5.10 DIFENOCONAZOLE (224)

RESIDUE AND ANALYTICAL ASPECTS

Difenoconazole was evaluated for the first time by JMPR 2007 when an acceptable daily intake (ADI) of 0–0.01 mg/kg bw and an acute reference dose (ARfD) of 0.3 mg/kg bw were established. In 2007, 2010, 2013 and 2015 the JMPR evaluated the compound for residues and recommended a number of maximum residue levels.

The definition of the residue for compliance with MRL and for dietary intake for plant commodities is parent *difenoconazole*, while for animal commodities it is defined as *sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol (CGA205375), expressed as difenoconazole*. The residue is fat-soluble.

The current Meeting received additional analytical methods, storage stability data for dried beans and oranges, processing data for rice, GAP information and residue trial data for uses on pome fruits (apples, pears), blueberries, strawberries, guava, dragon fruit, watermelon, chili peppers, sweet corn, pulses (beans, peas (except soya bean) and chickpeas), ginseng, globe artichoke, rice and coffee beans.

Methods of analysis

The Meeting received additional information on analytical methods for difenoconazole in plant matrices.

Method AG-676 employs refluxing with methanol/conc. ammonium hydroxide (8:2 v/v). Clean-up is performed by liquid-liquid partitioning against hexane followed by acetonitrile and SPE on silica and phenyl. Residues are determined by GC-NPD with a LOQ of 0.01 mg/kg.

The QuEChERS method employs shaking with acetonitrile/water (1/1, v/v) and clean-up by dispersive SPE with PSA. Residues are determined by LC-MS/MS using the ion transitions m/z 406→251, 406→337 with a LOQ of 0.005 mg/kg.

Method REM 147.08 employs refluxing with methanol/conc. ammonium hydroxide (8:2 v/v). Clean-up is performed by SPE on a HLB cartridge. Residues are determined by LC-MS/MS using the ion transition m/z 406→251 with a LOQ of 0.01 mg/kg.

The Modified Korean Food Code Method employs homogenization with acetone and clean-up by liquid-liquid partitioning against dichloromethane followed by SPE on a silica column. Residues are determined by LC-UV and LC-MS/MS using the ion transitions m/z 406→251, 406→337 with a LOQ of 0.03 mg/kg.

The Meeting concluded that the presented methods were sufficiently validated and are suitable to measure difenoconazole in plant commodities.

Stability of pesticides in stored analytical samples

Information provided for the 2007 JMPR indicated that difenoconazole residues were stable at approximately -20 °C for 2 years in matrices with high oil content, high water content matrices, high starch matrices and wheat forage and straw.

The Meeting received additional information on storage stability of difenoconazole in acidic and high protein content matrices, demonstrating a storage stability of at least 9 months.

Results of supervised residue trials on crops

Pome fruits

Difenoconazole is registered in the USA for use on pome fruit (apple and pear). The critical GAP involves five pre-harvest foliar applications at a rate of 77 g ai/ha with a 7 day interval and 14 days

PHI. After harvest, subsequent post-harvest treatments using either dip or drench at 30 g ai/hL or spraying at 1.3 g ai/tonne are applied. The Meeting received supervised field trial data from the USA on apples and pears matching the cGAP.

In pome fruit (apples and pears) the ranked residues of difenoconazole following GAP treatment (±25%) were:

Dip treatment (n=9): 0.59, 0.66, 0.85, 0.90, 0.93, 1.0, 1.1(3) mg/kg.

Drench treatment (n=9): 0.56, 0.76, 0.85, 0.86, 1.1(2), 1.2, 1.3, 2.6 mg/kg.

Spray treatment (n=9) 0.39, 0.56, 0.59, 0.60, 0.63, 0.66, 0.78, 1.1, 1.4 mg/kg.

The Meeting estimated a maximum residue level of 4 (Po) mg/kg, to replace its previous recommendation of 0.8 mg/kg, a STMR of 1.1 mg/kg and a HR of 2.6 mg/kg for difenoconazole in pome fruit (based on drench treatment).

Blueberries

Difenoconazole is registered in Canada for the use on blueberries with four foliar applications at a nominal rate of 127 g ai/ha with a 6–9 day interval between applications and 1 day PHI.

In blueberries from the USA and Canada, residues of difenoconazole following GAP treatment (±25%) were (n=10): 0.33, 0.65, 0.67, 0.84, 1.0 (2), 1.2, 1.4, 1.7, 1.9 mg/kg.

The Meeting estimated a maximum residue level of 4 mg/kg, a STMR of 1.0 mg/kg and a HR of 2.2 mg/kg (based on the highest individual sample) for difenoconazole in blueberries.

Strawberries

Difenoconazole is registered in the USA for the use on strawberries with four foliar applications at a nominal rate of 127.5 g ai/ha with a 7 day interval between applications and 0 day PHI.

In strawberries trials from the USA, residues of difenoconazole following GAP treatment (± 25%) were (n=8): 0.07, 0.19, 0.37, 0.41, 0.43, 0.63, 0.65, 1.2 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, a STMR of 0.42 mg/kg and a HR of 1.2 mg/kg for difenoconazole in strawberries.

Guava

Difenoconazole is registered in Egypt for the use on guava with three foliar applications at a nominal rate of 62.5 g ai/ha with a 6–8 day interval between applications and 10 days PHI.

It was noted that the trials did not match the GAP.

Pitaya (dragon fruit)

Difenoconazole is registered in Indonesia for the use on pitaya with three foliar applications at a nominal rate of 50 g ai/ha with a 9-11 day interval between applications and 7 days PHI. However, the treatment in the provided field trials was three exaggerated foliar applications of difenoconazole at a nominal rate of 94 g ai/ha.

Ranked residues in trials from Indonesia and Vietnam were (n=7): 0.022, 0.030, 0.051, 0.064, 0.071, 0.10, 0.15 mg/kg. The meeting decided that the proportionality principle could be applied in this case, as the application rate does not differ by more than five times. Therefore scaling factors of 0.47–0.54 were applied, resulting in residues of 0.012, 0.016, 0.027, 0.034, 0.037, 0.052, 0.080 mg/kg.

The Meeting estimated a maximum residue level of 0.15 mg/kg, a STMR of 0.034 mg/kg and a HR of 0.083 mg/kg (based on the highest individual analytical result) for difenoconazole in pitaya.

Watermelon

Difenoconazole is registered in Brazil for the use on watermelon with six foliar applications at a nominal rate of 50 g ai/ha with a 7 day interval between applications and 3 days PHI. However, the treatment in the provided field trials was six exaggerated foliar applications of difenoconazole at a nominal rate of 75 g ai/ha.

Ranked residues in trials from Brazil were (n=4): < 0.010(2), 0.020(2) mg/kg. The meeting decided that the proportionality principle could be applied in this case, as the application rate does not differ by more than five times. Therefore a scaling factor of 0.67 was applied to residues >LOQ, resulting in residues of < 0.010(2), 0.010(2) mg/kg.

The Meeting estimated a maximum residue level of 0.02 mg/kg, a STMR of 0.01 mg/kg and a HR of 0.01 mg/kg for difenoconazole in watermelon.

Chili peppers

Difenoconazole is registered in the Republic of Korea for the use on chili peppers with four foliar applications at a nominal rate of 80 g ai/ha with a 10 day interval between applications and 2 days PHI.

In chili peppers, residues of difenoconazole following GAP compliant treatment (± 25%) were (n=3): 0.24, 0.30, 0.41 mg/kg. The Meeting noted that the number of trials conducted according to GAP is insufficient for estimating a maximum residue level. The application rate of trial 6 was outside the ±25% tolerance range, however the meeting decided that the proportionality principle could be applied, as the application rate does not differ by more than five times. Therefore a scaling factor of 0.73–0.93 was applied to residues >LOQ, resulting in residues of: 0.19, 0.21, 0.27, 0.41 mg/kg.

The Meeting estimated a maximum residue level of 0.9 mg/kg, a STMR of 0.24 mg/kg and a HR of 0.41 mg/kg for difenoconazole in chili peppers.

In 2013 the JMPR recommended a maximum residue level of 0.6 mg/kg for fruiting vegetables other than cucurbits based on 20 trials performed with tomato, sweet pepper and chili pepper in the US. The Meeting estimated a maximum residue level for fruiting vegetables other than cucurbits (except chili peppers) of 0.6 mg/kg, to replace its previous recommendation of 0.6 mg/kg for fruiting vegetables other than cucurbits (except sweetcorn and mushrooms).

Based on experimental processing data, a processing factor of 4.5 was estimated for chili peppers dried. The Meeting estimated a STMR-P and HR-P for dried chili peppers of 1.08 mg/kg and 1.85 mg/kg, respectively. Since the previously established maximum residue level of 5 mg/kg for chili peppers dried also covers residues according to the new GAP, the Meeting agreed to maintain its previous recommendation.

Pulses

Difenoconazole is registered in the USA for the use on pulses (dry beans, dry peas (except soya bean)) and dry chickpeas with four foliar applications at a nominal rate of 127.5 g ai/ha with a 14 ± 2 day interval, between applications and 14 days PHI. Supervised residue trials from the USA were submitted on dry peas, dry bean and chick peas.

Dry beans

In dry bean, residues of difenoconazole following GAP treatment (± 25%) were (n=7): < 0.01 (2), 0.010, 0.011, 0.012, 0.013, 0.030 mg/kg.

The Meeting estimated a maximum residue level of 0.05 mg/kg and a STMR of 0.011 mg/kg for difenoconazole in the subgroup of dry beans (except soya bean).

Dry peas

In dry pea, residues of difenoconazole following GAP treatment (± 25%) were (n=4): 0.016, 0.028, 0.029, 0.087 mg/kg, while residues in chick peas were (n=3) < 0.010 (2), 0.031 mg/kg. The Meeting decided to combine the residue data for the subgroup of dry peas: (n=7) < 0.010 (2), 0.016, 0.028, 0.029, 0.031, 0.087 mg/kg.

The Meeting estimated a maximum residue level of 0.15 mg/kg and a STMR of 0.028 mg/kg for difenoconazole in the subgroup of dry peas.

Ginseng, dried

Difenoconazole is registered in the USA for the use on ginseng with four foliar applications at a nominal rate of 127.5 g ai/ha with a 6–8 day interval between applications and 0 day PHI.

In ginseng trials from the USA, residues of difenoconazole following GAP treatment (± 25%) were (n=4): 0.06, 0.15, 0.21, 0.39 mg/kg.

The Meeting estimated a maximum residue level of 0.8 mg/kg, a STMR of 0.18 mg/kg and a HR of 0.42 mg/kg (based on the highest individual analytical result) for difenoconazole in dried ginseng.

The Meeting estimated a maximum residue level for dried ginseng of 0.8 mg/kg, to replace its previous recommendation of 0.2 mg/kg.

Artichoke, globe

Difenoconazole is registered in the USA for the use on globe artichoke with four foliar applications at a nominal rate of 127.5 g ai/ha with a 12-16 day interval between applications and 3 days PHI.

In globe artichoke from trials in the USA, residues of difenoconazole following GAP treatment (± 25%) were (n=4): 0.30, 0.49, 0.52, 0.57 mg/kg.

The Meeting estimated a maximum residue level of 1.5 mg/kg, a STMR of 0.505 mg/kg and a HR of 0.64 mg/kg (based on the highest individual analytical result) for difenoconazole in globe artichoke.

Rice grain

Difenoconazole is registered in the USA for the use on rice with two foliar applications at a nominal rate of 137 g ai/ha with a 14 day interval between applications and 35 days PHI.

In rice grain trials from the USA, residues of difenoconazole following GAP treatment (± 25%) were (n=15): 0.42, 0.46, 0.51, 0.57, 0.72, 0.98, 1.0(2), 1.2, 1.3, 1.4, 1.5, 2.1, 4.3, 6.2 mg/kg.

The Meeting estimated a maximum residue level of 8 mg/kg and a STMR of 1.1 mg/kg for difenoconazole in rice grain.

Sweet corn (Corn-on-the-cob) (kernels plus cob with husk removed)

Difenoconazole is registered in the USA for the use on sweet corn as seed treatment with one application at a nominal rate of 300 g ai/tonne seed.

In sweet corn (ears) trials from the USA, residues of difenoconazole following GAP treatment (± 25%) were (n=9): < 0.01 mg/kg (9).

The Meeting estimated a maximum residue level of 0.01* mg/kg, a STMR of 0.01 mg/kg and a HR of 0.01 mg/kg for difenoconazole in sweet corn (corn-on-the-cob) (kernels plus cob with husk removed).

Coffee beans

Difenoconazole is registered in Brazil for the use on coffee beans with three foliar applications at a nominal rate of 50 g ai/ha with a 12–16 day interval between applications and 30 days PHI. Four

independent supervised residue trials on coffee beans (green beans) from Brazil were submitted using 5×38 g ai/ha applications, totalling 190 g ai/ha compared to 150 g ai/ha from the cGAP.

The meeting concluded that the submitted trials can be accepted since they were conducted at a higher application rate than the cGAP and since residues were < 0.01 mg/kg throughout the trials.

The Meeting estimated a maximum residue level of 0.01* mg/kg and a STMR of 0.01 mg/kg for difenoconazole in coffee beans.

Animal feedstuffs

Pea vines and pea hay

Difenoconazole is registered in the USA for the use on pulses with four foliar applications at a nominal rate of 127.5 g ai/ha with a 14±2 day interval between applications and 14 days PHI. For pea vines and hay, a total of five supervised residue trials with two applications at ~130 g ai/ha and 0 days PHI from the USA were submitted. As these trials were not in compliance with the cGAP they were not considered here.

Sweet corn forage and sweet corn fodder (stover)

Difenoconazole is registered in the USA for use on sweet corn as a seed treatment with one application at a nominal rate of 300 g ai/tonne seed. Nine independent supervised residue trials on sweet corn from the USA were submitted matching the GAP.

Residue concentrations of difenoconazole in sweet corn forage with ears were (n=9): < 0.01 (9) mg/kg.

Residue concentrations of difenoconazole in sweet corn forage without ears were (n=9): < 0.01 (9) mg/kg.

Residue concentrations of difenoconazole in sweet corn fodder (stover) were (n=9): < 0.01 (9) mg/kg as received.

The Meeting estimated a maximum residue level of 0.01* mg/kg (dry weight) for sweet corn fodder and median and highest residues of 0.01 mg/kg (as received) for difenoconazole in sweet corn forage and fodder (stover).

Rice straw

Difenoconazole is registered in the USA for the use on rice with two foliar applications at a nominal rate of 137 g ai/ha with a 14 day interval between applications and 35 days PHI.

Residue concentrations of difenoconazole in rice straw from trials in the USA were (n=14): 0.90, 1.2, 1.3, 1.5 (2), 1.7, 2.1, 2.2 (2), 3.3, 3.4, 6.1, 6.9, 10 mg/kg as received.

The Meeting estimated a maximum residue level of 17 mg/kg (DM, based on 90% DM content), a median residue of 2.15 mg/kg (as received) and a highest residue of 10 mg/kg (as received) for difenoconazole in rice straw.

Fate of residues during processing

The Meeting received new information on the fate of difenoconazole residues during processing in rice and chili peppers.

Estimated processing factors for the commodities considered at this Meeting are summarised below.

Raw commodity	Processed commodity	Individual processing factors	Mean or best estimate processing factor	STMR-P = $STMR_{RAC}$ × PF (mg/kg)	HR-P = HR_{RAC} × PF (mg/kg)
Rice grain	Hulls	3.3	3.3	3.6	-
	Bran	0.69	0.69	0.76	-

Raw commodity	Processed commodity	Individual processing factors	Mean or best estimate processing factor	STMR-P = $STMR_{RAC}$ × PF (mg/kg)	HR-P = HR_{RAC} × PF (mg/kg)
	Polished Rice	0.0078	0.0078	0.0086	-
Fresh chili peppers	Dried chili peppers	3.4, 5.0, 5.3, 4.0, 4.4, 4.9, 2.9, 5.2, 5.5	4.5	1.08	1.85

Using the estimated maximum residue level of 8 mg/kg for rice grain and applying the processing factor of 0.0078, the Meeting estimated a maximum residue level of 0.07 mg/kg for difenoconazole in polished rice.

Residues in animal commodities

Estimated maximum and mean dietary burdens of livestock and animal commodities maximum residue levels

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6. The calculations were made according to the livestock diets from US-Canada, EU, Australia and Japan in the OECD diets listed in Appendix IX of the 2016 edition of the FAO Manual.

Previous evaluations included the following potential feed items: almond hulls, apple pomace, bean forage, cabbages, carrot culls, citrus dried pulp, grape pomace, dry, bean vines, potato culls, potato process waste (wet peel), rape seed fodder, rape seed meal, soya bean seed, sugar beet leaves or tops, sunflower seed meal, wheat straw and fodder. Additional feed items from this evaluation were sweet corn forage and fodder (stover) and rice grain, straw, bran and hulls.

The estimation of residues of difenoconazole in the crops considered by the current Meeting does not impact on the previous recommendations for residues in animal commodities made by 2013 JMPR.

RECOMMENDATIONS

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

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant commodities: *difenoconazole*.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for animal commodities: *sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol), expressed as difenoconazole*.

The residue is fat-soluble.

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for difenoconazole is 0–0.01 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for difenoconazole were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the previous and present JMPR. The results are shown in Annex 3 of the 2017 JMPR Report. The IEDIs ranged 9–80% of the maximum ADI.

The Meeting concluded that the long-term dietary exposure to residues of difenoconazole from uses considered by the JMPR is unlikely to present a public health concern.

Short-term dietary exposure

The ARfD for difenoconazole is 0.3 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for difenoconazole were calculated for the food commodities for which STMRs or HRs were

estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2017 JMPR Report. The IESTIs varied from 0–60% of the ARfD for children and 0–20% for the general population.

The Meeting concluded that the short-term dietary exposure to residues of difenoconazole from uses considered by the present Meeting is unlikely to present a public health concern.