

Respondent's Pre-Hearing Exchange: Index of Exhibits

Exhibit Number	Exhibit Title
1	EPA Decision Memorandum for Registration of Flubendiamide (August 1, 2008)
2	Letter from Lois Rossi (EPA Registration Division) re: Preliminary Assessment Letter for Flubendiamide Registrations (July 31, 2008)
3	Notices of Registration for Flubendiamide Technical (EPA Reg. No. 71711-26) and Belt SC Insecticide (EPA Reg. No. 264-1025) (Aug. 1, 2008); Vetica Insecticide (EPA Reg. No. 71711-32) and Tourismo Insecticide (EPA Reg. No. 71711-33) (Mar. 4, 2009)
4	Emails between Clive A. Halder, director of Regulatory Affairs, BayerCropScience; Danielle A. Larochelle, Registration Product Manager, Bayer CropScience and EPA Registration Division (July 17, 2008 thru July 31, 2008)
5	EPA Decision Memorandum for Flubendiamide Cancellation (Jan. 29, 2016)
6	Letter from Jack Housenger (EPA Office of Pesticide Programs) re Request for Voluntary Cancellation of Flubendiamide Registrations (Jan. 29, 2016)
7	Letter from Dana Sargent (Bayer CropScience LP) re Refusal to Request Voluntary Cancellation of Flubendiamide Registrations (Feb. 5, 2016)
8	Flubendiamide; Notice of Intent to Cancel Pesticide Registrations, 81 Fed. Reg. 11,558 (Mar. 4, 2016)
9	Existing Stocks of Pesticide Products; Statement of Policy, 56 Fed. Reg. 29,362 (June 26, 1991)

RESPONDENT EXHIBIT 1



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

DECISION MEMORANDUM

SUBJECT: Section 3 New Chemical Registration of Flubendiamide

FROM: Lois Rossi, Director
Registration Division (7505P)

TO: Debra Edwards, Ph.D., Director
Office of Pesticide Programs (7501P)

Donald, 2 Staff 8/1/08

This action reflects the first registration in the U.S. for the insecticide flubendiamide. The Registration Division (RD) has prepared a final rule for the tolerances for your signature, if you concur. The enclosed final rule is based on the Health Effects Division (HED) and Office of General Counsel's review for domestic food tolerances and addresses the risk from use of flubendiamide on the proposed crops referenced below.

Background: Flubendiamide (N²-[1,1-Dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N¹-[2-methyl-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]phenyl]-1,2-benzenedicarboxamide) belongs to the novel phthalic acid diamide class of insecticides which acts through a new biochemical mode of action against adult and larval forms of lepidopterous insect pests (such as armyworms, bollworms, corn borers, cutworms, diamondback moth, fruitworms and loopers) by interfering with the calcium release channel, which is involved in muscle contraction. It is known to target/stabilize insect ryanodine receptors in an open state in a species-specific manner and to desensitize the calcium dependence of channel activity. Continuous stimulation of muscle contraction by "locking" the calcium channel in an "open" state, leads to muscle paralysis and eventual death of the target organism.

Nihon Nohyaku Co., Ltd. (NNC) developed the new insecticidal active ingredient flubendiamide. On April 5, 2006, Bayer CropScience LP (BCS) and Nichino America, Inc. (U.S. subsidiary of NNC) jointly submitted an application for registration of flubendiamide technical product, EPA File Symbol NNI-0001 Technical. In addition, BCS submitted an application for registration of 2 flubendiamide end-use products as follows: (1) a 24% a.i water dispersible granule [WG], EPA File Symbol 264-RNEA; [NNI-0001 24 WG]; and (2) a 39% a.i. soluble concentrate [SC], EPA File Symbol 264-RNEL; [NNI-0001 480 SC] as well as a petition to establish crop tolerances to support the use of flubendiamide on corn, cotton, tobacco, pome and stone fruit, tree nut crops, grapes and vegetable crops (including cucurbit vegetables, fruiting vegetables and okra, leafy vegetables [except *Brassica*] and *Brassica* [cole] leafy vegetables). The registration of the technical product is to be held by Nichino America, Inc. and the registration of the 2 end-use products are to be held by BCS. There are currently no established CODEX, Canadian or Mexican MRLs established for residues of flubendiamide *per se* in crop or livestock commodities.

This memorandum recommends that you concur with the establishment of tolerances for residues of the insecticide flubendiamide *per se*, in or on the following commodities:

Alfalfa, forage at 0.15 ppm; Alfalfa, hay at 0.04 ppm; Almond, hulls at 9.0 ppm; Apple, wet pomace at 2.0 ppm; Barley, hay at 0.04 ppm; Barley, straw at 0.07 ppm; *Brassica*, head and stem, subgroup 5A at 0.60 ppm; *Brassica*, leafy greens, subgroup 5B at 5.0 ppm; Buckwheat at 0.07 ppm; Cattle, fat at 0.30 ppm; Cattle, kidney at 0.30 ppm; Cattle, liver at 0.30 ppm; Cattle, muscle at 0.05 ppm; Clover, forage at 0.15 ppm; Clover, hay at 0.04 ppm; Corn, field, forage at 8.0 ppm; Corn, field, grain at 0.02 ppm; Corn, field, stover at 15 ppm; Corn, pop, grain at 0.02 ppm; Corn, pop, stover at 15 ppm; Corn, sweet, forage at 9.0 ppm; Corn, sweet, kernel plus cob with husks removed at 0.01 ppm; Corn, sweet, stover at 25 ppm; Cotton gin byproducts at 60 ppm; Cotton, undelinted seed at 0.90 ppm; Egg at 0.01 ppm; Fruit, pome, group 11 at 0.70 ppm; Fruit, stone, group 12 at 1.6 ppm; Goat, fat at 0.30 ppm; Goat, kidney at 0.30 ppm; Goat, liver at 0.30 ppm; Goat, muscle at 0.05 ppm; Grain,

aspirated fractions at 5.0 ppm; Grape at 1.4 ppm; Grass, forage at 0.15 ppm; Grass, hay at 0.04 ppm; Horse, fat at 0.30 ppm; Horse, kidney at 0.30 ppm; Horse, liver at 0.30 ppm; Horse, muscle at 0.05 ppm; Milk at 0.04 ppm; Milk, fat at 0.30 ppm; Millet, pearl, forage at 0.15 ppm; Millet, pearl, hay at 0.04 ppm; Millet, proso, forage at 0.15 ppm; Millet, proso, hay at 0.04 ppm; Millet, proso, straw at 0.07 ppm; Nut, tree, group 14 at 0.06 ppm; Oats, forage at 0.15 ppm; Oats, hay at 0.04 ppm; Oats, straw at 0.07 ppm; Okra at 0.30 ppm; Poultry, fat at 0.02 ppm; Poultry, liver at 0.01 ppm; Poultry, muscle at 0.01 ppm; Rye, forage at 0.15 ppm; Rye, straw at 0.07 ppm; Sheep, fat at 0.30 ppm; Sheep, kidney at 0.30 ppm; Sheep, liver at 0.30 ppm; Sheep, muscle at 0.05 ppm; Sorghum, grain, forage at 0.03 ppm; Sorghum, grain, stover at 0.06 ppm; Soybean, forage at 0.02 ppm; Soybean, hay at 0.04 ppm; Teosinte, forage at 0.15 ppm; Teosinte, hay at 0.04 ppm; Teosinte, straw at 0.07 ppm; Triticale, forage at 0.15 ppm; Triticale, hay at 0.04 ppm; Triticale, straw at 0.07 ppm; Vegetable, cucurbit, group 9 at 0.20 ppm; Vegetable, fruiting, group 8 at 0.60 ppm; Vegetable, leafy, except *Brassica*, group 4 at 11 ppm; Wheat, forage at 0.15 ppm; Wheat, hay at 0.03 ppm and Wheat, straw at 0.03 ppm.

Based upon review of the nature of the residue data submitted in support of this tolerance petition for flubendiamide, as well as EPA policy, HED has revised commodity definitions and/or some of the proposed tolerances. No residue data were submitted to support the proposed uses on okra and popcorn. The available field trial data for fruiting vegetables may be translated to okra, and the submitted data for field corn may also be translated to popcorn. The proposed uses on all types of corn (field, pop and sweet) are identical.

Parent residue levels vary based on crop (for edible commodities; residues ranged from 0.018 ppm, corn, field, grain to 6.7 ppm, spinach). Most crops indicated parent residues declined with successive sampling dates and were determined to be available on the surface of plants/RACs. HED will allow translation of residue data from trials conducted on rotated barley, sorghum and wheat to support the proposed rotational crop tolerances for the forages, hay and straw of other types of cereal grains and grasses. HED will also allow translation of residue data from trials conducted on rotated soybean to support the proposed rotational crop tolerances for the forages, fodder, hay and straw of alfalfa and clover to support the proposed rotational plant-back intervals. Based on the transfer coefficients for livestock tissues and the relatively low dietary burden for swine of 0.02 ppm for flubendiamide, tolerances for hogs are not needed.

HUMAN HEALTH EFFECTS

Toxicity Summary

Acute Toxicity: Flubendiamide has a low acute oral ($LD_{50} > 2,000$ mg/kg body weight/day (mkd)), dermal ($LD_{50} > 2,000$ mkd) and inhalation toxicity ($LC_{50} > 68.5$ mg/m³ air, which is the mean maximum attainable concentration) in male and female rats. Though it is a slight irritant to the eye, flubendiamide is not a skin irritant and it is not a skin sensitizer.

Subchronic Toxicity: In the subchronic oral toxicity studies in the rat (MRID 46817210), mouse (MRID 46817211) and dog (MRIDs 46817212 and 46817242) and a 28-/29-day dermal toxicity study in the rat (MRID 46817213), the primary target organs identified were the liver, thyroid, kidney and eyes. Liver effects reported in rats, mice and/or dogs include organ weight increase, periportal fatty change, hypertrophy and minimal foci of cellular alteration. Thyroid effects include organ weight increase, follicular cell hypertrophy and slight perturbations of triiodothyronine (T3) and thyroid stimulating hormone (TSH) in the rat and mouse. Kidney effects include increases in absolute and/or relative to body kidney weights and chronic nephropathy in the rat. Eye effects include eye enlargement, opacity and exophthalmus with hemorrhage and appear only in rat pups.

The hazard assessment indicated potential toxicity resulting from exposure to flubendiamide via different routes over different durations. **The observed eye effects¹ were selected as a critical effect for the acute dietary exposure scenario; whereas liver and thyroid effects were determined critical for the chronic**

¹ The weight of evidence from various studies suggest that the finding of enlarged eyeballs in rat offspring is a rat-specific phenomenon, resulting from exposure to higher steady-state concentrations of flubendiamide which may be due to the uniquely diminished capacity of the female rat to oxidize the parent compound. While human microsomes have been shown to be capable of approximately 4 times higher hydroxylation rates than female mouse microsomes and may be able to efficiently metabolize/excrete flubendiamide, preventing accumulation of the parent compound, it remains unclear whether this ability is the only requirement to avoid ocular toxicity. Due to the potential concern for increased susceptibility of human neonates vs. adults, this perinatal ocular effect is considered in the HED risk assessment.

dietary exposure scenario. Short- and intermediate-term dermal risks were also based on liver and thyroid effects, as well as blood effects. Short- and intermediate-term inhalation risks are based on liver toxicity, as well as adrenal weight increase and an increase in adrenal cortical cell hypertrophy.

Chronic Toxicity: In the 1-year chronic rat study (MRID 46817217), the LOAEL is 97.5 mkd in females, based on indications of slight hepatotoxicity in females. The NOAEL is 2.4 mkd in females. In the 1-year chronic dog study (MRID 46817218), the LOAEL is 35.2/37.9 mkd in M/F, based on decreased bodyweight and bodyweight gain in males; increased ALP in both sexes; and increased absolute and relative liver weights in both sexes. The NOAEL is 2.21/2.51 mkd in M/F. In the 24-month rat carcinogenicity study (MRID 46817219), the LOAEL is 33.9/43.7 mkd in M/F, based on hepatotoxicity and nephrotoxicity in both sexes, and hair loss and folliculitis in females. The NOAEL is 1.70/2.15 mkd in M/F. In the 18-month mouse carcinogenicity (feeding) study (MRID 46817220), the LOAEL is 94/93 mkd in M/F, based on hepatotoxicity in both sexes. The NOAEL is 4.85/4.44 mkd in M/F. **At the doses tested, there was no treatment-related increase in tumor incidence when compared to controls. Dosing was considered adequate based on hepatotoxicity and nephrotoxicity in both sexes and hair loss, folliculitis and decreased body weight gain in females.**

Carcinogenicity: Flubendiamide is considered to be "Not Likely to be Carcinogenic to Humans." There was no evidence of carcinogenicity in rats and mice up to the limit dose at 24- and 18-months, respectively. Flubendiamide was determined to be non-mutagenic in bacteria, negative in an *in vivo* mammalian cytogenetics assay and did not cause unscheduled DNA synthesis (repair of DNA damage) in mammalian cells *in vitro*. **Overall, there was no clear evidence that flubendiamide was either mutagenic or clastogenic in either *in vivo* or *in vitro* assays. Quantification of cancer risk is; therefore, not needed for flubendiamide.**

Developmental Toxicity: Maternal toxicity was very slight (effects included loose stool, decreased food consumption and increased liver weight). Toxicity to the offspring occurred at equivalent or higher doses than maternal toxicity. **No effect on embryo/fetal development was observed in either species and there was no evidence to suggest that flubendiamide possessed a teratogenic potential up to the limit dose of 1,000 mkd.**

Reproductive Toxicity: In the 2-generation rat reproduction study (MRID 46817216), the only parental/systemic effects were observed on the liver, thyroid and kidneys as indicated by changes in organ weights corroborated by gross and microscopic lesions on the liver at the LOAEL of 146.3/167.5 mkd in M/F. The NOAEL is 3.68/4.27 mkd in M/F. **No effects on reproduction were observed at any dose. The LOAEL for offspring toxicity is 146.3/167.5 mkd in M/F, based on effects on the liver and thyroid as indicated by changes in organ weights corroborated by gross and microscopic lesions.** In addition, at 20,000 ppm, pup body weights were decreased on PND 21 in both sexes in both generations. Sexual maturation was delayed in males, as indicated by a dose-dependent increase in the mean number of days until preputial separation at 50 ppm (42.5 days), 2,000 ppm (43.0 days) and 20,000 ppm (43.7 days) as compared to controls (41.3 days).

Neurotoxicity: **There are no treatment-related neurotoxic findings in the acute neurotoxicity and DNT studies in rats.** Although eye effects were observed in the DNT study, the toxicological PODs employed in the HED risk assessment are protective of this effect.

Dermal Toxicity: In the 28-/29-day dermal toxicity study in rats (MRID 46817213), statistically significant decreases in erythrocyte counts, hematocrit and hemoglobin were noted in males at 10 mkd and above. These slight differences were not correlated with dose and were considered incidental to lower water intakes in control rats. Absolute and relative liver weights were statistically increased relative to controls in both sexes at 1,000 mkd. Microscopically, females showed a slightly elevated fat-positive reaction in the periportal zone, but not in males. In the thyroid, an increased incidence of follicular cell hypertrophy relative to other groups also was noted in 1,000 mkd females. Additionally, the tinctorial density of the follicular colloid was considered slightly reduced in the majority of these animals.

Human Study: The HED risk assessment for flubendiamide relies in part on data from studies in the Pesticide Handlers Exposure Database (PHED), Version 1.1 (August 1998). Some of the studies involved adult human subjects that were intentionally exposed to a pesticide or other chemical and; therefore, may be relied upon by EPA in actions under FIFRA only if the research meets the standards set forth in EPA's Human Studies rule, 40

CFR part 26. These studies were determined to require a review of their ethical conduct, which subsequently determined these studies to be ethical.

HED Risk Assessment Summary

Endpoints

Acute: The 2-generation reproduction (MRID 46817216), 1-generation reproduction (MRID 46817239) and DNT studies (MRIDs 46817214 and 46817240) as 3 co-critical studies were selected for the acute reference dose (aRfD) of 0.995 mkd. Using 99.5 mkd from the DNT study (the highest NOAEL) and a LOAEL from the 1-generation reproduction study of 127 mkd (the lowest LOAEL) based on buphthalmia (enlargement of eyes), ocular opacity, retinal degeneration, hemorrhage, cataract and atrophy of the optic nerve. Uncertainty factors (UFs) (100x) include: 10x interspecies extrapolation and 10x intraspecies variability. The resulting acute population adjusted dose (aPAD) is 0.995 mkd. The NOAEL/LOAEL chosen result in a more refined yet health protective acute dietary risk assessment.

Chronic: The 1-year chronic rat study (MRID 46817217), 1-year chronic dog study (MRID 46817218) and the 24-month rat carcinogenicity study (MRID 46817219) were selected as 3 co-critical studies for the chronic reference dose (cRfD) of 0.024 mkd with a NOAEL/LOAEL of 2.4/33.9 mkd (highest NOAEL of 2.4 mkd from the 1-year chronic rat study and lowest LOAEL of 33.9 mkd from the 24-month rat study. Although the 1-year dog study had NOAELs of 2.21/2.51 mkd, the lowest NOAELs from each study were considered when comparing NOAELs among the 3 studies, respectively, based on the consistent liver toxicity reported across multiple studies, different durations and multiple species. UFs (100x) include: 10x interspecies extrapolation and 10x intraspecies variability. The resulting chronic population adjusted dose (cPAD) is 0.024 mkd. The NOAEL/LOAEL are protective of effects seen in other long-term studies.

Carcinogenicity: Flubendiamide has been classified as "Not Likely to be Carcinogenic to Humans" and is not expected to pose a cancer risk.

Short- and Intermediate-Term Dermal Occupational Exposure: A 28-/29-day dermal toxicity study in the rat (MRID 46817213) was used to select the dose and endpoint for short- and intermediate-term dermal exposure. A LOAEL for local skin reactions was not determined (>1,000 mkd). The LOAEL for systemic effects is 1,000 mkd and is based on increased liver weight, thyroid follicular cell hypertrophy, slight decreases in hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, decreased aspartate aminotransferase in females and a slightly elevated fat-positive reaction in periportal hepatocytes in both sexes. The NOAEL for local skin reaction is 1,000 mkd; the NOAEL for systemic effects is 100 mkd. Although neurotoxicity is not assayed for in the referenced dermal toxicity study, the only neurotoxic-related effect observed in the toxicity database was related to an acute exposure, and the NOAEL was determined to be 99.5 mkd (the dermal NOAEL is approximately equivalent and; therefore, protective for this effect). Although balanopreputial separation was observed at the LOAEL of 99.5 mkd (NOAEL 9.9 mkd) and is a perinatal effect not assayed for in the dermal toxicity study, due to the low dermal absorption of flubendiamide (0.02%), this POD is protective of this post-natal effect.

Short- and Intermediate-Term Inhalation Occupational Exposure: In lieu of a repeat longer term inhalation study, the 90-day oral toxicity study in the dog (MRID 46817212) was used to select the dose and endpoint for short- and intermediate-term inhalation exposure. A NOAEL of 2.6 mkd was selected for this route-specific exposure scenario and would be protective for liver and adrenal toxicities, as well as acute ocular toxicity reported in the 2-generation reproduction, 1-generation reproduction and DNT studies. This assumes that absorption via inhalation is equivalent to oral absorption.

FQPA Safety Factor

EPA evaluated the quality of the toxicity/exposure data and has determined that the safety of infants and children would be adequately protected if the FQPA SF were reduced to 1x based on the following findings: (1) The toxicology database for flubendiamide is complete for purposes of risk assessment and the characterization of potential pre- and/or post-natal risks to infants and children. Although susceptibility was identified in the toxicological database (eye effects), the selected regulatory PODs (which are based on clear NOAELs) are protective of these effects; therefore, the human health risk assessment is protective; (2) There are no

treatment-related neurotoxic findings in the acute neurotoxicity and DNT studies in rats. Although eye effects were observed in the DNT study, the PODs employed in the HED risk assessment are protective of this effect; and (3) There are no residual uncertainties identified in the exposure databases and the exposure assessment is protective.

Exposure and Risk

Acute Dietary Assessment: The acute dietary assessment (using the DEEM-FCID™ model) incorporates the highest relevant estimates of drinking water concentrations (EDWCs) provided from EFED directly into the analysis. By using these screening-level exposure assessments in the acute dietary (food and drinking water) assessment, risk is not underestimated for the exposure and risks posed by flubendiamide. The analysis assumed that 100% of crops with requested uses of flubendiamide are treated and that all treated crops contain residues at tolerance-level. In addition, tolerance-level residues for livestock commodities were included in these analyses to account for the potential transfer of plant residues to livestock tissues. **These assumptions result in conservative, health-protective estimates of exposure which are well below the Agency's LOC (100% of the aPAD). The maximum exposure estimate is less than 8% of the aPAD for the most highly exposed population subgroup, children 1-2 years old. These analyses indicate that there are no acute dietary exposure considerations that would preclude registration of flubendiamide for the requested uses.**

Chronic Dietary Assessment: The chronic dietary assessment (also using the DEEM-FCID™ model) incorporates the highest relevant EDWCs provided from EFED directly into the analysis. By using these screening-level exposure assessments in the chronic dietary (food and drinking water) assessment, risk is not underestimated for the exposure and risks posed by flubendiamide. The analysis assumed that 100% of requested crops are treated and that all treated crops contain residues at the average residue levels found in the crop field trials and experimentally-determined processing factors where available. In addition, average-level residues for livestock commodities were also included in these analyses to account for the potential transfer of plant residues to livestock tissues. **These assumptions result in conservative, health-protective estimates of exposure which are well below the Agency's LOC (100% of the cPAD). The maximum exposure estimate is less than 15% of the cPAD the most highly exposed population subgroup, children 1-2 years old. These analyses indicate that there are no chronic dietary exposure considerations that would preclude registration of flubendiamide for the requested uses.**

Residential Assessment: Flubendiamide is not registered for any specific use patterns that would result in residential exposure. That is, no residential uses are being requested for flubendiamide at this time; therefore, no residential risk assessment has been conducted.

Smoker Exposure Assessment: Although residential uses are not being requested at this time for flubendiamide, there is a proposed use on tobacco, and subsequently, a potential for exposure to flubendiamide via smoking tobacco products. The short-term inhalation NOAEL is 2.6 mkd and is based on liver toxicity and adrenal weight increase and increase in adrenal cortical cell hypertrophy in females observed in the 90-day oral toxicity dog study. HED has not examined intermediate- or long-term exposure to flubendiamide via tobacco due to the severity and quantity of health effects associated with the use of tobacco products. **Based on the inhalation NOAEL, the short-term MOE for flubendiamide exposure from the use of tobacco is estimated to be greater than 130, which is higher than the target MOE of 100 for the U.S. General Population. This is a highly conservative value for the reasons stated above and is not a risk concern.**

Aggregate Risk Assessment: The aggregate risk assessment considers dietary exposures from food and drinking water to flubendiamide consumed over the acute and chronic durations. **Acute and chronic dietary exposure is well below the Agency's LOC and there are no acute or chronic dietary exposure considerations that would preclude registration of flubendiamide for the requested uses.**

Cumulative Risk Assessment: Section 408(b)(2)(D)(v) of FFDCRA requires that, when considering whether to establish, modify or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA has not found flubendiamide to share a common mechanism of toxicity with any other substances, and flubendiamide does not appear to produce a toxic metabolite produced by other substances. **For the purposes**

of this tolerance action; therefore, EPA has assumed that flubendiamide does not have a common mechanism of toxicity with other substances.

Occupational Risk Assessment: Based upon the proposed use patterns for flubendiamide (3 to 5 applications per season), the following occupational pesticide handler scenarios were assessed: (1) Mixing/loading liquid concentrates to support aerial, airblast, chemigation and ground boom applications; (2) Mixing/loading water-dispersible granules to support aerial, chemigation and ground boom applications; (3) Applying sprays with aircraft, airblast and ground boom equipment; and (4) Flagging to support aerial applications. Short- (1 to 30 days) and possibly intermediate-term (1 to 6 months) exposures are possible for occupational flubendiamide handlers. Dermal, inhalation and combined (dermal plus inhalation) risks were assessed because both endpoints are based on liver toxicity. An MOE ≥ 100 is adequate to protect occupational pesticide handlers, based on conventional uncertainty factors (10x interspecies extrapolation and 10x intraspecies variation). No chemical-specific data were available to assess potential exposure to occupational pesticide handlers; therefore, estimates of exposure to pesticide handlers are based upon surrogate study data from PHED, Version 1.1 (August 1998).

All occupational handler MOEs for flubendiamide are estimated to be >100 at some level of risk mitigation for the proposed uses. Combined dermal plus inhalation risks are not a concern, provided that: (1) Baseline attire (long-sleeved shirt and long pants and shoes plus socks) is worn by all occupational handlers; (2) Handlers mixing and loading liquid concentrates to support aerial and chemigation applications wear chemical-resistant gloves such as barrier laminate, butyl rubber, nitrile rubber or viton; and (3) Pilots use enclosed cockpits.

There is the possibility for agricultural workers to have post-application exposure to flubendiamide following its proposed agricultural crop uses. Therefore, occupational post-application exposures and risks were assessed using data from flubendiamide-specific DFR studies and using HED's default assumptions that 20% of the initial application is available for transfer on day 0 (*i.e.*, 12 hours after application) and that the residue dissipates at a rate of 10% per day following treatment.

For flubendiamide, the exposure durations for non-cancer post-application risk assessment were short- (30 days) and intermediate-term (>30 days and up to several months). However, since the dermal toxicological endpoint of concern is the same for short- and intermediate-term exposures, the short- and intermediate-term post-application risks are numerically identical. HED has established levels of concern (LOC) for occupational post-application risks. Margins of exposure of <100 for occupational non-cancer dermal risks are a concern.

Inhalation exposures are thought to be negligible in outdoor post-application scenarios, since flubendiamide has a relatively low vapor pressure (7.5×10^{-7} mm Hg).

It should be noted that the grape and corn flubendiamide-specific DFR data indicate that flubendiamide does not dissipate characteristically in a steady state. Rather, there is evident fluctuation up and then down, though the ultimate trend is downwards. In at least one case, the highest study DFR values were detected 5 days after the last treatment. In fact, the highest residue value detected in the entire study was detected on corn on the 2nd day after the last treatment. That observation ($0.390 \mu\text{g}/\text{cm}^2$) is higher than the residue value calculated for corn using HED default assumptions ($0.21 \mu\text{g}/\text{cm}^2$) by a factor of 1.86 ($0.390/0.21 = 1.86$). To ensure that the post-application assessments, using default DFRs are protective, HED conducted a highly conservative assessment assuming that all the default DFRs would be 1.86x higher if flubendiamide-specific data were generated on each of those crops (an assumption that is not likely, since in the case of grapes, the DFR residues were less than the default assumptions). **Therefore, even when assuming an extraordinarily worse-case scenario, post-application exposure to flubendiamide does not pose a risk to occupational workers.**

Flubendiamide is classified in acute toxicity category III for acute oral, dermal and inhalation toxicity and acute toxicity category IV for primary eye irritation and primary skin irritation. It is not a dermal sensitizer. **A restricted entry interval (REI) of 12 hours is appropriate and meets the requirements of the Worker Protection Standard for Agricultural Pesticides (WPS).**

Residue Chemistry: The nature of the residue in plants, rotational crops and ruminants is adequately understood. For the purposes of tolerance establishment and dietary/drinking water risk assessment, the residue of concern in plants, animals and rotational crops is the parent flubendiamide *per se*.

ECOLOGICAL EFFECTS & ENVIRONMENTAL FATE CHARACTERISTICS

Environmental Fate and Transport: Data were submitted regarding the hydrolysis, photolysis, biodegradation, soil adsorption properties and terrestrial field dissipation of flubendiamide. These data are sufficient to characterize the transport, partitioning, mobility and degradation of flubendiamide technical in the environment.

Hydrolysis/Photolysis: Flubendiamide is stable to hydrolysis under laboratory conditions, but direct aqueous photolysis appears to be a main route of degradation. Flubendiamide degrades to NNI-0001-des-iodo (des-iodo), with a half-life estimated as 11.56 days. Flubendiamide degrades to des-iodo under laboratory soil photolysis with a half-life estimated as 35.3 days. Volatilization from soil and water surfaces is not expected to be an important dissipation route since flubendiamide has a relatively low vapor pressure (7.5×10^{-7} mm Hg) and Henry's Law constant (8.9×10^{-11} atm·m³/mol).

Mobility/Transport: Flubendiamide is expected to be slightly to hardly mobile ($K_{FOC} = 1,076$ to $3,318$ L/Kg). Des-iodo is expected to be moderately mobile ($K_{FOC} = 234$ to 581 L/kg). The main transformation product, des-iodo, is more mobile than the parent; however, des-iodo was only detected in a small quantity (<3.4% of the applied) at the 0 to 15 cm soil depth at 3 sites in the terrestrial field studies. **Flubendiamide and des-iodo have the potential to contaminate surface water through run-off due to their persistence in soil and also have the potential for groundwater contamination in vulnerable soils with low organic carbon content, after heavy rainfall and/or in areas with high water tables (because there is less depth to travel before reaching groundwater).**

Soil/Water Degradation: Flubendiamide is stable under aerobic and anaerobic soil metabolism and aerobic aquatic metabolism laboratory conditions. In aerobic and anaerobic aqueous environments, flubendiamide is expected to dissipate somewhat faster than in aerobic soil, likely as a result of metabolism. Laboratory experiments using anaerobic and aerobic aquatic systems resulted in flubendiamide half-lives (water plus soil/sediment) of 127 to 364 days and 32.8 to 533.2 days, respectively. Anaerobic aquatic metabolism is another main route of degradation for flubendiamide. Flubendiamide degrades to des-iodo under anaerobic aquatic conditions with a half-life estimated as 365 days. **Flubendiamide and des-iodo's overall stability/persistence suggests that they will accumulate in soils, water column and sediments with each successive application.**

Terrestrial Field Dissipation: Flubendiamide also degrades in the field condition very slowly. In terrestrial field experiments, flubendiamide half-lives in 3 soils ranging from loamy sand to silt loam were 210 to 770.2 days (leaching to a depth of 30 to 60 cm) and in a sandy loam soil under outdoor conditions, the half-life was 322 days. In an aerobic soil environment, flubendiamide is expected to dissipate slowly. In the laboratory using 4 soils ranging from loamy sand to silt, flubendiamide was stable with <5% of the applied chemical dissipating at 371 days post-treatment.

Bioaccumulation: Flubendiamide has a potential for bioaccumulation in fish due to flubendiamide being stable to hydrolysis and having a relatively high log K_{ow} (4.1 at pH 7). However, in general, chemicals are a concern for bioaccumulation with bioconcentration factors (BCFs) of 1,000 or greater and log K_{ow} of 4.5 - 5.0 or greater. Flubendiamide residues in bluegill sunfish in the high dose study had a maximum mean fish BCFs of 109.9x, 57.0x and 206.3x for edible, non-edible and whole fish tissue, respectively. After a 14-day depuration period, flubendiamide residues in the whole fish declined by a mean of 83% (low dose) and 86% (high dose). The residues depurated with a half-life of 4.6 and 4.8 days, from the low and high dose studies.

The des-iodo degradate is also not of concern for bioaccumulation in that it has a octanol-water partition coefficient of log K_{ow} 3.40 and calculated mean BCF values, based on total radioactive residues, of 12.6, 20.4, and 7.7 for whole fish, viscera, and edible tissues, respectively.

Ecological Effects: The Agency has determined, based on the proposed uses, that there is no potential risk to freshwater and marine fish, marine crustaceans, marine mollusks and aquatic plants at the limit of solubility for parent flubendiamide. In addition, there is no potential acute risk or reproductive effects to birds and mammals, earthworms, beneficial insects including honey bees and natural Lepidoptera predators, and terrestrial plants for all of the proposed uses.

There is a potential risk to freshwater benthic invertebrates exposed to flubendiamide and its degradate des-iodo. EPA has compared the body of toxicological data for the parent compound and des-iodo. With the possible

exception of chronic testing with chironomid midges, there is no apparent difference in toxicity evident from the available data. In the case of the chironomid data, conversion of effect endpoints to pore water units results in an estimated NOAEC for the parent compound of approximately 1 µg/L. The corresponding NOAEC for des-iodo is 0.28 µg/L. Because of the estimated nature of the parent compound NOAEC (the value is estimated from the relationship between nominal and pore water measurements at other dose levels because actual measurements of pore water concentrations were not made at the NOAEC level) and because NOAEC comparisons are usually confounded by the dose selections at study design onset, EFED concluded that there was insufficient data to demonstrate a significant difference in toxicity between the parent and degradate. However, for the purposes of risk assessment and in consideration of the use of data as prescribed in the Agency's Risk Assessment Overview Document, risk calculations are based on the chronic endpoints established for each chemical, specifically.

Using these NOAEC values, RQs for parent flubendiamide would range from 0.94 to 21.3. Considering only the accumulation within the first 30 years of use for all of the crop scenarios, RQs for the des-iodo degradate would range from 0.03 to 6.9 in the 1st year, 2.9 to 64 in the 10th year, 4.9 to 127 in the 20th year and 12 to 190 in the 30th year. Uncertainties in the model results make longer term estimates of accumulation and risk unreliable. However, due to the persistence of both the parent and degradate, there is a concern for potential accumulation in aquatic sediments over time.

Testing of the formulated products 480 SC and 24 WG resulted in RQs ranging up to 0.1 for freshwater invertebrates. Results of a mesocosm study conducted with the formulated products also did not identify any serious risk concerns for water column invertebrates.

Adult ladybird beetles are potentially at risk due to ingestion of food items (aphids and pollen) containing flubendiamide residues. In addition, there is a potential direct risk to non-target lepidopterous species, including endangered species. Lepidoptera may occur in areas adjacent to treated fields, where they may be exposed to spray drift, and will likely move through treated fields. Further, the larvae of some lepidopterous species are aquatic and; therefore, may be exposed to both the parent formulation and the des-iodo degradate.

The Agency is concerned about the possible accumulation of flubendiamide and des-iodo in aquatic sediments and the effects that this would have on freshwater benthic organisms. However, given the benefits described below, the Agency is granting registration for this chemical at this time. The risk mitigation required and conditions of registration for this chemical, as described below, are designed to address these concerns and to provide adequate information that will allow the Agency to determine: (1) if the required risk mitigation is adequate or, if this is still uncertain, (2) through a monitoring program, determine the rate and extent of accumulation of the parent and degradate in the most vulnerable areas of use during the time period of the 5-year conditional registration. There is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations.

PROPOSED REGULATORY DECISION: A 5-year conditional registration is proposed for flubendiamide use as an insecticidal control of various lepidopterous insect pests on corn, cotton, tobacco, tree fruit, tree nuts, vine crops and vegetable crops.

Flubendiamide may be a viable alternative to comparably registered and existing pesticides that tend to pose greater risk concerns and may also be an important tool as a rotational insecticide to limit or prevent the development of resistance to other insecticide chemistries. Flubendiamide has also been identified as an OP alternative for the control of leafroller and fruitworm pests in tree fruit production, where the dominant pesticides used have been azinphos-methyl, chlorpyrifos and phosmet.

The EFED risk assessment; however, suggests that both flubendiamide and des-iodo will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. As a result, EPA is requiring certain measures which the Agency believes may be effective in mitigating the apparent risk, including the requirement of 15-foot vegetative buffer zones which are expected to reduce run-off of both parent and degradate to the aquatic environment, reduced application rates and other labeling statements which reduce the allowable total loading in one year and environmental hazards, ground water and surface water advisories.

To confirm the utility of the 15-foot vegetative buffers, the Agency is requiring a small-scale run-off/vegetative buffer strip study. If the utility of the 15-foot buffers cannot be demonstrated to achieve reductions in off-site transport and aquatic organism risk that would alleviate the risk concern, the Agency is requiring a monitoring program, the results of which allow the Agency to determine, at the end of the 5-year conditional registration, the rate and extent of accumulation in the most vulnerable use areas. If there are risk concerns at that time that result in the Agency being unable to determine that there are no unreasonable adverse effects to the environment, the registrants have agreed that the pesticide will be voluntarily cancelled.

DATA REQUIRED AND LABEL REVISIONS:

Data Required: The registrant has committed to submit the following data:

1. Flubendiamide

(Non-guideline) **Small-Scale Run-Off/Vegetative Buffer Strip Study** – The quantitative efficacy of vegetative buffers for flubendiamide use is uncertain. To determine the magnitude of the parent, flubendiamide, retained in buffer strips, the small-scale run-off/vegetative buffer strip study and monitoring program will allow the Agency to quantitatively consider the impact of such buffers on the risk picture. The protocols for the studies will be mindful of the need to consider both the variety of proposed use sites as well as a variety of buffer conditions.

If the employment of label enforceable buffers is empirically demonstrated to alleviate the risk concern, then no further work need be conducted. However, if buffers cannot be demonstrated to achieve these meaningful risk reductions, the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations. Therefore, a monitoring study of receiving waters within watersheds where flubendiamide will be used will be required.

2. Des-Iodo Degradate

- (161-1) **Hydrolysis** – A hydrolysis study to establish the significance of chemical hydrolysis as a route of degradation for des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.
- (162-4) **Aerobic Aquatic Metabolism** – An aerobic aquatic metabolism study to determine the effects of des-iodo on aerobic conditions in water and sediments during the period of dispersal of des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modeling uncertainty.

3. For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), the registrant will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.

Label Revisions: The proposed end-use labels for 480 SC and 24 WG, were updated/revised on July 24, 2008, to include the following revisions:

1. Requirement of 15-foot vegetative buffer zones and the addition of updated spray drift language as is used for aerial/ground applications as is used for similar products with similar use patterns on both end-use labels.
2. On the proposed label for 24 WG, the registrant will reduce application rates, revise the maximum amount of product applied per acre "per year" to a "per crop season" basis and remove the number of applications per crop season for the *Brassica*, Cucurbits, Leafy Vegetables and Fruiting Vegetables crop groupings in order to reduce the per year loading allowed.

3. Addition of revised environmental hazards, ground water and surface water advisories to both end-use labels.
4. On the proposed label for 480 SC, the registrant will be required to clearly articulate what application method(s) are proposed for each listed crop.
5. The proposed rotational crop restriction for root crops (root, tuber and bulb vegetables), which specifies that *"treated areas may be replanted immediately following harvest, or as soon as practical following the last application"* will be revised to a 30-day plant-back interval on both end-use labels.

BENEFIT DETERMINATIONS: Since flubendiamide is a novel chemistry, the Agency believes that it may be a viable alternative to comparably registered and existing pesticides that tend to pose greater risk concerns. Also, it may be an important tool as a rotational insecticide to limit or prevent the development of resistance to other insecticide chemistries. BEAD's preliminary analysis of the material submitted by the registrant concludes that flubendiamide provides Lepidoptera control equivalent or superior to the insecticides currently being used for pest control in the evaluated crops. Materials submitted also suggest low toxicity to terrestrial insect predators and honey bees which should make flubendiamide an important component in IPM programs.

When assessing recent pesticide usage data for currently registered insecticide products aimed at controlling lepidopterous pests in corn, several market leaders are of concern to the Agency. Flubendiamide's toxicity to terrestrial organisms is low, especially in comparison to the current active ingredients most commonly used against the labeled target pests.

For pesticides used to control cotton pests such as the beet armyworm and bollworm, the usage information for products used in 2007 was more broadly distributed among chemical pesticides than that indicated for corn usage, with a number of synthetic pyrethroids, namely lambda cyhalothrin, and other chemistries such as acephate and chlorpyrifos leading the usage profile.

In addition, flubendiamide has been identified as an organophosphorus pesticide alternative for the control of leafroller and fruitworm pests in tree fruit production, where the dominant pesticides used have been azinphos-methyl, chlorpyrifos and phosmet. Therefore, flubendiamide is a chemical that broadens the diversity of pest control measures available to growers for the reasons stated above.

GOVERNMENT PERFORMANCE ACT: Registration of flubendiamide will meet the objectives of GPRA title 3.1.1 by assuring new pesticides entering the market are safe for humans and the environment.

RECOMMENDATION: I recommend that you concur with the conditional registration of this new insecticide flubendiamide under FIFRA section 3(c)(7)(C).

Heather E. Swann ds August 1, 2008
 CONCUR DATE

 DO NOT CONCUR DATE

RESPONDENT EXHIBIT 2



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Thursday, July 31, 2008

CERTIFIED MAIL: (Article Number 7008 0150 0002 6191 4899)

Ms. Danielle A. Larochele,
Registration Product Manager,
Authorized Agent for Nichino America, Inc.
c/o Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709-2014

Subject: Application for a New Section 3 Registration of Flubendiamide with Associated Tolerance NNI-0001 Technical (EPA File Symbol 71711-EA); NNI-0001 24 WG (EPA File Symbol 264-RNEA); NNI-0001 480 SC (EPA File Symbol 264-RNEL); and Tolerance Petition No. 6F7065

Dear Ms. Larochele:

The products referred to above will be acceptable for registration under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, provided that Bayer CropScience LP (Bayer), as authorized agent for Nichino America, Inc. (Nichino), agree/concur with the following conditions of registration and provided that the Director of the Office of Pesticide Programs concurs with the registration:

- The subject products will be conditionally registered for a period of five (5) years from the date of the "Notice of Registration." In addition, this regulatory action will establish permanent tolerances in primary crops for residues of flubendiamide.
- Bayer, as authorized agent for Nichino, will generate/submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

Guideline Number	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July 31, 2010
NOTE: Bayer will submit a final protocol for the small-scale run-off/vegetative buffer strip study on or before January 31, 2009. Bayer will submit one (1) progress report by December 31, 2009 and a final report on or before July 31, 2010.		
Non-Guideline	Monitoring Program -If risk assessment, based on the results from the small-scale run-off/vegetative buffer strip study and additional available data indicates that there are still risk concerns, there will be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used.	July 31, 2012
NOTE: Bayer will submit to EPA a final protocol for the monitoring program on or before March 1, 2010. Bayer will revise the protocol for the monitoring study, as necessary, within one (1) month following receipt of the Agency's decision that a monitoring program is necessary.		

The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. Open literature and Bayer-conducted studies on compounds with similar characteristics to flubendiamide provide information that permits an estimation of the impact of such buffers on the risk picture. A confirmatory small-scale run-off/vegetative buffer strip study with flubendiamide would allow the Agency to quantitatively consider the impact of such buffer strips on risk reduction in critical use areas. It is recommended that the protocol for the referenced study, like in past cases, be a product of a dialogue between EPA and Bayer scientists. Such dialogue, the protocols arising from it and assessment of supporting literature, should be mindful of the need to address

vulnerable use patterns and sites as well as a variety of buffer conditions. The buffer conditions used for this study should support potential mitigation enforceable by label language if, in the future, they are demonstrated to achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.

The Agency will make use of the results of the small-scale run-off/vegetative buffer strip study in refining the aquatic exposure and risk assessment.¹ If the employment of the data from the small-scale run-off/vegetative buffer strip study, together with other available data, result in the Agency's conclusion that there are no risk concerns, then no further work, including the monitoring program, need be conducted. However, if risk concerns remain, then the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations.

3. The Environmental Fate and Effects risk assessment (copy enclosed), suggests that both flubendiamide and its NNI-0001-des-iodo (des-iodo) degradate will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. The available mesocosm data does not provide evidence to refute these conclusions. No degradation pathway was identified for des-iodo. As such, Bayer will commit to generate and submit the following data (studies) on the des-iodo degradate to determine if Agency assumptions of chemical stability are appropriate:

Guideline Number	Title of Study	Date Due
161-1	Hydrolysis – A hydrolysis study is requested to establish the significance of chemical hydrolysis as a route of degradation for des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.	October 30, 2010
162-4	Aerobic Aquatic Metabolism – An aerobic aquatic metabolism study is requested to assist in determining the effects of des-iodo on aerobic conditions in water and sediments during the period of dispersal of des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modelling uncertainty.	October 30, 2010

4. For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), Bayer will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.
5. Nichino America Inc. (Nichino) (or some other person who consents to Nichino's reliance on the data) understands and agrees that the time-limited registration of the flubendiamide technical product shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.
6. The EPA and Nichino (or some other person who consents to Nichino's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide technical product, as well as Nichino's (or some other person who consents to Nichino's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:
 - (a) Nichino (or some other person who consents to Nichino's reliance on the data) shall submit all data identified in paragraphs 2-4, on or before July 31, 2012, according to the schedules set forth in those paragraphs.

¹ The goal of the vegetative buffer strip study is to determine how much of a buffer is necessary to prevent both flubendiamide applied to a field and des-iodo formed in the field from accumulating to levels in aquatic environments that pose risk to freshwater benthic invertebrates. Therefore, showing "that the level of the des-iodo degradate leaving the field (prior to reaching the buffer) is insignificant," would be insufficient justification to remove "the 15 foot buffer requirement."

- (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Nichino (or some other person who consents to Nichino's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists, as agents for Nichino, shall engage in dialogue about the data and the Agency's conclusions.
 - (c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide technical product unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Nichino will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide technical product.
 - (d) If, after EPA's review of the data as set forth in 6(b) above, the Agency makes a determination that further registration of the flubendiamide technical product will result in unreasonable adverse effects on the environment, within one (1) week of this finding, to be effective no earlier than September 1, 2013, Nichino will submit a request for voluntary cancellation of the flubendiamide technical product registration. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.
 - (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide technical product registration could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Nichino agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.
7. Bayer understands and agrees that the time-limited registration of the flubendiamide end-use products shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment. In addition, this regulatory action will establish permanent tolerances in primary crops for residues of flubendiamide.
8. The EPA and Bayer (or some other person who consents to Bayer's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide end-use products, as well as Bayer's (or some other person who consents to Bayer's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:
- (a) Bayer (or some other person who consents to Bayer's reliance on the data) shall submit all data identified in paragraphs 2-4, on or before July 31, 2012, according to the schedules set forth in those paragraphs.
 - (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Bayer (or some other person who consents to Bayer's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists shall engage in dialogue about the data and the Agency's conclusions.
 - (c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide end-use products unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Bayer will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide end-use products.
 - (d) If, after EPA's review of the data as set forth in 8(b) above, the Agency makes a determination that further registration of the flubendiamide end-use products will result in unreasonable adverse effects on the environment, within one (1) week of this finding, to be effective no earlier than September 1, 2013, Bayer will submit a request for voluntary cancellation of the flubendiamide end-use product registrations. That request shall include a statement that Bayer recognizes and agrees that the cancellation request is irrevocable.

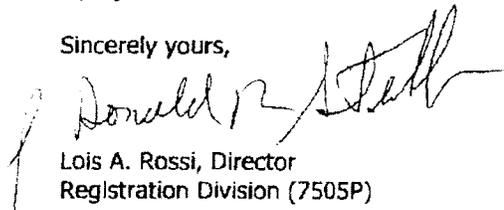
- (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide end-use product registrations could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Bayer agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.

The "Notice of Registration" will be issued under separate cover when you have agreed in writing to the conditions stated within this letter. **Further, this letter DOES NOT constitute registration, and the products MAY NOT be lawfully marketed until they are registered.**

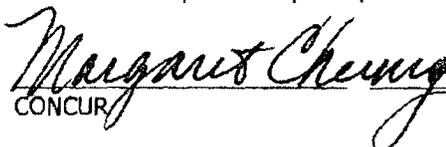
Nichino and Bayer should recognize that if EPA issues any technical and/or end-use product registration pursuant to the requirements of section 3(c)(7)(C) of FIFRA, such registration will contain any conditions that are a necessary component of EPA's findings that the statutory requirements for issuing a registration are met. Any such registration will provide that Nichino's or Bayer's release for shipment of any product pursuant to any such registration signals Nichino's or Bayer's acceptance of all of those conditions. If either Nichino or Bayer does not agree with any of the conditions of registration, they should consider any such registration to be null and void. If either Nichino or Bayer notifies EPA that it is unwilling to accept any of those conditions, EPA will commence the appropriate denial process under section 3(c)(6) of FIFRA.

If you have any questions regarding anything in this letter, please contact Mr. Carmen J. Rodia, Jr. directly at (703) 306-0327 or via e-mail at Rodia.Carmen@epa.gov.

Sincerely yours,


Lois A. Rossi, Director
Registration Division (7505P)

Bayer CropScience LP hereby concurs with the time-limited conditional registration of the new insecticide flubendiamide under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as outlined in this preliminary acceptance letter, dated July 31, 2008.

 7/31/08
CONCUR DATE

DO NOT CONCUR

DATE

Enclosures:

- Copy of Human Health Effects Risk Assessment for Flubendiamide, dated April 3, 2008
- Copy of Environmental Fate and Effects Risk Assessment for Flubendiamide, dated June 23, 2008
- Copy of Public Interest Finding for Flubendiamide, dated April 15, 2008
- Copy of Acute Toxicity Review for NNI-0001 Technical, dated October 12, 2007
- Copy of Acute Toxicity Review for NNI-0001 24 WG, dated July 15, 2007
- Copy of Acute Toxicity Review for NNI-0001 480 SC, dated October 12, 2007
- Copy of Product Chemistry Review for NNI-0001 Technical, dated October 24, 2007
- Copy of Product Chemistry Review #1 for NNI-0001 24 WG, dated October 18, 2007
- Copy of Product Chemistry Review #2 for NNI-0001 24 WG, dated January 25, 2008
- Copy of Product Chemistry Review for NNI-0001 480 SC, dated October 19, 2007

071711-00026 0366875
000264-01026 0366877
000264-01025 0366876
PP# 6F7063 0366884

RESPONDENT EXHIBIT 3

 <p align="center"> U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs Registration Division (7505C) 1200 Pennsylvania Ave., N.W. Washington, D.C. 20460 </p> <p align="center"> NOTICE OF PESTICIDE: <input checked="" type="checkbox"/> Registration <input type="checkbox"/> Reregistration <small>(under FIFRA, as amended)</small> </p>	EPA Reg. Number: 71711-26	Date of Issuance: AUG 0 1 2008
	Term of Issuance: Conditional	
	Name of Pesticide Product: NNI-0001 Technical	
Name and Address of Registrant (include ZIP Code): Nichino America, Inc. c/o Bayer CropScience LP 2 T.W. Alexander Drive Research Triangle Park, NC 27709-2014		
<p>Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.</p>		
<p>On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.</p> <p>Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.</p> <p align="center">This product is conditionally registered in accordance with FIFRA section 3(c)(7) provided that you:</p> <ol style="list-style-type: none"> 1. Make the following change to the label: <ol style="list-style-type: none"> a. Change the product registration number to "EPA Reg. No. 71711-26" 		
<p>(continued on page 2)</p>		
Signature of Approving Official: Refer to Page #2. Richard J. Gebken, Product Manager (10) Insecticide Branch, Registration Division (7505P)	Date: AUG 0 1 2008	

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12

2. Submit two (2) copies of the final printed labeling before releasing the product for shipment.

Your release for shipment of these products constitutes acceptance of the conditions of registration as outlined in the preliminary acceptance letter for flubendiamide, dated July 31, 2008. If these conditions are not complied with, the registration will be subject to cancellation in accordance with section 6(e) of FIFRA.

A stamped "Accepted" copy of the label for this product is enclosed for your records.

Sincerely yours,



Richard J. Gebken,
Product Manager (10)
Insecticide Branch,
Registration Division (7505P)

Enclosures: Copy of label for NNI-0001 480 SC stamped "Accepted," dated August 1, 2008

000264-01025 D366878

264-1025

8/01/2008

1/12



U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg. Number:

264-1025

Date of Issuance:

AUG 01 2008

NOTICE OF PESTICIDE:

Registration
 Reregistration
(under FIFRA, as amended)

Term of Issuance:

Conditional

Name of Pesticide Product:

NNI-0001 480 SC

Name and Address of Registrant (include ZIP Code):

Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709-2014

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7) provided that you:

1. Make the following change to the label:
 - a. Change the product registration number to "EPA Reg. No. 264-1025"

(continued on page 2)

Signature of Approving Official:

Refer to Page #2.

Richard J. Gebken, Product Manager (10)
Insecticide Branch, Registration Division (7505P)

Date:

AUG 01 2008

2. Submit two (2) copies of the final printed labeling before releasing the product for shipment.

2/4

Your release for shipment of these products constitutes acceptance of the conditions of registration as outlined in the preliminary acceptance letter for flubendiamide, dated July 31, 2008. If these conditions are not complied with, the registration will be subject to cancellation in accordance with section 6(e) of FIFRA.

A stamped "Accepted" copy of the label for this product is enclosed for your records.

Sincerely yours,



Richard J. Gebken,
Product Manager (10)
Insecticide Branch,
Registration Division (7505P)

Enclosures: Copy of label for NNI-0001 Technical stamped "Accepted," dated August 1, 2008

071711-00264 D366875

71711-32

03/04/2009

1/13



U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg. Number:

71711-32

Date of Issuance:

MAR 4 2009

NOTICE OF PESTICIDE:

Registration
 Reregistration
(under FIFRA, as amended)

Term of Issuance:

Conditional

Name of Pesticide Product:

NNI-0871 SC (Vetica™
Insecticide)

Name and Address of Registrant (include ZIP Code):

Nichino America, Inc.
4550 New Linden Hill Road, Suite 501
Wilmington, DE 19808-2951

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with section 3(c)(7) of FIFRA provided that you:

1. Make the following change(s) to the label:
 - a. Change the product registration number to "EPA Reg. No. 71711-32"

(continued on page 2)

Signature of Approving Official:

Refer to Page #2.

Richard J. Gebken, Product Manager (10)
Insecticide Branch, Registration Division (7505P)

Date:

MAR 4 2009

2
13

Data Requirements:

1. Within one (1) year from the date of this registration, Bonide Products, Inc. is obligated to submit an Enforcement Analytical Method (830.1800) study, a One Year Storage Stability (830.6317) study and a Corrosion Characteristics (830.6320) study on this product in support of this registration.¹
2. Submit two (2) copies of the final printed labeling before releasing the product for shipment.

Your release for shipment of these products constitutes acceptance of the conditions of registration as outlined in the preliminary acceptance letter for the flubendiamide + buprofezin premix products, dated March 4, 2009. If these conditions are not complied with, the registration will be subject to cancellation in accordance with section 6(e) of FIFRA.

A stamped "Accepted" copy of the label for this product is enclosed for your records.

Sincerely yours,



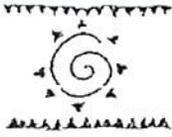
Richard J. Gebken,
Product Manager (10)
Insecticide Branch,
Registration Division (7505P)

Enclosure: Copy of label for NNI-0871 SC (Vetiva™ Insecticide) stamped "Accepted," dated March 4, 2009

071711-00032 D398900

¹For more detailed information, please refer to the product chemistry review for this product

RESPONDENT EXHIBIT 4



{In Archive} Draft Copy of Preliminary Acceptance Letter for Flubendiamide

Carmen Rodia to: clive.halder

07/17/2008 02:44 PM

Cc: Danielle.Larochelle, Lois Rossi, Marion Johnson, Richard Gebken, George LaRocca, Kimberly Nesci

Archive:

This message is being viewed in an archive.

Hello Clive:

As per Lois Rossi's direction, attached please find a draft copy of the preliminary acceptance letter for flubendiamide. Regards, Carmen Rodia.



Flubendiamide, DRAFT Preliminary Acceptance Letter (07-17-08).pdf

Carmen J. Rodia, Jr.
Environmental Protection Specialist
U.S. EPA, Office of Pesticide Programs,
Registration Division, Insecticide Branch
(703) 306-0327 (tel)
(703) 308-0029 (fax)
Rodia.Carmen@epa.gov



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

___ day, July __, 2008

CERTIFIED MAIL: (Article Number 7008 0150 0002 6191 4899)

Ms. Danielle A. Larochelle, Registration Product Manager
Agent for Nichino America, Inc.
c/o Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709-2014

Subject: Application for a New Section 3 Registration of Flubendiamide with Associated Tolerance NNI-0001 Technical (EPA File Symbol 71711-EA); NNI-0001 24 WG (EPA File Symbol 264-RNEA); NNI-0001 480 SC (EPA File Symbol 264-RNEL); and Tolerance Petition No. 6F7056

Dear Ms. Larochelle:

The products referred to above will be acceptable for registration under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, provided that you agree in writing that:

- The subject products will be conditionally registered for a period of 5 years from the date of the Notice of Registration.
- You will generate and submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

Guideline Reference No.	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study and Monitoring Program - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July __, 2013
NOTE: You will submit to EPA a final protocol for the above study on or before ____, 200__. You will submit annual monitoring progress reports on or before December 31 st of each year during the study. You will provide the Agency with a final monitoring report on or before ____, 2013.		

The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. The small-scale run-off/vegetative buffer strip study and monitoring program would allow the Agency to quantitatively consider the impact of such buffers on the risk picture. Such studies have been proposed and conducted for other relatively persistent and sediment-bound chemicals in Bayer CropScience LP's inventory. In order for a similar course of study to be implemented with flubendiamide, it is recommended that the protocol for such studies, like in past cases, be a product of a dialogue between Agency and registrant scientists. Such dialogue, and protocols arising from it, should be mindful of the need to both consider the variety of proposed use sites as well as a variety of buffer conditions. The buffer conditions used for this study should constitute methods deemed enforceable by label language if, in the future, they are

demonstrated to achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.

If the employment of label enforceable buffers is empirically demonstrated to meet the goal of meaningful reductions in off-site transport and risk, then no further work need be conducted. However, if buffers cannot be demonstrated to achieve these meaningful risk reductions, the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations. Like other chemicals with persistent properties in the Bayer CropScience LP's inventory, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used. Again, previous cases with Bayer CropScience LP chemicals have provided a relatively straight forward path for developing such data and what issues need to be negotiated between Bayer CropScience LP and EPA scientists.

- The Environmental Fate and Effects risk assessment (copy enclosed), suggests that both flubendiamide and its NNI-0001-des-iodo degradate (des-iodo) will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. The available mesocosm data does not provide evidence to refute these conclusions. No degradation pathway was identified for des-iodo. As such, you will commit to generate and submit the following data (studies) on the des-iodo degradate to determine if Agency assumptions of chemical stability are appropriate:

Guideline Reference No.	Title of Study	Date Due
161-1	Hydrolysis – A hydrolysis study is requested to establish the significance of chemical hydrolysis as a route of degradation for NNI-0001-des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.	May __, 2009
161-2	Photodegradation in Water – Pesticides introduced into aqueous systems in the environment can undergo photolytic transformation by sunlight. Data on rates of photolysis are requested to establish the importance of this transformation process and the persistence characteristics of the photoproducts formed.	May __, 2009
162-3	Anaerobic Aquatic Metabolism – An anaerobic aquatic metabolism study is requested to assess the effects the nature and extent of formation of NNI-0001-des-iodo residues in water and in hydrosol since anaerobic conditions are more likely to exist in aquatic environments.	October __, 2010
162-4	Aerobic Aquatic Metabolism – An aerobic aquatic metabolism study is requested to determine the effects on NNI-0001-des-iodo to aerobic conditions in water and sediments during the period of dispersal of NNI-0001-des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modeling uncertainty.	October __, 2010
164-1	Terrestrial Field Dissipation Studies – NNI-0001-des-iodo is persistent and moderately mobile which increases the likelihood for run-off and leaching. Terrestrial field dissipation studies are requested for NNI-0001-des-iodo since no definitive studies on the field dissipation and degradation properties of NNI-0001-des-iodo have been submitted to the Agency.	October __, 2010

4. For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), you will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.
5. All end-use product labeling submitted to EPA on April 7, 2006, and updated/revised on July 3, 2008, must be further revised by incorporating the following label revisions before you package and release these products for shipment:

(a) On the proposed label for NNI-0001 480 SC (EPA File Symbol 264-RNEL), you will be required to clearly articulate what application method(s) are proposed for each listed crop.

(b) Both end-use labels, NNI-0001 24 WG (EPA File Symbol 264-RNEA) and NNI-0001 480 SC (EPA File Symbol 264-RNEL), restrict use to once per season; however, there are crops such as *Brassica*, Cucurbits, Leafy Vegetables and Fruiting Vegetables that often have more than 1 season in a year. In the EFED risk assessment for flubendiamide, RQs are based on 1 season per year and risk is underestimated for crops that have more than 1 growing season per year. This concern was discussed with Bayer CropScience LP and a proposed label revision was presented to EPA on July 9, 2008, identifying the following label changes: reduced application rates, changing from "per year" to "per crops season" and removing the number of applications per crop season for *Brassica*, Cucurbits, Leafy Vegetables and Fruiting Vegetables. **The Agency accepts your proposed changes to the labels for the referenced crop groupings.**

(c) Insert the following new subsection into the "**DIRECTIONS FOR USE**" section, immediately preceding the "**AGRICULTURAL USE REQUIREMENTS**" text box as follows:

BUFFER ZONES

Vegetative Buffer Strip

Construct and maintain a minimum 15-foot wide vegetative filter strip of grass or other permanent vegetation between field edge and down gradient aquatic habitat (such as, but not limited to, lakes; reservoirs; rivers; permanent streams; marshes or natural ponds; estuaries; and commercial fish farm ponds).

Only apply products containing flubendiamide onto fields where a maintained vegetative buffer strip of at least 15 feet exists between the field edge and down gradient aquatic habitat.

For guidance, refer to the following publication for information on constructing and maintaining effective buffers:

Conservation Buffers to Reduce Pesticide Losses. Natural Resources Conservation Services. USDA, 2000. Fort Worth, Texas. 21 pp.

<http://www.in.csusda/v/techpical/aronom/newconbuf.pdf>

(d) Replace the last sentence in the "**Importance of Droplet Size:**" subsection of the "**SPRAY DRIFT REDUCTION MANAGEMENT**" section with: "Use only Medium or coarser spray nozzles (for ground and non-ULV aerial application) according to ASAE (S572) definition for standard nozzles. In conditions of low humidity and high temperatures, applicators should use a coarser droplet size."

- (e) Insert the following new subsection immediately following the **"Importance of Droplet Size:"** subsection of the **"SPRAY DRIFT REDUCTION MANAGEMENT"** section as follows:

"Ground Applications:

Wind speed must be measured adjacent to the application site on the upwind side, immediately prior to application. For ground boom applications, apply using a nozzle height of no more than 4 feet above the ground or crop canopy. For airblast applications, turn off outward pointing nozzles at row ends and when spraying the outer two (2) rows. To minimize spray loss over the top in orchard applications, spray must be directed into the canopy."

- (f) Replace the 2nd and 3rd sentences in the **"Aerial Applications:"** subsection of the **"SPRAY DRIFT REDUCTION MANAGEMENT"** section with: "The minimum practical boom length should be used, and must not exceed 75% of the wing span or 80% rotor diameter. Flight speed and nozzle orientation must be considered in determining droplet size. Spray must be released at the lowest height consistent with pest control and flight safety. Do not release spray at a height greater than 10 feet above the crop canopy unless a greater height is required for aircraft safety. When applications are made with a cross-wind, the swath will be displaced downwind. The applicator must compensate for this displacement at the downwind edge of the application area by adjusting the path of the aircraft upwind."

- (g) Replace the 1st, 2nd and 3rd sentences in the **"Wind Speed Restrictions:"** subsection of the **"SPRAY DRIFT REDUCTION MANAGEMENT"** section with: "Drift potential increases at wind velocities of less than 3 mph (due to inversion potential) or more than 10 mph. However, many factors, including droplet size, canopy and equipment specifications determine drift potential at any given wind speed. Only apply this product if the wind direction favors on-target deposition. Do not apply when wind velocity exceeds 15 mph and avoid gusty and windless conditions."

- (h) Replace the 4th sentence in the **"Restrictions During Temperature Inversions:"** subsection of the **"SPRAY DRIFT REDUCTION MANAGEMENT"** section with: "Temperature inversions are characterized by stable air and increasing temperatures with altitude and are common on nights with limited cloud cover and light to no wind."

- (i) Replace the 6th and 7th sentences in the **"Restrictions During Temperature Inversions:"** subsection of the **"SPRAY DRIFT REDUCTION MANAGEMENT"** section with: "Their presence can be indicated by mist or ground fog; however if fog is not present, inversions can also be identified by the movement of smoke from a ground source. Smoke that layers and moves laterally near the ground surface in a concentrated cloud (under low wind conditions) indicated an inversion, while smoke that moves upward and rapidly dissipates indicated good vertical mixing."

6. Bayer CropScience LP shall submit a request for voluntary cancellation of this registration within sixty (60) days of the grant of the registration. That request shall include a statement that Bayer CropScience LP recognizes and agrees that the cancellation request is irrevocable. That request may include the following conditions:

(a) The cancellation will not become effective before July __, 2013.

(b) The cancellation will not become effective if Bayer submits the data identified in paragraphs 2-4 according to the schedules set forth in those paragraphs, and EPA has not determined in writing on or before July __, 2013, that, after review of the data, the Agency is unable to make a determination that further registration of flubendiamide will not result in unreasonable adverse effects on the environment.

7. Notwithstanding Item #6 above, this registration will expire on July __, 2013, unless EPA determines, at its sole discretion, to extend the registration.

The proposed labeling will be further revised to incorporate the label changes specified in Item #5 above before being approved/registered. In addition, the "Notice of Registration" will be issued under separate cover when you have agreed in writing to the conditions stated within this letter. **Further, this letter does not constitute registration, and the products may not be lawfully marketed until they are registered.**

If Bayer CropScience LP complies with the conditions set forth in this letter, it is EPA's current intention to: (1) Complete its review of all relevant data and other information that are available to the Agency and make a determination as to whether flubendiamide registrations can meet the standards for registration set forth in section 3(c)(5) of FIFRA by December __, 2012.

Bayer CropScience LP should recognize that if EPA issues a registration pursuant to the requirements of section 3(c)(7)(C) of FIFRA, that registration will contain any conditions that are a necessary component of EPA's findings that the statutory requirements for issuing a registration are met. The registration will provide that Bayer CropScience LP's release for shipment of any product pursuant to the registration signals Bayer CropScience LP's acceptance of all those conditions. If Bayer CropScience LP does not agree with any of the conditions of registration, it should consider the registration to be null and void. If Bayer CropScience LP notifies EPA that it is unwilling to accept any of those conditions, EPA will commence the appropriate denial process under section 3(c)(6) of FIFRA.

If you have any questions regarding anything in this letter, please contact Mr. Carmen J. Rodia, Jr. directly at (703) 306-0327 or via e-mail at Rodia.Carmen@epa.gov.

Sincerely yours,

Lois A. Rossi, Director
Registration Division (7505P)

Enclosures:

- Copy of Human Health Effects Risk Assessment for Flubendiamide, dated April 3, 2008*
- Copy of Environmental Fate and Effects Risk Assessment for Flubendiamide, dated June 23, 2008*
- Copy of Public Interest Finding for Flubendiamide, dated April 15, 2008*
- Copy of Acute Toxicity Review for Flubendiamide Technical, dated October 12, 2007*
- Copy of Acute Toxicity Review for 24 WG, dated July 15, 2007*
- Copy of Acute Toxicity Review for 480 SC, dated October 12, 2007*
- Copy of Product Chemistry Review for Flubendiamide Technical, dated October 24, 2007*
- Copy of Product Chemistry Review #1 for 24 WG, dated October 18, 2007*
- Copy of Product Chemistry Review #2 for 24 WG, dated January 25, 2008*
- Copy of Product Chemistry Review for 480 SC, dated October 19, 2007*

071711-00026 D366875
000264-D1026 D366877
000264-D1025 D366878
PP# 6F7065 D366884



Archive:

{In Archive} Flubendiamide - Preliminary Acceptance Letter

Danielle Larochelle to: Carmen Rodia
Cc: clive.halder, Richard Gebken, Marion Johnson

07/23/2008 09:31 AM

This message is being viewed in an archive.

Carmen,
Attached is Bayer CropScience counter proposal to EPA's draft preliminary acceptance letter for Flubendiamide.

Best regards,

Danielle

The information contained in this e-mail is for the exclusive use of the intended recipient(s) and may be confidential, proprietary, and/or legally privileged. Inadvertent disclosure of this message does not constitute a waiver of any privilege. If you receive this message in error, please do not directly or indirectly use, print, copy, forward, or disclose any part of this message. Please also delete this e-mail and all copies and notify the sender. Thank you.

For alternate languages please go to <http://bayerdisclaimer.bayerweb.com>



07-23-08 Flubendiamide Pre-Registration Agreement - Counter Language from BCSI.pdf

Bayer CropScience



July 23, 2008

Mr. Richard Gebken, PM 10
Registration Division
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, Virginia 22202-4501

Dear Mr. Gebken,

Re: **Flubendiamide (NNI-0001) – Petition 6F7065**
Pre-Registration Agreement

Bayer CropScience
RTP
P.O. Box 10074
RTP, NC 27709
Tel: 919 649 2000

On behalf of Nichino America, Inc., Bayer CropScience LP is providing in the attached document counter language to the draft preliminary acceptance letter that EPA sent by email on July 17, 2008.

Please let me know if you would like to discuss any of the changes proposed. You can reach me by phone at (919) 549-2718 (cell: 919 368-3448) or by email at Danielle.Larochelle@bayercropscience.com.

Sincerely,

A handwritten signature in cursive script that reads "Danielle A. Larochelle".

Danielle A. Larochelle
Registration Product Manager
Agent for Nihon Nohyaku Co. Ltd.

Attachment: Flubendiamide Pre-Registration Agreement, Bayer CropScience LP counter proposal, July 23, 2008

cc: Mr. Carmen Rodia, Team 10

EPA Corr. No. daL070-08

On behalf of Nichino America, Inc., Bayer CropScience LP herein provides counter language to the draft pre-registration agreement, as issued via e-mail by EPA to Bayer CropScience LP on July 17th:

Part 2: In the first table box, delete Due Date of "July ____, 2013" for the Vegetative Buffer Strip Study and replace with "July 31, 2012" and under NOTE: insert the following dates: _____ and July 31, 2012.

Replace the paragraph following the first table box with the following modified language:

The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. Open literature and Bayer CropScience LP conducted studies on compounds with similar characteristics to flubendiamide provide information that permits an estimation of the impact of such buffers on the risk picture. A confirmatory small-scale run-off/vegetative buffer strip study and monitoring program with flubendiamide will allow the Agency to quantitatively consider the impact of such buffers strips on risk reduction in critical use areas. It is recommended that the protocol for such studies, like in past cases, be a product of a dialogue between Agency and registrant scientists. Such dialogue, the protocols arising from it and assessment of supporting literature should be mindful of the need to address vulnerable use patterns and sites as well as a variety of buffer conditions. The buffer conditions used for this study should support potential mitigation enforceable by label language if, in the future, they are demonstrated to achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.

Part 3: Date Due for all Guideline Reference No's should be revised as follows:

<u>Guideline</u>	<u>Date</u>
Non-Guideline	July 31, 2012
Non-Guideline	July 31, 2012
#161-1	December 15, 2009

Part 6 of draft pre-registration agreement should be entirely replaced with the following language:

Bayer CropScience LP understands and agrees the time-limited registration of flubendiamide shall be cancelled if the EPA determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.

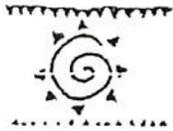
The EPA and Bayer CropScience LP agree on the following data review guidelines and timelines related to the conditions of registration for flubendiamide and its subsequent registration under section 3(c)(5) of FIFRA, as well as Bayer Crop Science's generation of, and the EPA's review of, such additional data during the term of the time-limited registration, as follows:

- (a) Bayer CropScience, LP shall submit to the EPA all data required under this Agreement by the specified timelines as described in Parts 2, 3, and 4, with the submission of the final study report [the Vegetative Buffer Strip Study] by July 31, 2012.
- (b) The EPA shall complete its review of the entire required data set and any additional data and supporting information voluntarily submitted by Bayer CropScience LP by January 31, 2013.
- (c) Between February 1, 2013 and July 31, 2013 EPA scientists and Bayer CropScience LP scientists shall engage in dialogue about the data and the EPA's conclusions.
- (d) By September 1, 2013, the EPA shall either: (1) approve the registration of Flubendiamide unconditionally; or (2) the EPA and Bayer CropScience LP mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) the EPA cancels the time-limited registration of flubendiamide, the cancellation of which shall not take effect until September 15, 2013.

Part 7: Entirely delete the first paragraph. "Notwithstanding Item #6 above, this registration will expire on July ____, 2013, unless EPA determines, at its sole discretion, to extend the registration."

Entirely delete the third paragraph "If Bayer CropScience LP complies with the conditions set forth in this letter, it is EPA's current intention to: (1) complete its review of all relevant data and other information that are available to the Agency and make a determination as to whether flubendiamide registrations can meet the standards for registration set forth in section 3(c)(6) of FIFRA by December __, 2012."

On the last page, before the last paragraph "If you have any questions regarding ... Rodia.Carmen@epa.gov.", add: "The terms of the time-limited registration of flubendiamide do not preclude the Agency from working on additional actions for flubendiamide including the review of (1) petitions for the establishment of tolerances for flubendiamide in or on additional crops and (2) applications for the registration of new formulations containing flubendiamide that may be submitted between July 26, 2008 and September 15, 2013.



{In Archive} Re: Flubendiamide - Preliminary Acceptance Letter 

Carmen Rodia to: Danielle Larochelle

07/29/2008 04:31 PM

Cc: Marion Johnson, Richard Gebken

Archive:

This message is being viewed in an archive.

Danielle, attached is an MS Word version of the draft preliminary acceptance letter for flubendiamide for your use and reference. Regards, Carmen Rodia.



Flubendiamide, Preliminary Acceptance Letter (07-29-08).doc

Carmen J. Rodia, Jr.
Environmental Protection Specialist
U.S. EPA, Office of Pesticide Programs,
Registration Division, Insecticide Branch
(703) 306-0327 (tel)
(703) 308-0029 (fax)
Rodia.Carmen@epa.gov



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
 WASHINGTON, D.C. 20460-0001

OFFICE OF
 PREVENTION, PESTICIDES
 AND TOXIC SUBSTANCES

____ day, July __, 2008

CERTIFIED MAIL: (Article Number 7008 0150 0002 6191 4899)

Ms. Danielle A. Larochelle, Registration Product Manager
 Agent for Nichino America, Inc.
 c/o Bayer CropScience LP
 2 T.W. Alexander Drive
 Research Triangle Park, NC 27709-2014

Subject: Application for a New Section 3 Registration of Flubendiamide with Associated Tolerance
 NNI-0001 Technical (EPA File Symbol 71711-EA); NNI-0001 24 WG (EPA File Symbol 264-RNEA);
 NNI-0001 480 SC (EPA File Symbol 264-RNEL); and Tolerance Petition No. 6F7056

Dear Ms. Larochelle:

The products referred to above will be acceptable for registration under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, provided that you agree in writing that:

1. The subject products will be conditionally registered for a period of five (5) years from the date of the "Notice of Registration."
2. Bayer CropScience LP (Bayer) will generate and submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

Guideline Reference Number	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July 31, 2010
Non-Guideline	Monitoring Program – If vegetative buffers cannot be demonstrated to achieve meaningful risk reductions, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used.	July 31, 2012

NOTE: Bayer will submit to EPA a final protocol for the small-scale run-off/vegetative buffer study on or before January 31, 2009. Bayer will submit annual monitoring progress reports on or before December 31st of each year during the study. Bayer will provide the Agency with a final monitoring report on or before July 31, 2012.

The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. Open literature and Bayer-conducted studies on compounds with similar characteristics to flubendiamide provide information that permits an estimation of the impact of such buffers on the risk picture. A confirmatory small-scale run-off/vegetative buffer strip study with flubendiamide would allow the Agency to quantitatively consider the impact of such buffer strips on risk reduction in critical use areas. It is recommended that the protocol for the referenced study, like in past cases, be a product of a dialogue between EPA and Bayer scientists. Such dialogue, the protocols arising from it and assessment of supporting literature, should be mindful of the need to address vulnerable use patterns and sites as well as a variety of buffer conditions. The buffer conditions used for this study should support potential mitigation enforceable by label language if, in the future, they are demonstrated to

achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.¹

If the employment of label enforceable buffers is empirically demonstrated to meet the goal of meaningful reductions in off-site transport and risk, then no further work need be conducted. However, if buffers cannot be demonstrated to achieve these meaningful risk reductions, the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations. Like other chemicals with persistent properties in the Bayer's inventory, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used. Again, previous cases with Bayer chemicals have provided a relatively straight forward path for developing such data and what issues need to be negotiated between EPA and Bayer scientists.

The Environmental Fate and Effects risk assessment (copy enclosed), suggests that both flubendiamide and its NNI-0001-des-iodo degradate (des-iodo) will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. The available mesocosm data does not provide evidence to refute these conclusions. No degradation pathway was identified for des-iodo. As such, Bayer will commit to generate and submit the following data (studies) on the des-iodo degradate to determine if Agency assumptions of chemical stability are appropriate:

Guideline Reference Number	Title of Study	Date Due
161-1	<u>Hydrolysis – A hydrolysis study is requested to establish the significance of chemical hydrolysis as a route of degradation for des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.</u>	December 15, 2009
162-4	<u>Aerobic Aquatic Metabolism – An aerobic aquatic metabolism study is requested to assist in determining the effects of des-iodo on aerobic conditions in water and sediments during the period of dispersal of des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modeling uncertainty.</u>	October 30, 2010

- For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), Bayer will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.
- Nichino America Inc. (Nichino) (or some other person who consents to Nichino's reliance on the data) understands and agrees that the time-limited registration of the flubendiamide technical product shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.
- The EPA and Nichino (or some other person who consents to Nichino's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide technical product, as well as Nichino's (or some other person who consents to Nichino's reliance on the data) generation of, and the EPA's subsequent review of, such additional data during the term of the time-limited registration, as follows:

¹ The goal of the vegetative buffer strip study is to determine how much of a buffer is necessary to prevent both flubendiamide applied to a field and des-iodo formed in the field from accumulating to levels in aquatic environments that pose risk to freshwater benthic invertebrates. Therefore, showing "that the level of the des-iodo degradate leaving the field (prior to reaching the buffer) is insignificant," would be insufficient justification to remove "the 15 foot buffer requirement.

- (a) Nichino (or some other person who consents to Nichino's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.
 - (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Nichino (or some other person who consents to Nichino's reliance on the data) by January 31, 2013. EPA scientists and Nichino scientists shall engage in dialogue about the data and the EPA's conclusions.
 - (c) If EPA has not determined in writing on or before September 1, 2013, that, after review of the data, the Agency is unable to make a determination that further registration of the flubendiamide technical product will not result in unreasonable adverse effects on the environment, within one (1) week of this finding, Nichino will submit a request for voluntary cancellation of the registration of the flubendiamide technical product. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.
 - (d) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide technical product unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Nichino will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide technical product.
 - (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide technical product registration could meet the standards for FIFRA registration, and Nichino agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.
6. Bayer understands and agrees that the time-limited registration of the flubendiamide end-use products shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.
 7. The EPA and Bayer (or some other person who consents to Bayer's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide end-use products, as well as Bayer's (or some other person who consents to Bayer's reliance on the data) generation of, and the EPA's subsequent review of, such additional data during the term of the time-limited registration, as follows:
 - (a) Bayer (or some other person who consents to Bayer's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.
 - (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Bayer (or some other person who consents to Bayer's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists shall engage in dialogue about the data and the EPA's conclusions.
 - (c) If EPA has not determined in writing on or before September 1, 2013, that, after review of the data, the Agency is unable to make a determination that further registration of the flubendiamide end-use products will not result in unreasonable adverse effects on the environment, within one (1) week of this finding, Bayer will submit a request for voluntary cancellation of the registration of the flubendiamide end-use products. That request shall include a statement that Bayer recognizes and agrees that the cancellation request is irrevocable.



Archive:

{In Archive} Fw: Flubendamide

Marion Johnson to: Carmen Rodia, Richard Gebken

07/30/2008 11:18 AM

This message is being viewed in an archive.

FYI !!!

Marion J. Johnson, Jr.,
Chief, Insecticide Branch
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
(703) 305-6788 (tel.)
(703) 308-0029 (fax)
johnson.marion@epa.gov
visit: <http://www.epa.gov/pesticides>

----- Forwarded by Marion Johnson/DC/USEPA/US on 07/30/2008 11:16 AM -----

Lois Rossi/DC/USEPA/US

07/30/2008 11:09 AM

To "Marion Johnson" <johnson.marion@epa.gov>, "Kathy
Monk" <monk.kathy@epa.gov>

cc

Subject Fw: Flubendamide

Here is what he sent. I isn't open the attachment on my blackberry.

Sent by EPA Wireless E-Mail Services.

From: Clive Halder [clive.halder@bayercropscience.com]
Sent: 07/30/2008 08:08 AM AST
To: Lois Rossi
Cc: Clive Halder <clive.halder@bayercropscience.com>; Danielle Larochelle
<danielle.larochelle@bayercropscience.com>
Subject: Re: Flubendamide

Hi Lois:

I am attaching a word copy of our response back to EPA below:

I am also extracting out the two, more salient components that we are addressing in order for you to

capture it on Blackberry. Basically, there is only one remaining "sore point", which revolves around paragraphs 5(c) and 7(c) (which are close duplicates of each other). It is a "sore point" because, first off, it is so vague as to not be understandable to us. Second, it appears to allow EPA to demand cancellation without any due process from us. My take is that the Agency would like to avoid having to go through Section 6 cancellation proceedings. We understand this, so have little problem with fitting in the "fast death" approach, i.e. voluntary cancellation within a week of the decision. From our side, we expect that a fair cancellation demand can only occur after the conditions of part 5(b) and 7(b) have been met, specifically, that all the submitted data have been reviewed alongside all voluntary data submitted by Bayer, plus following a measured dialogue between the scientists.

Item #1: Given that this is a legal agreement, we wanted to make sure we obtain as much clarity around the process of the conduct of the "run-off" studies where the outcome, as with any scientific data, do not lend themselves to the exactness of a legal document. Having said that, you can see we have no problem with what is being asked for. Our changes are mostly in the notes clarifying if/when the 2nd study may need to be initiated.

Guideline Reference Number	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July 31, 2010
	NOTE: Bayer will submit to EPA a final protocol for the small-scale run-off/vegetative buffer study on or before January 31, 2009. Bayer will submit annual progress reports on or before December 31st of each year during the study. Bayer will provide the Agency with a final monitoring report on or before July 31, 2010. The Agency will provide reviews of the annual and final reports within 60 days of the submission of each report.	
Non-Guideline	Monitoring Program - If risk assessment based on results from the small scale runoff/vegetative buffers study does not result in acceptable risk, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used.	July 31, 2012
	NOTE: If the monitoring study is deemed necessary, Bayer will submit to EPA a final protocol for the monitoring program on or before July 31, 2010. Bayer will submit annual monitoring progress reports on or before December 31st of each year during the study. Bayer will provide the Agency with a final monitoring report on or before July 31, 2012.	

Item #2: The "sore point". We have hopefully addressed our collective needs of the original sections 5(c) and 7(c) by deleting them in their entirety and rewriting them, respectively, so that they now read as follows:

5(c) If after review of the data, as set forth in 5 (b) above, the Agency makes a determination that further registration of the flubendiamide technical product will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Nichino will submit a request for voluntary cancellation of the registration of the flubendiamide technical product. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.

7(c) If after review of the data, as set forth in 7(b) above, the Agency makes a determination that further registration of the flubendiamide end-use products will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Bayer will submit a request for voluntary cancellation of the registration of the flubendiamide end-use products. That request shall include a statement that Bayer recognizes and agrees that the cancellation request is irrevocable.

With Best Regards,

Clive A. Halder
Bayer CropScience
Director of Regulatory Affairs
Business Unit - Insecticide & Seed Treatment
Tel: 919. 549. 2824
e-mail: clive.halder@bayercropscience.com

Rossi.Loïs@epamail.epa.gov

07/30/2008 01:41 AM

To "Clive Halder" <clive.halder@bayercropscience.com>
cc
Subject Re: Flubendamide

If you can cut and paste into a message I will read it. I didn't think we were to far. Need to take advantage of Friday window of time.

Sent by EPA Wireless E-Mail Services.

From: Clive Halder [clive.halder@bayercropscience.com]
Sent: 07/29/2008 06:57 PM AST
To: Lois Rossi
Cc: Clive Halder <clive.halder@bayercropscience.com>
Subject: Re: Flubendamide

Hi Lois:

Hope I am not interfering with your vacation already. We had a talk with Carmen Rodia this afternoon, and will be submitting some adjustments to the language tomorrow morning. We believe we are not far apart now. We will have a conference call with Marion, Carmen, some EFED folks tomorrow (probably by noon-ish). Hopefully, we will get to the point of sign-off this week (before Friday).

If you would like to see a copy of the 2nd-round letter from us, let me know. Otherwise, I do not want to mess with vacation time.

Cheers!

Clive A. Halder
Bayer CropScience
Director of Regulatory Affairs



{In Archive} Updated Draft Preliminary Acceptance Letter for
Flubendiamide

Carmen Rodia to: Danielle.Larochelle
Cc: Marion Johnson, Richard Gebken, Lois Rossi, Kathy Monk

07/30/2008 03:55 PM

Archive: This message is being viewed in an archive.

Danielle, Marion and I will call you and Clive in just a few minutes. I wanted you both to be able to look at the attached document as we speak. Regards, Carmen Rodia.



Flubendiamide, Preliminary Acceptance Letter (07-31-08).doc

Carmen J. Rodia, Jr.
Environmental Protection Specialist
U.S. EPA, Office of Pesticide Programs,
Registration Division, Insecticide Branch
(703) 306-0327 (tel)
(703) 308-0029 (fax)
Rodia.Carmen@epa.gov



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Thursday, July 31, 2008

CERTIFIED MAIL: (Article Number 7008 0150 0002 6191 4899)

Ms. Danielle A. Larochelle, Registration Product Manager
Agent for Nichino America, Inc.
c/o Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709-2014

Subject: Application for a New Section 3 Registration of Flubendiamide with Associated Tolerance NNI-0001 Technical (EPA File Symbol 71711-EA); NNI-0001 24 WG (EPA File Symbol 264-RNEA); NNI-0001 480 SC (EPA File Symbol 264-RNEL); and Tolerance Petition No. 6F7056

Dear Ms. Larochelle:

The products referred to above will be acceptable for registration under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, provided that Bayer CropScience LP (Bayer), as authorized agent for Nichino America, Ltd. (Nichino), agree/concur with the following conditions of registration:

- The subject products will be conditionally registered for a period of five (5) years from the date of the "Notice of Registration." ~~Notwithstanding the time-limited period of the registration, the tolerances will be unconditional and permanent.~~
- Bayer, as authorized agent for Nichino, will generate/submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

Guideline Number	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July 31, 2010
NOTE: Bayer will submit to EPA a final protocol for the small-scale run-off/vegetative buffer strip study on or before January 31, 2009. Bayer will submit annual monitoring progress reports on or before December 31st of each year during the study one (1) monitoring progress report by December 31, 2009 and a final report on or before July 31, 2012. Bayer will provide the Agency with a final monitoring report on or before July 31, 2012.		
Non-Guideline	Monitoring Program - If vegetative buffers cannot be demonstrated to achieve meaningful risk reductions, If risk assessment based on the results from the small-scale run-off/vegetative buffer strip study and additional available data demonstrate unacceptable risk, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used.	July 31, 2012
NOTE: Bayer will submit to EPA a final protocol for the monitoring program on or before January 31, 2009. Bayer will revise the protocol for the monitoring study, as necessary, within one (1) month following receipt of the Agency's decision that a monitoring program is necessary. If the monitoring program is deemed necessary, Bayer will discuss the decision of the monitoring study with EPA before initiating, and will provide the Agency with a final protocol on or before July 31, 2012.		

The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. Open literature and Bayer-conducted studies on compounds with similar characteristics to flubendiamide provide information that permits an estimation of the impact of such buffers on the risk picture. A confirmatory small-scale run-off/vegetative buffer strip study with flubendiamide would allow the Agency to quantitatively consider in the exposure assessment, the mass loadings expected from the application of the product and the impact of such buffer strips on risk reduction in critical use areas. It is recommended that the protocol for the referenced study, like in past cases, be a product of a dialogue between EPA and Bayer scientists. Such dialogue, the protocols arising from it and assessment of supporting literature, should be mindful of the need to address vulnerable use patterns and sites as well as a variety of buffer conditions. The buffer conditions used for this study should support potential mitigation enforceable by label language if, in the future, they are demonstrated to achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.¹

The Agency will make use of the results of the small-scale run-off/vegetative buffer strip study in refining the aquatic exposure and risk assessment. If the employment of label enforceable buffers is empirically demonstrated to meet the goal of the data from the small-scale run-off/vegetative buffer strip study, together with other available data, result in the Agency's conclusion that there are risk concerns meaningful reductions in off-site transport and risk, then no further work, including the monitoring program, need be conducted. However, if risk concerns remain, then buffers cannot be demonstrated to achieve these meaningful results from the refined exposure and risk assessment do not achieve acceptable risk reductions, the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations. Like other chemicals with persistent properties in the Bayer's inventory, there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used. Again, previous cases with Bayer chemicals have provided a relatively straight forward path for developing such data and what issues need to be negotiated between EPA and Bayer scientists.

The Environmental Fate and Effects risk assessment (copy enclosed), suggests that both flubendiamide and its NNI-0001-des-iodo (des-iodo) degradate will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. The available mesocosm data does not provide evidence to refute these conclusions. No degradation pathway was identified for des-iodo. As such, Bayer will commit to generate and submit the following data (studies) on the des-iodo degradate to determine if Agency assumptions of chemical stability are appropriate:

Guideline Number	Title of Study	Date Due
161-1	<u>Hydrolysis – A hydrolysis study is requested to establish the significance of chemical hydrolysis as a route of degradation for des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.</u>	December 15, 2009
162-4	<u>Aerobic Aquatic Metabolism – An aerobic aquatic metabolism study is requested to assist in determining the effects of des-iodo on aerobic conditions in water and sediments during the period of dispersal of des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modeling uncertainty.</u>	October 30, 2010

- For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), Bayer will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.

¹ The goal of the vegetative buffer strip study is to determine how much of a buffer is necessary to prevent both flubendiamide applied to a field and des-iodo formed in the field from accumulating to levels in aquatic environments that pose risk to freshwater benthic invertebrates. Therefore, showing "that the level of the des-iodo degradate leaving the field (prior to reaching the buffer) is insignificant," would be insufficient justification to remove "the 15 foot buffer requirement.

4. Nichino America Inc. (Nichino) (or some other person who consents to Nichino's reliance on the data) understands and agrees that the time-limited registration of the flubendiamide technical product shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.
5. The EPA and Nichino (or some other person who consents to Nichino's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide technical product, as well as Nichino's (or some other person who consents to Nichino's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:
 - (a) Nichino (or some other person who consents to Nichino's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.
 - (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Nichino (or some other person who consents to Nichino's reliance on the data) by January 31, 2013. EPA scientists and Bayer Nichino-scientists, as agents for Nichino, shall engage in dialogue about the data and the Agency's conclusions.
 - (c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide technical product unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Nichino will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide technical product.
 - ~~(c) If EPA has not determined in writing on or before September 1, 2013, that, after review of the data, the Agency is unable to make a determination that further registration of the flubendiamide technical product will not result in unreasonable adverse effects on the environment, within one (1) week of this finding, Nichino will submit a request for voluntary cancellation of the flubendiamide technical product registration. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.~~
 - ~~(d) If, by September 1, 2013, after review of the data as set forth in 5(b) above, the Agency makes a determination that further registration of the flubendiamide technical product will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Nichino will submit a request for voluntary cancellation of the flubendiamide technical product registration. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.~~
 - ~~(d) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide technical product unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Nichino will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide technical product.~~
 - (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide technical product registration could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Nichino agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.
6. Bayer understands and agrees that the time-limited registration of the flubendiamide end-use products shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.

7. The EPA and Bayer (or some other person who consents to Bayer's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide end-use products, as well as Bayer's (or some other person who consents to Bayer's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:
- (a) Bayer (or some other person who consents to Bayer's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.
 - (b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Bayer (or some other person who consents to Bayer's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists shall engage in dialogue about the data and the Agency's conclusions.
 - (c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide end-use products unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Bayer will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide end-use products.
 - ~~(c) If EPA has not determined in writing on or before September 1, 2013, that, after review of the data, the Agency is unable to make a determination that further registration of the flubendiamide end-use products will not result in unreasonable adverse effects on the environment, within one (1) week of this finding, Bayer will submit a request for voluntary cancellation of the flubendiamide end-use product registrations. That request shall include a statement that Bayer recognizes and agrees that the cancellation request is irrevocable.~~
 - ~~(d) If, by September 1, 2013, after review of the data as set forth in 7(b) above, the Agency makes a determination that further registration of the flubendiamide end-use products will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Bayer will submit a request for voluntary cancellation of the flubendiamide end-use product registrations. That request shall include a statement that Bayer recognizes and agrees that the cancellation request is irrevocable.~~
 - ~~(d) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide end-use products unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Bayer will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide end-use products.~~
 - (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide end-use product registrations could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Bayer agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.

The "Notice of Registration" will be issued under separate cover when you have agreed in writing to the conditions stated within this letter. **Further, this letter does not constitute registration, and the products may not be lawfully marketed until they are registered.**

~~If Nichino and Bayer comply with the conditions set forth in this letter, it is EPA's current intention to complete its review of all relevant data and other information that are available to the Agency and make a determination as to whether flubendiamide technical and end-use product registrations can meet the standards for registration set forth in section 3(c)(5) of FIFRA by January 31, 2013.~~

Nichino and Bayer should recognize that if EPA issues any technical and/or end-use product registration pursuant to the requirements of section 3(c)(7)(C) of FIFRA, such registration will contain any conditions that are a necessary component of EPA's findings that the statutory requirements for issuing a registration are met. Any such registration will provide that Nichino's or Bayer's release for shipment of any product pursuant to any such registration signals Nichino's or Bayer's acceptance of all of those conditions. If either Nichino or Bayer does not agree with any of the conditions of registration, they should consider any such registration to be null and void. If either Nichino or Bayer notifies EPA that it is unwilling to accept any of those conditions, EPA will commence the appropriate denial process under section 3(c)(6) of FIFRA.

If you have any questions regarding anything in this letter, please contact Mr. Carmen J. Rodia, Jr. directly at (703) 306-0327 or via e-mail at Rodia.Carmen@epa.gov.

Sincerely yours,

Lois A. Rossi, Director
Registration Division (7505P)

Bayer CropScience LP hereby concurs with the time-limited conditional registration of the new insecticide flubendiamide under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as outlined in this preliminary acceptance letter, dated July 31, 2008.

CONCUR

DATE

DO NOT CONCUR

DATE

Enclosures:

Copy of Human Health Effects Risk Assessment for Flubendiamide, dated April 3, 2008
Copy of Environmental Fate and Effects Risk Assessment for Flubendiamide, dated June 23, 2008
Copy of Public Interest Finding for Flubendiamide, dated April 15, 2008
Copy of Acute Toxicity Review for NNI-0001 Technical, dated October 12, 2007
Copy of Acute Toxicity Review for NNI-0001 24 WG, dated July 15, 2007
Copy of Acute Toxicity Review for NNI-0001 480 SC, dated October 12, 2007
Copy of Product Chemistry Review for NNI-0001 Technical, dated October 24, 2007
Copy of Product Chemistry Review #1 for NNI-0001 24 WG, dated October 18, 2007
Copy of Product Chemistry Review #2 for NNI-0001 24 WG, dated January 25, 2008
Copy of Product Chemistry Review for NNI-0001 480 SC, dated October 19, 2007

071711-00026 D366875
000264-01026 D366877
000264-01025 D366878
PP# 6P7065 D366884



{In Archive} Fw: Updated Draft Preliminary Acceptance Letter for
Flubendiamide

Danielle Larochelle to: Carmen Rodia

07/31/2008 10:07 AM

Cc: Marion Johnson, Richard Gebken

Archive:

This message is being viewed in an archive.

Carmen,

Thank you for arranging the conference call yesterday. It was helpful to discuss the remaining issues with you and Marion.

The following is revised language that we are proposing to incorporate in the last paragraph that begins on page 1 ("The Agency believes ..."), We proposed to revise the third sentence to (the text in blue italics is new language):

"... A confirmatory small-scale run-off/vegetative buffer strip study with flubendiamide would allow the Agency *to refine the modeling of the fate and mobility of flubendiamide in the field and* to quantitatively consider the impact of such buffer strips on risk reduction in critical use areas."

This would replace the statement we previously included in the sentence and that we discussed yesterday (" ... in the exposure assessment the mass loadings expected").

We believe it is important to include this statement for the following reason: The field study will provide data on the mobility of the compound in runoff water and sediment, as well as the effectiveness of vegetative filter strip (VFS) in reducing pesticide loading. The exposure assessment needs to be refined to capture both the behavior of the compound and the effectiveness of VFS observed in that study. Furthermore, the technology for modeling the effectiveness of VFS exists, and such technology coupled with PRZM/EXAMS models, will allow the calculation of the daily exposure levels.

I have attached below a copy of the letter you sent us yesterday. Most changes are now "accepted" on the document. The only changes tracked are the new revisions we discussed with you yesterday and the issues that remain to be addressed (e.g., page 1- tolerances are not time-limited, revised language and dates in the table; Parts 5d and 7d - "...by September 1, 2013..")

Also, I wanted to ask you if you discussed the buffer strip issue with your team. I had the impression that the vegetative buffer strip was supposed to be consistent with that required for the pyrethroids. Richard Gebken thought that it was changed to 15 ft. However, George LaRocca confirmed a couple of days ago that it is 10 ft and that no changes will be made. Let me know what you find out.

Please call if you and Marion would like to discuss any of the remaining issues.

Best regards,

Danielle

Corr. # daL076-08

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For alternate languages please go to <http://bayerdisclaimer.bayerweb.com>



Flubendiamide, Preliminary Acceptance Letter (07-31-08) Bayer Comments.doc



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Thursday, July 31, 2008

CERTIFIED MAIL: (Article Number 7008 0150 0002 6191 4899)

Ms. Danielle A. Larochelle, Registration Product Manager
Agent for Nichino America, Inc.
c/o Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709-2014

Subject: Application for a New Section 3 Registration of Flubendiamide with Associated Tolerance
NNI-0001 Technical (EPA File Symbol 71711-EA); NNI-0001 24 WG (EPA File Symbol 264-RNEA);
NNI-0001 480 SC (EPA File Symbol 264-RNEL); and Tolerance Petition No. 6F7056

Dear Ms. Larochelle:

The products referred to above will be acceptable for registration under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, provided that Bayer CropScience LP (Bayer), as authorized agent for Nichino America, Ltd. (Nichino), agree/concur with the following conditions of registration:

1. The subject products will be conditionally registered for a period of five (5) years from the date of the "Notice of Registration." *(Tolerances will not be time-limited)*
2. Bayer, as authorized agent for Nichino, will generate/submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

Guideline Number	Title of Study	Date Due
Non-Guideline	Small-Scale Run-Off/Vegetative Buffer Strip Study - A run-off study is requested to determine the magnitude of the parent, flubendiamide, retained in buffer strips of various widths.	July 31, 2010
NOTE: Bayer will submit to EPA a final protocol for the small-scale run-off/vegetative buffer strip study on or before January 31, 2009. Bayer will submit one (1) progress report by December 31, 2009 and a final report on or before July 31, 2010.		
Non-Guideline	Monitoring Program - If risk assessment based on the results from the small-scale run-off/vegetative buffer strip study and additional available data indicates that there are still risk concerns , there may be a need to conduct monitoring of receiving waters within watersheds where flubendiamide will be used.	July 31, 2012
NOTE: Bayer will submit to EPA a final protocol for the monitoring program on or before March 1, 2010 . Bayer will revise the protocol for the monitoring study, as necessary, within one (1) month following receipt of the Agency's decision that a monitoring program is necessary.		

Deleted: monitoring

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The Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain. Open literature and Bayer-conducted studies on compounds with similar characteristics to flubendiamide provide information that permits an estimation of the impact of such buffers on the risk picture. A confirmatory small-scale run-off/vegetative buffer strip study with flubendiamide would allow the Agency to refine the modeling of the fate and mobility of flubendiamide in the field and to quantitatively consider the impact of such buffer strips

on risk reduction in critical use areas. It is recommended that the protocol for the referenced study, like in past cases, be a product of a dialogue between EPA and Bayer scientists. Such dialogue, the protocols arising from it and assessment of supporting literature, should be mindful of the need to address vulnerable use patterns and sites as well as a variety of buffer conditions. The buffer conditions used for this study should support potential mitigation enforceable by label language if, in the future, they are demonstrated to achieve meaningful reductions in off-site transport and aquatic organism risk of the pesticide.¹

The Agency will make use of the results of the small-scale run-off/vegetative buffer strip study in refining the aquatic exposure and risk assessment. If the employment of the data from the small-scale run-off/vegetative buffer strip study, together with other available data, result in the Agency's conclusion that there are no risk concerns, then no further work, including the monitoring program, need be conducted. However, if risk concerns remain, then, the other areas of critical uncertainty in the modeling assumptions must be considered. In this case, there is considerable uncertainty in the application of the EXAMS pond scenario for chemicals with suspected aquatic system accumulation. Additional information on the actual potential for the pesticide to build up in receiving waters would address the uncertainty associated with current model limitations.

The Environmental Fate and Effects risk assessment (copy enclosed), suggests that both flubendiamide and its NNI-0001-des-iodo (des-iodo) degradate will accumulate to concentrations in aquatic environments that will pose risk to freshwater benthic invertebrates. The available mesocosm data does not provide evidence to refute these conclusions. No degradation pathway was identified for des-iodo. As such, Bayer will commit to generate and submit the following data (studies) on the des-iodo degradate to determine if Agency assumptions of chemical stability are appropriate:

Guideline Number	Title of Study	Date Due
161-1	Hydrolysis – A hydrolysis study is requested to establish the significance of chemical hydrolysis as a route of degradation for des-iodo and to identify, if possible, the hydrolytic products formed to provide initial information on whether they may exhibit structures that may potentially adversely affect non-target organisms.	December 15, 2009
162-4	Aerobic Aquatic Metabolism – An aerobic aquatic metabolism study is requested to assist in determining the effects of des-iodo on aerobic conditions in water and sediments during the period of dispersal of des-iodo throughout the aquatic environment and to compare rates and formation of metabolites. The data from this study would provide the aerobic aquatic input parameter for PRZM/EXAMS; therefore, potentially reducing modeling uncertainty.	October 30, 2010

- For the submitted GLN 860.1850 Confined Rotational Crop studies (MRIDs 46817133 and 46817134), Bayer will submit extraction and analysis dates of samples in order to confirm that samples were extracted and analyzed within the stated intervals (or within 6 months of harvest). Otherwise, additional storage stability data may be required by EPA.
- Nichino America Inc. (Nichino) (or some other person who consents to Nichino's reliance on the data) understands and agrees that the time-limited registration of the flubendiamide technical product shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment.
- The EPA and Nichino (or some other person who consents to Nichino's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide technical product, as well as Nichino's (or some other person who consents to Nichino's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:

¹ The goal of the vegetative buffer strip study is to determine how much of a buffer is necessary to prevent both flubendiamide applied to a field and des-iodo formed in the field from accumulating to levels in aquatic environments that pose risk to freshwater benthic invertebrates. Therefore, showing "that the level of the des-iodo degradate leaving the field (prior to reaching the buffer) is insignificant," would be insufficient justification to remove "the 15 foot buffer requirement."

(a) Nichino (or some other person who consents to Nichino's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.

(b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Nichino (or some other person who consents to Nichino's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists, as agents for Nichino, shall engage in dialogue about the data and the Agency's conclusions.

(c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide technical product unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Nichino will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide technical product.

(d) If, after review of the data as set forth in 5(b) above, the Agency makes a determination that further registration of the flubendiamide technical product will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Nichino will submit a request for voluntary cancellation of the flubendiamide technical product registration. That request shall include a statement that Nichino recognizes and agrees that the cancellation request is irrevocable.

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(e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide technical product registration could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Nichino agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.

6. Bayer understands and agrees that the time-limited registration of the flubendiamide end-use products shall be cancelled if the Agency determines that the continued use of flubendiamide will result in unreasonable adverse effects on the environment. (Tolerances will not be time-limited)

7. The EPA and Bayer (or some other person who consents to Bayer's reliance on the data) agree on the following data review guidelines and timelines related to the conditions of registration under section 3(c)(5) of FIFRA for the flubendiamide end-use products, as well as Bayer's (or some other person who consents to Bayer's reliance on the data) generation of, and the EPA's subsequent review of such additional data during the term of the time-limited registration, as follows:

(a) Bayer (or some other person who consents to Bayer's reliance on the data) shall submit all data identified in paragraphs 2-3, on or before July 31, 2012, according to the schedules set forth in those paragraphs.

(b) The EPA shall complete its review of the entire required data set and will consider any additional data and supporting information voluntarily submitted by Bayer (or some other person who consents to Bayer's reliance on the data) by January 31, 2013. EPA scientists and Bayer scientists shall engage in dialogue about the data and the Agency's conclusions.

(c) By September 1, 2013, the EPA shall either: (1) Approve the registration of the flubendiamide end-use products unconditionally, notwithstanding any restrictions that are deemed necessary; or (2) The EPA and Bayer will mutually agree on a path forward, revising or providing additional data under a conditional registration; or (3) The Agency will accept the voluntary cancellation of the time-limited registration of the flubendiamide end-use products.

(d) If, after review of the data as set forth in 7(b) above, the Agency makes a determination that further registration of the flubendiamide end-use products will result in unreasonable adverse effects on the environment, within one (1) week of this finding, Bayer will submit a request for voluntary cancellation of the flubendiamide end-use product registrations. That request shall include a

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statement that Bayer recognizes and agrees that the cancellation request is irrevocable.

- (e) No cancellation shall occur if EPA determines, after review of the data, that the flubendiamide end-use product registrations could meet the standards for registration set forth in section 3(c)(5) of FIFRA, and Bayer agrees in writing to comply with any conditions (including, but not limited to, revised label language, use deletions or conditions of registration) that EPA finds necessary in order to make the registration determination.

The "Notice of Registration" will be issued under separate cover when you have agreed in writing to the conditions stated within this letter. **Further, this letter does not constitute registration, and the products may not be lawfully marketed until they are registered.**

Nichino and Bayer should recognize that if EPA issues any technical and/or end-use product registration pursuant to the requirements of section 3(c)(7)(C) of FIFRA, such registration will contain any conditions that are a necessary component of EPA's findings that the statutory requirements for issuing a registration are met. Any such registration will provide that Nichino's or Bayer's release for shipment of any product pursuant to any such registration signals Nichino's or Bayer's acceptance of all of those conditions. If either Nichino or Bayer does not agree with any of the conditions of registration, they should consider any such registration to be null and void. If either Nichino or Bayer notifies EPA that it is unwilling to accept any of those conditions, EPA will commence the appropriate denial process under section 3(c)(6) of FIFRA.

If you have any questions regarding anything in this letter, please contact Mr. Carmen J. Rodia, Jr. directly at (703) 306-0327 or via e-mail at Rodia.Carmen@epa.gov.

Sincerely yours,

Lois A. Rossi, Director
Registration Division (7505P)

Bayer CropScience LP hereby concurs with the time-limited conditional registration of the new insecticide flubendiamide under section 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as outlined in this preliminary acceptance letter, dated July 31, 2008.

CONCUR

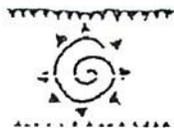
DATE

DO NOT CONCUR

DATE

Enclosures: *Copy of Human Health Effects Risk Assessment for Flubendiamide, dated April 3, 2008*
Copy of Environmental Fate and Effects Risk Assessment for Flubendiamide, dated June 23, 2008
Copy of Public Interest Finding for Flubendiamide, dated April 15, 2008
Copy of Acute Toxicity Review for NNI-0001 Technical, dated October 12, 2007
Copy of Acute Toxicity Review for NNI-0001 24 WG, dated July 15, 2007
Copy of Acute Toxicity Review for NNI-0001 480 SC, dated October 12, 2007
Copy of Product Chemistry Review for NNI-0001 Technical, dated October 24, 2007
Copy of Product Chemistry Review #1 for NNI-0001 24 WG, dated October 18, 2007
Copy of Product Chemistry Review #2 for NNI-0001 24 WG, dated January 25, 2008
Copy of Product Chemistry Review for NNI-0001 480 SC, dated October 19, 2007

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00264-0124 014437
00264-0125 014438
FOR 47045 014436



{In Archive} Flubendiamide - Copy of Preliminary Acceptance Letter

Carmen Rodia to: Danielle.Larochelle

07/31/2008 11:48 AM

Cc: Lois Rossi, Marion Johnson, Richard Gebken, Kathy Monk

Archive:

This message is being viewed in an archive.

Danielle, attached is an MS Word version of the latest draft preliminary acceptance letter for flubendiamide for your use and reference. I will call you in a few minutes to discuss your availability, along with Clive, for a teleconference with Marion Johnson, Richard Gebken, Kathy Monk and myself. Regards, Carmen Rodia.



Flubendiamide, Preliminary Acceptance Letter (07-31-08).doc

Carmen J. Rodia, Jr.
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Registration Division, Insecticide Branch
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1. The subject products will be conditionally registered for a period of five (5) years from the date of the "Notice of Registration." In addition, this regulatory action will establish permanent tolerances in primary crops for residues of flubendiamide.
2. Bayer, as authorized agent for Nichino, will generate/submit acceptable data listed in the following tables, in accordance with 40 CFR §158, as follows:

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 - (a) Nichino (or some other person who consents to Nichino's reliance on the data) shall submit all data identified in paragraphs 2-4, on or before July 31, 2012, according to the schedules set forth in those

¹ The goal of the vegetative buffer strip study is to determine how much of a buffer is necessary to prevent both flubendiamide applied to a field and des-iodo formed in the field from accumulating to levels in aquatic environments that pose risk to freshwater benthic invertebrates. Therefore, showing "that the level of the des-iodo degradate leaving the field (prior to reaching the buffer) is insignificant," would be insufficient justification to remove "the 15 foot buffer requirement.