Fipronil sulfone (MB46513)
BASF Response: It is not expected that this data requirement will add meaningful information to the risk assessment. The estuarine/marine invertebrate (mysid shrimp) is clearly more sensitive than the freshwater invertebrate (daphnid) with fipronil (parent). Additionally, aquatic invertebrates are consistently more sensitive to MB46136 than MB46513. As such, BASF requests that this EPA-anticipated data requirement be waived.

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Guideline Number: 850.1300
Study Type: Freshwater Aquatic Invertebrate Life-Cycle
Test Substance: Fipronil sulfide (MB45950)
BASF Response: A freshwater aquatic invertebrate (*Daphnia magna*) life-cycle study was conducted with MB45950 *(MRID No. 42918670: McNamara, P. (1990) MB45950 -- Chronic Toxicity to Daphnids (Daphnia magna) Under Flow-through Conditions: Final Report: Lab Project Number: 90-4-3292: 10566.1089.6147.130. Unpublished study prepared by Springborn Laboratories Inc. 76p)*, and reviewed by EPA and considered invalid. However, the EPA reviewer did not have the raw data at the time of the review. At the request of the reviewer, the raw data were subsequently submitted *(MRID No. 43291724: Mihaich, E. (1994) Raw Data Submission Pertaining to (MB45950): Chronic Toxicity to Daphnids (Daphnia magna) under Flow-Through Conditions: Addendum: Lab Project Number: 90/4/3292. Unpublished study prepared by Rhone-Poulenc Ag Co. 63p.)* The results of the data review are unknown and it is not clear if the status of the study changed after EPA reviewed the raw data. BASF requests that EPA review the history of this submission and provide its conclusion to BASF and the public prior to the release of the Final Work Plan.

It should be noted that a NOEC of 13 µg/L was obtained from the original MB45950 study *(MRID No. 42918670: McNamara, P. (1990) MB45950 -- Chronic Toxicity to Daphnids (Daphnia magna) Under Flow-through Conditions: Final Report: Lab Project Number: 90-4-3292: 10566.1089.6147.130. Unpublished study prepared by Springborn Laboratories Inc. 76p.)* A significantly lower NOEC of 0.63 µg/L was obtained from the same type of study conducted with MB46136. As aquatic invertebrates are consistently more sensitive to MB46136 than MB45950, repeating a freshwater aquatic invertebrate life-cycle study with MB45950 is not expected to provide meaningful information for risk assessment purposes. Currently, effect levels listed in the public literature on black fly are driving the risk assessment (refer to Overmyer, J.P., B.N. Mason, K.L. Armbrust. 2005. Acute toxicity of imidacloprid and fipronil to a nontarget aquatic insect, *Simulium vittatum* Zetterstedt cytospecies IS-7. Bull. Environ. Toxicol. 74:872-879). Given all the data generated to date, a new study is not expected to provide significant new information. As such, BASF requests that this EPA-anticipated data requirement be waived.

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Guideline Number: 850.1300
Study Type: Freshwater Aquatic Invertebrate Life-Cycle
Test Substance: Fipronil sulfone (MB46136)
BASF Response: A freshwater aquatic invertebrate (*Daphnia magna*) life-cycle study was conducted with MB46136 and submitted to EPA *(MRID No. 42918672: McNamara, P. (1992) MB46136 -- Chronic Toxicity to Daphnids (Daphnia magna) Under Flow-through Conditions: Lab Project Number: 91-8-3886: 10566.1090.6175.130. Unpublished study prepared by Springborn Laboratories, Inc. 83p.)* The raw data were subsequently submitted to EPA *(MRID No. 43291725: Mihaich, E. (1994) Raw Data Submission Pertaining to (MB46136): Chronic Toxicity to Daphnids (Daphnia magna) under Flow-Through Conditions: Addendum: Lab Project Number: 91/8/3886. Unpublished study prepared by Rhone-Poulenc Ag Co. 62p.)* BASF has never received a Data Evaluation Record (DER) from EPA for this study, nor is it mentioned in EPA's Problem Formulation. As such, BASF is unsure of its classification. BASF requests that EPA inform BASF of the status of this study. **NOTE**: Regardless of the study classification for MRID 43291725, given the relative insensitivity of daphnids, it is not clear to BASF what value these data would contribute to the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.1350
Study Type: Estuarine/Marine Invertebrate Life-Cycle
Test Substance: Fipronil (parent)
BASF Response: A fipronil mysid chronic study *(MRID No. 43681201: Machado, M. (1995) Fipronil -- Chronic Toxicity to Mysids (Mysidopsis bahia) Under Flow-Through Conditions: Final Report: Lab Project Number: 95-4-5820: 10566.1294.6353.530. Unpublished study prepared by Springborn Labs, Inc. 107p)* was submitted to EPA and classified as supplemental. On August 2, 1996 EPA authored a memorandum defining the chronic endpoint from the study and concluding that no new study was required. A copy of this memorandum is attached in Appendix 2.

Additionally, a higher tiered mysid life-cycle study *(MRID No. 46619103: Cafarella, M. (2005) Fipronil - Life-Cycle Toxicity Test with Mysids (Americamysis bahia) Under Static Conditions in a Water Sediment System. Project Number: 986/6163, 198247, 2005/5000047. Unpublished study prepared by Springborn Smithers Laboratories. 68 p)* was conducted and submitted for EPA review. This study,

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which EPA did not mention in the Problem Formulation, was run under more environmentally realistic conditions, resulted in an NOEC twelve times higher than the one from the original study. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.1350
Study Type: Estuarine/Marine Invertebrate Life-Cycle
Test Substance: MB46513 (photolytic degradate)
BASF Response: Aquatic invertebrates are consistently more sensitive to MB46136 than MB46513. The NOEC for MB46513 is expected to be at least an order of magnitude greater than the NOEC for MB46136. If conducted, data from a mysid life-cycle with MB46513 is not expected to inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.1400
Study Type: Freshwater Fish Early Life Stage
Test Substance: Fipronil sulfide (MB45950)
BASF Response: The fipronil metabolite MB45950 was identified in freshwater bioaccumulation studies *(MRID No. 43291706: Chapleo, S.; Hall, B. (1992) (Carbon 14)-MB46030: Bioaccumulation Test in Bluegill Sunfish: Lab Project Number: 381457: 8892. Unpublished study prepared by Inveresk Research International. 95p; MRID No. 43291707: Roohi, A.; Coote, A.; Savage, E. (1993) (Carbon 14) MB46030: Investigation into the Nature and Possible Structures of Metabolites in Fish used in a Bioaccumulation Study at Inveresk Research International (Study IRI/381457): Lab Project Number: P/92/302. Unpublished study prepared by Rhone-Poulenc Agriculture Ltd. 62p; and MRID No. 44298002: Theissen, R. (1997) Fipronil (MB46030): Bioaccumulation in Bluegill Sunfish: Supplemental Response for Storage Stability Data (for MRID Nos. 43291706 & 43291707): Lab Project Number: IRI 381457: RPAL P92/302: IRI 381457/RPAL/P92/302. Unpublished study prepared by Rhone-Poulenc Ag Co. 8p)* and would have also been formed via metabolism during the freshwater fish early life stage study *(MRID No. 42918627: Machado, M. (1992) MB46030 - The Toxicity to Rainbow Trout (Oncorhyncus mykiss) during an Early Life-stage Exposure: Amended Final Report: Lab Project Number: 92-1-4084:10566. 0391.6209.121. Unpublished study prepared by Springborn Laboratories, Inc. 81p)* with fipronil (parent). Given that each of

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these studies resulted in exposure to MB45950, this data requirement would not result in new information and should not be required. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.1400
Study Type: Freshwater Fish Early Life Stage
Test Substance: Fipronil sulfone (MB46136)
BASF Response: Fipronil metabolite MB46136 was identified in freshwater bioaccumulation studies *(MRID No. 43291706: Chapleo, S.; Hall, B. (1992) (Carbon 14)-MB46030: Bioaccumulation Test in Bluegill Sunfish: Lab Project Number: 381457: 8892. Unpublished study prepared by Inveresk Research International. 95p; MRID No. 43291707: Roohi, A.; Coote, A.; Savage, E. (1993) (Carbon 14) MB46030: Investigation into the Nature and Possible Structures of Metabolites in Fish used in a Bioaccumulation Study at Inveresk Research International (Study IRI/381457): Lab Project Number: P/92/302. Unpublished study prepared by Rhone-Poulenc Agriculture Ltd. 62p; and MRID No. 44298002: Theissen, R. (1997) Fipronil (MB46030): Bioaccumulation in Bluegill Sunfish: Supplemental Response for Storage Stability Data (for MRID Nos. 43291706 & 43291707): Lab Project Number: IRI 381457: RPAL P92/302: IRI 381457/RPAL/P92/302. Unpublished study prepared by Rhone-Poulenc Ag Co. 8p)* and would have also been formed via metabolism during the freshwater fish early life stage study *(MRID No. 42918627: Machado, M. (1992) MB46030 - The Toxicity to Rainbow Trout (Oncorhyncus mykiss) during an Early Life-stage Exposure: Amended Final Report: Lab Project Number: 92-1-4084:10566. 0391.6209.121. Unpublished study prepared by Springborn Laboratories, Inc. 81p)* with fipronil (parent). Given that each of these studies resulted in exposure to MB46136, this data requirement would not result in new information and should not be required. As such, BASF requests that this EPA-anticipated data requirement be waived.

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Guideline Number: 850.1400
Study Type: Freshwater Fish Early Life Stage
Test Substance: MB46513 (photolytic degradate)
BASF Response: If this data requirement is requested in the Data Call-In, BASF recommends testing the sheepshead minnow in lieu of the fathead minnow as freshwater and marine fish species are nearly equally sensitive to fipronil and its metabolites and degrades and there is more relevant data for the sheepshead minnow than fathead minnow.

Guideline Number: 850.1500
Study Type: Estuarine Marine Fish Early Life Stage
Test Substance: Fipronil sulfide (MB45950)
BASF Response: MB45950 was formed during a fish (bluegill sunfish) bioaccumulation study and would have also been formed via metabolism (and consequently tested, albeit indirectly) during the estuarine marine fish early life stage studies with fipronil (parent) *(MRID No. 44605501: Sousa, J. (1998) Fipronil Technical-Early Life-Stage Toxicity Test with Sheepshead Minnow (Cyprinodon variegatus): Final Report: Lab Project Number: 96-12-6799: 10566.0796.6402.520. Unpublished study prepared by Springborn Laboratories, Inc. 89p)* and fish full life-cycle *(MRID No. 45265101: Dionne, E. (2000) Fipronil-Chronic Toxicity to the Sheepshead Minnow (Cyprinodon variegatus) During a Full Life-Cycle Exposure: Lab Project Number: 10566.6580: 16958. Unpublished study prepared by Springborn Laboratories, Inc. 469p.)* Additionally, the acute LC50 values for MB45950, MB46513 and MB46136 are nearly identical for the trout; the acute LC50 values for MB46513 and MB46136 are nearly identical for the bluegill; and the acute LC50 value for fipronil (parent) in the sheepshead minnow falls between the LC50 values for the bluegill and trout. Taken together, these data suggest that the results of an estuarine marine fish early life stage study with MB45950 will be similar to those with MB46513, which should be an appropriate surrogate for the other metabolites. Since BASF agrees with EPA that an estuarine/marine fish early life stage study with MB46513 should be conducted, BASF requests that the EPA-anticipated data requirement for MB45950 be waived.

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Guideline Number: 850.1500
Study Type: Estuarine Marine Fish Early Life Stage
Test Substance: Fipronil sulfone (MB46136)
BASF Response: MB46136 was formed during a fish (bluegill sunfish) bioaccumulation study and would have also been formed via metabolism (and consequently tested, albeit indirectly) during the estuarine marine fish early life stage studies with fipronil (parent) *(MRID No. 44605501: Sousa, J. (1998) Fipronil Technical-Early Life-Stage Toxicity Test with Sheepshead Minnow (Cyprinodon variegatus): Final Report: Lab Project Number: 96-12-6799: 10566.0796.6402.520. Unpublished study prepared by Springborn Laboratories, Inc. 89p)* and fish full life cycle *(MRID No. 45265101: Dionne, E. (2000) Fipronil-Chronic Toxicity to the Sheepshead Minnow (Cyprinodon variegatus) During a Full Life-Cycle Exposure: Lab Project Number: 10566.6580: 16958. Unpublished study prepared by Springborn Laboratories, Inc. 469p.)* Additionally, the acute LC50 values for MB45950, MB46513 and MB46136 are nearly identical for the trout; the acute LC50 values for MB46513 and MB46136 are nearly identical for the bluegill; and the acute LC50 value for fipronil (parent) in the sheepshead minnow falls between the LC50 values for the bluegill and trout. Taken together, these data suggest that the results of an Estuarine Marine Fish Early Life Stage study with MB46136 will be similar to those with MB46513, which should be an appropriate surrogate for the other metabolites. Since BASF agrees with EPA that an estuarine/marine fish early life stage study with MB46513 should be conducted, BASF requests that the EPA-anticipated data requirement for MB45950 be waived.

Guideline Number: 850.1730
Study Type: Bioaccumulation in Fish
Test Substance: Fipronil sulfide (MB45950)
BASF Response: Information on residue levels and depuration of MB45950 is available in the fipronil (parent) bioconcentration reports *(MRID No. 43291706: Chapleo, S.; Hall, B. (1992) (Carbon 14)-MB46030: Bioaccumulation Test in Bluegill Sunfish: Lab Project Number: 381457: 8892. Unpublished study prepared by Inveresk Research International. 95p; MRID No. 43291707: Roohi, A.; Coote, A.; Savage, E. (1993) (Carbon 14) MB46030: Investigation into the Nature and Possible Structures of Metabolites in Fish used in a Bioaccumulation Study at Inveresk Research International (Study IRI/381457): Lab Project*

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Number: P/92/302. Unpublished study prepared by Rhone-Poulenc Agriculture Ltd. 62p; and MRID No. 44298002: Theissen, R. (1997) Fipronil (MB 46030): Bioaccumulation in Bluegill Sunfish: Supplemental Response for Storage Stability Data (for MRID Nos. 43291706 & 43291707): Lab Project Number: IRI 381457: RPAL P92/302: IRI 381457/RPAL/P92/302. Unpublished study prepared by Rhone-Poulenc Ag Co. 8p.) The data indicate that the metabolites MB46136 and MB45950 were found at significant levels in all analyzed tissues. Additionally, fipronil (parent) and the metabolites MB46136 and MB45950 were rapidly eliminated. Therefore, the findings of the two reports indicate that the potential for bioaccumulation reported for fipronil (parent) (BCF=321) was tested and confirmed for the metabolites MB46136 and MB45950.

Furthermore, MB46136 and MB45950 are common metabolites found in metabolism studies with other vertebrates (rat, goat and hen). The rapid and extensive clearance of residues of MB46136 and MB45950 observed in fish is consistent with the elimination pattern in other vertebrates.

Additional aquatic bioconcentration testing with MB45950 is not expected to yield data that will be pertinent to the risk assessment of fipronil. BASF requests that this EPA-anticipated data requirement for MB46136 be waived.

Guideline Number: 850.1730
Study Type: Bioaccumulation in Fish
Test Substance: Fipronil sulfone (MB46136)
BASF Response: Information on residue levels and depuration of MB46136 is available in the fipronil parent bioconcentration reports *(MRID No. 43291706: Chapleo, S.; Hall, B. (1992) (Carbon 14)-MB46030: Bioaccumulation Test in Bluegill Sunfish: Lab Project Number: 381457: 8892. Unpublished study prepared by Inveresk Research International. 95p; MRID No. 43291707: Roohi, A.; Coote, A.; Savage, E. (1993) (Carbon 14) MB46030: Investigation into the Nature and Possible Structures of Metabolites in Fish used in a Bioaccumulation Study at Inveresk Research International (Study IRI/381457): Lab Project Number: P/92/302. Unpublished study prepared by Rhone-Poulenc Agriculture Ltd. 62p; and MRID No. 44298002: Theissen, R. (1997) Fipronil (MB 46030): Bioaccumulation in Bluegill Sunfish: Supplemental Response for Storage Stability Data (for MRID Nos.*

43291706 & 43291707): Lab Project Number: IRI 381457: RPAL P92/302: IRI 381457/RPAL/P92/302. Unpublished study prepared by Rhone-Poulenc Ag Co. 8p.) The data indicate that the metabolites MB46136 and MB45950 were found at significant levels in all analyzed tissues. Additionally, fipronil (parent) and the metabolites MB46136 and MB45950 were rapidly eliminated. Therefore, the findings of the two reports indicate that the potential for bioaccumulation reported for fipronil (parent) (BCF=321) was tested and confirmed for the metabolites MB46136 and MB45950.

Furthermore, MB46136 and MB45950 are common metabolites found in metabolism studies with other vertebrates (rat, goat and hen). The rapid and extensive clearance of residues of MB46136 and MB45950 observed in fish is consistent with the elimination pattern in other vertebrates.

Additional aquatic bioconcentration testing with MB46136 is not expected to yield data that will be pertinent to the risk assessment of fipronil. BASF requests that this EPA-anticipated data requirement for MB46136 be waived.

Guideline Number: 850.1730
Study Type: Bioaccumulation in Fish
Test Substance: MB46513 (photolytic degradate)
BASF Response: The bioaccumulation potential of fipronil (parent) and the metabolites MB46136 and MB45950 has been tested and has proven to be low. MB46513 has a similar chemical structure and slightly lower log P_{ow} (MB46513 = 3.4) than the other three compounds tested (fipronil (parent) = 3.5-4.0, MB46136 = 3.8, and MB45950 = 3.7). Therefore, it is reasonable to assume that MB46513 will not bioaccumulate. Consequently, the need for this study is not scientifically justified. As such, BASF requests that this EPA-anticipated data requirement be waived.

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Guideline Number: 850.1735
Study Type: Whole sediment acute freshwater invertebrate toxicity
Test Substance: MB45950
BASF Response: BASF directs EPA to the following previously submitted study to address guideline 850.1735, MRID No. 45084801 *(Putt, A. (2000) (Carbon-14) MB 45950-Toxicity to Midge (Chironomus tentans) during a 10-Day Sediment Exposure: Lab Project Number: 10566.6536: 10397. Unpublished study prepared by Springborn Labs., Inc. 74p.)*

Guideline Number: 850.1735
Study Type: Whole sediment acute freshwater invertebrate toxicity
Test Substance: MB46136
BASF Response: BASF directs EPA to the following previously submitted study to address guideline 850.1735, MRID No. 45084801 *(Putt, A. (2000) (Carbon-14) MB 45950-Toxicity to Midge (Chironomus tentans) during a 10-Day Sediment Exposure: Lab Project Number: 10566.6536: 10397. Unpublished study prepared by Springborn Labs., Inc. 74p.)*

Guideline Number: 850.1735
Study Type: Whole sediment acute freshwater invertebrate toxicity
Test Substance: MB46513
BASF Response: BASF directs EPA to the following previously submitted study to address guideline 850.1735, MRID No. 45084801 *(Putt, A. (2000) (Carbon-14) MB 45950-Toxicity to Midge (Chironomus tentans) during a 10-Day Sediment Exposure: Lab Project Number: 10566.6536: 10397. Unpublished study prepared by Springborn Labs., Inc. 74p.)*

Guideline Number: 850.2100
Study Type: Avian Oral (Quail)
Test Substance: MB46513 (photolytic degradate)
BASF Response: Avian oral reports for both quail *(MRID No. 43776601: Pedersen, C.; Solatycki, A. (1993) MB46513: 21-Day Acute Oral LD50 Study in Bobwhite Quail: Lab Project Number: 108-017-03. Unpublished study prepared by Bio-Life Associates, Ltd. 62p)* and mallard *(MRID No. 43776602: Helsten, B.; Solatycki, A. (1994) 14-Day Acute Oral LD50 Study with MB46513 in Mallard Ducks: Lab Project Number: 108-027-04. Unpublished study prepared by Bio-Life Associates, Ltd. 58p)* were submitted to the Agency on 08/18/1995. As such, BASF requests

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that EPA review these previously submitted studies and remove this EPA-anticipated data requirement.

Guideline Number: 850.2100
Study Type: Avian Oral (House Sparrow)
Test Substance: Fipronil sulfide (MB45950)
BASF Response: There is an important pattern with regard to the sensitivity of organisms to fipronil (parent) and its metabolites and degrades: "If an organism is sensitive to fipronil (parent) it is also sensitive to its metabolites and degrades. Conversely, if an organism is less sensitive to fipronil (parent) it is also less sensitive to its metabolites and degrades".

The bobwhite quail is clearly the most sensitive avian species tested to date. Comparative quail and house sparrow acute oral studies with fipronil (parent) resulted in LD50 values which find the quail being 100 times more sensitive than the sparrow. Since the quail is clearly more sensitive than the house sparrow to fipronil (parent), it follows that the same pattern would hold true for the metabolites and degradates of fipronil.

Therefore, this study is not necessary as it will not provide meaningful information for risk assessment purposes. Additionally, conducting this study would require the unnecessary use and subsequent death of at least 60 birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2100
Study Type: Avian Oral (House Sparrow)
Test Substance: Fipronil sulfone (MB46136)
BASF Response: There is an important pattern with regard to the sensitivity of organisms to fipronil (parent) and its metabolites and degrades: "If an organism is sensitive to fipronil (parent) it is also sensitive to its metabolites and degrades. Conversely, if an organism is less sensitive to fipronil (parent) it is also less sensitive to its metabolites and degrades".

The bobwhite quail is clearly the most sensitive avian species tested to date. Comparative quail and house sparrow acute oral studies with fipronil (parent) resulted in LD50 values which find the quail being 100 times more sensitive than the sparrow. Since

the quail is clearly more sensitive than the house sparrow to fipronil (parent), it follows that the same pattern would hold true for the metabolites and degradates of fipronil.

Therefore, this study is not necessary as it will not provide meaningful information for risk assessment purposes. Additionally, conducting this study would require the unnecessary use and subsequent death of at least 60 birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2100
Study Type: Avian Oral (House Sparrow)
Test Substance: MB46513 (photolytic degradate)
BASF Response: There is an important pattern with regard to the sensitivity of organisms to fipronil (parent) and its metabolites and degrades: "If an organism is sensitive to fipronil (parent) it is also sensitive to its metabolites and degrades. Conversely, if an organism is less sensitive to fipronil (parent) it is also less sensitive to its metabolites and degrades".

The bobwhite quail is clearly the most sensitive avian species tested to date. Comparative quail and house sparrow acute oral studies with fipronil (parent) resulted in LD50 values which find the quail being 100 times more sensitive than the sparrow. Since the quail is clearly more sensitive than the house sparrow to fipronil (parent), it follows that the same pattern would hold true for the metabolites and degradates of fipronil.

Therefore, this study is not necessary as it will not provide meaningful information for risk assessment purposes. Additionally, conducting this study would require the unnecessary use and subsequent death of at least 60 birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2300
Study Type: Avian Reproduction (Quail)
Test Substance: Fipronil sulfide (MB45950)
BASF Response: MB45950 was formed during a fipronil (parent) hen metabolism study *(MRID No. 43401106: Stewart, F. (1994) (Carbon 14)-MB46030: Distribution, Metabolism, and Excretion Following Multiple Oral Administration to the Laying Hen: Revised Final Report: Lab*

Project Number: 68/120R-1011. Unpublished study prepared by Hazleton Europe. 273p) and therefore would be formed (and consequently tested, albeit indirectly) during a quail reproduction study with fipronil (parent). Conducting this study would not provide additionally relevant data and would require the unnecessary use and subsequent death of many birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2300
Study Type: Avian Reproduction (Quail)
Test Substance: Fipronil sulfone (MB46136)
BASF Response: MB46136 was formed during a fipronil (parent) hen metabolism study *(MRID No. 43401106: Stewart, F. (1994) (Carbon 14)-MB46030: Distribution, Metabolism, and Excretion Following Multiple Oral Administration to the Laying Hen: Revised Final Report: Lab Project Number: 68/120R-1011. Unpublished study prepared by Hazleton Europe. 273p)* and therefore would be formed (and consequently tested, albeit indirectly) during a quail reproduction study with fipronil (parent). Conducting this study would not provide additionally relevant data and would require the unnecessary use and subsequent death of many birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2300
Study Type: Avian Reproduction (Quail)
Test Substance: MB46513 (photolytic degradate)
BASF Response: MB46513 is a minor photolytic degradate of fipronil in terrestrial environments, including relevant avian food items. Sensitive birds (i.e., upland game species) are not expected to be exposed to quantities of MB46513 that would adversely effect their reproduction. Additionally, this study would require the unnecessary use and subsequent death of many birds. As such, BASF requests that this EPA-anticipated data requirement be waived.

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Guideline Number: 850.2300
Study Type: Avian Reproduction (Mallard)
Test Substance: Fipronil sulfide (MB45950)
BASF Response: MB45950 was formed during a fipronil (parent) hen metabolism study *(MRID No. 43401106: Stewart, F. (1994) (Carbon 14)-MB46030: Distribution, Metabolism, and Excretion Following Multiple Oral Administration to the Laying Hen: Revised Final Report: Lab Project Number: 68/120R-1011. Unpublished study prepared by Hazleton Europe. 273p)* and therefore would be formed (and consequently tested, albeit indirectly) during a quail reproduction study with fipronil (parent). Conducting this study would not provide additionally relevant data and would require the unnecessary use and subsequent death of many birds. Additionally, mallards are consistently less sensitive than bobwhite quail. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2300
Study Type: Avian Reproduction (Mallard)
Test Substance: Fipronil sulfone (MB46136)
BASF Response: MB46136 was formed during a fipronil (parent) hen metabolism study *(MRID No. 43401106: Stewart, F. (1994) (Carbon 14)-MB46030: Distribution, Metabolism, and Excretion Following Multiple Oral Administration to the Laying Hen: Revised Final Report: Lab Project Number: 68/120R-1011. Unpublished study prepared by Hazleton Europe. 273p)* and therefore would be formed (and consequently tested, albeit indirectly) during a quail reproduction study with fipronil (parent). Additionally, mallards are consistently less sensitive than bobwhite quail. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.2300
Study Type: Avian Reproduction (Mallard)
Test Substance: MB46513 (photolytic degradate)
BASF Response: MB46513 is a minor photolytic degradate of fipronil (parent) in terrestrial environments. Water fowl are not expected to be exposed to quantities of MB46513 that would adversely effect their reproduction. Additionally, this study would require the unnecessary use and subsequent death of many birds. Mallards are consistently less sensitive than bobwhite quail. As such,

BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3020
Study Type: Honeybee Acute Contact
Test Substance: Fipronil sulfide (MB45950)
BASF Response: Within the current uses, there does not appear to be a relevant route of exposure. It is unclear what value the data from an acute contact study with MB45950 will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3020
Study Type: Honeybee Acute Contact
Test Substance: Fipronil sulfone (MB46136)
BASF Response: Within the current uses, there does not appear to be a relevant route of exposure. It is unclear what value the data from an acute contact study with MB46136 will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3020
Study Type: Honeybee Acute Contact
Test Substance: MB46513 (photolytic degradate)
BASF Response: Within the current uses, there does not appear to be a relevant route of exposure. It is unclear what value the data from an acute contact study with MB46513 will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will

not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3030
Study Type: Honeybee Foliage Residue Study
Test Substance: Fipronil (parent)
BASF Response: As there are no currently registered foliar applications of fipronil in the U.S., a relevant route of exposure does not appear to exist. It is unclear what value the data from a honeybee foliage residue study will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3030
Study Type: Honeybee Foliage Residue Study
Test Substance: Fipronil sulfide (MB45950)
BASF Response: As there are no currently registered foliar applications of fipronil in the U.S., a relevant route of exposure does not appear to exist. It is unclear what value the data from a honeybee foliage residue study will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3030
Study Type: Honeybee Foliage Residue Study
Test Substance: Fipronil sulfone (MB46136)
BASF Response: As there are no currently registered foliar applications of fipronil in the U.S., a relevant route of exposure does not appear to exist. It is unclear what value the data from a honeybee foliage residue study will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications,

of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3030
Study Type: Honeybee Foliage Residue Study
Test Substance: MB46513 (photolytic degradate)
BASF Response: As there are no currently registered foliar applications of fipronil in the U.S., a relevant route of exposure does not appear to exist. It is unclear what value the data from a honeybee foliage residue study will provide. In the in-furrow corn assessment (PC code 129121, dated November 15, 2001), EPA stated that such a study would be necessary to support foliar ground or aerial applications, of which there are none in the U.S. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.3040
Study Type: Field Testing for Pollinators
Test Substance: Fipronil (parent)
BASF Response: As there are no currently registered foliar applications of fipronil in the U.S., a relevant route of exposure does not appear to exist. It is unclear what value the data generated from field testing with pollinators will provide. Since the Agency agrees fipronil is non-systemic, these data will not inform the risk assessment. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 850.4100
Study Type: Seedling Emergence Tier II
Test Substance: Fipronil (parent)
BASF Response: It is unusual that a seedling emergence study be requested for an active ingredient rather than a formulation. An OECD seedling emergence study has been conducted with formulated product (BASF Registration Document No. 2004/1027260 and amendment 2005/1006512) and will be submitted to EPA. As would be expected of an insecticide, effects on terrestrial plants were minimal. BASF requests that EPA review the results of the

OECD guideline report. As a report is being submitted, BASF requests that EPA removed this anticipated data requirement.

Guideline Number: 850.4150
Study Type: Vegetative Vigor Tier II
Test Substance: Fipronil (parent)
BASF Response: It is unusual that a vegetative vigor study be requested for an active ingredient rather than a formulation. Additionally, since there are no currently registered foliar uses for fipronil in the U.S., there are no relevant routes of exposure that would trigger this study. Finally, the above referenced seedling emergence study (Guideline Number 850.4100) clearly concludes that fipronil (an insecticide), which is applied at exceptionally low rates, poses no risk to terrestrial plant species. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: Non-Guideline
Study Type: *Hyalella azteca* 42-d Test for Measuring the Effects of Sediment-associated Contaminants on Survival, Growth, and Reproduction
Test Substance: Fipronil – incurred residues
BASF Response: A comprehensive 1-year evaluation (final and interim reports) of the impact of fipronil and its metabolites and degradate on sediment dwelling organisms (multiple taxa) from several sites encompassing ponds, lakes and stream environments has been conducted and was submitted to EPA previously. *(MRID No. 47245001: Burton, G.; LaPoint, T.; Kennedy, J.; *et. al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems: Final Report. Project Number: 2007/7009480, 47152301, 46936104. Unpublished study prepared by BASF Corporation, University of North Texas and Wright State University. 1013p; MRID No. 47152301: Burton, G.; Lapoint, T.; Kennedy, J.; et al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems Supplemental Interim Report to MRID No. 46936104. Project Number: 2007/7006915, 137834, EBFIY003. Unpublished study prepared by BASF Corporation, Wright State University and University of North Texas. 875p; and MRID No. 46936104U: Burton, G.; La Point, T.; Kennedy, J. (2006) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems, An Interim Report. Project Number: 137834, 2006/7010016. Unpublished study prepared by Wright State University, University of North Texas and Bayer CropScience LP. 45p.)*

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This EPA-suggested non-guideline study is not as comprehensive and is not necessary given that "real world" data has been collected and already provided to EPA. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: Non-Guideline
Study Type: Life-cycle Test for Measuring the Effects of Sediment-associated Contaminants on *Chironomus dilutus* (formerly known as C. *tentans)*
Test Substance: Fipronil – incurred residues
BASF Response: Numerous higher tier, "real world" studies have been conducted to examine potential effects of fipronil in the environment. A simulated pond study *(MRID No. 46733901: Hoberg, J. (2005) Chipco Topchoice - Effects on Aquatic Fauna in Outdoor Simulated Ponds. Project Number: 13798/6164, EBFIY001, 2005/7004401. Unpublished study prepared by Springborn Smithers Laboratories. 281p)*, as well as a comprehensive 1-year evaluation (final and interim reports) of the impact of fipronil and its metabolites and degradate on sediment dwelling organisms (multiple taxa) from several sites encompassing ponds, lakes and stream environments has been conducted and was submitted to EPA previously. *(MRID No. 47245001: Burton, G.; LaPoint, T.; Kennedy, J.; *et. al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems: Final Report. Project Number: 2007/7009480, 47152301, 46936104. Unpublished study prepared by BASF Corporation, University of North Texas and Wright State University. 1013p; MRID No. 47152301: Burton, G.; Lapoint, T.; Kennedy, J.; et al. (2007) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems Supplemental Interim Report to MRID No. 46936104. Project Number: 2007/7006915, 137834, EBFIY003. Unpublished study prepared by BASF Corporation, Wright State University and University of North Texas. 875p; and MRID No. 46936104U: Burton, G.; La Point, T.; Kennedy, J. (2006) An Assessment of Fipronil Effects on Benthic Invertebrates in Freshwater Ecosystems, An Interim Report. Project Number: 137834, 2006/7010016. Unpublished study prepared by Wright State University, University of North Texas and Bayer CropScience LP. 45p.)*

The EPA-suggested non-guideline study is not as comprehensive and is not necessary given that "real world" data has been

collected and already provided to EPA. As such, BASF requests that this EPA-anticipated data requirement be waived.

Guideline Number: 870.3250
Study Type: 90-day dermal
Test Substance: Fipronil (parent)
BASF Response: The 90-day dermal study is requested based on the rationale that the existing 21-day dermal study in rabbits *(MRID No. 42918644: Hermansky, S.; Wagner, C. (1993) MB46030: Twenty-One Day Repeated Cutaneous Dose Toxicity Study in New Zealand White Rabbits #2: Lab Project Number: 92N1165. Unpublished study prepared by Union Carbide Chemicals and Plastics Co., Inc., Bushy Run Research Center. 209p)* is insufficient to identify potential hazards for longer duration exposures. However, in the 21-day study, effects on body weight and food consumption were observed only at the highest dose tested of 10 mg/kg/day (LOAEL), whereas no effects were observed at the NOAEL of the study (5 mg/kg/day).

At the NOAEL, there were no effects on food consumption, and males and female animals gained weight throughout the study, comparable to control animals. Therefore, it is unlikely, considering the low dermal absorption of fipronil, that the NOAEL of a 90-day study will be considerably lower than the existing 21-day study NOAEL. Therefore, BASF proposes that the existing dermal toxicity data is appropriate for risk assessment purposes and requests that this EPA-anticipated data requirement be waived.

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Appendix 1

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Appendix 2

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

AUG 2 1996

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Appropriate LCx/NOEC regarding repeat of mysid chronic study (MRID# 436812-01) and calculation of an NOEC to be used in future risk assessments.

From: Anthony F. Maciorowski, Chief 8/2/96
Ecological Effects Branch
Environmental Fate and Effects Division (7507C)

To: Richard Keigwin
Product Manager 10
Registration Division (7505C)

After discussing issues related to the Fipronil mysid chronic study (MRID# 436812-01) at a meeting held with the registant on 6/18/96, it was decided that the Agency would evaluate the data presented and arrive at a toxicity endpoint estimate usable for a risk assessment. Rhone-Poulenc requested that a memo be written within 30 days stating the endpoint and the decision for a waiver for repeating the study. Calculation of an EC5 was discussed as a possible endpoint. The Aquatic Risk Evaluation Team (ARET) has reviewed this request and have provided guidance in addressing this issue.

The Agency has completed review of the mysid chronic toxicity study with Fipronil and proposes the use of 5.0 pptr as a NOEC for this study (actual NOEC < 5 pptr). The NOEC is based on the most sensitive endpoint, reduction in male body weights. Because the exposure of mysid shrimp to 57 pptr resulted in mortality, this value is inappropriate for use in the risk assessment.

In addition, determination of the EC_5 requires double transformation. In order to assume linearity, the data set should be expressed as percent reduction in probit units with dosage in log units. Furthermore, the Williams test is inappropriate for data sets which fail to demonstrate dose response.

OPTIONAL FORM 99 (7-90)
FAX TRANSMITTAL | # of pages ▶ 2
To: Larry Hodges | From: Ann S. Isbell
Dept./Agency: Rhone Poulenc | Phone #
Fax #: (919) 549-2545 | Fax #
NSN 7540-01-317-7368 5099-101 GENERAL SERVICES ADMINISTRATION

cc: E. Mihaich
B. Tepper
M. Cherry
R. Theisen

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Finally, the pooling of positive and negative controls is unwarranted for this data set, because it confounds the solvent effect. The Agency believes that the solvent control is more appropriate for this statistical analysis. Using the solvent control for the basis of male body weight comparisons, the Agency determined the EC_{10} and EC_5 (SAS software, Probit Analysis) to be 10.6 and 0.73 pptr respectively. For purposes of this risk assessment, 5 pptr will be used as the hazard value. A new study is not required.

If any questions should arise concerning this memo, please contact Ann Stavola (305-5354) or Nick Federoff (305-5064) of my staff.

TOTAL P.02

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