

5.3 BOSCALID (221)

TOXICOLOGY

Boscalid (2-chloro-*N*-[2-(4-chlorophenyl)phenyl]pyridine-3-carboxamide) was evaluated by JMPR in 2006, when an ADI of 0–0.04 mg/kg bw was established. The Meeting concluded that it was not necessary to establish an ARfD for boscalid (Annex 5, reference 109).

Following a request for additional maximum residue levels by CCPR, boscalid was placed on the agenda of the present Meeting, which assessed additional toxicological information available on boscalid and its metabolites since the last review. The Meeting also applied the “Plant and animal metabolite assessment scheme” of JMPR for the assessment of these metabolites.

The newly submitted studies investigated absorption, excretion and metabolism, dermal sensitization, mechanism of the thyroid effects and reversibility of toxicity of the parent compound and the toxicity of two metabolites that have been found in groundwater.

All critical studies contained statements of compliance with good laboratory practice (GLP) and were conducted in accordance with relevant national or international test guidelines, unless otherwise specified. No additional information from a literature search was identified that complemented the toxicological information submitted for the current assessment.

Biochemical aspects

The toxicokinetics of boscalid in rats following the administration of a single dose of ¹⁴C-labelled boscalid at 500 mg/kg bw or multiple dosing of unlabelled boscalid at 500 mg/kg bw per day for 14 or 28 days followed by a single dose of ¹⁴C-labelled boscalid at 500 mg/kg bw indicated no significant differences in the excretory (approximately 70% in the faeces) or metabolic patterns in urine and faeces, regardless of dosing regimen or sex (Fabian, Grosshans & Mellert, 2003).

In dermal penetration studies using human skin *in vitro*, the dermal penetration estimates were 0.07% and 1% for the formulation concentrate (50% boscalid) and the 1:1300 spray dilution, respectively.

In an *in vitro* study comparing the metabolism of boscalid in human, rat and dog hepatocytes, no human-specific metabolites of boscalid were identified, and the metabolic pathways were similar in the tested species.

Toxicological data

In rats, the acute oral median lethal dose (LD₅₀) for boscalid was greater than 2000 mg/kg bw. Boscalid was not sensitizing to the skin of guinea-pigs.

In a study to investigate the induction of metabolizing enzymes in the liver and changes in thyroid hormone levels in rats, treatment with boscalid led to decreases in thyroxine (T₄) levels, increases in thyroid stimulating hormone (TSH) levels, increased liver and thyroid weights and increased activities of phase I and phase II enzymes. It was concluded that the mild imbalance in thyroid hormone levels caused by boscalid was due to the induction of the hepatic microsomal enzyme system. The effects of boscalid on liver and thyroid were reversible, and the effect on the thyroid was considered indirect.

Toxicological data on metabolites and/or degradates

M510F47 (Reg. No. 107371; 2-chloronicotinic acid; low-level rat metabolite, soil and potentially groundwater degradate)

M510F47 had low acute toxicity (LD₅₀ > 2000 mg/kg bw) and showed no evidence of genotoxicity *in vitro*.

M510F49 (Reg. No. 391572; N-(4'-chlorobiphenyl-2-yl)-2-hydroxynicotinamide; soil and potentially groundwater degradate)

M510F49 had low acute toxicity ($LD_{50} > 2000$ mg/kg bw) and showed no evidence of genotoxicity in vitro or in vivo.

The no-observed-adverse-effect level (NOAEL) for M510F49 identified in a 90-day feeding study in rats was 968 mg/kg bw per day, the highest dose tested. The Meeting noted that the NOAELs for boscalid in 90-day feeding studies were 34 mg/kg bw per day in rats, 29 mg/kg bw per day in mice and 7.6 mg/kg bw per day in dogs, as identified by the 2006 Meeting (Annex 5, reference 109).

Human data

No adverse effects of boscalid were reported in medical surveillance of manufacturing plant personnel. One case of slight skin irritation was registered in an employee accidentally exposed to boscalid in combination with another product. Therefore, it was not clear whether the effect was attributable to boscalid. No data on exposure of the general public or epidemiological studies are available for boscalid.

Toxicological evaluation

The Meeting concluded that no revision of the ADI for boscalid was necessary.

The Meeting concluded that metabolite M510F47 was unlikely to be genotoxic. Following JMPR's "Plant and animal metabolite assessment scheme", the Meeting concluded that for chronic toxicity, M510F47 could be assessed using the TTC approach. M510F47 is categorized in Cramer class III, and therefore a TTC of 1.5 µg/kg bw per day applies.

On the basis of a comparison of NOAELs in short-term studies of toxicity, the Meeting concluded that the toxicity of M510F49 was lower than that of the parent compound. Owing to the limited database on M510F49, the Meeting was unable to conclude that this metabolite was of no concern but concluded that M510F49 would be covered by the ADI of the parent compound.

The ADI of 0–0.04 mg/kg bw applies to boscalid plus metabolite M510F49, expressed as boscalid.

An addendum to the toxicological monograph was prepared.

Acceptable daily intake (ADI) (applies to boscalid plus metabolite M510F49, expressed as boscalid)

0–0.04 mg/kg bw

Critical end-points for setting guidance values for exposure to boscalid and metabolites

| | |
|-----------------------------------|--|
| Acute toxicity | |
| Rat, LD_{50} , oral | >2 000 mg/kg bw |
| Dermal sensitization (guinea-pig) | Not sensitizing (maximization test) |
| Short-term studies of toxicity | |
| Target/critical effect | None |
| Lowest relevant inhalation NOAEC | 616.7 mg/m ³ , highest concentration tested (rat) |
| Studies on metabolites | |
| M510F47 | Oral $LD_{50} > 2\ 000$ mg/kg bw No evidence of genotoxicity in vitro |
| M510F49 | Oral $LD_{50} > 2\ 000$ mg/kg bw |

No evidence of genotoxicity

Short-term study of toxicity: NOAEL 968 mg/kg bw per day, highest dose tested (rat)

RESIDUE AND ANALYTICAL ASPECTS

Boscalid is a systemic fungicide first evaluated by JMPR in 2006 for residues and toxicology as a new active substance. An ADI of 0–0.04 mg/kg bw was established for boscalid, while no ARfD was considered necessary.

The 2006 JMPR recommended the following residue definition for boscalid:

Definition of the residue for compliance with the MRL in plant and animal commodities and for dietary risk assessment in plant commodities: *boscalid*

Definition of the residue for dietary risk assessment in animal commodities: *sum of*

boscalid, 2-chloro-N-(4'-chloro-5-hydroxybiphenyl-2-yl)nicotinamide (M510F01) including its conjugate, expressed as boscalid

The residue is fat-soluble.

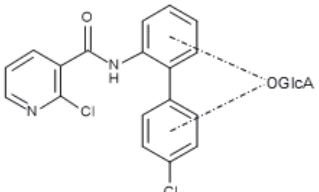
In 2008 and 2010 additional uses (and in 2009 residues in follow crops) were reviewed for residues by the Meeting. Boscalid was scheduled at the Fiftieth Session of the CCPR for the evaluation of additional uses for the Extra 2019 JMPR Meeting.

The current Meeting received new information on use patterns for boscalid in pome fruit, stone fruit, berry fruit, tropical fruit and tea supported by additional plant and animal metabolism studies, field rotational crop studies, analytical methods and recovery data, supervised field trials and studies simulating typical processing conditions.

The current Meeting also received additional data on environmental fate and on corresponding analytical methods in environmental matrices (see evaluation). The Meeting concluded that these data are not directly linked to the current consideration of additional uses on permanent crops and decided to postpone the assessment of the data until the next periodic review of boscalid.

The following abbreviations are used for the metabolites discussed below:

| Code Names | Structure | Where found |
|---------------------|-----------|---|
| Boscalid BAS510F | | Rat, plants, animals, rotational crops, soil |
| M510F01 | | Rat, animals |

| Code Names | Structure | Where found |
|------------|---|--------------|
| M510F65 |  | Rat, animals |

Plant metabolism

The fate of boscalid in plants was evaluated by the 2006 Meeting following foliar spray application of ^{14}C -diphenyl- or ^{14}C -pyridine-radiolabelled substance to grapes, lettuce and green beans. A detailed assessment of these studies is presented in the 2006 JMPR Report. For the current Meeting, an additional plant metabolism study on green beans was submitted.

The metabolism of ^{14}C -diphenyl-boscalid in common beans was investigated under enclosed conditions by application of three foliar sprays at 0.52 kg ai/ha each. The treatments were performed at the beginning of flowering (BBCH 61, 33 days before harvest), 11 days later (22 days before harvest) and 13 days before harvest (BBCH 75–79). Samples of plants and whole pods were collected 3 days before and 13 days after final treatment. Pods collected at harvest were additionally separated into hulls and green seeds.

In all samples except green seeds, the extraction of radioactivity with methanol, followed by water, was nearly complete (>98% TRR). In green seeds 70% of the TRR was extracted by the solvents used. TRR levels ranged from 29–52 mg eq/kg in plants, 0.79–1.2 mg eq/kg in whole pods, 0.80 mg eq/kg in hulls and 0.065 mg eq/kg in green seeds.

The identification of the radioactive residues revealed only unchanged boscalid in plants, pods and hulls, representing 97–102% of the TRR. In green seeds, only 17% of the TRR (0.011 mg eq/kg) was identified as boscalid. The majority of the extracted radioactivity (53% TRR) was characterised as five minor components, two of them present up to 0.011 mg eq/kg (up to 17% TRR) and three of them up to 0.006 mgeq/kg (up to 9% TRR).

Post-extraction solids were not investigated and represented 30% TRR in green seeds (0.019 mg eq/kg) and <2% TRR in all other matrices.

The Meeting concluded that parent boscalid is the predominant residue in all plant parts directly treated (plant, whole pods, hulls). In green seeds, it is also present as a major component by proportion, but absolute concentrations are much lower. No metabolites were identified in bean plants, pods or hulls. In green seeds, characterised metabolites were present in minor amounts.

Animal metabolism

The fate of boscalid in lactating goats and laying hens was evaluated by the 2006 Meeting following administration of ^{14}C -diphenyl-radiolabelled substance. A detailed assessment of these studies is presented in the 2006 JMPR Report. For the current Meeting, an additional metabolism study on laying hens was submitted.

For the investigation of the metabolism of boscalid in laying hens ten animals received a dose of ^{14}C -pyridin-labelled boscalid equivalent to 12 ppm for 13 consecutive days via capsule administration. Animals were sacrificed approximately 6 hrs after the final dosing. During the whole dosing period eggs and excreta were collected and analysed with pooled tissue samples for each group at the end of the study.

TRR levels found were highest in liver (0.44 mg eq/kg), followed by egg yolk (0.12 mg eq/kg), fat (0.095 mg eq/kg), muscle (0.051 mg eq/kg) and egg white (0.03 mg eq/kg).

Solvent extraction using acetonitrile or methanol released the majority of the residue from all matrices (63–94% TRR). In addition, 2–10% TRR could be released from liver and eggs with water extraction while only 1.4% TRR was additionally released with dichloromethane from liver. Post extraction solids ranged from 6–32% TRR. Their characterisation by enzymatic hydrolysis released most of the radioactivity with protease treatment (22–35% TRR). The pepsin and pancreatin solubilizate contained only minor radioactivity ($\leq 2\%$ TRR).

Parent boscalid was found as a major residue in the extracts of fat (85% TRR), egg white/yolk (34% TRR) and muscle (29% TRR). In liver, only 1.8% of the TRR (0.008 mg eq/kg) were identified as unchanged parent. The major residue in liver extracts was M510F01 representing 35% TRR (0.16 mg eq/kg), which was also present in major proportions in egg white/yolk (27–28% TRR, 0.008–0.034 mg eq/kg) but not in muscle or fat (5–11% TRR, 0.005 mg eq/kg). Additionally, M510F65 (glucuronides of M510F01) was found as a major metabolite, representing 16–32% TRR in egg white/yolk (0.005–0.039 mg eq/kg) and 20% TRR in liver (0.09 mg eq/kg). In egg yolk, the majority of the M510F65 was recovered after enzymatic hydrolysis of the post-extraction solids (24% TRR, 0.029 mg eq/kg).

The metabolic pathway of ^{14}C -pyridin-labelled boscalid in laying hens was limited. In the first step, hydroxylation at the diphenyl-ring was observed forming M510F01. In a second step, glucuronidation occurs into M510F65. All metabolites identified in laying hens were also found in the rat.

Environmental fate

The current Meeting received one additional field rotational crop study involving application of 2.1 kg ai/ha to bare soil at four sites in Europe. Zucchini, cucumbers, tomatoes and lettuce were planted as rotational crops 30 days after treatment. In all fruiting vegetables (cucumber, zucchini and tomato), no residues above the LOQ of 0.01 mg/kg were found (66–140 days after treatment). Only lettuce contained quantifiable residues ranging from 0.014–0.12 mg/kg.

The Meeting noted that boscalid residues found in rotated lettuce (up to 0.12 mg/kg) surpass findings in rotated Brassica vegetables (up to 0.05 mg/kg). However, the Meeting confirmed its previous conclusion that residues taken up from soil add insignificantly compared to directly treated leafy vegetables (maximum residue level recommendation of the 2010 JMPR was 40 mg/kg for leafy vegetables).

Methods of analysis

The current Meeting received additional analytical methods for the determination of boscalid in plant commodities and additional concurrent recovery information for method 471/0 evaluated by the 2006 Meeting, measuring boscalid and M510F01 (incl. conjugates) in animal matrices.

For plant matrices, three new single residue analytical methods were provided involving initial extraction with methanol/water/hydrochloric acid (70:25:5) or acetonitrile, followed by partitioning against cyclohexane or hexane, respectively. The first solvent system does not require further clean-up while the acetonitrile/hexane system includes a C_{18} - and Silica Gel-solid-phase extraction step. All methods involve analysis by LC-MS/MS at LOQs of 0.01 mg/kg for high water, high starch and high acid content matrices as well as for hops, spices and herbal infusions. For high oil content matrices, a LOQ of 0.05 mg/kg was validated.

In addition, the QuEChERS-Multimethod was successfully tested in high water, high acid and high starch content matrices at a LOQ of 0.01 mg/kg for boscalid.

In animal matrices, additional concurrent recovery data were submitted for method 471/0. LOQs of 0.01 mg/kg were validated each for boscalid and M510F01 (incl. conjugates) in bovine tissues, milk, cream and eggs.

Definition of the residue

The current Meeting received new data on the metabolism of boscalid in green beans and laying hens.

Following foliar application to green beans, boscalid was the only residue identified. The Meeting therefore confirms its previous recommendation of boscalid for compliance with the MRL and for the estimation of the dietary exposure for plant commodities.

In laying hens parent boscalid was found as a major residue in fat (85% TRR), egg white/yolk (34% TRR) and muscle (29% TRR) and in lower proportions in the liver (1.8% TRR). The Meeting confirms its previous recommendation of boscalid for compliance with the MRL for animal commodities and also on the fat-solubility of the residue.

Besides boscalid, its hydroxylated metabolite M510F01 and glucuronides thereof (M510F65) were the only components identified in hen matrices. Therefore the Meeting confirmed its previous recommendation for the estimation of the dietary exposure to be the sum of boscalid and M510F01 (2-chloro-N-(4'-chloro-5-hydroxybiphenyl-2-yl)nicotinamide) including its conjugate, expressed as boscalid.

Based on new information submitted, the present Meeting assessed the toxicity of M510F49 and considered it to be covered by the ADI for the parent substance. Since this metabolite was exclusively found in hen liver hydrolysate representing 12% of the TRR, no inclusion into the residue definition for compliance with the MRL or for the estimation of the dietary exposure is required.

Results of supervised residue trials on crops

The Meeting received supervised trial data for applications of boscalid on pome fruit, stone fruit, bush berries, cane berries, avocado, mango, pomegranate and tea, respectively.

Pome fruit

For boscalid, the 2006 JMPR Meeting recommended a maximum residue level of 2 mg/kg and estimated an STMR value of 0.365 mg/kg for apples based on a GAP from the UK (4×0.2 kg ai/ha, 7 day PHI). The current Meeting received new GAP information with supporting supervised field trials on apples and pears.

Boscalid is registered in the USA for the use pome fruits with a critical GAP involving four foliar sprays of 0.33 kg ai/ha each (7 day interval) and a PHI of 0 days.

Supervised field trials conducted in the USA on apples and pears were submitted which matched the individual application rates, their interval and the PHI, but six instead of four treatments were conducted.

In absence of decline data from Northern America on pome fruits, the Meeting decided to use decline trials from Europe reported by the current and by the 2006 JMPR, which were conducted at growth stages comparable to the US GAP. In total, 31 trials on apples and eight trials on pears were identified with reported residues at 0 days and sampling intervals up to 29 days. Based on first-order kinetics, decline rates of $k=-0.0197$ for apples and $k=-0.0307$ for pears were estimated.

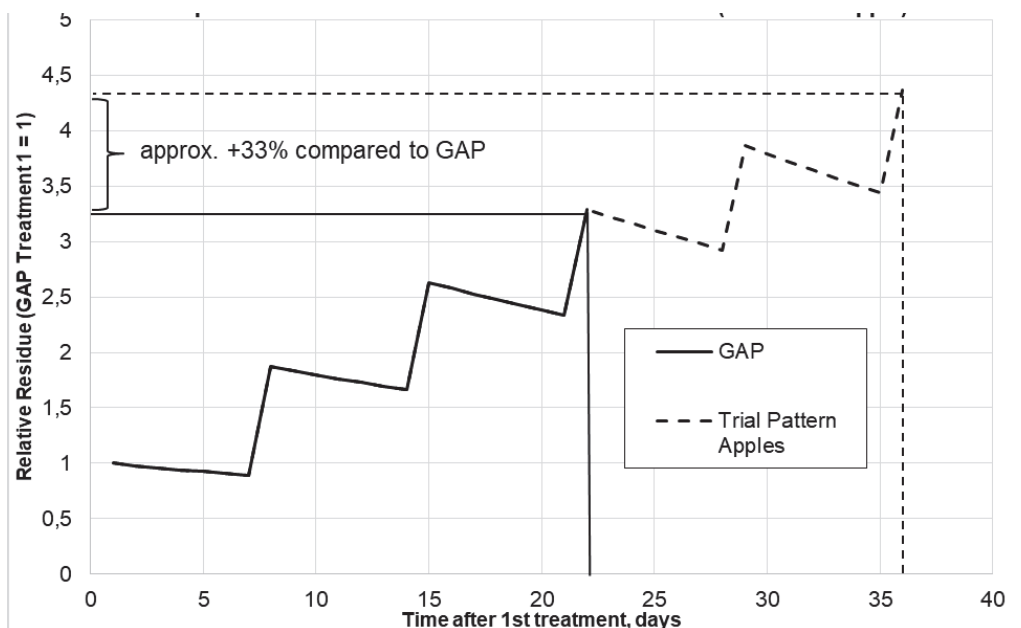


Figure 1 Anticipated residues at GAP vs Field trials (Boscalid – Apple)

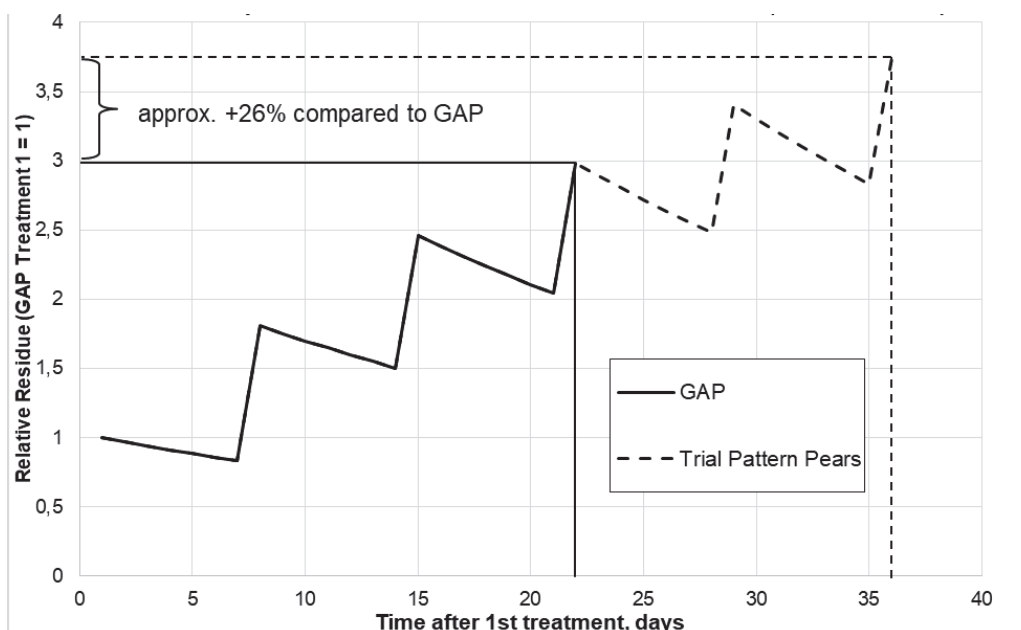


Figure 2 Anticipated residues at GAP vs Field trials (Boscalid – Pear)

The Meeting concluded that the supervised field trial data submitted for apples and pears from the USA overestimate the residue according to the US GAP by more than +25% and cannot be used to estimate maximum residue levels in pome fruits. The Meeting also concluded that proportional adjustment of these trials is inappropriate due to the deviating treatment regime compared to the critical GAP from the USA.

Boscalid is also registered in the Czech Republic for the use on pome fruits with a maximum GAP involving four foliar sprays of 0.2 kg ai/ha each (8 day interval) and a PHI of 7 days.

New supervised field trials conducted in Europe on pears approximating this GAP were submitted to the Meeting. In addition, residue data on apples assessed by the 2006 JMPR against a comparable GAP from the UK were considered.

Residues of boscalid in apples submitted to the 2006 JMPR were (n=22): 0.15, 0.19, 0.2, 0.24, 0.29, 0.29, 0.3, 0.32, 0.32, 0.34, 0.36, 0.37, 0.39, 0.42, 0.42, 0.43, 0.51, 0.53, 0.55, 0.65, 0.86, 1.2 mg/kg.

Residues of boscalid in pears were (n=8): 0.086, 0.11, 0.16, 0.29, 0.33, 0.39, 0.48, 1.3 mg/kg.

The Meeting noted that residues in apples and pears are not significantly different, which was confirmed by the Mann-Whitney-U Test, and decided to combine the datasets.

Residues of boscalid in apples and pears were (n=30): 0.086, 0.11, 0.15, 0.16, 0.19, 0.2, 0.24, 0.29, 0.29, 0.29, 0.3, 0.32, 0.32, 0.33, 0.34, 0.36, 0.37, 0.39, 0.39, 0.42, 0.42, 0.43, 0.48, 0.51, 0.53, 0.55, 0.65, 0.86, 1.2, 1.3 mg/kg (italic = pear residues).

Based on the combined dataset for apples and pears, the Meeting estimated a maximum residue level of 2 mg/kg and a STMR value of 0.35 mg/kg for boscalid in pome fruit.

The Meeting withdraws its previous recommendation of 2 mg/kg for boscalid in apples.

Stone fruit

The 2006 JMPR Meeting estimated a maximum residue level of 3 mg/kg and a STMR value of 1.21 mg/kg for boscalid in stone fruit based on a GAP from the USA (5×0.26 kg ai/ha, 0 day PHI). The current Meeting received new GAP information for stone fruit with supporting supervised field trials on cherries, peaches and plums.

Boscalid is registered in Austria for use on stone fruits with a maximum GAP involving three foliar sprays of 0.19 kg ai/ha each (10 day interval) and a PHI of 7 days.

Supervised field trials conducted in Europe on cherries were newly submitted approximating the GAP from Austria. Although treated at intervals slightly longer than the cGAP, the Meeting considered this deviation as insignificant since boscalid residues remain stable on treated fruits.

For peaches and plums, new supervised field trials from Europe were submitted involving four or five instead of three sprays at 0.2 kg ai/ha. However, the Meeting noted that the first sprays were conducted at flowering and/or beginning of fruit development, not contributing to the final residue at harvest. Therefore, the Meeting concluded that the treatment regime used in the submitted trials approximates the Austrian GAP and that the data can be used for an assessment.

Residues of boscalid in cherries were (n=16): <0.05, < 0.05, 0.052, 0.088, 0.096, 0.14, 0.14, 0.16, 0.22, 0.36, 0.37, 0.39, 0.47, 0.66, 0.7, 1.3 mg/kg.

Residues of boscalid in peaches were (n=8): 0.05, 0.15, 0.17, 0.21, 0.21, 0.29, 0.35, 0.35 mg/kg.

Residues of boscalid in plums were (n=10): 0.057, 0.07, 0.08, 0.11, 0.13, 0.15, 0.18, 0.23, 0.27, 0.45 mg/kg.

Boscalid is registered in the USA for use on stone fruits with a critical GAP involving five foliar sprays of 0.26 kg ai/ha each (7 day interval) and a PHI of 0 days.

New supervised field trials conducted in Canada and in the USA on cherries, peaches and plums approximating the GAP from the USA were submitted. In addition, the current Meeting considered residue data on stone fruit evaluated by the 2006 JMPR against the GAP from the USA.

Residues of boscalid in cherries were (n=14): 0.055, 0.76, 1.0, 1.2, 1.2, 1.4, 1.5, 1.5, 1.5, 1.5, 1.6, 1.6, 2.6, 2.6 mg/kg.

Residues of boscalid in peaches were (n=19): 0.19, 0.32, 0.4, 0.42, 0.48, 0.49, 0.49, 0.52, 0.6, 0.60, 0.64, 0.71, 0.73, 0.75, 0.78, 0.79, 1.0, 1.2, 3.6 mg/kg.

Residues of boscalid in plums were (n=15): <0.05, 0.1, 0.11, 0.12, 0.13, 0.15, 0.17, 0.25, 0.32, 0.46, 0.54, 0.57, 0.6, 0.7, 0.76 mg/kg.

(italic = 2006 residue data)

The Meeting noted that the US GAP for stone fruit results in higher residues than the Austrian GAP and decided to explore the possibility for a group recommendation based on it. However, median

residues differ by more than a factor of 5, suggesting significant differences in residues between the three commodities investigated. Therefore, the Meeting decided to base its recommendation on the individual sub-groups of cherries, plums and peaches.

The Meeting estimated maximum residue levels and STMR values for boscalid of 5 mg/kg and 1.5 mg/kg for cherries (subgroup 003A) and of 4 mg/kg and 0.6 mg/kg for peaches (subgroup 003C), respectively.

The Meeting also estimated a maximum residue level of 1.5 mg/kg and a STMR value of 0.25 mg/kg for plums (subgroup 003B), because of the significantly lower residue population in plums compared to other members of the stone fruit group and due to the availability of a specific subgroup for plums.

The Meeting withdraws its previous recommendation of 3 mg/kg for boscalid in stone fruit.

Berries and other small fruits, except strawberries and grapes

For boscalid, the 2006 JMPR Meeting recommended a maximum residue level of 10 mg/kg and estimated a STMR value of 2.53 mg/kg for berries and other small fruits, except strawberries and grapes based on a US GAP (4×0.4 kg ai/ha, PHI 0 days). The current Meeting received new GAP information for bush berries and cane berries with supporting supervised field trials.

Boscalid is registered in the USA for use on bush berries and cane berries with a maximum GAP identical to the one considered by the 2006 Meeting involving four foliar sprays of 0.4 kg ai/ha each (7 day interval) and a PHI of 0 days.

Two new supervised field trials conducted in Canada and the USA on blueberries were submitted to the Meeting approximating the GAP from the USA. In addition, supervised field trials on blueberries and caneberries were evaluated by the 2006 Meeting against the same GAP.

Residues of boscalid in blueberries were (n=12): 0.84, 1.2, 1.2, 1.3, 1.4, 2.0, 2.4, 2.6, 3.8, 4.4, 5.4, 6.8 mg/kg (*italic=new trial data*).

Residues of boscalid in raspberries were (n=6): 1.5, 2.0, 2.4, 2.7, 3.5, 3.7 mg/kg.

The Meeting noted that residues in blueberries and raspberries were not significantly different (confirmed by Whitney-Mann-U Test) and decided to combine the data for a group recommendation.

Combined residues of boscalid in blueberries and raspberries were (n=18): 0.84, 1.2, 1.2, 1.3, 1.4, 1.5, 2.0, 2.0, 2.4, 2.4, 2.6, 2.7, 3.5, 3.7, 3.8, 4.4, 5.4, 6.8 mg/kg.

The Meeting noted that the OECD MRL Calculator result for the combined dataset is 10 mg/kg, which is covered by the previous recommendation. The Meeting confirmed its previous recommendation for boscalid in small fruits and berries, except strawberry and grapes.

Avocado

Boscalid is registered for use on tropical fruits (including avocado) in the USA with a maximum GAP involving two foliar sprays of 0.33 kg ai/ha each (7 day interval) and a PHI of 0 days.

Supervised field trials conducted in the USA on avocado were submitted involving four instead of two treatments (7 day interval) with higher individual rates per treatment than the GAP (0.41 kg ai/ha vs. 0.33 kg ai/ha).

The Meeting concluded that the supervised field trial data submitted was conducted at significantly more critical conditions (>+25%) than the US GAP and decided that the data is insufficient for a recommendation.

Mango

The critical GAP for boscalid in mangoes is from Mexico, involving two foliar sprays at 0.3 kg ai/ha each (7 day interval) with a PHI of 0 days. Two supervised field trials from Brazil approximating this

GAP were submitted.

Residues of boscalid in mango (whole fruits, calculated) approximating the Mexican GAP were (n=2): 0.032 and 0.54 mg/kg.

The Meeting concluded that two trials are insufficient for a recommendation based on the Mexican GAP.

The critical GAP for boscalid on mango in Brazil is two foliar sprays of 0.024 kg ai/hl each (15 day interval) with a PHI of 7 days.

Supervised field trials conducted in Brazil were submitted approximating the GAP. In some trials, the stone was removed already in the field. Since metabolism information indicates that boscalid is stable both in primary plants and rotational crops, in freezer storage and during simulated hydrolysis, the Meeting decided that no significant impact on the residue in the remaining fruit has to be expected from the procedure in the field.

Residues of boscalid in mango (whole fruits, calculated) approximating Brazilian GAP were (n=8): 0.032, 0.1, 0.22, 0.25, 0.26, 0.55, 0.68, 1.0 mg/kg.

Based on the dataset for mango according to the Brazilian GAP, the Meeting estimated a maximum residue level of 2 mg/kg and a STMR value of 0.255 mg/kg for boscalid in mangoes.

Pomegranate

Boscalid is registered in Turkey for use on pomegranates with a maximum GAP involving three foliar sprays of 0.0126 kg ai/hl each (bud formation, end of flowering (loss of calix) and close to harvest) without specified PHI.

Supervised field trials on pomegranate from Europe were submitted, involving two applications directly before harvest at a 5 day interval.

The Meeting concluded that these trials do not match the GAP from Turkey.

Tea, green, black (black, fermented and dried)

Boscalid is registered in Japan for use on tea with a maximum GAP involving two foliar sprays of a factor 2000 diluted product (WG formulation, 13.6% boscalid, calculated: 0.0068 kg ai/hL) each corresponding to a maximum calculated rate of 0.27 kg ai/ha in combination with a PHI of 7 days.

The Meeting received eight supervised trials from China, India, Japan and Taiwan Province of China on tea approximating the highest calculated rate per hectare according to GAP.

Based on the calculated maximum treatment rate of 0.27 kg ai/ha the estimated residues in dried green tea were (n=8): 1.7, 4.1, 5.6, 6.2, 6.3, 7.3, 16, 19 mg/kg.

Based on the dataset for tea according to the Japanese GAP, the Meeting estimated a maximum residue level of 40 mg/kg and a STMR value of 6.25 mg/kg for tea, green, black (black, fermented and dried).

Fate of residues during processing

Processing factors for the commodities considered at this Meeting are summarised below based on the estimations of the 2006 JMPR.

| Raw commodity | Processed commodity | Boscalid | |
|----------------------------|---------------------|---|----------------|
| | | Median or best estimate processing factor | STMR-P (mg/kg) |
| Apple (STMR:0.35 mg/kg) | Wet apple pomace | 6.06 | 2.121 |
| | Juice | 0.08 | 0.028 |
| Plums (STMR:0.25 mg/kg) | Dried prunes | 2.8 | 0.7 |
| | Puree | 1.95 | 0.49 |

| Raw commodity | Processed commodity | Boscalid | |
|---------------------------------|---------------------|---|----------------|
| | | Median or best estimate processing factor | STMR-P (mg/kg) |
| Tea, black (STMR=6.25 mg/kg) | Infusion | <0.002, <u>0.002</u> , <0.02 | 0.0125 |
| | Instant tea | 0.005, <u>0.007</u> , <0.02 | 0.044 |

Based on a maximum residue level of 1.5 mg/kg for plums the Meeting estimated a maximum residue level of 5 mg/kg for boscalid in prunes, dried to replace its previous recommendation of 10 mg/kg.

Residues in animal commodities

The only feed commodity affected by the current recommendations is dry apple pomace, which was already considered by all previous Meetings for boscalid residues. Since the new recommendation for boscalid in pome fruit is slightly lower than the previous recommendation for apples (2006: STMR 0.365 mg/kg for apples, 2019: 0.35 mg/kg for pome fruit), no re-calculation of the livestock animal dietary burden is necessary.

RECOMMENDATIONS

On the basis of the data obtained from supervised trials, the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for compliance with the MRL for plant and animal commodities and dietary risk assessment for plant commodities: *boscalid*.

Definition of the residue for dietary risk assessment for animal commodities: *sum of boscalid, 2-chloro-N-(4'-chloro-5-hydroxybiphenyl-2-yl)nicotinamide (M510F01) including its conjugate, expressed as boscalid*.

The residue is fat-soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for boscalid is 0–0.04 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for boscalid were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2019 Extra JMPR Report.

The IEDIs ranged from 10–60% of the maximum ADI. The Meeting concluded that long-term dietary exposure to residues of boscalid from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The 2006 JMPR decided that an ARfD for boscalid was unnecessary. The Meeting therefore concluded that the acute dietary exposure to residues of boscalid from the uses considered is unlikely to present a public health concern.

Assessment of metabolites using the threshold of toxicological concern (TTC) approach

The metabolite M510F47 could be assessed using the TTC approach (Cramer Class III threshold of 1.5 µg/kg bw per day). Since this metabolite was not identified in food or feed commodities, the Meeting concluded that it is unlikely to present a public health concern.

