## 5.9 DIFLUBENZURON (130)

### RESIDUE AND ANALYTICAL ASPECTS

Diflubenzuron [1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea] is an agricultural insect growth regulator. It was originally evaluated by the JMPR in 1981 and re-evaluated for residues several times up to 1988.

Under the periodic review program, toxicology data was re-evaluated by JMPR in 2001. The original ADI of 0–0.02 mg/kg bw/day was re-confirmed and an acute reference dose was unnecessary. The compound was re-evaluated for residues by the JMPR in 2002.

This Meeting received information on the residue analysis, storage stability, use patterns and supervised field residue trials for peaches, plums, peppers, mustard greens, barley, wheat, almond, pecan and peanut.

#### *Analytical methods*

The Meeting received details of several analytical methods used in supervised residue trials and in studies on storage stability, which are primarily based on the methods previously reviewed by JMPR in 2002, with some modifications to minimize matrix interference. All methods are single methods for determination of diflubenzuron.

For determination of diflubenzuron, HPLC analysis with UV detection was validated for almond, mustard greens, peppers, peanuts, barley and wheat. The limits of quantification were 0.005 or 0.05 mg/kg for almond hulls, 0.05 mg/kg for almond nutmeat, mustard green, peach, peanut nutmeat and oil, wheat and wheat processed commodities, 0.005 mg/kg for peppers, 0.5 mg/kg for peanut meal and peanut hay. GC-ECD analysis was validated for peppers with an LOQ of 0.05 mg/kg.

#### *Stability of residues in stored analytical samples*

The Meeting received data on the stability of residues in plant products (almond nutmeat and hulls, peach, plum, mustard greens, peanut nutmeat, peanut hay, peanut meal, peanut oil, wheat forage, wheat hay, wheat grain, wheat straw, wheat flour and wheat germ) in the corresponding supervised residue trials. The storage stability data covered the period of storage of field samples for residue analysis. The lowest freezer temperature was -24 ºC. The average freezer temperature was -18 ºC.

Diflubenzuron residues in fortified samples were stable over a period of 13 months frozen storage for peaches, 12 months for peppers and 14 months for mustard greens. Residues in fortified samples of wheat grain were stable for 296 days, barley straw for 301 days, wheat forage for 422 days and wheat hay for 337 days of frozen storage.

For wheat processed commodities, diflubenzuron residue is also stable in wheat flour for 6 months and wheat germ for 12 months of frozen storage.

In almond nutmeat, diflubenzuron residues were stable over a period of 12 months of frozen storage.

In peanuts, diflubenzuron was stable in nutmeat for 295 days, hay for 356 days, peanut meal for 643 days, and refined oil for 365days.

#### *Results of supervised trials on crops*

The Meeting received supervised residue trials data following foliar application of diflubenzuron on peaches, plums, peppers, mustard greens, barley, wheat, almonds, pecans and peanuts.

Residues of diflubenzuron were reported in all studies. Supervised field trials conducted with different formulations (wettable powders, suspensions concentrates and wettable granules), but with identical crop varieties, locations and spray dates were not considered as independent. The highest result according to the corresponding GAP was selected in these cases. Where multiple samples were taken from a single plot and individual results are reported, the mean value is used for estimation of maximum residue level.

The OECD calculator was used as a tool in the estimation of the maximum residue level from the selected residue data set obtained from trials conducted according to GAP. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at a best estimate of the maximum residue level using expert judgment. Then, the OECD calculator was employed. If the statistical calculation spreadsheet suggested a different value from that recommended by the JMPR, a brief explanation of the deviation was supplied.

*Peaches and Plums*

Five field trials on peaches and three trials on plums conducted in 2005 in the USA matched the critical USA GAP for stone fruit, which is two applications at a rate of 0.28 kg ai/ha (interval 14 days) with a PHI of 14 days.

Residues of diflubenzuron in peaches from trials matching GAP, in ranked order, were (n = 5): 0.12, 0.17, 0.20, 0.21 and 0.23 mg/kg.

The ranked order of diflubenzuron residue data in plums matching GAP were (n = 3): 0.08, 0.17 and 0.17 mg/kg.

Individually there were insufficient trials from each crop to estimate commodity maximum residue levels. As the residue levels found were from similar populations, the Meeting agreed that the two data sets could be used for mutual support and decided to combine the data for evaluation. Residues found on peaches and plums, in ranked order, were (n = 8): 0.08, 0.12, 0.17, 0.17, 0.17, 0.20, 0.21 and 0.23 mg/kg.

The Meeting agreed to estimate an STMR of 0.17 mg/kg, and recommended a maximum residue level of 0.5 mg/kg for diflubenzuron in peaches and plums (including prunes). Further the Meeting agreed to extrapolate these recommendations to nectarines.

*Mustard greens*

Eight field trials on mustard greens were conducted in the USA during 2001 growing season matched the USA GAP, which is a maximum of four foliar applications at a rate of 0.07 kg ai/ha with a PHI of 7 days.

Residues of diflubenzuron found on mustard greens, in ranked order, were (n = 8): < 0.05, 1.0, 1.1, 1.2, 1.5, 2.1, 2.5 and 6.8 mg/kg.

The Meeting agreed to estimate an STMR of 1.35 mg/kg, and recommended a maximum residue level of 10 mg/kg for mustard greens.

*Sweet peppers*

Six field trials on sweet peppers and three field trials on chili peppers were conducted in the USA in 1997 according to the GAP of the USA, i.e., a maximum of five foliar applications at a rate of 0.14 kg ai/ha with a PHI of 7 days.

Residues of diflubenzuron found on sweet peppers, in ranked order, were (n = 6): 0.07, 0.07, 0.08, 0.24, 0.24, and 0.33 mg/kg.

The ranked order of diflubenzuron residue data in chili peppers were (n = 3): 0.25, 0.92 and 0.94 mg/kg.

It was considered that the datasets for sweet peppers and chili peppers were not from similar residue populations and as a consequence could not be combined. On the basis of the data fro sweet peppers the Meeting agreed to estimate an STMR of 0.16 mg/kg, and recommended a maximum residue level of 0.7 mg/kg for sweet peppers.

As chili peppers are a minor crop, the Meeting agreed to estimate an STMR of 0.92 mg/kg, and recommended a maximum residue level of 3 mg/kg for chili peppers.

On the basis of the STMR and maximum residue level for chili peppers and the default dehydration factor of 7, the Meeting estimated an STMR of 6.44 mg/kg, and recommended a maximum residue level of 20 mg/kg for chili peppers, dry.

*Cereal grains*

*Wheat and barley*

Seven field trials on barley and three field trials on wheat were conducted in the USA between 2002 and 2003 growing seasons following the USA GAP for barley, wheat, oats and triticale, which is a maximum of one foliar application at a rate of 0.07 kg ai/ha up to boot stage (BBCH 41).

The diflubenzuron residue data in barley grain from trial according to GAP were (n = 7): < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, < 0.05 and < 0.05 mg/kg.

The diflubenzuron residue data in wheat grain from trial according to GAP were (n = 3): < 0.05, < 0.05 and < 0.05 mg/kg.

As the applications from seven trials on barley and three trials on wheat before boot stage (BBCH 41) resulted in residue data below the LOQ of 0.05 mg/kg, the Meeting decided to combine the two datasets together for the evaluation.

The Meeting agreed to estimate an STMR of 0.05 mg/kg, and recommended a maximum residue level of 0.05* mg/kg for barley and wheat, and agreed to extrapolate these recommendation to oats and triticale.

*Tree nuts*

*Almonds and pecans*

For almonds, five field trials in 1998 and two field trials in 2003 were conducted in the USA, and for pecan five trials were conducted in 1999 in the USA.

In almond nutmeat, two trials followed the USA GAP for tree nuts, which is a maximum of four foliar applications at a rate of 0.28 kg ai/ha with PHI 28 days, the residue data were 0.033 and 0.048 mg/kg. The LOQ for these trials was 0.005 mg/kg.

Five trials were conducted with twice rate at PHI of 28 days and all residue data were below LOQ of 0.05 mg/kg.

In pecan kernels, all residue data in five trials with twice rate at PHI of 28 days were below LOQ of 0.05 mg/kg

The Meeting agreed to combine all residue data for the evaluation. The diflubenzuron residue data in almond nutmeat and pecan kernels from trial were (n = 12): 0.033, 0.048 and < 0.05 (10) mg/kg.

Considering the maximum residue value on individual replicate sample prior to averaging up to 0.089 mg/kg (mean trial value was 0.045 mg/kg), the Meeting agreed to estimate an STMR of 0.05 mg/kg, and recommended a maximum residue level of 0.2 mg/kg for tree nuts.

*Peanuts*

Field trials were conducted in the USA in the 2001 growing season following the USA GAP of a maximum of three foliar applications at a rate of 0.14 kg ai/ha with PHI of 28 days.

The ranked order of diflubenzuron residue data in peanut nutmeat were (n = 9): < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, 0.05 and 0.06 mg/kg.

The Meeting agreed to estimate an STMR of 0.05 mg/kg, and recommended a maximum residue level of 0.15 mg/kg for peanut nutmeat.

***Animal feed commodities***

*Hay or fodder (dry) of grasses*

Seven field trials on barley and three field trials on wheat were conducted in the USA between 2002 and 2003 growing seasons following the USA GAP for barley, wheat, oats and triticale, which is a maximum of one foliar application at a rate of 0.07 kg ai/ha up to boot stage.

In barley hay, the diflubenzuron residue data from trial matching GAP were (n = 7): 0.11, 0.46, 0.58, 0.61, 0.64, 0.74 and 1.4 mg/kg.

Residues of diflubenzuron found in wheat hay following treatments complying with the US GAP were (n = 3): 0.18, 0.88 and 1.2 mg/kg.

The Meeting agreed that the residues found in wheat and barley were from the same population and could be combined for evaluation. The ranked order of diflubenzuron residues found in barley and wheat hay were (n = 10): 0.11, 0.18, 0.46, 0.58, 0.61, 0.64, 0.74, 0.88, 1.2 and 1.4 mg/kg.

The Meeting agreed to estimate a median residue of 0.625 mg/kg, a highest residue of 1.4 mg/kg, and recommend a maximum residue level of 3 mg/kg for hay or fodder (dry) of grasses.

*Straw and fodder (dry) of cereal grain*

Seven field trials on barley and three field trials on wheat were conducted in the USA between 2002 and 2003 growing seasons matching the GAP of the USA in barley, wheat, oats and triticale, which is a maximum of one foliar application at a rate of 0.07 kg ai/ha up to boot stage.

In barley straw, the diflubenzuron residue data from trial matching GAP were (n = 7): < 0.05, 0.12, 0.18, 0.30, 0.46, 0.54 and 0.56 mg/kg.

In wheat straw, the diflubenzuron residue data from trial matching GAP were (n = 3): 0.06, 0.28 and 0.90 mg/kg.

The Meeting agreed that the residues found in wheat and barley were from the same population and could be combined for evaluation. The ranked order of diflubenzuron residues found in barley and wheat straw were (n = 10): < 0.05, 0.06, 0.12, 0.18, 0.28, 0.30, 0.46, 0.54, 0.56 and 0.90 mg/kg.

The Meeting agreed to estimate a median residue of 0.29 mg/kg, a highest residue of 0.90 mg/kg, and recommend a maximum residue level of 1.5 mg/kg for straw and fodder (dry) of cereal grain.

*Almond hulls*

Field trials in 1998 and four field trials in 2003 on almonds were conducted in the USA complying with the GAP of the USA, i.e., a maximum of four foliar applications at a rate of 0.28 kg ai/ha with a PHI of 28 days.

Residues in almond hulls from two trials, matching the US GAP, were 2.1 mg/kg and 4.0 mg/kg.

Five trials were conducted at a double rate (0.56 kg ai/ha) and a PHI of 28 days. Residue data from these trials were: 1.0, 1.6, 2.1, 2.3 and 4.4 mg/kg. The Meeting agreed that the results from these trials could be scaled to match the US GAP (0.28 kg ai/ha application rate) by dividing by 2 (0.56/0.28). The proportionally adjusted residues in almond hull were: 0.5, 0.8, 1.05, 1.15 and 2.2 mg/kg.

The Meeting agreed that the two dataset matching the USA GAP were not significantly different and could be combined for evaluation. The combined residue data were (n = 7): 0.5, 0.8, 1.05, 1.15, 2.1, 2.2 and 4.0 mg/kg.

The Meeting agreed to estimate a median residue of 1.15 mg/kg.

*Peanut hay*

Field trials were conducted in the USA in 2001 growing season following the USA GAP, i.e., 3 × 0.14 kg ai/ha with a PHI of 28 days.

The ranked order of diflubenzuron residue concentrations in peanut hay were (n = 8): 1.6, 1.9, 2.6, 7.1, 7.9, 8.4, 17.0 and 18.4 mg/kg.

The Meeting agreed to estimate a median residue of 7.5 mg/kg, a highest residue of 18.4 mg/kg and recommended a maximum residue level of 40 mg/kg for peanut hay.

***Fate of residues during processing***

The Meeting did not receive any information on the fate of incurred residue of diflubenzuron in processing of relevant commodities.

***Residues of animal commodities***

*Farm animal dietary burden*

In 2002, the JMPR estimated the dietary burden from residues in wet pomace of apples, grass forage, rice grain and rice straw of diflubenzuron residues in farm animals from the diets listed in Appendix IX of the FAO Manual (FAO, 2002).

The present Meeting estimated the dietary burden of diflubenzuron in farm animals on the basis of the diets listed in Appendix X of the FAO Manual (OECD Feedstuffs Derived from Field Crops, FAO, 2009). Calculation from the highest residues, the STMRs (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating maximum residue levels, while calculation from the STMRs and STMR-P values for feed is suitable for estimating STMR values for animal commodities. Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6.

The present Meeting calculated the dietary burdens from residues in wet pomace of apples, grass forage, rice grain, rice straw, barley and wheat grain, hay, straw, almond hulls, and peanut hay. The results are summarized in the following table.

| | Livestock dietary burden, diflubenzuron, ppm of dry matter diet | | | |
|---|---|---|---|---|
| | US/CAN | EU | Australia | Japan |

| | max | mean | max | mean | max | mean | max | mean |
|---|---|---|---|---|---|---|---|---|
| Beef cattle | 0.27 | 0.13 | 11.52 | 4.82 | 20.99[a] | 8.11[b] | 1.41 | 0.38 |
| Dairy cattle | 13.45 | 5.19 | 12.77 | 4.73 | 20.99[c] | 8.02[d] | 2.14 | 0.69 |
| Poultry-broiler | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.006 | 0.006 |
| Poultry-layer | 0.04 | 0.04 | 2.05[e] | 0.71[f] | 0.04 | 0.04 | | |

[a] Highest maximum beef or dairy cattle burden suitable for maximum residue level estimates for mammalian meat

[b] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[c] Highest maximum dairy cattle dietary burden suitable for maximum residue level estimates for milk.

[d] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[e] Highest maximum poultry dietary burden suitable for maximum residue level estimates for poultry meat and eggs.

[f] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs.

The dietary burdens were recalculated using the OECD tables and the addition of barley and wheat grain, hay straw, almond hulls, and peanut hay to the animal feed diet did not significantly increase the dietary burden value. The Meeting decided that it is not necessary to re-evaluated animal commodities for maximum residue levels.

## DIETARY RISK ASSESSMENT

### *Long-term intake*

The acceptable daily intake (ADI) of 0–0.02 mg/kg bw/day based on the NOAEL for haematological effects of 2 mg/kg bw per day in a 2-year studies in rats and the 52-week study in dogs was re-confirmed by 2001 JMPR.

International Estimated Daily Intake (IEDI) was calculated for commodities of human consumption for which STMRs for diflubenzuron were estimated. Results are presented in Annex 3. The IEDI for the 13 GEMS/Food cluster diets were only 2–10% of the maximum ADI. The intake of residues of diflubenzuron resulting from its proposed uses is unlikely to present a public health concern.

### *Short-term intake*

The JMPR in 2001 concluded that it was unnecessary to establish an ARfD, and therefore the short-term intake of diflubenzuron residues is unlikely to present a public health concern.