UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

**MEMORANDUM**

DATE: 11/3/2005

SUBJECT: PP#s 1F6313 and 3E6791, 4F6875, and 5E6933 **Human Health Risk Assessment for Boscalid.** Proposal for Tolerances for Residues in/on Celery, Spinach, and Imported Bananas.

| | | | |
|---|---|---|---|
| DP Barcode: | D321910 | | |
| Chemical#: | 128008 | | |
| Class: | Fungicide | | |
| Trade Name: | Endura™ | EPA Reg#: | 7969-197 |
| | Pristine™ | EPA Reg#: | 7969-199 |
| | BAS 510 04 F | EPA Reg#: | 7969-197 |
| 40 CFR: | §180.589 | | |

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## 1.0 EXECUTIVE SUMMARY

### General Background

Boscalid, 3-pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl), is a fungicide and a member of the carboxamide (anilide) class of compounds. The Interregional Research Project #4 (IR-4) has proposed tolerances on celery and spinach. The registrant, BASF, has requested the establishment of a tolerance for imported bananas, an increase in the tolerance for strawberries, decreased PHIs for almonds and potatoes, and seed treatment uses for bulb vegetables, *Brassica* leafy vegetables, legumes, cucurbits, peanuts, and sunflowers.

Permanent tolerances have been established in 40 CFR §180.589 for residues of boscalid in/on numerous plant commodities, ranging from 0.05 ppm in/on peanuts and tuberous and corm vegetables (subgroup 1C) to 35 ppm in/on dried hops cones. Separate tolerances have also been established for indirect or inadvertent residues of boscalid in rotational crops, ranging from 0.05 ppm in several commodities to 8.0 ppm in grass forage, fodder, and hay (Crop Group 17). Tolerances for the combined residues of boscalid and its glucuronic acid conjugate are also established on animal commodities, ranging from 0.02 ppm in eggs to 0.35 ppm in meat byproducts of cattle, goats, horses, and sheep. Finally, a time-limited tolerance of 2.0 ppm has been established in conjunction with a Section 18 request for the use of boscalid on tangerines in California.

Since the first risk assessment for boscalid that was performed in 2003, there have been no additions to the toxicological database and no changes in either the toxicological endpoints chosen for hazard evaluation or the FQPA Safety Factor determination. Therefore, reference may be made to the initial risk assessment for information pertaining to the toxicological database as well as much of the information pertaining to the residue chemistry database (i.e., the information which does not pertain specifically to the commodities in this assessment).

The following end-use products are used on the crops in these tolerance petitions: Endura Fungicide (EPA Reg. No. 7969-197), Pristine Fungicide (EPA Reg. No. 7969-199), Cantus Fungicide, Banastar Fungicide, and BAS 510 04 F Seed Treatment Fungicide (EPA Reg. No. 7969-197). Endura contains 70% by weight boscalid and 30% inert ingredients. Pristine contains boscalid and a second fungicide, pyraclostrobin, in a 2:1 ratio (25.2% boscalid, 12.8% pyraclostrobin). Both Pristine and Endura are proposed for use on celery and spinach. In addition, they are both currently being used on almonds. Pristine alone is used on strawberries. Cantus and Banastar are used on imported bananas. Cantus contains 50% boscalid and Banastar contains 50 g/L boscalid. BAS 510 04 F is a seed treatment formulation that contains 70% boscalid and 30% inert ingredients.

The hazard assessment for boscalid was summarized in the initial risk assessment. As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD) for the general population or females 13-50 years old. Chronic toxicity was seen in several species of animals. Effects were seen in the thyroid and liver. The chronic NOAEL was 21.8 mg/kg bw/day. The FQPA Safety Factor was reduced to 1x, and the uncertainty factor for

intraspecies variability and interspecies extrapolation was 100x. As a result, the chronic population adjusted dose was 0.218 mg/kg/day. For the dermal route, the absorption rate is 15% relative to oral. For the inhalation route, the absorption rate is assumed to be 100%. The residential and occupational level of concern (LOC) for all routes is an MOE of 100. The Cancer Assessment Review Committee (CARC) classified boscalid as having "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential." The quantification of human cancer risk was therefore not recommended.

**Residential Exposure Estimates**

The non-occupational/residential exposure/risk assessment is based on HED's initial assessment for boscalid (D290072). All MOEs exceeded HED's level of concern (100). The daily dermal dose and dermal MOE for the postapplication activity, golfing, are 0.0008 mg/kg/day and 27,000, respectively, based on the highest daily average transferable turf residue for wet turf.

**Dietary Exposure Estimates**

In target crops, rotational crops, and drinking water, parent boscalid is the only residue of concern for both tolerance expression and risk assessment. In animal commodities, parent boscalid, a hydroxy metabolite, and the glucuronide of the hydroxy metabolite are the residues of concern for tolerance expression and risk assessment.

Method D9908 was used for data collection in the crop field trials. This method has been adequately validated for data collection, and the reported limit of quantitation (LOQ) is 0.05 ppm for residues of boscalid in/on plant matrices. Submitted freezer storage stability data support the freezer storage intervals used in the field trial studies.

The submitted field trials performed on celery, spinach, bananas, strawberries, and almonds are adequate to support the recommended tolerances. No deficiencies were noted in the submitted data that would preclude establishing new tolerances for boscalid on celery, spinach, and bananas. In addition, based on the submitted field trial data, the current tolerances for strawberries and almond hulls should be increased. The rotational crop tolerances should be decreased for all of the following: garden beet roots, sugar beet roots, radish roots, turnip roots, and Crop Group 2 (the tops of root and tuber vegetables).

*Dietary Exposure Analysis*

The chronic dietary exposure analysis was performed using DEEM-FCID™. The analysis was based on tolerance-level residues (in some cases modified by DEEM™ (Version 7.81) default processing factors), and assumed 100% crop treated. The risk estimates are below HED's level of concern for the general U.S. population and all population subgroups. The most highly exposed population subgroup is children 1-2 years, which utilizes 31% of the chronic population adjusted dose, (cPAD). The general U.S. population utilizes 9.3% of the cPAD.

*Drinking Water Exposure Estimates*

EFED provided the Tier I estimated drinking water concentrations (EDWCs) for boscalid in surface water and in groundwater for use in the human health risk assessment. EFED used the simulation model FIRST to calculate the surface water EDWCs and used the simulation model SCI-GROW to calculate the groundwater concentration. The turf use represents the highest annual application rate for boscalid. The environmental drinking water concentrations from FIRST are 87.53 ppb for acute and 25.77 ppb for chronic. The SCI-GROW estimate for groundwater exposure is 0.63 ppb.

**Aggregate Exposure Scenarios and Risk Conclusions**

*Acute Aggregate Risk*

As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD) for the general population or females 13-50 years old. An acute aggregate risk assessment is not needed.

*Short-Term Aggregate Risk*

The short-term aggregate risk assessment takes into account average exposure estimates from dietary consumption of boscalid (food and drinking water) and non-occupational uses (golf course exposure). Postapplication exposures from the use on golf courses is considered short-term, and applies to adults and youth. Therefore, a short-term aggregate risk assessment was conducted. As all endpoints are from the same study, exposures from different routes can be aggregated. The exposure to residues in drinking water were included in the dietary exposure analysis. As a result, the aggregate exposure is the sum of two exposure values: dietary (food + water) and residential. The target maximum daily exposure to boscalid residues is 0.22 mg/kg/day. The sum of the food, water, and residential exposures is 0.021 mg/kg/day. As a result, the short-term aggregate risk of exposure to boscalid residues is below HED's level of concern. The exposure estimate was calculated using the general U.S. population, but is considered to be representative of youth because youth and adults possess similar body surface area to weight ratios and because the dietary exposure for youth (13-19 years old) is less than that of the general U.S. population.

*Intermediate-Term Aggregate Risk*

As no intermediate-term non-occupational exposures are anticipated, an intermediate-term aggregate risk assessment is not needed.

*Chronic Aggregate Risk*

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of boscalid (food and drinking water) and residential uses. As the exposure resulting from contact with turf grass (golf courses) is considered short term rather than chronic, the chronic aggregate assessment includes food and drinking water only. As drinking water residues were included in the dietary exposure analysis, the chronic aggregate risk assessment is equivalent to the chronic dietary risk assessment. Aggregate chronic exposure to boscalid in food and drinking water is below HED's level of concern for the general U.S. population and all population subgroups.

**Occupational Exposure Estimates**

There is potential for exposures to boscalid during activities performed by occupational handlers and postapplication workers. All MOEs for handlers performing crop protection uses were above the level of concern (MOE = 100) at the baseline level (4,500 ~ 17,000). All MOEs for handlers performing seed treatment uses were also above the level of concern (MOE = 100) at the single layer level (450 ~ 61,000). All crop protection postapplication MOEs on the day of application exceeded the level of concern (570 ~ 2,800). The postapplication MOEs for seed treatment uses also exceeded the level of concern (8,400 ~ 370,000). The technical material has a Toxicity Category IV for eye irritation/skin irritation, and a Category III for acute dermal toxicity. Per the Worker Protection Standard (WPS), a 12-hr restricted entry interval (REI) is required. The 12 hour REI appearing on the labels is appropriate.

**Recommendations**

HED concludes that there is a reasonable certainty that no harm will result to the general U.S. population, including infants and children, from short-term and chronic aggregate exposure to boscalid residues. No deficiencies were noted in the submitted data that would preclude establishing tolerances for boscalid on celery, spinach, and bananas. In addition, based on the submitted field trial data, the current tolerances for strawberries and almond hulls should be increased. In addition, the rotational crop tolerances should be decreased for all of the following: garden beet roots, sugar beet roots, radish roots, turnip roots, and Crop Group 2 (the tops of root and tuber vegetables). Revised Sections F should be submitted that propose tolerances of 45 ppm for celery, 60 ppm for spinach, 4.5 ppm for strawberries, 17 ppm for almond hulls, 0.20 ppm for banana, and 0.1 ppm for garden beet roots, sugar beet roots, radish roots, turnip roots, and Crop Group 2 (the tops of root and tuber vegetables). HED determined the recommended tolerances for celery, spinach, bananas, strawberries, and almond hulls using its Statistically-Based Method for Establishing NAFTA-Harmonized Tolerances. A summary of the recommended tolerances and the correct commodity definitions is given below in Table 1.

| Table 1. Tolerance Summary for Boscalid | | | |
|---|---|---|---|
| Commodity | Current Tolerance (ppm) | Recommended Tolerance (ppm) | Comments (correct commodity definition) |
| [§180.589(a)(1)] | | | |
| Celery | None | 45 | The available data indicate that a crop group tolerance for leafy vegetables is not appropriate. The data support separate tolerances of 45 ppm for residues in/on celery and 60 ppm for residues in/on spinach. Maximum residues from the field trials were 19.7 ppm in/on celery and 41.8 ppm in/on spinach. |
| Spinach | None | 60 | |
| Strawberry | 1.2 | 4.5 | Strawberry |
| Almond Hulls | 3.0 | 17 | Almond Hulls |
| Banana (Imported) | None | 0.20 | Banana |
| [§180.589(d)] | | | |
| Beet, garden, roots | 1.0 | 0.1 | Adequate residue data are available to support reducing tolerances on the separate rotational root crops and to establish a single tolerance for inadvertent residues in/on *vegetable, root, subgroup 1A*. In the extensive rotational crop field trials on root crops, maximum residues were 0.053 ppm in/on turnip roots |
| Radish, roots | 1.0 | | |
| Turnip, roots | 1.0 | | |
| Beet, sugar, roots | 1.0 | | |
| Vegetable, root and tuber, tops, Crop Group 2 | 1.0 | 0.1 | In the extensive rotational crop trials on sugar beets, garden beets, and turnips, the maximum residues were 0.082 ppm in/on turnip tops. |

The following deficiencies noted in the Agency's earlier review (D278385, M. Nelson, 8/15/03) remain outstanding:

1. Submission of radiovalidation data demonstrating the efficiency of the hydrolysis step in the proposed tolerance enforcement method (DFG S19) for livestock matrices. These radiovalidation data will also be used in support of the data collection method (471/0) for livestock matrices.

2. Submission of radiovalidation data demonstrating the efficiency of the microwave hydrolysis step in Method 476/0 which determines bound residues of boscalid in milk and liver.

3. Submission of data demonstrating the frozen storage stability of boscalid residues in processed grape juice (2 months).

4. Submission of the following additional field trials, conducted per their respective proposed use pattern: 3 tests on mustard greens (one each from Regions 2, 3, and 10); 2 tests on cucumber (one each from Regions 2 and 10); and 1 test on sunflower (Region 5).

5. In order to obtain a seed treatment use on peanuts, the registrant should perform additional field trials in which peanuts have been subjected to both the seed treatment as well as the foliar application. The seed should be treated at the proposed maximum label rate and the foliar applications should be at the maximum label rate. In addition, samples must be taken at the minimum PHI. If residues in the peanut RAC samples exceed the 0.05 ppm tolerance already established for peanuts, the tolerance will likely need to be increased.

## 2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

For a discussion of the physical and chemical properties of boscalid see the initial boscalid risk assessment (D290022, Y. Donovan, *et al.*, 9/8/2003) or the attached residue chemistry summary document (D322235, D. Dotson, 11/3/2005, Attachment 4).

## 3.0 HAZARD CHARACTERIZATION

As there have been no changes to the hazard characterization since the initial risk assessment, see the HED HIARC Report (TXR No. 0051713, 3/7/2003) or the initial risk assessment (D290022, Y. Donovan, *et al.*, 9/8/2003), for a discussion of this topic.

## 4.0 EXPOSURE ASSESSMENT

### 4.1 Summary of Registered and Proposed Uses

Permanent tolerances have been established in 40 CFR §180.589 for residues of boscalid in/on numerous plant commodities, ranging from 0.05 ppm in/on peanuts and tuberous and corm vegetables (subgroup 1C) to 35 ppm in/on dried hops cones. Separate tolerances have also been established for indirect or inadvertent residues of boscalid in rotational crops, ranging from 0.05 ppm in several commodities to 8.0 ppm in grass forage, fodder, and hay (Crop Group 17). Tolerances for the combined residues of boscalid and its glucuronic acid conjugate are also established on animal commodities, ranging from 0.02 ppm in eggs to 0.35 ppm in meat byproducts of cattle, goats, horses, and sheep. Finally, a time-limited tolerance of 2.0 ppm has been established in conjunction with a Section 18 request for the use of boscalid on tangerines in California.

The following end-use products are used on the crops in these tolerance petitions: Endura Fungicide (EPA Reg. No. 7969-197), Pristine Fungicide (EPA Reg. No. 7969-199), Cantus Fungicide, Banastar Fungicide, and BAS 510 04 F Seed Treatment Fungicide (EPA Reg. No. 7969-197). Endura contains 70% by weight boscalid and 30% inert ingredients. Pristine contains boscalid and a second fungicide, pyraclostrobin, in a 2:1 ratio (25.2% boscalid, 12.8%

pyraclostrobin). Cantus and Banastar are used on imported bananas. Cantus contains 50% boscalid and Banastar contains 50 g/L boscalid. BAS 510 04 F is a seed treatment formulation that contains 70% boscalid and 30% inert ingredients.

Pristine and Endura are both proposed for use on celery and spinach. Both formulations are currently being used on almonds, whereas the only formulation being used on strawberries is Pristine. BAS 510 04 F is proposed for use as a seed treatment on *Brassica* leafy vegetables (Crop Group 5), bulb vegetables (Crop Group 3), legume vegetables (Crop Group 6), peanuts, and sunflowers. Imported bananas are treated with Cantus and Banastar.

Crops are to be treated with a broadcast spray which can be made by either ground or aerial equipment. Bananas are treated aerially only. Celery and spinach may receive a maximum of two treatments per season at a rate of 0.40 lb ai/A for a total seasonal application rate of 0.80 lb ai/A. The proposed PHI is 0 days. Bananas receive four treatments per season at a rate of 0.13 lb ai/A for a total seasonal application rate of 0.53 lb ai/A. The PHI is 0 days. Strawberries may receive a maximum of five treatments per season at a rate of 0.18 lb ai/A for a total seasonal application rate of 0.92 lb ai/A. The PHI is 0 days. Almonds receive a maximum of four treatments per season at a rate of 0.23 lb ai/A for a total seasonal application rate of 0.93 lb ai/A. The proposed PHI is 25 days.

### 4.2 Dietary Exposure/Risk Pathway

#### 4.2.1 Residue Profile

For a discussion of the residue chemistry topics that do not pertain specifically to celery, spinach, bananas, strawberries, almonds, and the seed treatment uses on *Brassica* leafy vegetables (Crop Group 5), bulb vegetables (Crop Group 3), legume vegetables (Crop Group 6), peanuts, and sunflowers, (i.e., metabolism studies, analytical enforcement methods, frozen storage stability studies, etc.) see Memo (D290022, Y. Donovan, *et al.*, 9/8/2003). For a more detailed discussion of these topics, reference may also be made to the MARC Decision Memo (D286786, M. Nelson, 01/09/03) as well as the residue chemistry summary document associated with the previous risk assessments (D286787, M. Nelson, 8/15/03 and D290185, D. Dotson, 2/10/2004).

**Metabolism of Boscalid**

In target crops, rotational crops, and drinking water, parent boscalid is the only residue of concern for both tolerance expression and risk assessment. In animal commodities, parent boscalid, a hydroxy metabolite, and the glucuronide of the hydroxy metabolite are the residues of concern for tolerance expression and risk assessment (Memo, D286786, M. Nelson, 1/9/2003).

**Data Collection Method for Plants**

Method D9908 was used for data collection in the celery, spinach, banana, strawberry, and almond field trials as well as in the field rotational crop studies for sugar beets, garden beets, and turnips. This method determines residues of boscalid in plant matrices. Residues are extracted

with an aqueous organic solvent mixture followed by liquid/liquid partitioning and column clean-up. Quantitation is by LC/MS/MS. This method has been adequately validated for data collection, and the reported limit of quantitation (LOQ) is 0.05 ppm for residues of boscalid in/on plant matrices.

**Enforcement Methods**

Adequate methods are available to enforce tolerances on plants (Method D0008, GC/MS) and animals (Method DFG S19, GC/ECD).

**Freezer Storage Stability in Plant Commodities**

With the exception of grape juice, adequate storage stability data are available demonstrating that boscalid is stable under frozen conditions in diverse representative crop matrices for at least 24 months. In the current submissions, samples from the crop field trials and rotational crop studies were stored frozen for a maximum of 11.3 months.

**Magnitude of the Residue Studies**

Field trials were conducted to determine the magnitude of boscalid residues in celery, spinach, bananas, strawberries, almonds, garden beets, sugar beets, and turnips. The field trial studies, their results, and HED's conclusions concerning the adequacy of these studies are summarized below. HED determined the recommended tolerances for celery, spinach, bananas, strawberries, and almond hulls using its Statistically-Based Method for Establishing NAFTA-Harmonized Tolerances.

BASF submitted field trial data for celery and spinach in order to establish a crop group tolerance for the Leafy Vegetables (except *Brassica*) Group. The proposed crop group tolerance is 50 ppm. The available field trial data are adequate and support the proposed use patterns for celery and spinach. The total application rate used in field trials was 1x that specified on the current proposed label. Adequate numbers of field trials were conducted at the maximum proposed use rates, and the appropriate commodities were collected at the proposed PHI (0 days). Samples were analyzed using adequate analytical methods and the sample storage intervals are supported by the available storage stability data. The field trial data indicate that separate tolerances will be required for celery and spinach as maximum boscalid residues substantially exceeded the current tolerance of 11.0 ppm in/on leaf lettuce. The available data indicate that a crop group tolerance for leafy vegetables is not appropriate. The data support separate tolerances of 45 ppm for residues in/on celery and 60 ppm for residues in/on spinach. Maximum residues from the field trials were 19.7 ppm in/on celery and 41.8 ppm in/on spinach. The registrant needs to submit a revised Section F that proposes a tolerance of 45 ppm for celery and 60 ppm for spinach.

BASF has requested that the strawberry tolerance be increased from 1.2 ppm to 4.0 ppm. The available field trial data are adequate and support the request for an increase in the strawberry tolerance. The field trials were performed at the 1x application rate and the specified PHI, 0 days. Adequate numbers of field trials were conducted. Three field trials were performed in addition to the original eight trials. The OPPTS Series 860 Guidelines recommend that at least

eight field trials be performed. Samples were analyzed using adequate analytical methods and the sample storage intervals are supported by the available storage stability data. For a 0-day PHI, the available residue data support a 4.5 ppm tolerance for the raw agricultural commodity strawberry. BASF needs to submit a revised Section F that proposes a tolerance of 4.5 ppm for strawberry.

BASF submitted field trial data on almonds in order to support a request for an increase in the almond hull tolerance from 3.0 ppm to 15 ppm. The submitted field trials are adequate to evaluate the registrant's request. The OPPTS Series 860 Guidelines recommend that five field trials be performed in Growing Region 10. The registrant performed five field trials at two different spray dilutions for a total of ten trials. The trials were performed in Region 10. Based on the results of the almond hull analyses, HED recommends in favor of increasing the tolerance from 3.0 ppm to 17 ppm. The proposed PHI for almonds is 25 days, whereas the PHI for all other tree nuts is 14 days. In the five pecan field trials that were originally performed, residues in all samples were below the LOQ of 0.05 ppm. In the almond field trials performed at a 25-day PHI, residues in all samples were also below the LOQ of 0.05 ppm. Although almonds and pecans are the representative commodities of the tree nuts crop group and residues in all nutmeat samples were <0.05 ppm, HED recommends retaining the crop group tolerances for tree nut nutmeat and pistachios at 0.7 ppm. The existing 0.7 ppm tolerances for these commodities are based on the fact that the maximum residue in pistachios was 0.64 ppm (see 8/15/2003 M. Nelson summary document, PP#1F6313, D278385). The registrant needs to submit a revised Section F that proposes a tolerance of 17 ppm for almond hulls.

BASF has requested that the Agency establish a tolerance of 0.5 ppm on imported bananas. The submitted field trials are adequate to evaluate the registrant's request. The OPPTS Series 860 Guidelines recommend that for a domestic use five field trials be performed, one in Growing Region 3 and four in Region 13. The current request is for an import tolerance, however, so the field trials were performed in Central and South America. Twelve field trials were performed all together. This number is consistent with the import tolerance guidance published by the Agency in the Federal Register on June I, 2000. Based on the results of the analyses of the unbagged whole fruit samples, HED recommends in favor of establishing the import tolerance at 0.20 ppm. The registrant needs to submit a revised Section F that proposes a tolerance of 0.20 ppm for banana.

Adequate extensive field rotational crop trials are available on sugar beet, garden beet, and turnips. The representative crops were planted 14 days after soil applications of boscalid (WDG) totaling ~1.8 lb ai/A (1x the maximum seasonal rate), and adequate numbers of tests were conducted on each crop in the appropriate regions. The data support reducing the current tolerance for indirect residues on sugar beet roots, garden beet roots, turnip roots, radish roots, and the leaves of root and tuber vegetables (Group 2) from 1.0 ppm to 0.1 ppm.

The registrant has proposed a label amendment to decrease the tuberous and corm vegetable PHI from 30 days to 10 days. A tolerance of 0.05 ppm is currently in effect for tuberous and corm vegetables (Crop Subgroup 1C). The registrant performed 16 field trials on potatoes. The potatoes were harvested at a PHI of 30 days. Two residue decline studies were performed in which a PHI of 10 days was used. In addition, one of the field trials at the 30-day PHI was performed at a 5x application rate. In all samples including those performed at the 10-day PHI

and the one performed at the exaggerated rate, residues were below the LOQ of 0.05 ppm. Tuberous and corm vegetables grow underneath the soil surface. The primary means of uptake of residues from foliar applications is by translocation through the leaves. Very often residues increase with an increase in PHI because the residues have more time for translocation. As a result, HED feels that the two residue decline studies which include samples taken at a 10-day PHI support the request for the decreased PHI.

The registrant has requested the use of boscalid as a seed treatment on *Brassica* leafy vegetables (Crop Group 5), bulb vegetables (Crop Group 3), legume vegetables (Crop Group 6), peanuts, and sunflowers. Tolerances for foliar uses have already been established for all of these commodities. With the exception of peanuts, the tolerances for these commodities are 0.6 ppm or higher. The tolerance for peanuts is 0.05 ppm. As the tolerances for foliar uses are considerably higher than the residues that would result from seed treatment uses (for all of the proposed commodities except peanuts), HED recommends in favor of granting the seed treatment uses for all crops except peanuts. For a seed treatment use on peanuts, the registrant should perform additional field trials in which peanuts have been subjected to both the seed treatment as well as the foliar application. The seed should be treated at the proposed maximum label rate and the foliar applications should be at the maximum label rate. In addition, samples must be taken at the minimum PHI. If residues in the peanut RAC samples exceed the 0.05 ppm tolerance already established for peanuts, the tolerance will likely need to be increased.
The results of the celery, spinach, banana, almond, strawberry and rotational crop field trials are summarized in Table 2.

**Table 2. Summary of Residues from the Crop Field Trials with Boscalid**

| Crop Matrix | Total Seasonal Application Rate (lb ai/A) | PHI (days) | Residues (ppm) | | | | |
|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Dev. | HAFT | Min. | Max. |
| **Celery (proposed use = 0.80 lb ai/A total application rate, 0-day PHI)** | | | | | | | |
| Celery | 0.8 | 0 | 8.7 | 5.5 | 19.1 | 1.8 | 19.7 |
| **Spinach (proposed use = 0.80 lb ai/A total application rate, 0-day PHI)** | | | | | | | |
| Spinach | 0.8 | 0 | 24.9 | 9.9 | 39.5 | 12.6 | 41.8 |
| **Bananas (proposed use = 0.53 lb ai/A total applieation rate, 0-day PHI)** | | | | | | | |
| Banana | 0.13 | 0 | 0.08 | 0.04 | 0.18 | <0.05 | 0.18 |
| **Strawberries (proposed use = 1.81 lb ai/A total application rate, 0-day PHI)** | | | | | | | |
| Strawberries | 1.8 | 0 | 1.02 | 0.61 | 2.04 | 0.16 | 2.36 |
| **Almonds (proposed use = 0.93 lb ai/A total application rate, 21-day PHI)** | | | | | | | |
| Almond Nutmeat | 0.92 | 25 | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 |
| Almond Hulls | 0.92 | 25 | 5.3 | 3.3 | 11.3 | 1.8 | 13.4 |
| **Rotational Crops** | | | | | | | |
| Sugar Beet Roots | 1.8 | 14 (PBI)* | 0.050 | <0.05 | <0.05 | <0.05 | <0.05 |
| Sugar Beet Tops | 1.8 | 14 (PBI)* | 0.052 | <0.05 | 0.064 | <0.05 | 0.066 |

| Table 2. Summary of Residues from the Crop Field Trials with Boscalid | | | | | | | |
|---|---|---|---|---|---|---|---|
| Crop Matrix | Total Seasonal Application Rate (lb ai/A) | PHI (days) | Residues (ppm) | | | | |
| | | | Mean | Std. Dev. | HAFT | Min. | Max. |
| Garden Beet Roots | 1.8 | 14 (PBI)* | 0.050 | <0.05 | <0.05 | <0.05 | <0.05 |
| Garden Beet Tops | 1.8 | 14 (PBI)* | 0.050 | <0.05 | <0.05 | <0.05 | <0.05 |
| Turnip Roots | 1.8 | 13-14 (PBI)* | 0.050 | <0.05 | 0.052 | <0.05 | 0.053 |
| Turnip Tops | 1.8 | 13-14 (PBI)* | 0.055 | <0.05 | 0.074 | <0.05 | 0.082 |

* PBI: Plant Back Interval

**Magnitude of the Residue in Processed Food/Feed.**

As there are no processed food or feed commodities associated with spinach, celery, strawberries, almonds, or bananas, this guideline requirement is not relevant to the current submissions.

**International Harmonization**

There are currently no International or Codex MRLs for boscalid. Although the initial U.S. tolerances for boscalid were established in conjunction with a joint review with Canada's PMRA, MRLs have yet to be finalized in Canada. Regulatory Note for Boscalid REG2004-2 (1/30/2004) lists tolerances which have been proposed as part of the Canadian process. The strawberry tolerance in that Note is 1.2 ppm, which agrees with the established U.S. tolerance, but is less than the 4.5 ppm tolerance recommended by HED in the present action. This tolerance is being increased based on the submission of additional residue data to EPA and the use of the NAFTA statistical method that was not available at the time of the joint review. In a similar fashion, HED is recommending revision of rotational crop tolerances for the tops of root and tuber vegetables and for the roots of radishes, turnips, garden beets, and sugar beets. These tolerances are being decreased from 1.0 to 0.1 ppm based on the submission of field rotational crop data. As a result, these tolerances would differ from the proposed Canadian MRLs of 1.0 ppm for the tops and 0.7 ppm for the roots. The HED-recommended tolerances of 45 ppm on celery and 60 ppm on spinach are much higher than the proposed Canadian MRL of 1 ppm on these crops. However, that Canadian level is based on rotational crop residues, while the U.S. is now setting celery and spinach tolerances to cover direct use on these crops.

**4.2.2 Chronic Dietary Exposure and Risk**

The chronic dietary exposure assessment for boscalid is attached (Attachment 1, D321557, D. Dotson, 11/3/2005).

The chronic dietary exposure analysis was performed using the DEEM-FCID (Version 2.03) Model. The assessment was based on tolerance-level residues (in some cases modified by

DEEM (Version 7.81) default processing factors), and assumed 100% crop treated. Even with these highly conservative assumptions, the risk estimates are below HED's level of concern. The most highly exposed population subgroup is children 1-2 years, which utilizes 31% of the cPAD. The general U.S. population utilizes 9.3% of the cPAD.

**Table 3. Summary of Dietary Exposure and Risk for Boscalid**

| Population Subgroup | Acute Analysis | DEEM: Chronic Analysis | | Cancer Analysis |
|---|---|---|---|---|
| | | Dietary Exposure (mg/kg/day) | % cPAD | |
| General U.S. Population | Not Applicable: No Acute Dietary Endpoint | 0.020202 | 9.3 | Not Applicable: No cancer risk assessment is required |
| All Infants (< 1 year old) | | 0.047013 | 22 | |
| **Children 1-2 years old** | | **0.067046** | **31** | |
| Children 3-5 years old | | 0.046987 | 22 | |
| Children 6-12 years old | | 0.024451 | 11 | |
| Youth 13-19 years old | | 0.013912 | 6.4 | |
| Adults 20-49 years old | | 0.015423 | 7.1 | |
| Adults 50+ years old | | 0.017092 | 7.8 | |
| Females 13-49 years old | | 0.015606 | 7.2 | |

### 4.2.3 Cancer Dietary

The Cancer Assessment Review Committee (CARC) stated that boscalid exhibited "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential." The quantification of human cancer risk is therefore not necessary.

**4.3 Water Exposure/Risk Pathway** (Attachment 2, EFED memo of 5/5/2005, C. Salice, D313814).

EFED provided Tier I EDWCs for boscalid in surface water and in groundwater for use in the human health risk assessments. EFED used the simulation model FIRST to calculate the surface water EDWCs and used the simulation model SCI-GROW to calculate the groundwater concentration. The turf use represents the highest annual application rate for boscalid. The environmental drinking water concentrations from FIRST are 87.53 for acute and 25.77 ppb for chronic. The SCI-GROW estimate for groundwater exposure is 0.63 ppb.

| Table 4. Tier I EDWCs for Drinking Water Risk Assessment Based on Boscalid use on Turf. | |
|---|---|
| Surface water drinking water sources | acute: 87.5 ppb<br>chronic: 25.8 ppb |
| Groundwater drinking water sources | 0.63 ppb |

**4.4 Non-Occupational Exposure/Risk Pathway** (Attachment 3, HED ORE memo of 9/20/2005, Shih-Chi Wang, D321801)

As no new residential uses are proposed, a new residential exposure/risk assessment is not required. A short-term non-occupational dermal postapplication exposure/risk assessment for individuals golfing and harvesting fruit at "U-pick" farms and orehards was conducted in the initial boscalid assessment (D290072; S. Wang, M. Collantes, and G. Bangs, 6/23/03). The daily dermal dose and dermal MOE for the postapplication activity, golfing, are 0.0008 mg/kg/day and 27,000, respectively, based on the highest daily average transferable turf residue for wet turf. The turf study was performed in Pennsylvania.

**4.5 Other (Spray Drift, etc.)**

Spray drift is always a potential source of exposure to residents living in close proximity to spraying operations. This situation is particularly the case with aerial application. However, to a lesser extent, spray drift resulting from the ground application of boscalid could also be a potential source of exposure. The Agency has been working with the Spray Drift Task Force (a membership of U.S. pesticide registrants), EPA Regional Offices, State Lead Agencies for pesticide regulation, and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, and is developing a policy on how to apply appropriately the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast, and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with pesticide application.

## 5.0 AGGREGATE RISK ASSESSMENT AND RISK CHARACTERIZATION

Aggregate risk assessments were performed for short-term and chronic scenarios.

**5.1 Acute Risk**

As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute dietary risk to the general population or to the subpopulation females 13-50 years old. An acute aggregate risk assessment is not needed.

## 5.2 Short-Term Risk

The short-term aggregate risk assessment takes into account average exposure estimates from dietary consumption of boscalid (food and drinking water) and non-occupational uses. In this case, the only non-occupational use to be aggregated with dietary exposure is the turf use on golf courses. Postapplication exposures from the use on golf courses is considered short-term, and applies to adults and youth. Therefore, a short-term aggregate risk assessment was conducted. As all endpoints are from the same study, exposures from different routes can be aggregated. The exposure to residues in drinking water were included in the dietary exposure analysis. As a result, the aggregate exposure is the sum of two exposure values: dietary (food + water) and residential. Table 5 summarizes the results. The target maximum daily exposure to boscalid residues is 0.22 mg/kg/day. The sum of the food, water, and residential exposures is 0.021 mg/kg/day. As a result, the short-term aggregate risk of exposure to boscalid residues is below HED's level of concern.

The exposure estimate was calculated using the general U.S. population, but is considered to be representative of youth because youth and adults possess similar body surface area to weight ratios and because the dietary exposure for youth (13-19 years old) is less than that of the general U.S. population.

**Table 5. Short-Term Aggregate Risk and DWLOC Calculations for the General U.S. Population (Inhalation/Oral/Dermal Endpoints and NOAELs the Same)**

| Popula-tion | Short-Term Scenario | | | | | |
|---|---|---|---|---|---|---|
| | NOAEL mg/kg/day | Target MOE | Max Exposure[2] mg/kg/day | Average Dietary Exposure (food + water) mg/kg/day | Residential Exposure[3] mg/kg/day | Aggregate Food, Water, and Residential Exposure[4] mg/kg/day |
| U.S. | 21.8 | 100 | 0.218 | 0.020202 | 0.0008 | 0.0210 |

[1]The target MOE for dermal is 100.
[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE
[3] Residential Exposure = Dermal exposure from golf course only
[4] Aggregate Exposure = Dietary (food + water) Exposure + Residential Exposure

## 5.3 Intermediate-Term Risk

As no intermediate-term non-occupational exposures are anticipated, an intermediate-term aggregate risk assessment is not needed.

## 5.4 Chronic Risk

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of boscalid (food and drinking water) and residential uses. As the exposure resulting from contact with turf grass (golf courses) is considered short term, the chronic aggregate assessment includes food and drinking water only. Residues in drinking water were included in the chronic dietary analysis. As a result, the chronic aggregate risk assessment is equivalent to the chronic dietary analysis. See Table 3 for the results of the analysis. Chronic

aggregate risk is below HED's level of concern for the general U.S. population and all population subgroups.

### 5.5 Cancer Risk

The Cancer Assessment Review Committee (CARC) stated that boscalid exhibited "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential." The quantification of human cancer risk was not recommended.

## 6.0 CUMULATIVE RISK

FQPA (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this tolerance action for boscalid because HED has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of boscalid. For purposes of this tolerance action, EPA has assumed that boscalid does not have a common mechanism of toxicity with other substances.

On this basis, the registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether boscalid shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for boscalid need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with boscalid, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at: http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf. In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

**7.0 OCCUPATIONAL EXPOSURE AND RISK** (Attachment 3, HED ORE memo of 9/20/2005, Shih-Chi Wang, D321801)

Pesticide workers performing their activities will be exposed to boscalid during and after the application of the fungicide. For a discussion of products used, detailed use rates, and use patterns, see the attached HED ORE memo (D321801, S. Wang, 9/20/2005, Attachment 3).

## 7.1 Occupational Handler

There are six handler scenarios that are expected to result in the highest exposure for the proposed uses: (1) mixing/loading dry flowable for groundboom application, (2) applying sprays with groundboom equipment, (3) loading (open)/applying liquid for seed treatment, (4) sewing seeds after seed treatment, (5) bagging seeds after seed treatment, and (6) multiple worker activities for seed treatment.

The number of exposure days per year was not provided. Based on the frequency/interval of applications on the crops and the seasonal nature of seed treatment operation, EPA assumes that both application handlers and postapplication workers would be exposed for less than 6 months per year (short- and intermediate-term exposures). Long-term exposure is not expected.

As no chemical-specific data for assessing human exposures during pesticide handling activities were submitted to the Agency in support of the registration of boscalid, HED used surrogate data from the PHED Version 1.1 (PHED Surrogate Exposure Guide, 8/98) to assess exposures for crop protection uses. Defaults established by the HED Science Advisory Council for Exposure were used for acres treated per day and body weight. For seed treatment uses, handler assessments were based on data from two policy papers of the Science Advisory Council for Exposure (Exposure SAC). These data are (1) the unit exposure data from Policy #14: Standard Operating Procedures (SOP) for Seed Treatment (May 1, 2003) and (2) the treating/planting data from the Policy #15: Amount of Seed Treated or Planted Per Day (March 2, 2004).

All MOEs for handlers performing crop protection uses were above the level of concern (MOE = 100) at the baseline level (4,500 ~ 17,000). All MOEs for handlers performing seed treatment uses were also above the level of concern (MOE = 100) at the single layer level (450 ~ 61,000).

## 7.2 Postapplication Exposure and Risk Estimates

There is a potential for occupational exposure resulting from the entering of areas previously treated with boscalid and from the planting of treated seed. Occupational postapplication exposure is expected to be short- and intermediate-term in duration.

The occupational postapplication exposures/risks were calculated from activity-specific transfer coefficient (Tc) values from the HED Science Advisory Council for Exposure Policy Number

3.1 and from the unit exposures given in the Science Advisory Council for Exposure Policy Number 14 (May 1, 2003).

All crop protection postapplication MOEs on the day of application exceeded the level of concern (570 ~ 2,800). The postapplication MOEs for seed treatment uses also exceeded the level of concern (8,400 ~ 370,000). The technical material has a Toxicity Category IV for eye irritation/skin irritation, and a Category III for acute dermal toxicity. Per the Worker Protection Standard (WPS), a 12-hr restricted entry interval (REI) is required. The 12-hour REI appearing on the labels is appropriate.

## 8.0 DATA NEEDS

**8.1 Toxicology**: None

**8.2 Residue Chemistry**

Revised Sections F should be submitted that propose tolerances of 45 ppm for celery, 60 ppm for spinach, 4.5 ppm for strawberry, 17 ppm for almond hulls, and 0.20 ppm for banana. See Table 1 for a summary of the recommended tolerances and the correct commodity definitions.

The following deficiencies noted in the Agency's earlier review (D278385, M. Nelson, 8/15/03) remain outstanding:

1. Submission of radiovalidation data demonstrating the efficiency of the hydrolysis step in the proposed tolerance enforcement method (DFG S19) for livestock matrices. These radiovalidation data will also be used in support of the data collection method (471/0) for livestock matrices.

2. Submission of radiovalidation data demonstrating the efficiency of the microwave hydrolysis step in Method 476/0, which determines bound residues of boscalid in milk and liver.

3. Submission of data demonstrating the frozen storage stability of boscalid residues in processed grape juice (2 months).

4. Submission of the following additional field trials, conducted per their respective proposed use pattern: 3 tests on mustard greens (one each from Regions 2, 3, and 10); 2 tests on cucumber (one each from Regions 2 and 10); and 1 test on sunflower (Region 5).

5. In order to obtain a seed treatment use on peanuts, the registrant should perform additional field trials in which peanuts have been subjected to both the seed treatment as well as the foliar application. The seed should be treated at the proposed maximum label rate and the foliar applications should be at the maximum label rate. In addition, samples must be taken at the minimum PHI. If residues in the peanut RAC samples exceed the 0.05 ppm tolerance already established for peanuts, the tolerance will likely need to be increased.

Attachments:
1. HED Dietary Exposure Memo, D321557, D. Dotson, 11/3/2005.
2. EFED Memo, D313814, C. Salice, 5/5/2005.
3. HED ORE Memo, D290072, S. Wang, 9/20/2005.
4. HED Residue Chemistry Summary Document, D322235, D. Dotson, 11/3/2005.

cc without Attachments: D. Dotson, S. Wang