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MEMORANDUM

SUBJECT: Review of Three Reports Related to a 3-year Flubendiamide Water Monitoring Project in Support of the Conditional Registration of Flubendiamide

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Introduction

Flubendiamide, an insecticide, was conditionally registered in 2008 for aerial and/or ground application to corn, cotton, tobacco, pome fruit, stone fruit, tree nuts, grapes, cucurbit vegetables, fruiting vegetables, leafy vegetables, and brassica leafy vegetables. Registrant-submitted effects studies indicate that both the parent (flubendiamide) and degradate (des-iodo) exhibit chronic toxicity to aquatic invertebrates[1]. Submitted fate data indicate flubendiamide slowly converts to its des-iodo degradate, which does not breakdown. EFED modeling (D329613+) predicts that

[1] Flubendiamide's mode of action is taxa-specific to an unknown degree (targets lepidopteran ryanodine receptors). EFED does not have endpoints specific to lepidopterans. There are numerous species of aquatic lepidopterans of which four are listed species.

flubendiamide and its degradate (des-iodo) will accumulate in aquatic systems eventually exceeding Agency levels of concern (LOCs).

The registrant has argued that: 1) vegetative filter strips (VFSs) would prevent accumulation from exceeding Agency LOCs (flubendiamide labels require a 15 ft VFS buffer around aquatic areas); and 2) the Agency overestimates aquatic exposure because EFED modeling cannot account for the effect of VFSs. According to the flubendiamide preliminary acceptance letter, the Registration Division stated, the "Agency believes that the efficacy of vegetative buffers for flubendiamide use is uncertain." The conditions of registration required a VFS study and, if the VFS study did not allay the Agency's concerns, a pond monitoring study. EFED identified a major modeling error in the VFS study (MRIDs 48175602, 48175604, and 48175606) and asked the registrant to correct it and re-submit (D382010). The VFS study was never re-submitted, therefore, the monitoring study was required. The 3-year monitoring study of water column, sediments, and pore water in 3 ponds (2 in Georgia and 1 in North Carolina) was submitted in December of 2014.

EFED has reviewed the monitoring data and associated studies and has identified several issues with this monitoring data. Despite these issues, EFED believes the monitoring data shows clear evidence that both flubendiamide and des-iodo accumulate in the ponds monitored. The accumulation measured in the first three years of the pond data least impacted by the identified issues largely matches the initial 3 years of concentration predictions of EFED's aquatic exposure modeling. Because EFED's modeling does not account for the effect of VFSs, but still largely matches the monitoring data, EFED believes the effect of VFSs is not large enough to mitigate the ecological risks posed by flubendiamide applications. Therefore, EFED concludes the original and subsequent ecological risk assessments performed by the Agency adequately reflect the risks posed by flubendiamide applications and rejects the registrant's argument that the label-required 15 ft VFSs would prevent accumulation from exceeding Agency LOCs.

The registrant submitted three reports related to this monitoring study: 1) "Monitoring for Flubendiamide and its Metabolite Des-iodo Flubendiamide in Sediment and Surface Water" (MRID 49415303), "Flubendiamide Aquatic Risk – Summary of Surface Water Monitoring and Toxicity Testing" (MRID 49415302), and "Aquatic Exposure Assessment for Flubendiamide and its Metabolite Des-iodo Flubendiamide based on a 3-Year Monitoring Study" (MRID 49415301). This memo provides EFED's analysis of the monitoring data provided in the 3-year monitoring study, summarizes the individual registrant reports, and responds to the major issues raised in these reports.

EFED's Analysis of the Monitoring Data

The residues of flubendiamide and its metabolite Des-iodo were monitored in three ponds in two locations: one pond in Louisburg, NC, and two adjacent ponds (attached by a culvert) in Omega, GA (MRID 49415303). The monitoring study ponds in North Carolina (NC) (Negley et al. 2011; MRID 48535201) and Georgia (GA) (Hanzas et al. 2011; MRID 48644901) were approved by the Agency (D394006 and D398132, respectively). The ponds were selected from areas with high flubendiamide use based on confidential 2009 U.S. sales data. Ponds were selected based on the similarity of their surface area and watershed area to the standard pond that EFED uses in exposure modeling and the requirement that the entire watershed be planted to one crop. Additionally, an attempt was made to select ponds with watersheds that had similar characteristics to EFED standard scenarios for the crop planted in that watershed.

Although not requested by the Agency, the registrant also sampled intermittent and perennial streams near the monitored ponds. The *intermittent* stream sites were up and downstream of where the discharge of the pond(s) flowed into the intermittent stream, while the *perennial* stream sites were up and downstream of where the discharge of the intermittent stream flowed into the perennial stream. (Both Georgia ponds flowed into the same intermittent and perennial streams, so the total number of monitoring sites included 3 ponds, 4 intermittent stream sites (2 in GA and 2 in NC), and 4 perennial streams sites (2 in GA and 2 in NC).) Monthly water and sediment samples, with a few exceptions, were taken from each monitoring site for three years. Water quality parameters including pH, temperature, conductivity, dissolved oxygen, and oxidation/reduction potential (ORP) were measured on-site during each sampling event. Composite water and sediment (top 2 inches) samples were collected during each monthly sampling event. Applications of the flubendiamide product Belt™ were made to the watershed of the pond(s) at each location every year during the study period.

Pore water was separated from sediment samples by vacuum filtration at about 10 PSI to quantify the benthic water residue. Flubendiamide and des-iodo in the water column, pore water and sediment extracts were analyzed by LC/MS/MS, using isotopically-labelled internal standards for quantitation. The method detection limits were 0.004 μg/L for flubendiamide and des-iodo in water and pore water samples, and 0.02 μg/kg for flubendiamide and des-iodo in sediment samples.

Experimental Design and Data Quality Issues

EFED identified six major issues with the monitoring study that affect the interpretability of the study. The first four issues concern the experimental treatment of the watershed: 1) the variability in crops grown on the pond watersheds; 2) the variability in the date of application(s); 3) the variability in the application rates; and 4) the magnitude of the study application rates compared to the maximum annual label application rates (Table 1). Because the participation of the growers was voluntary, the registrant did not have much control over the treatment of the watersheds. The crops rotated in both watersheds – from tobacco (2011) to soybean (2012 and 2013) to tobacco (2014) in the NC pond watershed and from cotton (2011 and 2012) to peanut (2013) in the watershed of the GA ponds. The application dates were quite variable in the NC pond watershed with 15 months between the 1st and 2nd application, 12.5 months between the 2nd and 3rd, and 6.5 months between the 3rd and 4th application with a second application in 2014 occurring a month later. The application rates also varied in the NC pond watershed from 0.06 to 0.09 lb/A. Both the application dates (all in August) and rates (all 0.09 lb/A) in the watershed of the GA ponds were much more consistent.

Table 1. Timeline of applications within the watersheds of the monitoring study ponds and comparison to the maximum annual application rates allowed by flubendiamide labels.

Year	Crop	Application Date	Rate Applied (lb/A)	Label Maximum Annual Rate (lb/A)	Percent of Maximum Annual Rate (%)
North Carolina Pond Watershed					
2011	Tobacco	May 26	0.06	0.375	16
2012	Soybean	Aug 27	0.075	0.188	40
2013	Soybean	Nov 12	0.09	0.188	48
2014	Tobacco	May 31	0.0675	0.375	34
		June 28	0.06		
Georgia Ponds Watershed					
2011	Cotton	August 18 (25% of area) August 23, (75% of area)	0.09	0.282	32
2012	Cotton	August 13	0.09	0.282	32
2013	Peanut	August 30	0.09	0.375	24

The first three issues (variation in crops grown, application dates, and application rates) would be expected to add variability to the monitoring data; making it harder to detect trends in the data. The fourth issue (low application rates) reduces the magnitude of the trends, which makes it harder to detect trends from the noise in the data.

The fifth issue concerns the installation of maintained grass swales (grass waterways) in the watershed of the GA ponds. On page 15 of the GA Site selection Report (Hanzas, et al. 2011; MRID 48644901), it is stated “Primary entry points of runoff into the ponds originate from the southeast via two distinct, un-cropped (but not vegetated) drainage pathways.” However the Interim Report 1 (MRID 48892501; after the first year of monitoring data) p. 13, the Interim Report 2 (MRID 49139801; after the second year of monitoring data) p. 13, and the Final Monitoring Report (MRID 49415303) p. 15, all state the same sentence “Primary entry points of runoff into the ponds originated from the southeast via three maintained grass swales.” The Agency obtained aerial photography of the GA ponds and watershed from September 16, 2010 (Figure 5a) and September 13, 2013 (Figure 5b) from the National Agriculture Imagery Program (NAIP)[2].

[2] http://fsa.usda.gov/FSA/apfoapp?area=home&subject=prog&topic=nai

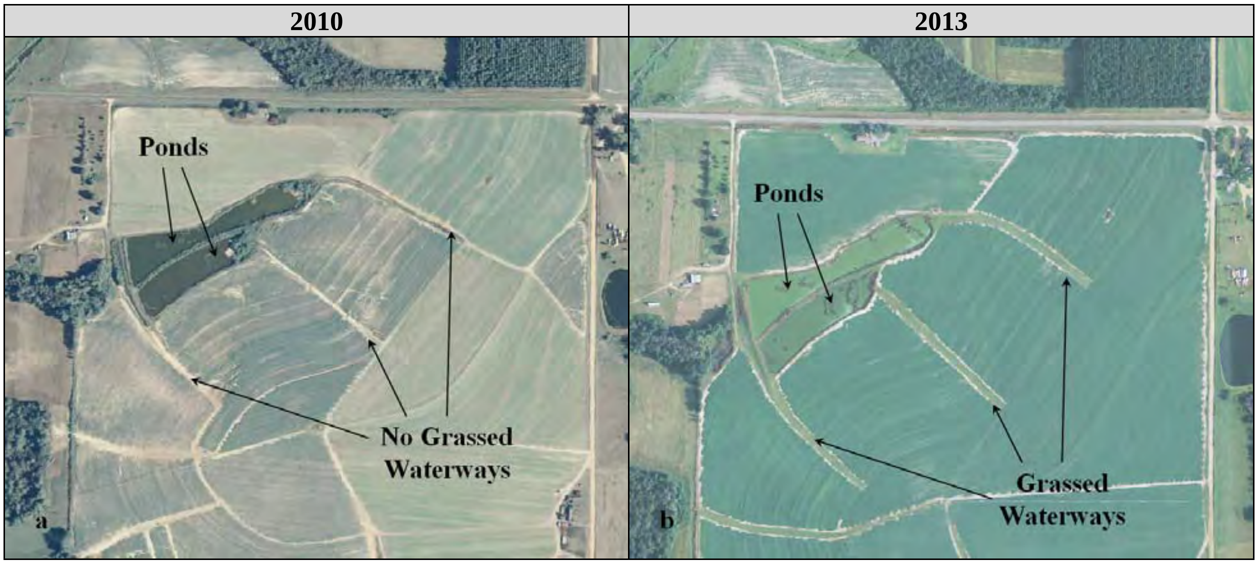


Figure 1. Aerial photography of the Georgia pond watershed taken before (a) and after (b) installation of grass waterways.

The purpose of grassed waterways is to reduce soil and chemical loadings to waterbodies. They occupy the main drainage pathways though which the majority of the pesticide in runoff and attached to eroded soil would travel. Grassed waterways are designed to trap eroded soil and allow runoff and the chemicals in the runoff to infiltrate into the ground. The flubendiamide labels require a 15 ft VFS between the treated field and waterbodies, but do *not* require grassed waterways. The presence of the grassed waterways would be expected to reduce the accumulation of flubendiamide and des-iodo in the GA ponds and therefore, make it more difficult to identify accumulation trends in the GA ponds. Additionally, the trends measured from water column, sediment, and pore water in the GA ponds would be diminished [*i.e.*, the magnitude (steepness) of those trends would be diminished relative to what would be expected in the absence of the grassed waterways].

The final issue with the submitted monitoring data concerns the magnitude of the pore water concentrations compared to the water column concentrations from samples collected from the same pond and at the same time. In the ponds, EFED expects the pore water and water column concentrations to equilibrate over time for both flubendiamide and des-iodo with only short-term excursions from nearly equal concentrations after drift and storm events. However, the observed pond pore water concentrations were typically much lower than the observed water column concentrations from samples collected from the same pond and at the same time.

To show the magnitude and pervasiveness of this discrepancy, the ratio of the pore water to water column concentration was plotted over time for all pond samples that had measured concentrations that were above the detection limit for both pore water and water column samples. If the pore water to water column concentration were equal, this ratio should equal 1. In the NC and GA pond samples (Figure 2a and c, respectively), almost all of the observed ratios plot below 1 (equilibrium) with many equal to, or less than, 0.1 indicating the pore water concentration is 10 times lower than the corresponding water column concentration for many of these samples. For comparison, similar ratios are plotted for samples from the up and downstream perennial stream sites (Figure 2b and d). The perennial stream site ratios tend to straddle a ratio value of 1 indicating much more equality between pore water and water column concentrations.

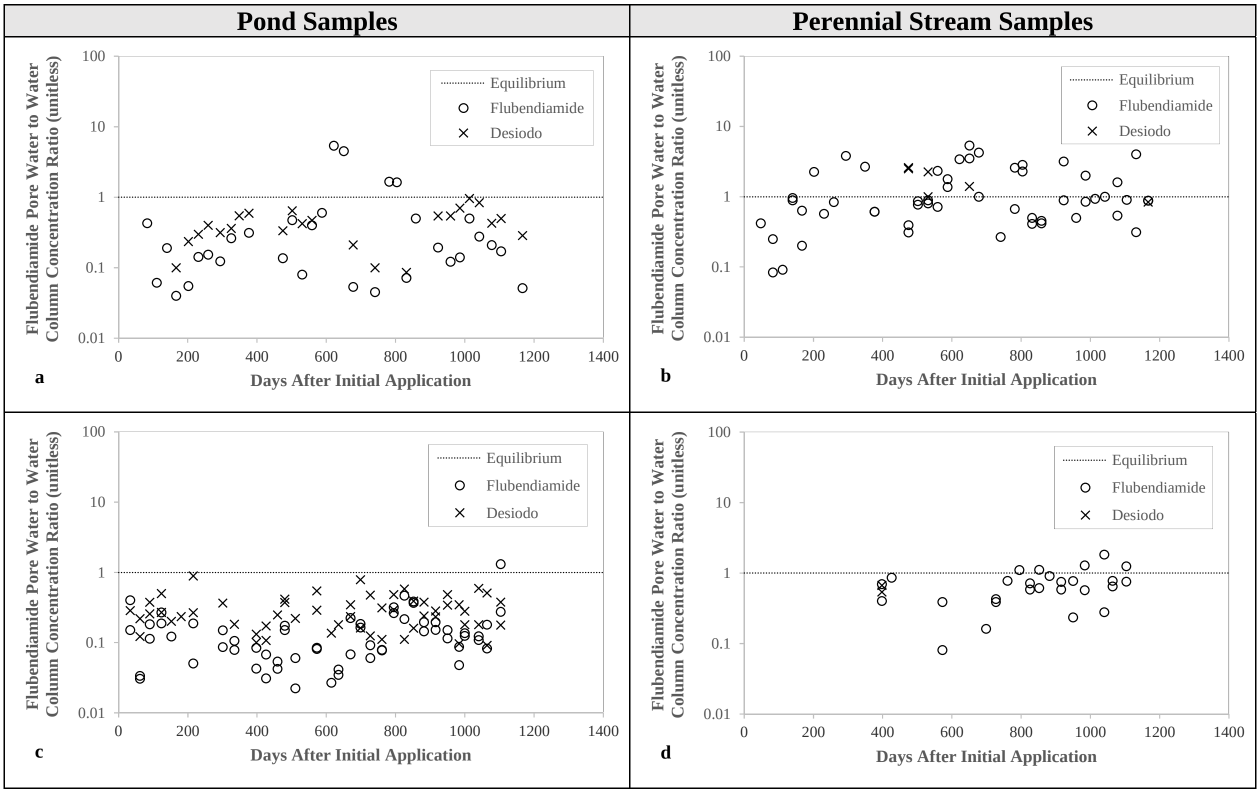


Figure 2. Comparison of observed pore water to water column concentration ratios for flubendiamide and des-iodo from the NC pond (a) the NC perennial stream (b) and GA ponds (c) the GA perennial stream (d) samples.

A potential explanation for why the pond pore water concentrations are so much lower relative to the pond water column concentrations may be that the depth of sediment and pore water contaminated with flubendiamide and des-iodo may be very shallow relative to the total depth of sediment and pore water extracted (~2 inches) during sample collection. Consequently, the pond sediment and pore water samples would constitute a mixture of flubendiamide/des-iodo and uncontaminated sediment and pore water, thus diluting the concentration flubendiamide and des-iodo in the sample.

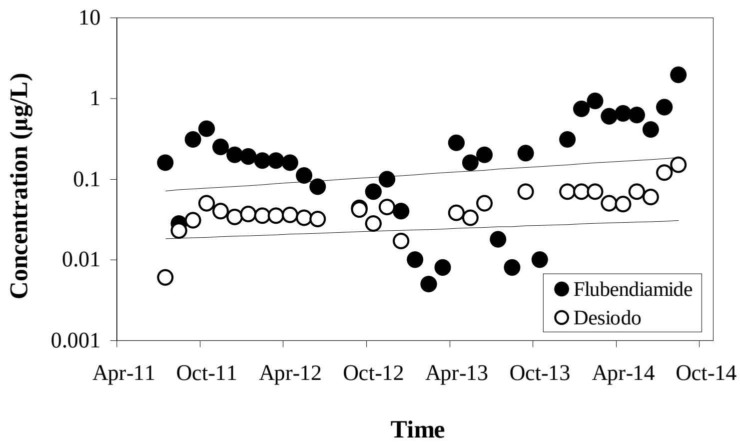
The NC perennial stream exhibits pore water to water column concentration ratios that are much closer to 1 (Figure 2b). This stream (the Tar River) is a large river at the sites sampled. Sediment depths are likely deeper and better mixed due to turbulent flow in the river, which may make it easier to sample sediment and pore water sample from a surficial layer with less dilution from deeper uncontaminated sediment and pore water. The GA perennial stream water column and pore water concentrations were relatively low, so that early in the monitoring time frame, ratios could not be calculated because one or both concentrations fell below the detection limit. However, the later ratios from the GA perennial stream sites (Figure 2d) were distributed closer to 1 than the pond ratios, but further from 1 than the Tar River (NC perennial stream) ratios (the GA perennial stream is much smaller at the GA sample sites than the NC perennial stream is at the NC sample sites). (Observed pore water to water column concentration ratios for flubendiamide and des-iodo for all stream sites are depicted in Appendix B.)

Assuming the measured sediment and pore water concentrations from the pond samples are biased low, it would be harder to detect trends in the sediment and pore water data because the observed rate of accumulation will have been diminished due to dilution with the uncontaminated layers. Additionally, these ‘diluted’ samples would be much lower than model predicted ‘non-diluted’ pore water concentrations.

Accumulation
EFED used the “LifeReg” regression procedure in SAS statistical software to fit trend lines to the pond concentration data because some of the data are only known to be less than the method detection limit (left-censored). This procedure better accounts for the presence of this left-censored data without biasing the fitted trend estimates. The fitted trends increase with time (accumulate) in all of the 18 time-series data sets collected from these ponds [3 ponds × 3 media (water column, sediments, and pore water) × 2 chemicals = 18 time series data sets]. Fitting these trends as exponential trends (*i.e.*, fitting a linear trend to the natural log of the concentration observations) indicated that 13 of these 18 trends were statistically significant at the $p = 0.05$ level of confidence (Figures 3, 4, and 5) despite the issues with this data described in the previous section. (The exponential trends appear as linear trends in these figures because the y-axis is presented as a log scale).

Concentration Data Over Time	Accumulation (change from beginning to end of trend line)

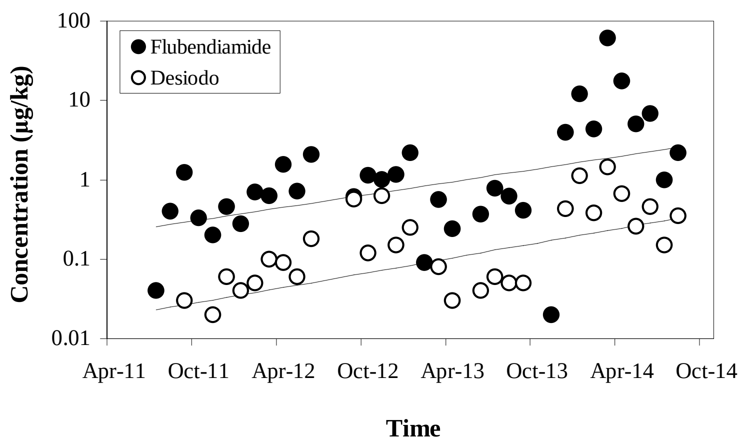
Water Column



Flubendiamide: Increased 2.60×
(0.071 to 0.19 µg/L)
Upward exponential trend is not statistically significant (P = 0.2840)

Des-iodo: Increased 1.68×
(0.018 to 0.031 µg/L)
Upward exponential trend is not statistically significant (P = 0.4675)

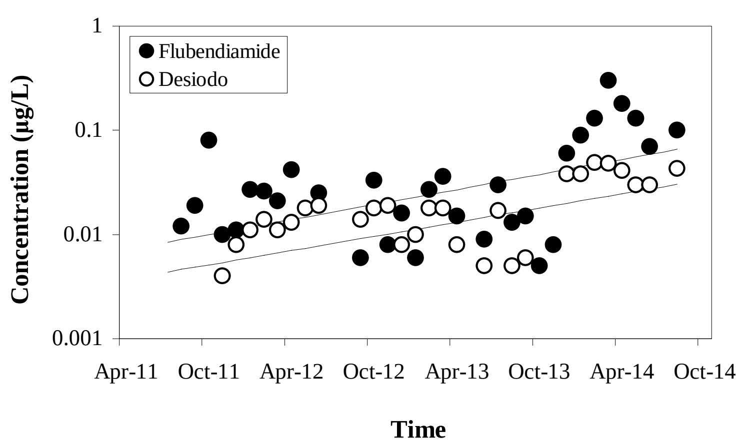
Sediment



Flubendiamide: Increased 10.0×
(0.26 to 2.57 µg/kg)
Upward exponential trend is statistically significant (P = 0.0088)

Des-iodo: Increased 10.55×
(0.023 to 0.33 µg/kg)
Upward exponential trend is statistically significant (P = 0.0002)

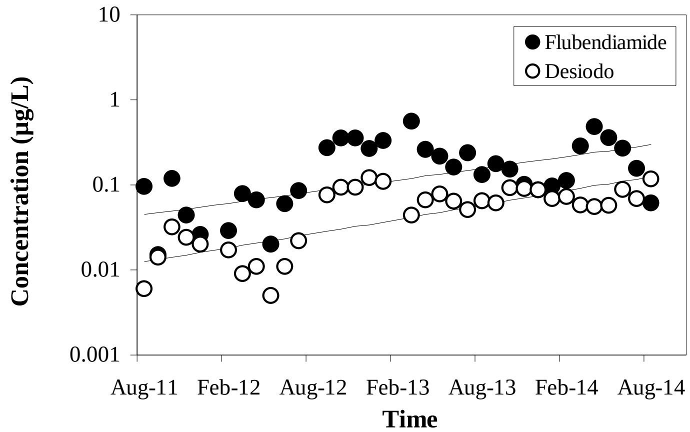
Pore Water

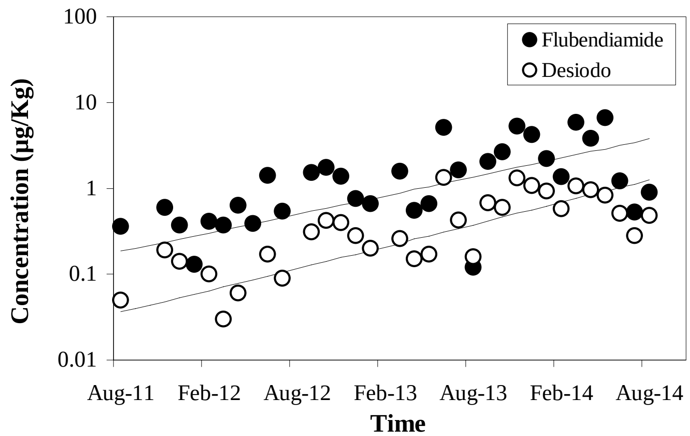


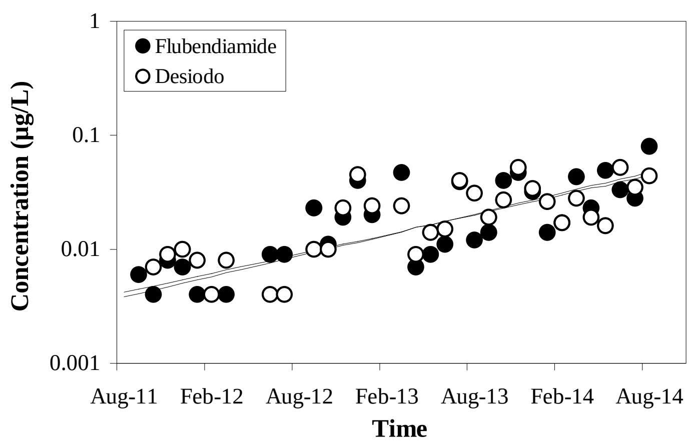
Flubendiamide: Increased 7.84×
(0.0084 to 0.66 µg/L)
Upward exponential trend is statistically significant (P = 0.0005)

Des-iodo: Increased 6.99×
(0.0044 to 0.030 µg/L)
Upward exponential trend is statistically significant ($P < 0.0001$)

Figure 3. Accumulation of flubendiamide and des-iodo in the water column (a), sediment (b), and pore water (c) of North Carolina pond.

<table>
<tr><th>Concentration Data Over Time</th><th>Accumulation (change from beginning to end of trend line)</th></tr>
<tr><td colspan="2">Water Column</td></tr>
<tr><td>
</td><td>Flubendiamide: Increased 6.6×
(0.045 to 0.30 µg/L)
Upward exponential trend is statistically significant (P = 0.0002)

Des-iodo: Increased 10.1×
(0.013 to 0.13 µg/L)
Upward exponential trend is statistically significant (P < 0.0001)</td></tr>
<tr><td colspan="2">Sediment</td></tr>
<tr><td>
</td><td>Flubendiamide: Increased 20.4×
(0.19 to 3.80 µg/kg)
Upward exponential trend is statistically significant (P < 0.0001)

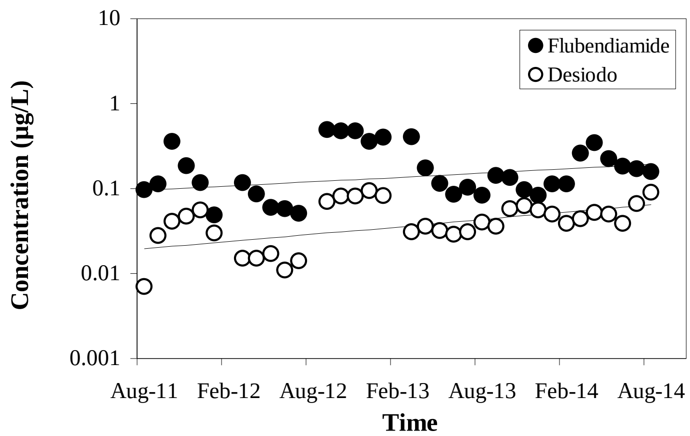
Des-iodo: Increased 34.6×
(0.037 to 1.27 µg/kg)
Upward exponential trend is statistically significant (P < 0.0001)</td></tr>
<tr><td colspan="2">Pore Water</td></tr>
<tr><td>
</td><td>Flubendiamide: Increased 12.5×
(0.0039 to 0.048 µg/L)
Upward exponential trend is statistically significant (P < 0.0001)

Des-iodo: Increased 10.7×
(0.0042 to 0.045 µg/L)
Upward exponential trend is statistically significant (P < 0.0001)</td></tr>
</table>

Figure 4. Accumulation of flubendiamide and des-iodo in the water column (a), sediment (b), and pore water (c) of Georgia pond #1.

Concentration Data Over Time	**Accumulation** (change from beginning to end of trend line)

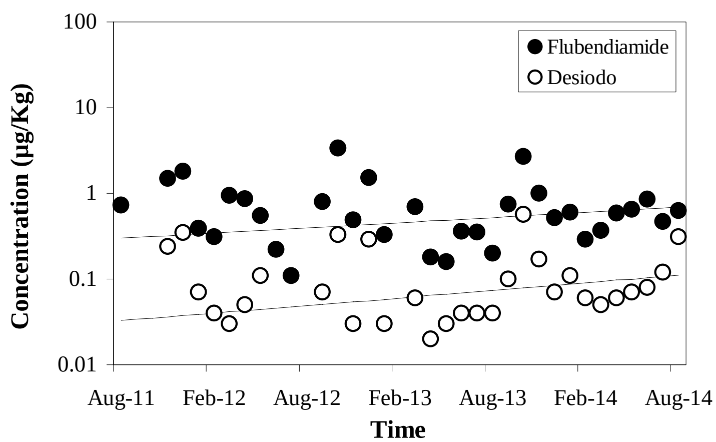
Water Column



Flubendiamide: Increased 2.02×
(0.096 to 0.19 µg/L)
Upward exponential trend is <u>not</u> statistically significant (P = 0.1588)

Des-iodo: Increased 3.30×
(0.020 to 0.065 µg/L)
Upward exponential trend is statistically significant (P = 0.0008)

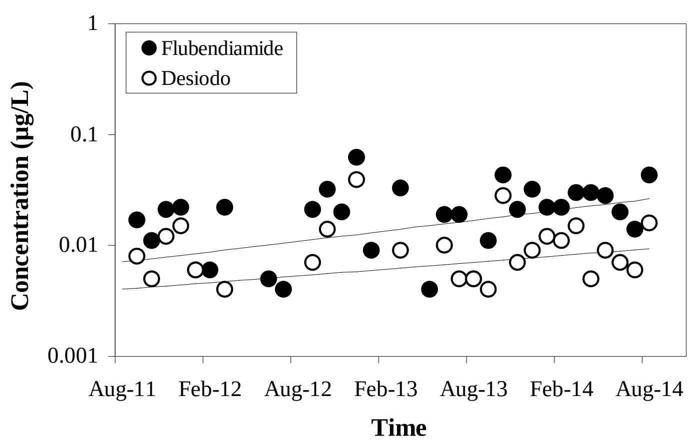
Sediment



Flubendiamide: Increased 2.30×
(0.30 to 0.69 µg/kg)
Upward exponential trend is <u>not</u> statistically significant (P = 0.1803

Des-iodo: Increased 3.38×
(0.033 to 0.11 µg/kg)
Upward exponential trend is statistically significant (P = 0.0377)

Pore Water



Flubendiamide: Increased 3.71×
(0.0071 to 0.026 µg/L)
Upward exponential trend is statistically significant (P = 0.0044)

Des-iodo: Increased 2.31×
(0.0041 to 0.0094 µg/L)
Upward exponential trend is <u>not</u> statistically significant (P = 0.0547)

Figure 5. Accumulation of flubendiamide and des-iodo in the water column (a), sediment (b), and pore water (c) of Georgia pond #2.

Comparison of Observed Concentrations in the Monitoring Study to Exposure Model Predictions
During the site selection phase of the monitoring study, the registrant made an attempt to select combinations of crops to be planted and pond watershed characteristics that were similar to EFED standard scenarios. However, EFED exposure scenarios are designed to represent high-end exposures and have many parameters embedded within the standard scenarios that would likely need adjustment to make a valid comparison between exposure model predictions to observed concentrations in a strict sense (field slopes, etc). Additionally, the SWCC cannot be parameterized for crop rotations, cannot account for VFSs (or the grassed waterways in the watershed of the GA ponds), assumes similar application timing and rates of pesticides applied each year, and assumes wind direction always deposits drift into the pond(s). Therefore the comparisons presented should be considered very "rough".

Figure 6 provides the comparison between exposure model predictions and observed concentrations for the NC pond. The SWCC modeling used the NC tobacco scenario[3] with the same input values as appear in Table 1 of the aquatic exposure report (MRID 49415301) with the exceptions that the benthic metabolism half-life value of 855 days was used (rather than the registrant modified value of 7300 days), the soil half-life of 0 (stable) was used (rather than the 10,000 day value in the aquatic exposure report), the efficiency (0.95) and drift (0.05) fractions were changed to 0.99 and 0.0082[4] because Table 1 indicates that these were ground applications under the application method section of this table, and standard pond dimensions were used. (EFED did not use the registrant modified weather files, files because they only provided to the agency in a pdf format as part of the report.)

The monitoring report does not contain sufficient information to identify a unique set of SWCC parameters for comparison with the NC pond data. For example, the report does not indicate whether the wind direction on the application date would have blown drift toward the pond. Therefore, three SWCC scenarios were run with different combinations of application rates and spray drift assumptions to bound reasonable SWCC parameterizations for the NC pond. The highest rates applied to the NC pond watershed (0.09 lb/A) with the EFED's current spray drift fraction (0.0082) is shown solid lines in Figures 6a to f). The lowest rates applied to the NC pond watershed (0.06 lb/A) with the EFED's current spray drift fraction (0.0082) is shown as dashed lines in Figures 6a to f. The third SWCC scenario used the lowest rates applied to the NC pond watershed (0.06 lb/A) with no drift (to simulate the lowest reasonable exposure scenario) and is show as dotted lines in Figures 6a to f. (Note: Figures 6a through f are presented with the y-axis as a log scale.)

The observed water column flubendiamide concentrations display a lot of scatter in Figure 6a, but contain concentrations that plot both above and below the SWCC predictions. Similarly, the observed water column des-iodo concentrations plot both above and below the SWCC predictions, but the concentrations that plot above the SWCC predictions occur toward the

[3] The crop in the NC pond watershed rotated from tobacco to soybean for two years and back to tobacco. EFED does not have mixed crop scenarios, but does have soybean scenarios from states other than NC. However, EFED simply used the scenario modeled by the registrant (MRID 49415301) without further exploration of alternative scenarios.
[4] Calculated with AgDrift based on a high boom ground application with a droplet size of ASAE fine to medium coarse (DV50 of 341um).

beginning of the monitoring. Additionally, the observed water column des-iodo concentrations display a lot less scatter (Figure 6b) than the flubendiamide concentrations (Figure 6a) and follow the trend much better in the latter half of the monitoring. The respective sediment concentrations (Figure 6c and d) and pore water concentrations (Figure 6e and f) all plot somewhat low compared to the SWCC predictions, consistent with the hypothesis that these samples are diluted with the underlying uncontaminated sediment and pore water lying below the higher surficial sediment and pore water concentrations (see previous discussion). Overall, the Agency believes the monitoring data tracks reasonably well with the modeled data and therefore, supports the previous predictions of aquatic exposure modeling and the prior flubendiamide risk assessments despite the fact that EFED's modeling cannot account any effect of the VFSs.

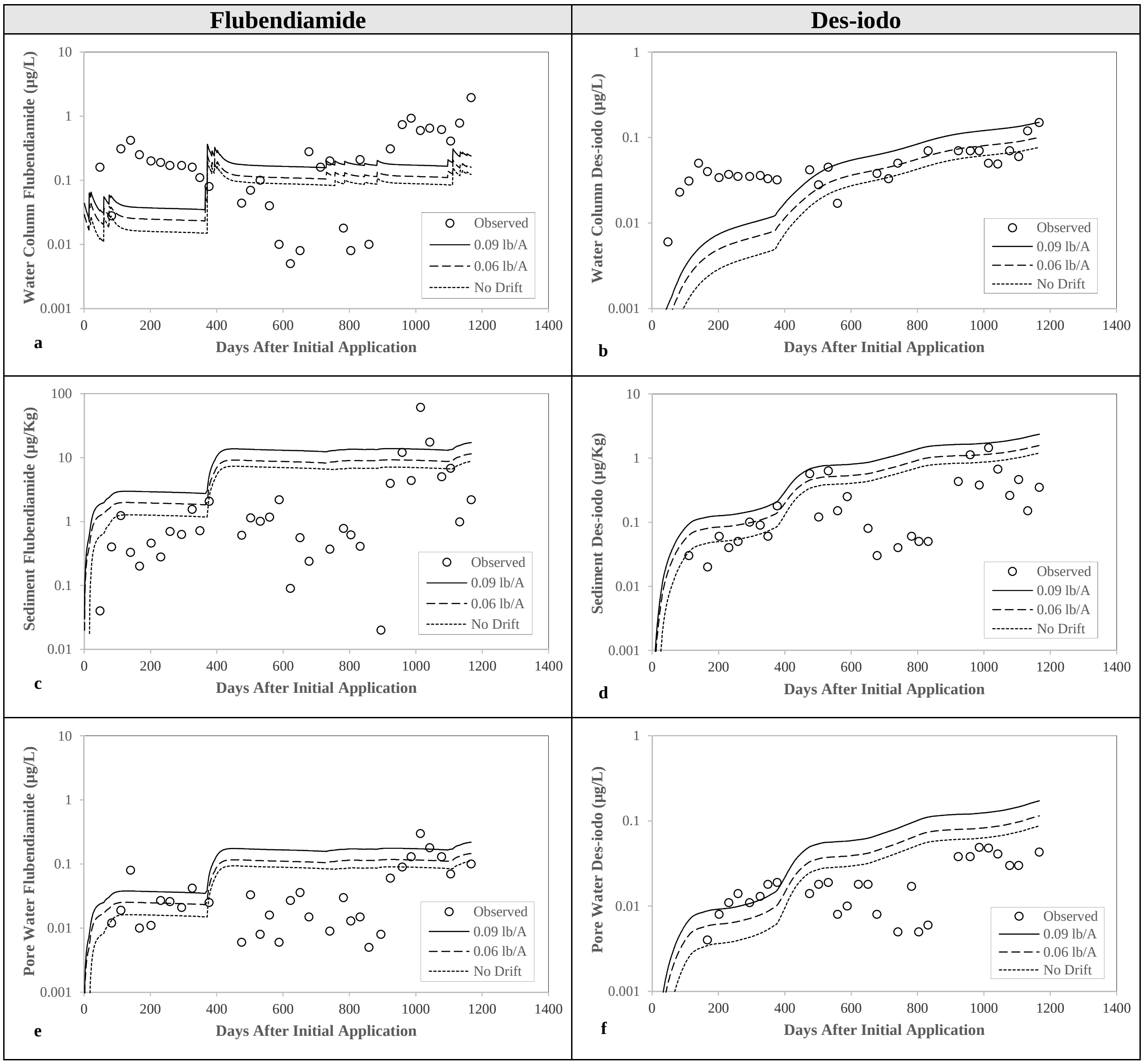


Figure 6. Comparison of Surface Water Concentration Calculator (SWCC) daily predictions from the North Carolina tobacco scenario to monitoring data from the North Carolina pond for water column flubendiamide (a) and des-iodo (b), sediment flubendiamide (c) and des-iodo (d), and pore water flubendiamide (e) and des-iodo (f) based on the range of application rates (0.06 to 0.09 lbs/A) used in the pond watershed during monitoring.

EFED assumes that any reduction in pond chemical concentrations in water column, sediment, and pore water concentrations from VFSs would be greatest when the chemical is first used and would diminish with time as the VFS became saturated with flubendiamide and des-iodo. Once saturated, the VFS might become a net source of the contaminants to the pond rather than a net sink. (EFED believes that VFSs would be more efficacious for pesticides that would rapidly breakdown into non-toxic degradates within the VFS.) From this rough comparison, the impact of the VFS does not appear to be large in the NC pond data.

Similar to the NC analysis, Figure 7 compares exposure model predictions and observed concentrations for the GA ponds. The SWCC modeling used the MS cotton[5] (solid lines in Figures 7a to f) and NC cotton[6] (dashed lines in Figures 6a to f) scenarios with the same input values as described for the NC scenario (only one application rate 0.09 lb/A was used since this did not vary in the GA pond watershed). A no drift scenario does not appear in the in Figure 7 because drift only accounts for ~2% of the flubendiamide reaching the pond in the MS and NC cotton scenarios and would have been indistinguishable from the predictions including drift. (Note: Figures 7a through f are presented with the y-axis as a log scale.)

Almost all of the GA ponds concentration data plots below the SWCC predictions. The interpretation of the GA ponds data is confounded by the presence of grassed waterways in the watershed. The combination of grassed waterways and VFSs (only VFSs are required by flubendiamide labels) would be expected to diminish transport of both flubendiamide and des-iodo to the ponds. The GA ponds data does appear to show the same pattern of sediment and pore water dilution in that the water column observations are much closer to the SWCC predictions (Figures 7a and b) than the sediment and pore water observations are (Figures 7c through d).

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[5] The MS cotton scenario was modeled by the registrant in MRID 49415301.
[6] The NC cotton scenario was added by EFED because it is located in the same general region and to provide comparison with the MS cotton scenario.

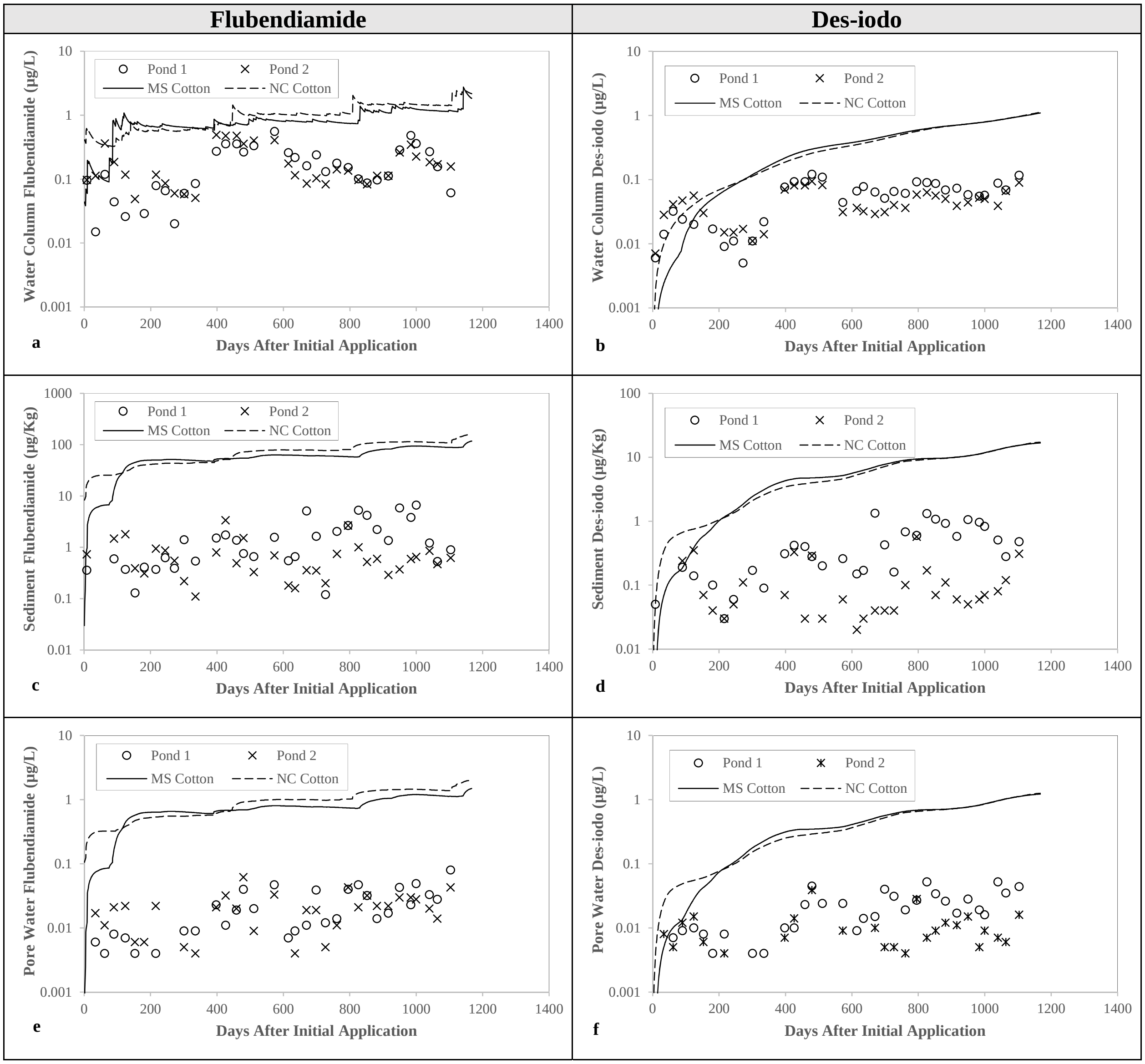

Figure 7. Comparison of Surface Water Concentration Calculator (SWCC) daily predictions from the Mississippi cotton and North Carolina cotton scenarios to monitoring data from the Georgia pond for water column flubendiamide (a) and des-iodo (b), sediment flubendiamide (c) and des-iodo (d), and pore water flubendiamide (e) and des-iodo (f).

Ecological Risk

Ecological risk is determined by comparing exposure estimates to Agency levels of concern (LOCs). Aquatic exposure is predicted over 30 years in Figure 8 for the NC tobacco scenario. These model results are based on the same parameters as the predictions that fit the NC pond data well, but use the maximum label rates instead (4 applications of 0.09 lb/A for an annual maximum of 0.375 lb/A assuming it is continuously planted to tobacco). Chronic aquatic invertebrate endpoints are also included in Figure 8. Because these chronic endpoints have an LOC of 1, an exposure exceeding an endpoint also exceeds the Agency LOC (*i.e.*, the LOC and the endpoint are the same number). Drawing a vertical line down from where the exposure crosses the appropriate endpoint indicates the time required for flubendiamide or des-iodo accumulation to exceed Agency LOCs. The water column des-iodo NOEC is exceeded after 8 years in Figure 8a and the pore water des-iodo NOEC is exceeded after 23 years in Figure 8b, while the pore water flubendiamide NOEC is exceeded after 7 years (also in Figure 8b). [Note: flubendiamide has already been on the market for 5 years (2009 to 2014). Also, at the lower application rates used in the monitoring study, it would take ~4 times as long to exceed all of these LOCs.] The NC tobacco scenario is not the worst case use (other scenarios exceed LOCs in shorter time periods).

Water Column	Pore Water
NC Tobacco	

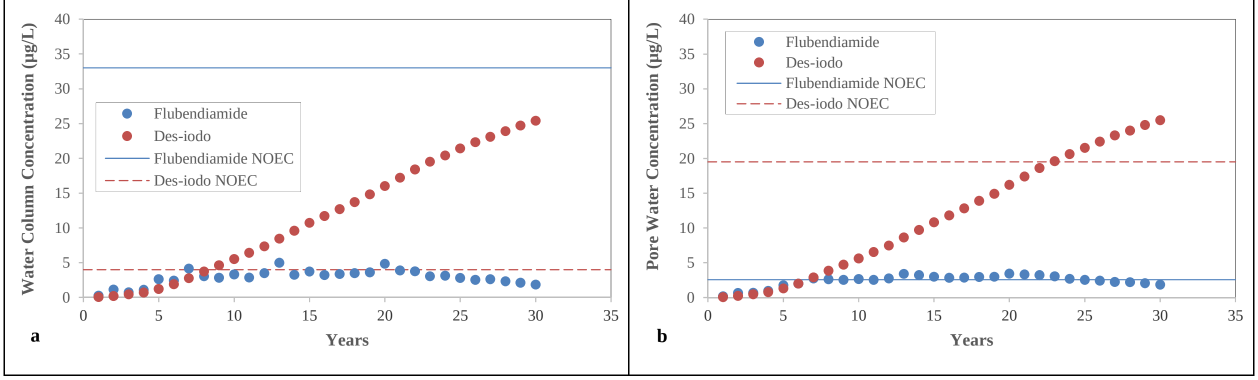

Figure 8. Accumulations of flubendiamide and its des-iodo degradate exceeding chronic risk endpoints in the standard pond water column (a) and pore water (b) based on ground applications to North Carolina tobacco at the maximum allowed application rate.

Additional monitoring at stream sites near these ponds found both flubendiamide and des-iodo in water column, sediment and pore water samples at all eight stream sites monitored (Appendix A). This stream data indicates low-level contamination in streams is currently pervasive in regions where flubendiamide is used.

The next section addresses each of the three submitted studies individually. For each study, a brief summary is provided with a list of issues raised in the study along with EFED comments on those issues.

Monitoring for Flubendiamide and its Metabolite Des-iodo Flubendiamide in Sediment and Surface Water (MRID 49415303)

Summary:
The objective of this study was to assess the potential for flubendiamide and its des-iodo metabolite to accumulate in aquatic environments (water and sediment) following drift and runoff of flubendiamide into surface water with multiple years of applications.

EFED Issue:
Much of the report only discusses measurements above the limit of quantitation (LOQ) rather than the method detection limits (MDL). For example, "(d)es-iodo flubendiamide was not detected above the LOQ in pore water in the farm pond in North Carolina" (p. 24). Yet, the flubendiamide data from the NC farm pond show a statistically significant ($P < 0.0001$) exponentially increasing trend according to the Agency's modeling from values below the LOQ. The Agency has discussed this issue with the registrant and has indicated that the registrant

should use all values down to the MDL. If the values between the MDL and LOQ are as randomly distributed as the registrant claims, including these values should make it more difficult to detect trends in accumulation over time. Use of these data should not spontaneously create trends where none actually occur.

Limits of quantitation are typically set between 3 and 10 times the MDL. The registrant has chosen 10 times the MDL for an accumulation study that modeling suggests will not accumulate to much more than the LOQ by the end of the monitoring study. Had the registrant applied the pesticide at the maximum application rate (and brought the grassed waterways to the attention of the Agency so that a different site could be monitored), using only the values above the LOQ may have been an option.

Registrant Comment:
"Overall, the results show negligible concentrations of des-iodo flubendiamide in water, pore-water or sediment, and no indication of formation of des-iodo flubendiamide in the water or sediment (*i.e.*, a decline in flubendiamide in sediment or water did not result in increases in des-iodo flubendiamide in sediment or water). Year-to-year variations in concentrations were observed, with highest residues occurring a few months after application, and then declining. There is no indication of accumulation of flubendiamide or des-iodo flubendiamide in pore-water, water or sediment in the pond, intermittent streams or permanent streams." (p. 27)

"These results indicate that low levels of flubendiamide residues can occur due to runoff from fields with recent applications of flubendiamide products. These residues are not significantly accumulating after three years of applications. This is expected due to the turnover of water and sediment in the moving water bodies, and water from the ponds. The sediment in the ponds, which might be expected to have accumulating residues, only showed year-to-year variations, and no indication of significant accumulation." (p. 30)

EFED Comments:
The report purports to look for accumulation over time, but there is no trend analysis presented. The Agency found that fitting trend lines to the data indicated that all 18 of the time series data sets from the ponds [3 ponds × 3 media [water column, sediments, and pore water] × 2 chemicals = 18 time series data sets] increased over time with 13 of the 18 identified as statistically significant. Considering just the sediment data discussed in the second quote above, five of the six sediment concentration trends were statistically significant. The Agency strongly disagrees with the registrant's assessment of no significant accumulation.

Flubendiamide Aquatic Risk – Summary of Surface Water Monitoring and Toxicity Testing (MRID 49415302)

Summary:
The registrant summarized the toxicity studies submitted to date for flubendiamide and des-iodo as well as a midge (*Chironomus riparius*) 28-d spiked sediment flubendiamide study that is yet to be submitted to the Agency.

Registrant Comment:
The appropriate chronic risk assessment endpoints to use for a flubendiamide and des-iodo flubendiamide sediment risk assessment are:

- Flubendiamide overlying water – NOEC 33 μg/L
- Flubendiamide pore water – NOEC 2.56 μg/L
- Des-iodo flubendiamide overlying water – NOEC 4 μg/L
- Des-iodo flubendiamide pore water – NOEC 19.5 μg/L

EFED Response:
EFED has evaluated all of these studies and provided a Data Evaluation Record (DER) for each with the exception of the aforementioned midge study that has yet to be submitted to the Agency. Some of these registrant-calculated endpoints differ slightly from the Agency determined endpoints. If the registrant believes the Agency-calculated endpoints are in error, the appropriate course of action would be to rebut the individual DERs. This report (MRID 49415302) does not contain sufficient explanation and analysis for the Agency to reconsider the endpoints. However for purposes of evaluating the studies submitted with the monitoring study (MRIDs 49415301 to 49415303), the Agency will use the registrant-calculated endpoints to avoid diverting focus from the issues the Agency has with the submitted monitoring and aquatic exposure reports.

Aquatic Exposure Assessment for Flubendiamide and its Metabolite Des-iodo Flubendiamide based on a 3-Year Monitoring Study (MRID 49415301)

Summary:
The overall objective of this report was to compare the results from a 3-year monitoring study at two locations with the potential aquatic estimated environmental concentrations (EECs) produced by the SWCC model. Both standard and modified scenarios were used as a means to better simulate field observations and to achieve insights into the factors governing the fate of flubendiamide and des-iodo at the field sites.

Registrant Comment:
"For GA, the SWCC overestimated peak flubendiamide concentrations in water and pore water by a factor of 3 and 17, respectively. Peak des-iodo concentrations were over-predicted by a factor of 11 and 26 in water and pore water, respectively." (p. 7)

EFED Response:
The Agency agrees the SWCC concentration predictions based on the MS cotton and NC cotton scenarios are higher than the concentrations observed in the GA pond. However, the Agency ascribes these discrepancies to problems with the registrant's data. The Agency believes the presence of the grassed waterways in the watershed of the GA ponds render these data unusable for comparison with the SWCC predictions. The pore water data discrepancy, which is larger than the water column data, is impacted by both the presence of the grassed waterways and potentially, the sample dilution issue. Additionally, there are other parameters such as field slope that would need adjustment before a direct comparisons could be made.

Registrant Comment:
"For NC, the SWCC under-predicted flubendiamide in water and pore water by a factor of 5 and 3 respectively. However, the NC site received an off-season, bare ground application in November of 2013 which led to greater runoff than would be expected in a typical growing season[7]. However, for des-iodo, the SWCC over-predicted water and pore water concentrations by a factor of 2 and 7, respectively." (p. 7)

EFED Response:
The Agency believes the SWCC predictions fit the water column data quite well (Figure 6a and b) and believes the differences in pore water concentrations (Figures 6e and f) are better ascribed to the previously discussed sample dilution issue.

Registrant Comment:
"The model also predicted exponential accumulation of both flubendiamide and des-iodo in the water and pore water, which was not observed in the field study." (p. 7)

EFED Response:
The Agency believes exponential accumulation was observed in the field study.

EFED Issue:
The registrant developed a series of increasingly complex model adjustments in order to get the SWCC predictions to align with the water column and pore water observations. The justification for making these adjustments was based almost entirely on the GA pond data and pore water data from both the GA and NC ponds, which the Agency believes to be inaccurate due to the presence of the grassed waterways (GA data) and the sample dilution issue (pore water data).

Conclusions

The monitoring study shows accumulation in all of the ponds monitored for both flubendiamide and des-iodo in water column, sediments, and pore water with 13 of the 18 pond accumulation trends identified as statistically significant. The VFS study (MRIDs 48175602, 48175604, and 48175606) and monitoring studies (MRIDs 49415301 to 49415303) did not provide evidence that VFSs provided significant reductions in flubendiamide and des-iodo transport to aquatic environments. The NC pond data provide a good match to the SWCC modeling (Figures 6a and b). This same model parameterization (after adjusting to maximum label application rates) produces exposure estimates that exceed Agency chronic LOCs (Figures 8a and b) for aquatic invertebrates in as little as 7 years. The NC tobacco scenario is not the worst case use (other scenarios exceed LOCs in shorter time periods). Flubendiamide and des-iodo are expected to accumulate in the environment and pose chronic risk concerns for aquatic invertebrates. Therefore, EFED concludes the original (D329613+) and subsequent ecological risk assessments performed by the Agency adequately reflect the risks posed by flubendiamide applications and

[7] According to the monitoring report, "The concentrations of flubendiamide and des-iodo flubendiamide were higher in 2013 and first part of 2014 which was mainly caused by the off-season application of Belt™ on bareground after soybean harvesting in 2013. Although application of Belt™ on bareground in November was not a good agricultural practice, the application was made to compensate for the grower not making a summertime application as expected."

rejects the registrant's argument that the label-required 15 ft VFSs would prevent accumulation from exceeding Agency LOCs.

Literature Cited

Dyer, D.G., and A.T. Hall. 2014. Flubendiamide Aquatic Risk – Summary of Surface Water Monitoring and Toxicity Testing. Bayer CropScience. Report Number: US0453. 16 pp. (MRID 49415302)

Hanzas, J.P., B. Toth, and J. White. 2011. Georgia Site Selection Report for "Monitoring for Flubendiamide and its Metabolite des-iodo Flubendiamide in Sediment and Surface Water". Bayer CropScience. Study Number: MEAMP011. 37 pp. (MRID 48644901)

Negley, T.L., D.K. Moore, and A.C. Newcombe. 2011. North Carolina Site Selection Report for "Monitoring for Flubendiamide and its Metabolite des-iodo Flubendiamide in Sediment and Surface Water" Bayer CropScience. Report Number: US0220. 50 pp. (MRID 48535201)

Pérez Ovilla, O. 2014. Aquatic Exposure Assessment for Flubendiamide and its Metabolite Des-iodo Flubendiamide based on a 3-Year Monitoring Study. Bayer CropScience. Report Number: US0453. 98 pp. (MRID 49415301)

Xu, T. 2012. Monitoring for Flubendiamide and its Metabolite Des-iodo Flubendiamide in Sediment and Surface Water: Interim Report 1. Bayer CropScience. Study Number: MEAMP011. 349 pp. (MRID 48892501)

Xu, T. 2013. Monitoring for Flubendiamide and its Metabolite Des-iodo Flubendiamide in Sediment and Surface Water: Interim Report 2. Bayer CropScience. Study Number: MEAMP011. 74 pp. (MRID 49139801)

Xu, T. 2014. Monitoring for Flubendiamide and its Metabolite Des-iodo Flubendiamide in Sediment and Surface Water: Final Report. Bayer CropScience. Study Number: MEAMP011. 518 pp. (MRID 49415303)

Appendix A. Additional Monitoring Data from Flowing-Water Sites

EFED does not anticipate continuous accumulation at these flowing-water sites because any accumulation is continuously (water) or periodically (sediment) flushed downstream. Data from the Georgia and North Carolina flowing-water sites (located at different points in the larger watersheds that contain the GA and NC ponds) with trend lines (solid for flubendiamide and dashed for des-iodo) are presented in Figure A1 and A2, respectively. Because some of the data time-series from stream sites have few concentrations measured above the detection limit, the trend lines appear counter-intuitive.

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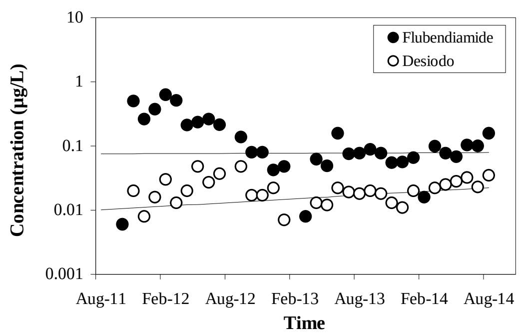
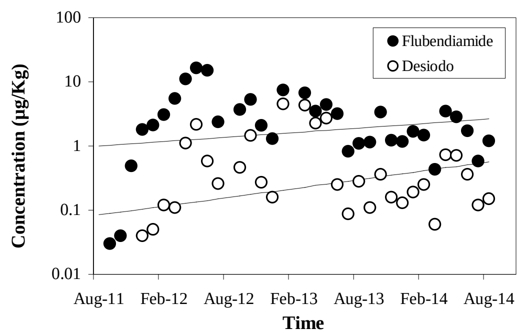
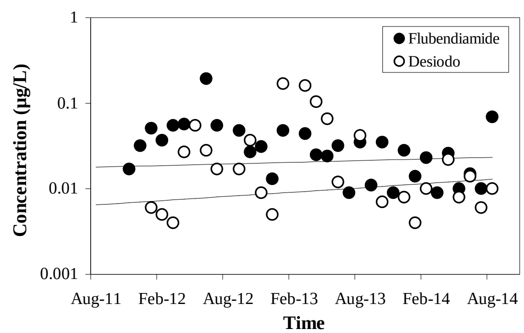

</td><td>
</td><td>
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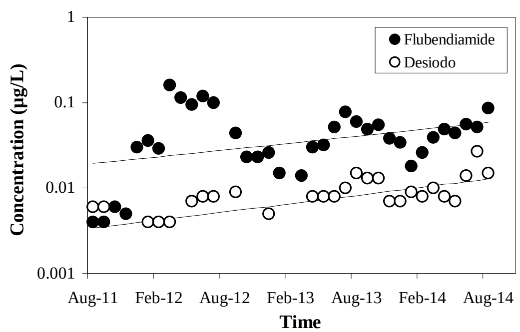
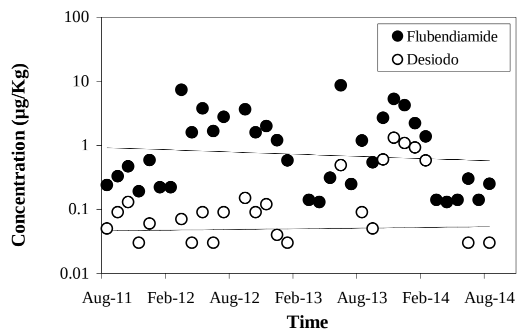
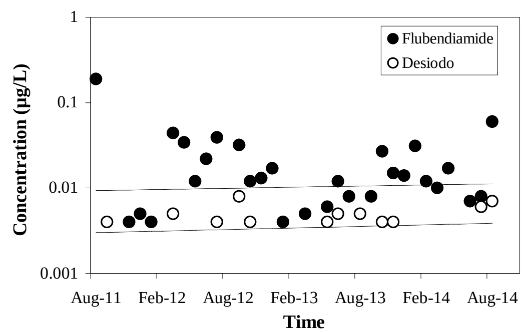

</td><td>
</td><td>
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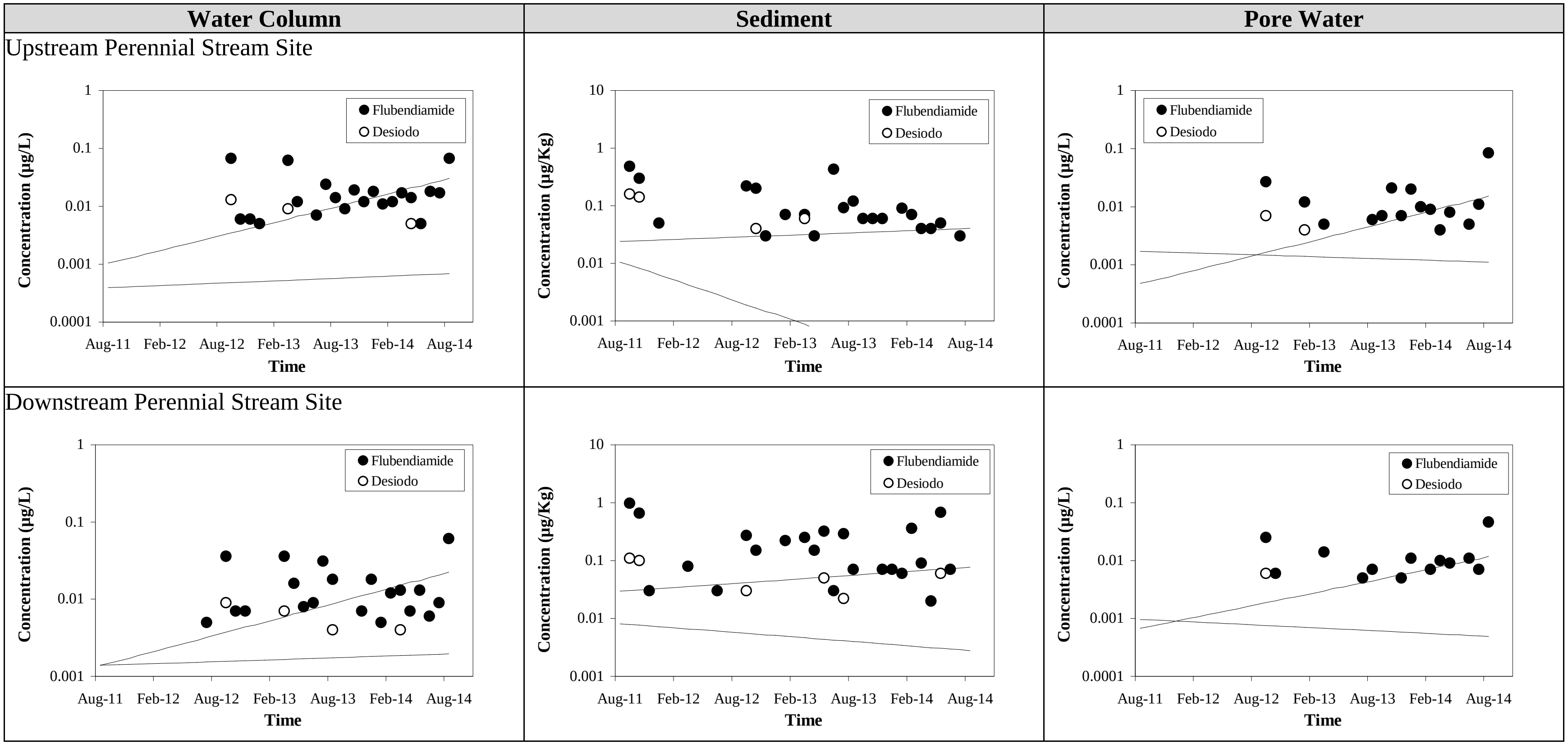


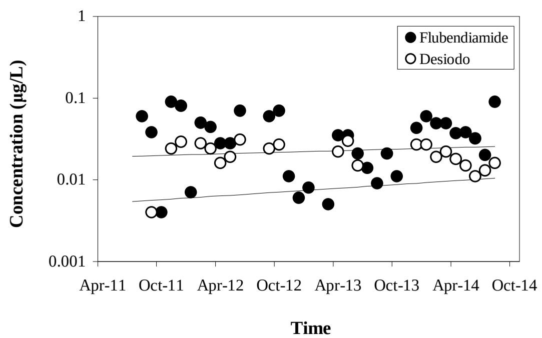
Figure A1. Georgia monitoring data from stream sites.

North Carolina Flowing-water Sites (located at different points in a larger watershed that contains the North Carolina Pond)

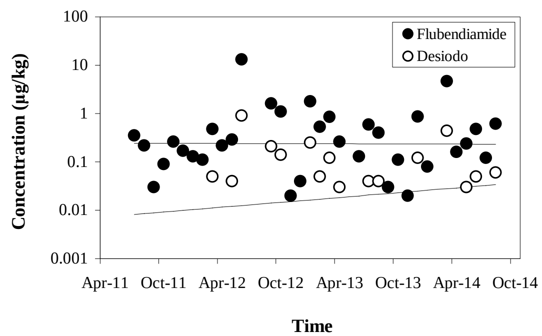
Water Column	Sediment	Pore Water

Upstream Intermittent Stream Site

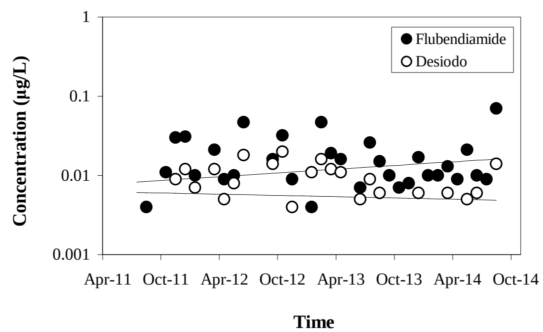
Water Column



Sediment

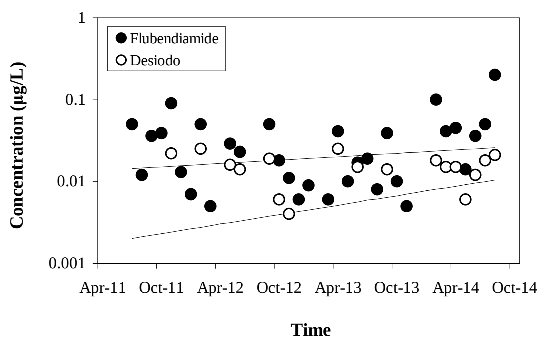


Pore Water

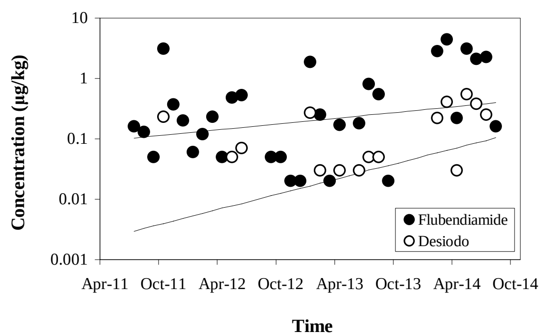


Downstream Intermittent Stream Site

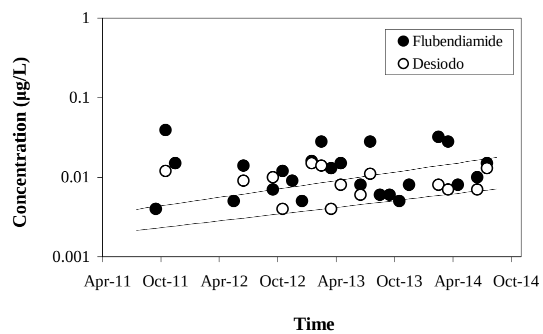
Water Column



Sediment

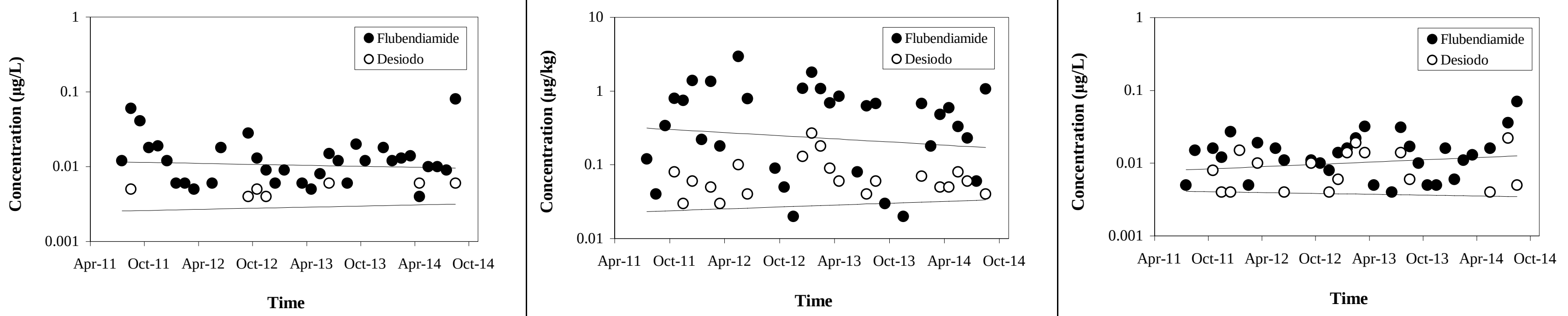


Pore Water



Water Column	Sediment	Pore Water

Upstream Perennial Stream Site



Downstream Perennial Stream Site

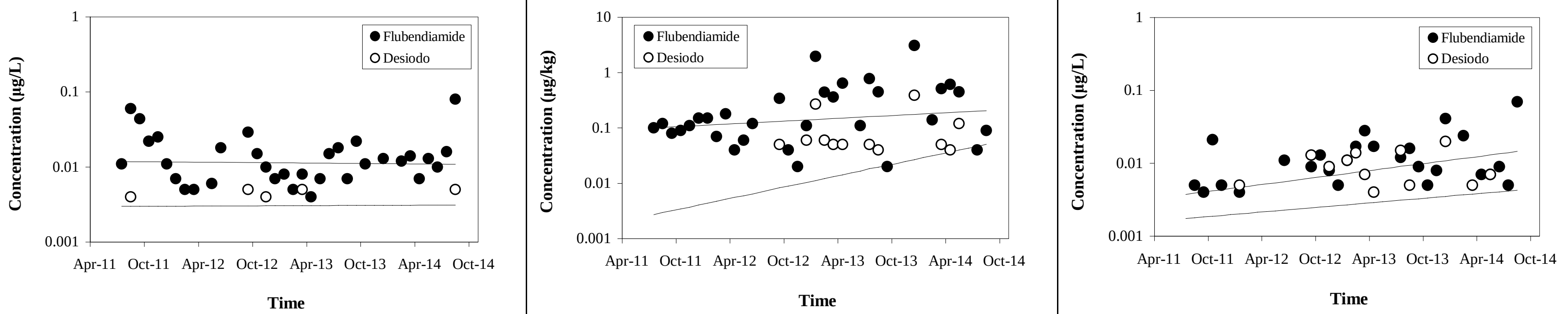


Figure A1. North Carolina monitoring data from stream sites.

Appendix B. Pore Water to Water Column Concentrations Ratios for Flowing Water Sites

The NC perennial stream exhibits pore water to water column concentration ratios that are much closer to 1 (Figure B1c and d) than the intermittent sites (Figure B1a and b) or the pond samples (see Figure 2a in the text). The NC perennial stream (the Tar River) is a large river at the sites sampled. Sediment depths are likely deeper and better mixed due to turbulent flow in the river, which may make it easier to sample sediment and pore water sample from a surficial layer with less dilution from deeper uncontaminated sediment and pore water. The intermittent stream samples had ratios that were intermediate in that they fell closer to 1 than the pond ratios, but further from 1 than the perennial stream samples.

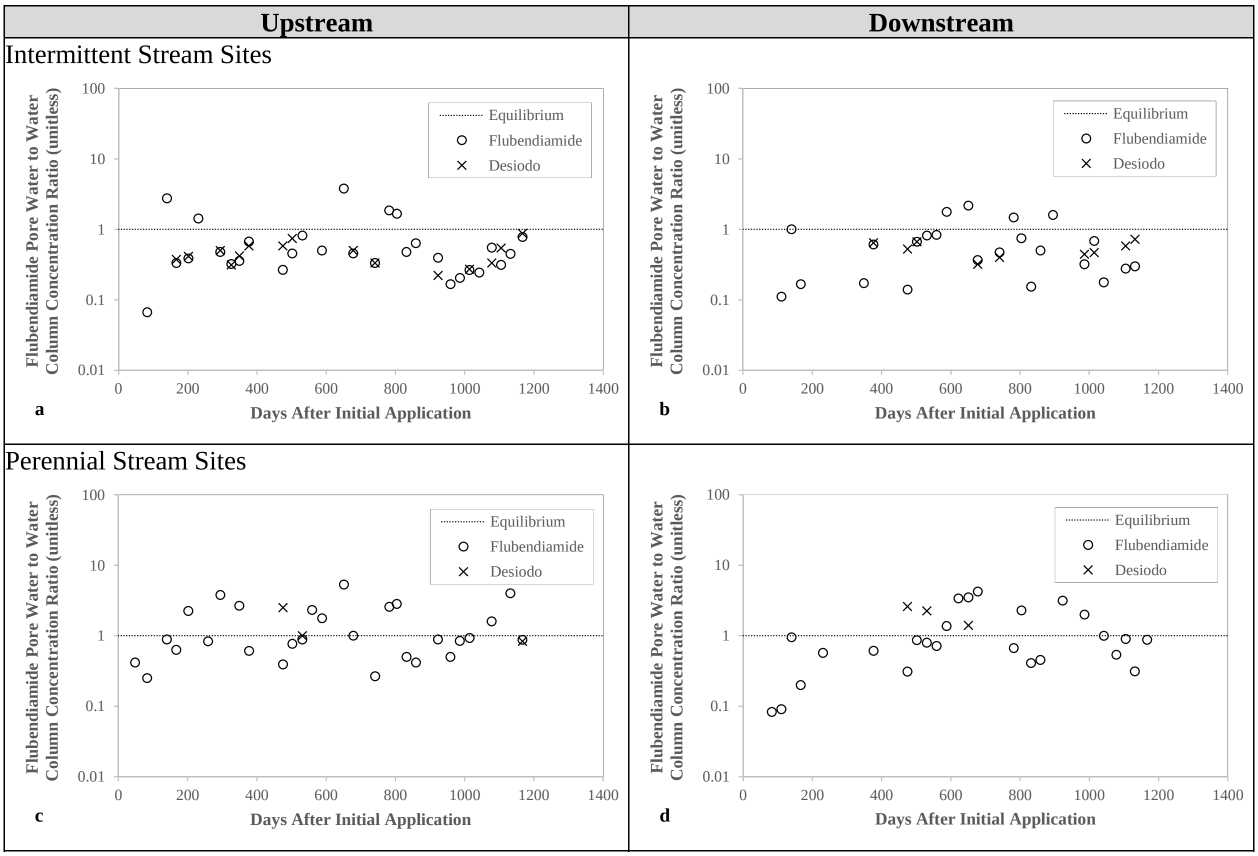
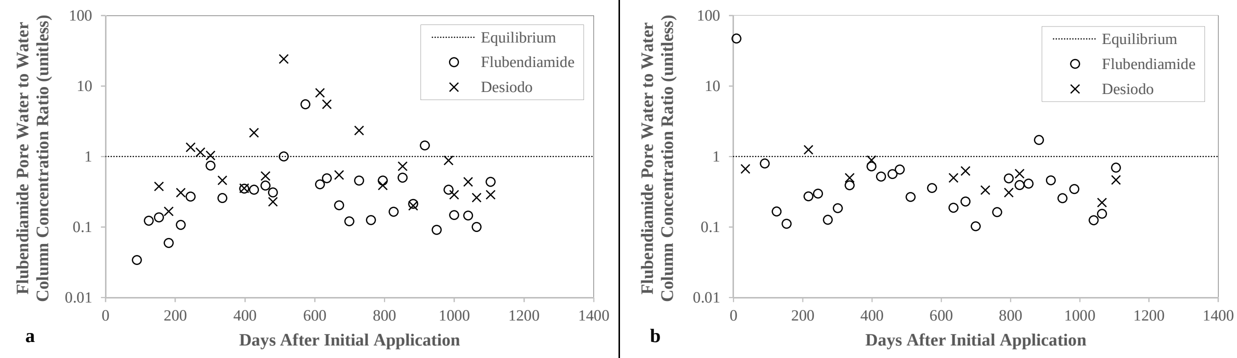


Figure B1. Comparison of pore water to water column concentration ratios for flubendiamide and des-iodo from intermittent (a and b) and perennial (c and d) near the North Carolina pond.

The GA perennial stream water column and pore water concentrations were relatively low. Therefore, early in the monitoring time frame, ratios could not be calculated because one or both concentrations fell below the detection limit. The later ratios from the GA perennial stream sites (Figure B2c and d) were distributed more like the GA (Figure B2a and b) and NC (Figure B1a and b) intermittent streams (the GA perennial stream is much smaller at the GA sample sites than the NC perennial stream is at the NC sample sites). Similar to the NC streams, the GA intermittent and perennial streams were much closer to a ratio of 1 than the GA pond ratios (Figure 2c in the text).

Upstream	Downstream

Intermittent Stream Sites



Perennial Stream Sites

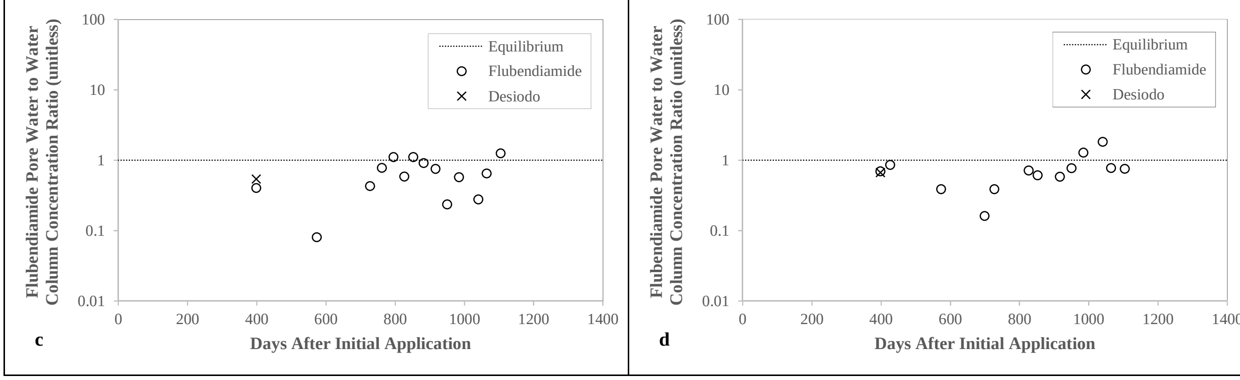


Figure B2. Comparison of pore water to water column concentration ratios for flubendiamide and des-iodo from intermittent (a and b) and perennial (c and d) near the Georgia ponds.