

5.18 FLUDIOXONIL (211)

RESIDUE AND ANALYTICAL ASPECTS

Fludioxonil was reviewed by the JMPR in 2004, 2006, 2010 and most recently in 2012. The ADI for fludioxonil is 0–0.4 mg/kg bw and an ARfD was considered unnecessary. Residue studies were submitted by the manufacturer for various crops, in addition to a hen feeding study and analytical method for poultry tissues and eggs.

The residue definition for fludioxonil for plant commodities for compliance with the MRL and estimation of dietary intakes is fludioxonil. For animal commodities the residue is the sum of fludioxonil and its benzopyrrole metabolites, determined as 2,2-difluoro-benzo[1,3]dioxole-4-carboxylic acid and expressed as fludioxonil. The residue is considered fat-soluble.

Methods of analysis

Method GRM025.03A, not previously evaluated by the JMPR, determines fludioxonil and its metabolites oxidisable to 2,2-difluorobenzo[1,3]dioxole-4-carboxylic acid (CGA192155) in poultry tissues and eggs. Samples of muscle, liver and kidney are homogenized, extracted by refluxing with ammonium hydroxide:acetonitrile and the aqueous phase is acidified and partitioned with toluene. Fludioxonil and its metabolites are converted to CGA192155 by heating in the presence of potassium permanganate and sodium hydroxide; the oxidation is quenched with sodium metabisulfite, the extracts are filtered, acidified, and partitioned into dichloromethane:ethyl acetate (80:20 v/v). Residues are determined as total fludioxonil by LC-MS/MS. A molecular weight correction factor of 1.23 is applied when calculating procedural recovery values and quantifying residues of CGA192155. The LOQ for fludioxonil and metabolites as CGA192155 in animal tissues was 0.01 mg/kg for fludioxonil (=0.0081 mg/kg for CGA192155). Residues of CGA192155 were shown to be stable at 0–9 °C for at least 7–9 days of storage.

Data evaluated by the 2004 JMPR showed that fludioxonil and CGA192155 are stable for at least 12 months in frozen muscle and for at least 18 months in frozen liver, milk and eggs.

Results from supervised residue trials on crops

Lemon

Five foliar supervised residue trials were conducted in the USA in lemons in 2004–2005 matching US GAP (1 × 0.245 kg ai/ha; 0 day PHI). Residues were 0.12 (3) and 0.16 (2) mg/kg.

Residues on lemons from foliar application are covered by the previous recommendation of maximum residue level of 10 mg/kg (Po) for fludioxonil on citrus

Avocado

Six supervised residue trials were conducted in USA in avocado in 2003 complying with US GAP (4 × 0.245 kg ai/ha; 0 day PHI). Residues were 0.02 (2), 0.04, 0.06, 0.11 and 0.19 mg/kg.

The Meeting estimated a maximum residue level of 0.4 mg/kg and a STMR of 0.05 mg/kg for fludioxonil in avocado.

Pineapple

Fludioxonil is registered in the USA for use in pineapple as a post-harvest high volume drench and/or directed peduncle spray at 1 × 0.06 kg ai/hL. Eight supervised residue trials were conducted in the

USA (Hawaii) in 2009 using a dip plus wax or drench application at 0.06 kg ai/hL followed by a spray directed to the peduncle at 0.87 kg ai/hL. Residues ranged from 4.8 to 6.6 mg/kg (n=8).

As no trials were conducted according to GAP, the Meeting could not estimate a maximum residue level for fludioxonil in pineapple.

Fruiting vegetables, Cucurbits

Eighteen supervised residue trials were conducted in the USA in 2004 complying with the US GAP for cucurbits (4×0.245 kg ai/ha; 1 day PHI).

Residues in cantaloupe were (n=6) 0.02, 0.07, 0.09, 0.13, 0.20 and 0.36 mg/kg.

Residues in cucumber were: (n=7) 0.03, 0.04 (2), 0.05, 0.06, 0.09 and 0.13 mg/kg.

Residues in summer squash were: (n=5) 0.01, 0.04 (2) and 0.08 (2) mg/kg

The median residues found in the three individual commodities were within a 5 times range, allowing a recommendation to be made for the cucurbits crop group.

As the residue populations are not statistically different, the Meeting agreed they could be combined as (n=18) 0.01, 0.02, 0.03, 0.04 (4), 0.05, 0.06, 0.07, 0.08 (2), 0.09 (2), 0.13 (2), 0.20 and 0.36 mg/kg.

The Meeting recommended a maximum residue level of 0.5 mg/kg and a STMR of 0.065 mg/kg for fludioxonil in fruiting vegetables, cucurbits.

The Meeting withdrew its previous recommendation of 0.03 mg/kg for Melons, except watermelon, and of 0.3 mg/kg for summer squash.

Tomato

Fludioxonil is registered in the USA for use on tomatoes as a post-harvest in line dip/drench at 1×0.06 kg ai/hL or high volume spray at 0.0044kg ai/1000 kg tomatoes (combined with propiconazole in a tank mix).

Residues in tomatoes from six trials at GAP using the dip or drench application were: 0.28, 0.43, 0.48, 0.73, 0.77 and 1.1 mg/kg (if drench and drip was used in one trial, only the highest residue was selected). Three trials conducted at GAP using spray application gave residues of 0.18, 0.66 and 1.8 mg/kg.

Residue data from the two application types were similar and could be combined for residues of 0.18, 0.28, 0.43, 0.48, 0.66, 0.73, 0.77, 1.1 and 1.8 mg/kg (n=9).

The Meeting estimated a maximum residue level of 3 mg/kg and a STMR of 0.66 mg/kg for fludioxonil in tomato (Po).

The Meeting withdrew its previous maximum residue level recommendation for fludioxonil in tomato of 0.5 mg/kg.

Peppers (Bell & Non-Bell)

Currently, there is a MRL of 1 mg/kg for fludioxonil in Peppers, sweet, based European trials matching the GAPs of Italy and Austria.

The GAP of the USA consists of 4×0.245 kg ai/ha; 0 day PHI. The current Meeting received 14 supervised field residue trials on bell (sweet pepper) and non-bell peppers (including chili pepper) from the USA and Canada and five greenhouse trials matching US GAP.

Residues in the field trials for sweet peppers were < 0.02 (2), 0.08, 0.09, 0.12, 0.13 (2), 0.16 (2) and 0.28 (2) mg/kg. Residues for non-bell peppers were 0.06, 0.07, 0.12 and 0.14 mg.

Residues found in the greenhouse trials were 0.10, 0.20, 0.21 and 0.22 mg/kg for sweet pepper and 0.20 mg/kg for non-bell peppers.

These data indicate that the current MRL of 1 mg/kg would accommodate the expected fludioxonil residues resulting in non-bell peppers when applied according to US GAP. The Meeting agreed to extend the previous recommendation of 1 mg/kg to peppers.

Based on the data on non-bell peppers (0.06, 0.07, 0.12, 0.14 and 0.20 mg) and a factor of 10, the Meeting estimates a maximum residue level of 4 mg/kg and a STMR of 1.2 mg/kg for dried chili peppers.

Leafy vegetables

Currently, there is a MRL of 10 mg/kg in Head lettuce, based on indoor trials matching the Italian GAP, and a MRL of 10 mg/kg in Mustard greens based on trials matching the GAP of the USA.

In the USA, GAP in leafy greens is 4×0.245 kg ai/ha; 0 day PHI. Twenty five trials were conducted in USA in 2001 in lettuce and spinach according to GAP were submitted to this Meeting. Additionally, trials evaluated by the 2004 JMPM according to GAP were also considered. Six trials conducted in USA in 2004 in radish tops were not at GAP.

Residue in head lettuce (with wrapper leaves) were (n=8) 0.42, 1.2, 1.4, 2.0 (2), 2.2, 2.8 and 4.6, mg/kg.

Indoor trials conducted in Europe in head lettuce at Italian GAP evaluated by the 2004 JMPM gave residues (n=11) ranging from 0.72 to 6 mg/kg, median of 2.7 mg/kg.

Residues in leafy lettuce were (n= 6) 4.8, 6.5, 6.7, 10, 16 and 22 mg/kg.

Residues in spinach were (n= 11) 1.9, 3.4, 4.6, 4.9 (2), 5.8, 7.5, 8.3, 9.8, 12 and 16 mg/kg.

Residues in watercress from trials evaluated in 2004 (USA GAP) were 4.2 and 4.5 mg/kg.

Residues in mustard greens from trials evaluated in 2004 (USA GAP) ranged from 0.06 to 7.1 mg/kg, median of 1.2 mg/kg (n=9).

The median residues found in the individual commodities from trials conducted matching USA GAP were outside the 5 times range, not allowing a recommendation for leafy vegetable group.

The Meeting therefore, estimated a maximum residue level of 40 mg/kg and a STMR of 8.3 mg/kg for fludioxonil in leafy lettuce

The Meeting estimated a maximum residue level of 30 mg/kg and a STMR of 5.8 mg/kg for fludioxonil in spinach.

The Meeting agreed that there were insufficient trials to estimate a maximum residue level for watercress.

The Meeting confirmed its previous recommendation of 10 mg/kg for fludioxonil in head lettuce and mustard greens.

Potato

Currently, there is a MRL of 0.02 mg/kg for potato, based on the Australian GAP as a seed treatment.

Fludioxonil is registered in the USA for use in potatoes as a post-harvest in line spray at 0.0045 kg ai/1000 kg tubers. Five trials were conducted in the USA and Canada in 2009/2010 matching the US GAP, giving residues of 0.66, 1.1, 1.5, 1.7 and 2.9 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg and a STMR of 1.5 mg/kg for fludioxonil in potato (Po).

The Meeting withdrew its previous recommendation for fludioxonil in potatoes of 0.02 mg/kg.

Radish

Six supervised residue trials were conducted in the USA in 2004 matching US GAP (2×0.245 kg ai/ha; 7 days PHI). Residues in the radish tops were: < 0.02 (2), 0.04, 0.08, and 0.10 (2) mg/kg.

The Meeting estimated a maximum residue level of .3 mg/kg and a STMR of 0.06 mg/kg for fludioxonil in radish.

Legume vegetables

Currently, there is a MRL of 0.3 mg/kg for beans, except broad beans and soya beans and for peas (pods and succulent=immature seeds), based on the GAP of France.

The GAP in USA for beans (dried and succulent, except cow beans) is 4×0.245 kg ai/ha; 7 days PHI). In eight trials conducted in snap beans (common beans) from the USA, matching US GAP, residues in snap beans pods were: < 0.02, 0.03 (2), 0.04 (2), 0.05 (2) and 0.38 mg/kg.

Based on the US data on snap beans, the Meeting estimated a maximum residue level of 0.6 mg/kg and a STMR of 0.04 mg/kg for fludioxonil in Beans, except broad bean and soya bean. The Meeting withdrew its previous recommendation of 0.3 mg/kg for beans, except broad bean and soya bean.

In seven trials conducted in lima beans in the USA according to US GAP, residues in succulent shelled beans were: < 0.02 (4), 0.03, 0.04 and 0.21 mg/kg.

The Meeting estimated a maximum residue level of 0.4 mg/kg and a STMR of 0.02 mg/kg for fludioxonil in Beans, Shelled. The Meeting agreed to withdraw its previous recommendation of 0.03 mg/kg for Beans, Shelled.

Fludioxonil is registered in USA to be used in peas as a seed treatment at 0.005 kg ai/100 kg seed. Five trials conducted at US GAP gave residues in mature fresh peas with pods of < 0.01 (5) mg/kg. Fifteen trials conducted at higher or lower GAP rate gave the same results.

The Meeting confirms its previous recommendation of 0.3 mg/kg for peas (pods and succulent=immature seeds).

Beans (dry)

Currently, there is a Codex MRL of 0.07 mg/kg for beans (dry) based on Spanish GAP.

Seven trials were conducted in USA in 2001 according to US GAP (4×0.245 kg ai/ha; 7 days PHI) gave residues in dry beans of 0.02 (2), 0.04 (2), 0.06, 0.12 and 0.23 mg/kg. In two trials harvested earlier or with 6 applications gave residues in the same range.

The Meeting estimated a maximum residue level of 0.5 mg/kg and a STMR of 0.04 mg/kg for fludioxonil in beans (dry) The Meeting withdrew its previous recommendation of 0.07 mg/kg for Beans (dry).

Herbs

Currently, there is a Codex MRL of 10 mg/kg for fludioxonil in fresh basil and chives and of 50 mg/kg for dried basil and chives.

The Meeting received four supervised residue trials in parsley from the USA matching US GAP in herbs (4×0.245 kg ai/ha; 7 days PHI). Residues in fresh parsley were 1.6, 2.3, 3.2 and 3.9 mg/kg and in dry parsley 8.9, 15, 18 and 23 mg/kg.

Data submitted to the 2004 JMPR matching US GAP showed residue of 1.8 and 3.9 mg/kg on fresh chives and 1.9 and 3.0 mg/kg on fresh basil, 14 and 31 mg/kg on dry chives and 15 and 24 mg/kg on dry basil.

The residues found in the individual fresh or dried commodities from trials conducted according to USA GAP are in the same range, and they are combined for allowing recommendations for herbs, fresh and dried.

The residues of fludioxonil in fresh parsley, basil and chives were considered similar and could be combined giving residues of 1.6, 1.8, 1.9, 2.3, 3.0, 3.2 and 3.9 (2) mg/kg.

The Meeting recommended a maximum residue level of 9 mg/kg and a STMR of 2.65 mg/kg for fludioxonil in herbs.

The residue data sets of fludioxonil from dried parsley, basil and chives were also considered similar and could be combined giving residues of 8.9, 14, 15 (2), 18, 22, 24 and 31 mg/kg.

The Meeting recommended a maximum residue level of 60 mg/kg and a STMR of 16.5 mg/kg for fludioxonil in dried herbs, except dried hops.

The Meeting agreed to withdraw its previous recommendations for chives and basil of 10 mg/kg and for dried chives and basil of 50 mg/kg.

Ginseng

Four supervised residue trials were conducted in the USA and Canada from 2005 to 2006 according to GAP (4×0.245 kg ai/ha; 14 days PHI). Residues were 0.16, 0.18, 0.40 and 1.7 mg/kg.

The Meeting recommends a maximum residue level of 4 mg/kg and a STMR of 0.29 mg/kg for fludioxonil in ginseng.

Residues in processed commodities

Pineapple fruit (5.62 mg/kg fludioxonil) processed to juice contained a residue of 5.40 mg/kg, with a processing factor (PF) of 0.96. However, as no maximum residue level recommendation on the raw commodity was made, the Meeting could not make an assessment of residues for pineapple juice.

Tomatoes containing 0.14 mg/kg of fludioxonil were processed to paste (0.15 mg/kg), giving a PF of 1.1. Processing factors estimated by the 2004 JMPR were 1.1, 1.4, 1.5 and 1.6. The best estimated processing factor for tomato paste is 1.4. Based on a STMR of 0.66 mg/kg for tomato, the Meeting estimated a of STMR-P of 0.924 mg/kg for tomato paste

Tomatoes was also processed to puree (0.05 mg/kg) giving a PF of 0.36. The Meeting estimated a STMR-P of 0.236 mg/kg for tomato puree.

The best estimate PF for tomato juice (2004 JMPR) was 0.22. The Meeting estimated a STMR-P of 0.145 mg/kg for fludioxonil.

Potato tubers containing 0.472 mg/kg fludioxonil were processed into chips. Residues were 0.797 mg/kg in wet peel (PF=1.69), 0.01 mg/kg in flakes (PF < 0.02) and 0.018 mg/kg in chips (PF of 0.04).

The Meeting estimated a STMR-P of 0.06 mg/kg for fludioxonil in potato chips (STMR in potato is 1.5 mg/kg).

Residues in animal commodities

Farm animal dietary burden

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Appendix IX of the FAO manual. The calculations were made according to the animal diets from US-Canada, EU, Australia and Japan in the Table (Appendix IX of the FAO manual). The STMR, STMR-Ps were estimated at the present Meeting. Dietary burden calculations are provided in Annex 5.

Livestock dietary burden for fludioxonil, ppm of dry mater diet

| Commodity | US-Canada | | EU | | Australia | | Japan | |
|-------------------|-----------|-------|---------------------|-------------------|-----------|-------|-------|-------|
| | Max | Mean | Max | Mean | Max | Mean | Max | Mean |
| Beef cattle | 0.029 | 0.018 | 0.56 ^a | 0.27 ^c | 0.24 | 0.13 | 0.017 | 0.017 |
| Dairy cattle | 0.39 | 0.18 | 0.57 ^{a b} | 0.27 ^d | 0.24 | 0.11 | 0.02 | 0.018 |
| Poultry - broiler | 0.017 | 0.017 | 0.38 ^e | 0.19 ^f | 0.035 | 0.035 | 0.002 | 0.002 |
| Poultry - layer | 0.017 | 0.017 | 0.38 | 0.19 | 0.035 | 0.035 | 0.002 | 0.002 |

^a Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimated for mammalian tissues

^b Highest maximum dairy cattle dietary burden suitable for maximum residue level estimated for mammalian milk

^c Highest mean beef or dairy cattle dietary burden suitable for STMR estimated for mammalian tissues.

^d Highest mean dairy cattle dietary burden suitable for STMR estimated for milk.

^e Highest maximum poultry dietary burden suitable for maximum residue level estimated for poultry tissues

^f Highest mean poultry dietary burden suitable for maximum residue level estimated for poultry tissues

Animal feeding study

A feeding study on poultry submitted to the current Meeting was conducted with fludioxonil at 1.54, 4.64 and 15.4 mg/kg feed on a 28-day daily dose regime via gelatine capsules.

Residues in eggs from the 15.4 ppm dose level hens were < 0.01 mg/kg 3 days after the initiation of dosing, increased to 0.024 mg/kg fludioxonil eq. (max. of 0.036 mg/kg), and reached 0.04 mg/kg at day 28. The Mean level during the study was 0.025 mg/kg and a maximum of 0.052 mg/kg fludioxonil eq. Eggs from the 4.64 ppm group had a mean and a maximum residue of 0.01 and 0.013 mg/kg fludioxonil eq., respectively. No residues were found in eggs from the 1.54 ppm dose group.

Only liver samples from the 1.54 ppm group were analysed, giving a mean of 0.05 mg/kg eq. (0.03 to 0.08 mg/kg).

In the 4.64 ppm group, residues in skin/fat (including abdominal fat) ranged from < 0.01 to 0.01 mg/kg eq. and residues in liver ranged from 0.06 to 0.21 mg/kg eq. (mean of 0.12 mg/kg).

In the 15.4 mg/kg ppm group, residues in muscle were < 0.01, from 0.01 to 0.04 mg/kg eq. in skin and fat (mean of 0.03 mg/kg) and 0.28 mg/kg eq. in liver.

A depuration study conducted at 15.4 ppm dosing level demonstrated that residues in the eggs ranged from 0.02 to 0.04 mg/kg eq. up to 3 days after termination of the study and were not detected further. Fludioxonil was not detected in any of the muscle, fat or liver samples, suggesting rapid elimination of fludioxonil following completion of dosing.

Animal commodity maximum residue levels

A feeding study in cattle evaluated by the 2004 JMPR showed that residues of fludioxonil and its metabolites found in the highest feeding level dose group (5.5 ppm) were 0.014–0.017 mg/kg in liver, 0.022–0.025 mg/kg in kidney (LOQ of 0.05 mg/kg) and none was detected in fat (< 0.05 mg/kg) or muscle (< 0.01 mg/kg). The highest and median residues in milk were 0.019 and 0.01 mg/kg, respectively (LOQ of 0.01 mg/kg). The feeding level in this study is about 10 times higher than the highest dietary burden estimated for cattle at this Meeting (0.57 ppm).

The Meeting confirmed its maximum residue level recommendation of 0.05* mg/kg for edible offal (mammalian), and 0.01* mg/kg for meat (from mammals other than marine mammals) and milks.

Based on an estimated dietary burden for poultry of 0.07 ppm and a metabolism study, the 2004 JMPR had estimated that residues of fludioxonil and metabolites were unlikely to be found in poultry commodities and recommended maximum residue levels of 0.05* mg/kg for eggs, 0.01* mg/kg for poultry meat and 0.05* mg/kg for poultry edible offal and STMRs of 0 mg/kg for eggs, poultry meat and poultry edible offal.

The highest calculated poultry dietary burden calculated by the current Meeting was 0.38 ppm. As the feeding study showed that no residues are expected at a dietary burden of 1.54 ppm (lowest dose tested), the Meeting confirmed that no residues are expected in poultry commodities.

The Meeting recommended a maximum residue level of 0.01* mg/kg and a STMR of 0 for fludioxonil in poultry edible offal and eggs.

The Meeting confirmed its previous recommendation of 0.01* mg/kg for poultry meat.

RECOMMENDATION

The residue definition: for plant commodities for compliance with the MRL and estimation of dietary intakes: *fludioxonil*.

For animal commodities the residue is the sum of fludioxonil and its benzopyrrole metabolites, determined as 2,2-difluoro-benzo[1,3]dioxole-4-carboxylic acid and expressed as fludioxonil.

The residue is fat-soluble.

DIETARY RISK ASSESSMENT***Long-term intake***

The IEDI of fludioxonil based on the STMRs estimated by this and previous Meetings for the 13 GEMS/Food regional diets were 2–6% of the maximum ADI of 0–0.4 mg/kg bw (see Annex 3 of the Report). The Meeting concluded that the long-term dietary intake of residues of fludioxonil is unlikely to present a public health concern.

Short-term intake

The 2004 JMPR decided that an ARfD for fludioxonil is unnecessary. The Meeting therefore concluded that the short-term dietary intake of fludioxonil residues is unlikely to present a public health concern.

