The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.09 mg/kg and an HR of 0.25 mg/kg for fresh chilli peppers.

Based on the concentration factor of 7 (for explanation and rational see report section on Chilli peppers), the Meeting estimated an STMR of 0.63 (7 × 0.09) mg/kg and a maximum residue level of 2 (7 × 0.25=1.75) mg/kg to replace its previous recommendation of 50 mg/kg for dried chilli pepper, which was based on an MRL of 5 for sweet peppers, and the default concentration factor of 10.

DIETARY RISK ASSESSMENT

Long- term intake

Using the consumption figures for chilli peppers and the STMR value of 0.63 for dried chilli peppers, the long term intake from use of carbaryl on chilli peppers and cranberries amounts to 0–2% of the ADI (0-0.008 mg/kg bw) in the 13 regional diets.

The Meeting concluded that the long-term intake of residues derived from carbaryl use on cranberries and chilli peppers that have been considered by the present JMPR will not, in practical terms, change the total intake of residues from other uses considered by the 2002 JMPR.

Short-term intake

The rounded cranberry short term intake is 0% of the ARfD (0.2 mg/kg bw) for both children and for adults. The short term intake derived from the consumption of dried chilli pepper is 0% for adults and 1% for children.

The Meeting concluded that the short-term intake estimate derived from residues of carbaryl use on cranberries and chilli peppers that has been considered by the JMPR is unlikely to present a public health problem.

5.6 CLOFENTEZINE (156)

RESIDUE AND ANALYTICAL ASPECTS

Clofentezine, an acaricide first evaluated by the JMPR in 1986 and re-evaluated for residues several times up to 1992. A toxicological review was conducted in 2005, when an ADI of 0-0.02 mg/kg bw was established. The 2005 JMPR concluded that an ARfD was not necessary. At the 37th session of the CCPR, clofentezine was scheduled for Periodic Re-evaluation of residues by the 2007 JMPR.

The manufacturer supplied information on identity; metabolism and environmental fate; residue analysis; use patterns; residues resulting from supervised trials on citrus, pome fruits, stone fruits, grapes, strawberries, currants, melons, tree nuts, tomatoes and cucumbers; and the fate of residues on apple, peach, almond and animal tissues during storage and orange, apple, grape and strawberries in processing. GAP information and enforcement methods were supplied by the manufacturer and the governments of the Netherlands and Australia.

Animal metabolism

The Meeting received animal metabolism studies with clofentezine in lactating cows, goats and laying hens. Clofentezine [^{14}C] labelled in the tetrazine ring was used in the animal metabolism studies.

The metabolism of clofentezine in rat, mouse, rabbit, calf and cow, dog, baboon and hen was qualitatively similar (details on laboratory animal metabolism are given in the toxicology report), with

hydroxylation of the phenyl ring and/or replacement of chlorine with a methylthio group being the 2 major pathways.

A lactating cow was orally dosed with [^{14}C] labelled clofentezine for 5 consecutive days at about 0.27 mg/kg bw per day. Residues in milk reached a plateau level of approximately 0.007 mg/L on the second day. Residues were highest in bile (1.1 mg/kg) and liver (0.09 mg/kg). Heart, muscle and fat contained residues less than 0.01 mg/kg.

A lactating cow was orally administered with [^{14}C] labelled clofentezine for 3 consecutive days at an exaggerated rate (2.2 mg/kg bw per day) in order to produce quantifiable residues. Levels of radioactivity in milk were shown to plateau at a level of 0.17 mg/kg clofentezine equivalents on day 3 after treatment. The major component of the residue in milk was 4-OH clofentezine (75 % TRR, total radioactive residues). The [^{14}C] residue was higher in the liver (0.76 mg/kg) than in other tissues, of which at least 67 % was identified as 4-OH clofentezine. In renal fat, 90% of the TRR (0.24 mg equivalents/kg) was confirmed to be 4-OH clofentezine. Residues in kidney were also found to be composed predominantly of 4-OH clofentezine (83% TRR, 0.30 mg equivalents/kg). The remaining components appeared to be hydrolysis products of 4-OH clofentezine.

A lactating goat was given a single oral dose (0.63 mg/kg bw per day) of [^{14}C]clofentezine. The results showed [^{14}C] in all tissues at levels below 0.05 mg/kg, with all the [^{14}C] being excreted within 72 hours of dosing. Highest TRR was in goat milk at a level of 0.049 mg/L clofentezine equivalents at a time of 24 h after dosing.

Another study at an exaggerated rate (2.2 mg/kg bw per day) was undertaken for 7 consecutive days, in which a plateau for TRR in milk was reached at days 3 or 4 of the test, with a maximum residue of 0.2 mg/L being obtained. Over 95% of the TRR was confirmed as 4-OH clofentezine.

In summary, most of the [^{14}C]clofentezine fed to ruminants was excreted within 72 h. Liver was the target tissue and the major part of the residue was 4-OH clofentezine. There are no qualitative differences in the comparative metabolism studies of rodents (rats) and ruminants (goats and cattle).

Laying hens were administered [^{14}C]clofentezine orally for 3 consecutive days at a dose level of 17 mg clofentezine/kg bodyweight/day. By far the greatest [^{14}C] residue was found in fat (3.0 mg/kg equivalents). The majority of each daily dose of clofentezine (71–79%) was excreted by hens during the subsequent 24 hour period. The majority of the identified component of the residue found in all tissue samples, was the parent clofentezine (fat: 70%, muscle: 34%, unlaid developing eggs: 32% and skin: 7.0%), with varying quantities of both 3 and 4-OH clofentezine. The remaining residue most likely consisted of conjugates of the 3 and 4-OH clofentezine metabolites.

Plant metabolism

The Meeting received plant metabolism studies with clofentezine on lemon, apple, peach and grapes.

In plants, parent clofentezine was the major component of the residue at shorter and longer intervals with lower and higher application rates. Levels of metabolites were usually much lower than parent clofentezine. Residues were mostly found as a surface residue.

The metabolism of [^{14}C]clofentezine (applied at 0.3 kg ai/ha) on lemon leaves was studied. Parent clofentezine was the main residue component and 2-chlorobenzonitrile was also present, at levels of 88% TRR and 8.1% TRR 25 days post-treatment, and 77% TRR and 6.8% TRR 103 days post-treatment, respectively.

The metabolism of [^{14}C]clofentezine in apple foliage was studied following application at a nominal dosage of 0.5 kg ai/ha. The main component of the residue found 25 days after treatment was parent clofentezine present amounting to 87% of TRR. Levels of parent clofentezine decreased over time to a level of 66% of TRR, with an increase of fibre bound residue. The metabolite NC 22505 (3, 6-bis(2-chlorophenyl)-1,2-dehydro -1,2,4,5-tetrazine) was present 10 and 100 days post-treatment but

was not found at intermediate time points. Other single metabolites appeared in concentrations less than 1% of TRR.

The metabolism of [^{14}C]clofentezine was investigated in apples treated at a field spray concentration of 0.03 kg ai/hL and the exaggerated spray concentration of 0.76 kg ai/hL. Residues in mature apple fruit 72 days post-treatment consisted predominantly of parent clofentezine and peel fibre bound residues. However, both residues were at levels of 0.012 mg/kg or less at a rate of 0.03 kg ai/hL. At the exaggerated spray concentration, the same components were present, however the level of the parent clofentezine was much higher, i.e., 82% of TRR (0.81 mg/kg).

Further investigation was made into the components of the fibre bound residue, with apples being treated at spray concentrations of 0.06 kg ai/hL and 0.48 kg ai/hL. Samples were taken at 25 and 64 days post-treatment. Only limited quantities (approximately 0.01 mg/kg) of fibre bound radioactivity was recovered in this trial. Base and enzyme hydrolysis revealed that approximately 50% of bound residue was likely to be unchanged clofentezine, with the remainder consisting of 2-chlorobenzoic acid, 2-chlorobenzylacohol and 2-chlorobenzaldehyde.

Peach trees in a glasshouse were treated with [^{14}C]clofentezine at spray concentrations of 0.01 and 0.1 kg ai/hL and peaches were harvested for analysis 62 days post-treatment. Following the application at 0.01 kg ai/hL the overall TRR was only 0.047 mg/kg, of which 0.036 mg/kg was parent clofentezine. At the higher treatment rate, the TRR was 0.70 mg/kg consisting of 0.63 mg/kg parent clofentezine and 0.038 mg/kg 2-chlorobenzonitrile.

Grape vines were treated in a glasshouse with [^{14}C]clofentezine at spray concentrations of 0.01 and 0.1 kg ai/hL (equivalent to application rates of 0.1 and 1.0 kg ai/ha). Grape samples were collected for analysis 25 and 46 days post-treatment. At 25 days post-treatment, the total radioactive residue found at the 0.1 kg ai/ha rate was 0.38 mg/kg and 2.5 mg/kg at the 1.0 kg ai/ha rate. At the lower rate, the majority of the residue was found to be parent clofentezine (0.29 mg/kg) followed by 2-chlorobenzonitrile (0.04 mg/kg), the remainder of the residue comprised of polar materials (< 0.01 mg/kg). At 46 DAT the overall residue levels were much lower (0.11 mg/kg at 0.1 kg ai/ha and 0.45 mg/kg at 1.0 kg ai/ha), and the parent clofentezine remained the prevalent component (69% of TRR or 0.31 mg/kg).

Environmental fate in soil

The Meeting received information on the environmental fate of clofentezine in soil, including studies on aerobic soil metabolism, field dissipation and crop rotational studies.

The environmental fate of clofentezine was investigated in a number of laboratory studies using either unlabelled or [^{14}C] tetrazine ring labelled material under aerobic conditions for various durations. The degradation rates were not strongly affected by soil organic carbon content, but greatly influenced by the soil pH, with the faster degradation at higher soil pH. The aerobic soil metabolism half-lives for clofentezine ranged from approximately 2 to 12 weeks. After one year, in the loamy sand, clay and clay loam, approximately 56%, 38% and 25% of the applied radioactivity respectively had been mineralized to [^{14}C]O_2, and 30–40% of the initial dose was extractable residue in the loamy sand, clay and clay loam respectively.

During the study period, the maximum concentrations of the major metabolites, expressed as the percentage of the initial dose, were: 13% of AEC 593600 [2-chlorobenzoic (2-chlorobenzylidene) hydrazide], 1.6% of AEC 512898 [N, N'-bis-(2-chlorobenzoyl)-hydrazine], 0.8% of AEF 092117 [2-chlorobenzamide] and 6.2% of AEC 500233 [2-chlorobenzoic acid].

Very little of the applied clofentezine moved below the top 15 cm of the soil during field dissipation trials of up to 8 months' duration in several different soils. Clofentezine concentrations declined to half of their initial values within 14 days to approximately 6 months. In orchard soil residue decline trials, quantifiable residues of clofentezine were mostly detected in the top soil layer and declined below the limit of determination within 60 days.

The low water solubility and relatively high octanol/water partition coefficient of clofentezine lessen the uptake of clofentezine residues from soil into following crops. A crop uptake study with orange and apple trees grown under glasshouse conditions indicated that the potential for uptake of clofentezine residues from the previously treated soil was low.

Methods of analysis

The Meeting received analytical methods descriptions and validation data for residues of clofentezine in a number of crops, and residues of clofentezine or 4-OH clofentezine or total residues of all compounds containing the 2-chlorobenzoyl moiety in animal tissues, milk and eggs.

Methods rely on HPLC-UV, HPLC-DAD, GC-ECD and GC-MSD for analysis of clofentezine or 4-OH clofentezine and all compounds containing the 2-chlorobenzoyl moiety in the various matrices. Several multi-residue methods with HPLC-DAD and GC-MSD were suitable for enforcement for plant and animal commodities (LOQ values 0.01–0.05 mg/kg).

In summary, numerous recovery data on a wide range of substrates showed that the methods for data collection and enforcement were valid over the relevant concentration ranges.

Stability of residues in stored analytical samples

The Meeting received information on the freezer storage stability of residues of clofentezine in apple, peach, almond (hulls and nutmeats), muscle, liver, fat and milk.

Residues were stable in apple, almond/nutmeat and peach samples for a period of at least one year when stored frozen.

After 6 months storage, the mean percentage of clofentezine fortified had fallen to 38% (muscle), 72% (liver), 50% peritoneal fat), and 50% (milk). The percentage of clofentezine-derived residues (all metabolites containing the 2-chlorobenzoyl moiety) determined by derivation to 2-chlorobenzoic acid was more than 90% of the original residue in muscle, liver and fat, and approximately 84% in milk after 15 months storage. Parent clofentezine is relatively unstable in products of animal origin, but the total residue of all metabolites containing the 2-chlorobenzoyl moiety was stable in animal products for at least 15 months.

Definition of the residue

The main residues in fruit crops were the parent clofentezine, and metabolite 2-chlorobenzonitrile. The levels of 2-chlorobenzonitrile found were < 0.05 mg/kg, which was approximately a tenth of those of the parent residue. Other metabolites identified were present only at low levels and these metabolites were not considered to be of toxicological significance. Therefore the parent compound is only included in the residue definition for plant matrices.

The metabolism data submitted for clofentezine in animal products showed the vast majority of the residue in cattle and goat tissues is 4-OH clofentezine. Poultry studies however, showed more significant quantities of parent clofentezine, in addition to 3 and 4-OH clofentezine. Quantities of 3 and 4-OH clofentezine were not separated in the poultry study, but quantities of 3-OH clofentezine are much smaller than the combined totals of parent and 4-OH clofentezine.

In the cow metabolism study, the TRRs in subcutaneous fat and muscle were about 0.02 mg/kg, but TRR in renal fat was about 16 times as high as that in muscle. The main component of the residue in poultry commodities is the parent clofentezine and the TRR in fat was approximately 22 times higher than in the muscle. Based on the above results and the octanol-water partition coefficient of clofentezine (log P_{OW}=4.1), clofentezine is considered as fat-soluble.

Based on the available comparative animal and plant metabolism studies, the Meeting recommended a residue definition for clofentezine as follows:

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

Definition of the residue (for compliance with the MRL and estimation of dietary intake) for animal commodities: *sum of clofentezine, and* a*ll metabolites containing the 2-chlorobenzoyl moiety, expressed as clofentezine.*

The Meeting decided that residue is fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for clofentezine uses on orange, lemon, mandarin, apple, pear, peach, apricot, cherry, nectarine, plum, grapes, strawberry, currant, gherkin, cucumber, melon, tomato, walnut and almond. Residue data were also provided on almond hulls.

Labels (or translations of labels) were available to the Meeting from Argentina, Australia, Belgium, Canada, France, Germany, Greece, Italy, the Netherlands, Portugal, South Africa, Spain, Switzerland, UK, and USA describing the relevant GAP for evaluation of clofentezine.

Citrus fruits

Supervised trials were conducted on orange trees in Greece (citrus GAP 0.015 kg ai/hL, one application, 30-day PHI), Italy (citrus GAP 0.015–0.02 kg/hL, one application, 30-day PHI) and Spain (citrus GAP 0.005–0.01 kg/hL, 21-day PHI) in 1984, 1990 and 2001.

In two orange trials from Greece with application conditions in line with GAP, clofentezine residues were 0.10 and 0.18 mg/kg, with residues in flesh at 0.02 and 0.03 mg/kg.

In six orange trials from Spain and two trials from Italy with application conditions matching Spanish GAP, clofentezine residues were: 0.06, 0.07, 0.09(3), 0.10, 0.12 and 0.14 mg/kg, with some residues in flesh at < 0.01, 0.01, 0.02(3) and 0.03 mg/kg.

In one trial on lemons from Greece with application conditions in line with GAP, clofentezine residue was 0.15 mg/kg, with residue in flesh at 0.03 mg/kg.

In one trial on lemons from Italy matching Spanish GAP, clofentezine residue in lemon was 0.09 mg/kg, with residue in flesh at 0.02 mg/kg.

In one trial on tangerines from Italy matching Spanish GAP, clofentezine residue was 0.24 mg/kg, with residue in flesh at 0.03 mg/kg.

In six mandarin trials from Spain with application conditions in line with GAP, clofentezine residues were 0.08(3), 0.15, 0.17 and 0.18 mg/kg, with residues in flesh for two trials at 0.02 and 0.17 mg/kg.

The Meeting noted that the residue data populations for orange, lemon, tangerine and mandarin were from similar populations and can be combined. The residues in ranked order on citrus fruits were: 0.06, 0.07, 0.08(3), 0.09(4), <u>0.10</u> (2), 0.12, 0.14, 0.15(2), 0.17, 0.18(2) and 0.24 mg/kg (n=19). A similar situation exists for the flesh and the ranked order of concentrations in flesh was: < 0.01, 0.01, <u>0.02</u>(5), 0.03(3) and 0.17 mg/kg (n=11).

The Meeting estimated a maximum residue level for citrus fruits and an STMR value for flesh of 0.5 and 0.02 mg/kg respectively. The Meeting also estimated an STMR value for clofentezine in whole citrus fruits of 0.10 mg/kg (for estimating STMR-R value in orange juice). The recommendation for a maximum residue level of 0.5 mg/kg for citrus fruits confirms the previous recommendation of 0.5 mg/kg.

Pome fruits

Supervised trials were conducted on apple trees in Australia (pome fruit GAP 0.015 kg/hL, one application, 21-day PHI), Canada (GAP 0.15–0.30 kg ai/ha, one application, 45-day PHI), UK (GAP 0.2 kg ai/ha, one application, 28-day PHI), France (GAP 0.02 kg ai/hL, one application, 42-day PHI), Greece (GAP 0.015 kg ai/hL, one application, 45-day PHI), Germany (pome fruit GAP 0.02 kg ai/hL, one application per year, 35-day PHI), Belgium (GAP 0.13 kg ai/ha, one application, no PHI), South Africa (GAP 0.02 kg ai/hL, 30-day PHI), USA (GAP 0.12–0.24 kg ai/ha, one application, 45-day PHI) annually from 1980 to 1987 and then 1992 and 1993.

In one trial from Canada with application conditions in line with GAP, the residue of clofentezine found in apple was 0.04 mg/kg.

In fifteen apple trials from France with application conditions in line with GAP, clofentezine residues were < 0.01(3), 0.01, 0.03, 0.05(2), 0.06, 0.07(3), 0.08, 0.10, 0.11 and 0.22 mg/kg.

In one apple trial from Greece with application conditions in line with GAP, clofentezine residue was 0.04 mg/kg.

In two apple trials from South Africa with application conditions in line with GAP, clofentezine residues were 0.09(2) mg/kg.

In sixteen apple trials from USA with application conditions in line with GAP, clofentezine residues were 0.01(2), 0.02(3), 0.04(3), 0.05(3), 0.07(2), 0.11 and 0.12(2) mg/kg.

In five apple trials from Germany with application conditions in line with GAP, clofentezine residues were 0.02, 0.03, 0.04, 0.05 and 0.09 mg/kg.

In four apple trials from UK with application conditions matching French GAP, clofentezine residues were 0.10, 0.16, 0.17 and 0.24 mg/kg.

The Meeting noted that the residues in apples from the above countries were from similar populations and could be combined. The ranked order of residues were: < 0.01(3), 0.01(3), 0.02(4), 0.03(2), 0.04(6), 0.05(6), 0.06, 0.07(5), 0.08, 0.09(3), 0.10(2), 0.11(2), 0.12(2), 0.16, 0.17, 0.22 and 0.24 mg/kg (n=44).

Supervised trials were conducted on pear trees in Australia (pome fruit GAP 0.015 kg/hL, one application, 21-day PHI), Canada (GAP 0.15-0.30 kg ai/ha, one application, 21-day PHI), Italy (GAP 0.02 kg ai/hL, one application, 30-day PHI), South Africa (GAP 0.02 kg ai/hL, 30-day PHI), USA (GAP 0.12-0.24 kg ai/ha, one application, 21-day PHI) in 1982, 1984, 1985, 1986, 1987, 1988 and 1993.

In one pear trial from Australia with application conditions in line with GAP, clofentezine residue was 0.02 mg/kg.

In four pear trials from Canada with application conditions in line with GAP, clofentezine residues were 0.12, 0.13, 0.14 and 0.19 mg/kg.

In one pear trial from Italy with application conditions in line with GAP, clofentezine residue was 0.04 mg/kg.

In two pear trials from South Africa with application conditions in line with GAP, clofentezine residues were 0.20 and 0.22 mg/kg.

In thirteen pear trials from USA with application conditions in line with GAP, clofentezine residues were 0.04, 0.05, 0.06(3), 0.08(2), 0.09(3), 0.15, 0.18 and 0.20 mg/kg.

The Meeting noted that the residues in pears from the above countries were from similar populations and could be combined. The residues in ranked order were: 0.02, 0.04(2), 0.05, 0.06(3), 0.08(2), 0.09(3), 0.12, 0.13, 0.14, 0.15, 0.18, 0.19, 0.20(2) and 0.22 mg/kg.

The Mann-Whitney test indicated the residue data populations for apple and pear were not significantly different and could be combined to support a pome fruit MRL. The ranked order of concentrations, median underlined, were < 0.01(3), 0.01(3),0.02(5), 0.03(2), 0.04(8), 0.05(7), 0.06(4), 0.07(5), 0.08(3), 0.09(6), 0.10(2), 0.11(2), 0.12(3), 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20(2), 0.22(2) and 0.24 mg/kg (n=65). The Meeting estimated a maximum residue level and an STMR value for clofentezine in pome fruits of 0.5 and 0.05 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for pome fruits confirms the previous recommendation.

Stone fruits

Supervised trials were conducted on peach in Australia (stone fruit GAP 0.015 kg ai/hL, one application, 21-day PHI), in Italy (no GAP), and USA (GAP 0.059–0.24 kg ai/ha, one application, 21-day PHI) in 1984, 1986, 1987, 1988, 1991, 1993 and 2002.

In two peach trials from Australia with application conditions in line with GAP, clofentezine residues in flesh were 0.06 and 0.13 mg/kg.

In eighteen peach trials conducted at GAP in USA, clofentezine residues were 0.02, 0.03, 0.04, 0.05, 0.06, 0.08(2), 0.09(2), 0.11, 0.12, 0.13, 0.14(2), 0.18(2), 0.24 and 0.35 mg/kg.

The Meeting noted that the residue data populations from Australia and USA for peach were from similar populations and should be combined. The residues in ranked order were: 0.02, 0.03, 0.04, 0.05, 0.06(2), 0.08(2), 0.09(2), 0.11, 0.12, 0.13(2), 0.14(2), 0.18(2), 0.24 and 0.35 mg/kg.

Supervised trials were conducted on apricot in Greece (GAP 0.015 kg ai/hL, one application, 45-day PHI) and USA (GAP 0.059-0.24 kg ai/ha, one application, 21-day PHI) in 1987, 1989 and 1993.

In one apricot trial conducted at GAP in Greece, clofentezine residue was 0.16 mg/kg.

In two apricot trials conducted at GAP in USA, clofentezine residues were 0.13 and 0.14 mg/kg.

Combined residues from Greek and USA apricot trials were 0.13, 0.14 and 0.16 mg/kg.

Supervised trials were conducted on cherries in UK (0.2 kg ai/ha, one application, 56-day PHI) in 1983.

In two cherry trials conducted in accordance with British GAP, clofentezine residues were 0.01 and 0.02 mg/kg.

Supervised trials were conducted on nectarines in USA (GAP 0.059–0.24 kg ai/ha, one application, 21-day PHI) in 1986 and 1987.

In three nectarine trials conducted in accordance with USA GAP, clofentezine residues were 0.04, 0.11 and 0.17 mg/kg.

Supervised trials were conducted on plums in Germany (GAP 0.02 kg ai/hL, one application limited by growth stage of the crop, no PHI) in 1985 and 1986. The last application was made during fruit development, which is not in accordance with German GAP, as a result the residue data could not be used for the evaluation.

The Meeting combined the residue data in peach, apricot, cherry and nectarine. The residues in ranked order were: 0.01, 0.02(2), 0.03, 0.04(2), 0.05, 0.06(2), 0.08(2), 0.09(2), 0.11(2), 0.12, 0.13(3), 0.14(3), 0.16, 0.17, 0.18(2), 0.24 and 0.35 mg/kg (n=28).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in stone fruits of 0.5 and 0.11 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for stone fruits replaces the previous recommendation of 0.2 mg/kg.

Grapes

Supervised trials were conducted on grapes in France (GAP 0.2 kg ai/ha, one application, 42-day PHI), in Greece (no GAP, use that of Spain), in Germany (GAP 0.06–0.24 kg ai/ha, one application, 35-day PHI), in Italy (GAP 0.01-0.015 kg ai/hL, one application, 30-day PHI) and in Spain (GAP 0.01-0.03 kg ai/hL, 30-day PHI) in 1984, 1985, 1986, 1987, 1991, 1992 and 2001.

In twelve trials conducted in line with German GAP, clofentezine residues were 0.09, 0.12, 0.14, 0.20, 0.22, 0.23, 0.39, 0.61, 0.69, 0.73, 0.79 and 0.89 mg/kg.

In one trial conducted in accordance with Italian GAP, clofentezine residue was 0.35 mg/kg.

In two trials conducted in accordance with Spanish GAP, clofentezine residues were 0.25 and 0.27 mg/kg.

In one trial in Greece conducted in accordance with Spanish GAP, clofentezine residue was 0.67 mg/kg.

In one trial in Italy conducted in accordance with Spanish GAP, clofentezine residue was 0.12 mg/kg.

In two trials in France conducted in accordance with Spanish GAP, clofentezine residues were 0.09 and 0.11 mg/kg.

The Meeting noted that the residues in grapes were from similar populations and could be combined. The residues in ranked order were: 0.09(2), 0.11, 0.12(2), 0.14, 0.20, 0.22, 0.23, 0.25, 0.27, 0.35, 0.39, 0.61, 0.67, 0.69, 0.73, 0.79 and 0.89 mg/kg (n=19).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in grapes of 2 and 0.25 mg/kg respectively. The recommendation for a maximum residue level of 2 mg/kg for grapes replaces the previous recommendation of 1 mg/kg.

Strawberries

Supervised trials were conducted on strawberries in France (GAP 0.2 kg ai/ha, 3-day PHI), in Germany (GAP 0.3 kg ai/ha, one application, no PHI, growth-stage restriction), in the Netherlands (GAP 0.075–0.15 kg ai/ha, one to two applications, no PHI, growth-stage restriction) and in Spain (GAP 0.01–0.02 kg ai/hL, 3-day PHI) in 1989, 1990, 1992, 2000 and 2001.

In eight outdoor trials in France conducted in line with French GAP, clofentezine residues were 0.08(2), 0.09, 0.13, 0.19, 0.20 and 0.24(2) mg/kg.

In two outdoor trials in the Netherlands conducted in accordance with Dutch GAP, clofentezine residues were 0.08 and 0.13 mg/kg.

In nine outdoor trials in Spain conducted in accordance with Spanish GAP, clofentezine residues were 0.50, 0.56, 0.60, 0.70, 0.72, 0.73, 0.75, 0.81 and 1.10 mg/kg.

In five outdoor trials in Germany conducted in line with French GAP, clofentezine residues were 0.09(2), 0.16, 0.18 and 0.23 mg/kg.

The data populations from France and those from the Netherlands and Germany were not significantly different and should be combined. The data from Spain were significantly different from those from France, Germany and the Netherlands in strawberries on a Mann-Whitney test.

Based on data from Spain, the Meeting estimated a maximum residue level and an STMR value for clofentezine in strawberries of 2 and 0.72 mg/kg respectively. The recommendation for a maximum residue level of 2 mg/kg for strawberry confirms the previous recommendation of 2 mg/kg.

Black, red and white Currants

Four supervised trials were conducted on blackcurrants in France (maximum GAP: 0.2 kg ai/ha, 45-day PHI) in 2001. The residues in ranked order on currants were: < 0.04(3) and 0.09 mg/kg.

The Meeting agreed to extrapolate from blackcurrants to red and white currants and estimated a maximum residue level and an STMR value for clofentezine in currants of 0.2 and 0.04 mg/kg respectively. The recommendation for a maximum residue level of 0.2 mg/kg for currants replaces the previous recommendation of 0.05 mg/kg.

Cucurbits

Supervised trials were conducted on cucumbers in France (cucurbits GAP 0.2 kg ai/ha, 3-day PHI), in Greece (cucumber GAP 0.015 kg ai/hL, one application, 4-day PHI) and in Switzerland (cucumber GAP 0.02 kg ai/hL, one application, 14-day PHI) in 1985, 1987, 1988 and 1991.

In one trial in France conducted on cucumber in accordance with French GAP, clofentezine residue was 0.07 mg/kg.

In four trials in Greece conducted on cucumber in accordance with Greek GAP, clofentezine residues were 0.12(2), 0.14 and 0.16 mg/kg.

In one trial in Switzerland conducted on cucumber in accordance with French GAP, clofentezine residue was 0.13 mg/kg.

The Meeting noted that the residue data in cucumber were from similar populations and could be combined. The residues in ranked order were: 0.07, 0.12(2), 0.13, 0.14 and 0.16 mg/kg (n=6).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in cucumber of 0.5and 0.125 mg/kg respectively. The recommendation for a maximum residue level of 0.5 mg/kg for cucumber replaces the previous recommendation of 1 mg/kg.

Melons

Supervised trials were conducted on melons in France (GAP 0.2 kg ai/ha, 3-day PHI), in Greece (no GAP, use that of France), in Italy (GAP 0.015–0.02 kg ai/hL, one application, 15-day PHI), in Portugal (no GAP, use that of France) and in Spain (GAP 0.01–0.02 kg ai/hL, 3-day PHI) in 1999 and 2000.

In two trials in France conducted in line with French GAP, clofentezine residues were < 0.05 and 0.05 mg/kg, with no detectable residue in pulp.

In one trial in Greece conducted in accordance with Greek GAP, clofentezine residue was 0.03 mg/kg, with no detectable residue in pulp.

In two trials in Portugal conducted in accordance with Portuguese GAP, clofentezine residues were < 0.05 mg/kg, with no detectable residue in pulp.

In two trials in Spain conducted in accordance with Spanish GAP, clofentezine residues were < 0.01 and < 0.05 mg/kg, with no detectable residue in pulp.

In two trials in Italy conducted in accordance with French GAP, clofentezine residues were 0.03 and 0.06 mg/kg, with no detectable residue in pulp.

The Meeting noted that the residues in melons were from similar populations and could be combined. The residues in ranked order were: < 0.01, 0.03(2), < 0.05(4), 0.05 and 0.06 mg/kg (n=9). The residues in all pulp samples were below the limit of quantification (n=9).

The Meeting estimated a maximum residue level of 0.1 mg/kg. Taking into account that the parent compound practically did not translocate in plants, the Meeting estimated an STMR value of 0 mg/kg for clofentezine in melons.

Tomato

Supervised trials were conducted on tomato in France (no GAP, use that of the Netherlands), in Germany (no GAP, use that of the Netherlands), in Greece (no GAP, use that of the Netherlands), in Italy (GAP 0.02-0.03 kg ai/hL, one application, 15-day PHI), in the Netherlands (GAP 0.075–0.23 kg ai/ha, 1-2 applications, 3-day PHI) and in Spain (0.01-0.02 kg ai/hL, one application, 3-day PHI) in 1986, 1992, 1999, 2000 and 2005.

In seven trials in Italy conducted in accordance with Italian GAP, clofentezine residues were 0.01, 0.03, 0.05(2), 0.06, 0.07 and 0.10 mg/kg.

In seven glasshouse trials in the Netherlands conducted in accordance with Dutch GAP, clofentezine residues were < 0.05, 0.09, 0.10, 0.11, 0.12, 0.16 and 0.18 mg/kg.

In four trials in France conducted matching Dutch GAP, clofentezine residues were < 0.05, 0.05, 0.06 and 0.09 mg/kg.

In three trials in Germany conducted matching Dutch GAP, clofentezine residues were < 0.05, 0.06 and 0.11 mg/kg.

In one trial in Greece conducted matching Dutch GAP, clofentezine residue was < 0.05 mg/kg.

In one trial in Italy conducted matching Dutch GAP, clofentezine residue was < 0.05 mg/kg.

In one trial in Spain conducted matching Dutch GAP, clofentezine residue was 0.09 mg/kg.

The Meeting noted that the residues from France, Germany and the Netherlands, in line with Dutch GAP, were from similar populations and could be combined. The data populations from France, Germany and the Netherlands and from Greece, Italy and Spain were not from similar populations based on the Mann-Whitney test, and could not be combined. The residues in ranked order based on France, Germany and the Netherlands were: < 0.05(3), 0.05, 0.06(2), 0.09(2), 0.10, 0.11(2), 0.12, 0.16 and 0.18 mg/kg (n=14).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in tomato of 0.5 and 0.09 mg/kg respectively.

Tree nuts

Eight supervised trials were conducted on walnut in USA (maximum GAP: 0.24 kg ai/ha, one application, 30-day PHI) in 1987 and 1988. The ranked order of concentrations on walnut was: < 0.02(8) mg/kg.

Thirty four supervised trials were conducted on almond in USA (maximum GAP: 0.24 kg ai/ha, 30-day PHI) in 1985, 1987, 1993, 1998 and 2002. The ranked order of concentrations on almond was: < 0.01(9), < 0.02(3), < 0.05(13), 0.10(3), 0.20(2), and 0.30(4) mg/kg.

The residue data for walnut and almond were from similar populations and could be combined. The residues in ranked order on tree nuts were: < 0.01(9), < 0.02(11), < 0.05(13), 0.10(3), 0.20(2), and 0.30(4) mg/kg (n=42).

The Meeting estimated a maximum residue level and an STMR value for clofentezine in tree nuts of 0.5 and 0.05 mg/kg respectively.

Animal feedstuffs

Almond hull

In 34 supervised trials on almond compliant with US GAP, residues of clofentezine in almond hulls in rank order, median and highest residue underlined, were: 0.06, 0.10, 0.11, 0.12(2), 0.20(2), 0.30,

0.40(2), 0.50(2), 0.60(2), 0.70(2), 0.90, 0.91, 1.00, 1.10(2), 1.20, 1.40(2), 1.50(2), 1.60, 1.70, 1.80, 2.00, 2.20, 2.30, 2.50 and 2.70 mg/kg (fresh weight) (n=34).

The meeting estimated an STMR value of 0.91 mg/kg and a highest residue of 2.70 mg/kg for clofentezine in almond hulls (fresh weight).

Allowing for the standard 90% dry matter for almond hulls (*FAO Manual*, p. 147) the residues in almond hulls were: 0.07, 0.11, 0.12, 0.13(2), 0.22(2), 0.33, 0.44(2), 0.56(2), 0.67(2), 0.78(2), 1.00, 1.01, 1.11, 1.22(2), 1.33, 1.56(2), 1.67(2), 1.78, 1.89, 2.00, 2.22, 2.44, 2.56, 2.78 and 3.00 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 1.01 mg/kg for almond hulls (dry weight). A highest residue level of 3.00 mg/kg was estimated for calculating the dietary burden of farm animals.

Fate of residues during processing

The Meeting received information on the fate of clofentezine residues during aqueous hydrolysis under conditions representing pasteurisation, baking, brewing, boiling and sterilisation. Information was also provided on the fate of clofentezine residues during the food processing of citrus, apples, grapes and strawberries.

Clofentezine was stable at pH 4 for 20 minutes at 90 °C with no degradation products formed, and moderately stable at pH 5 at 100 °C for 60 minutes. In this latter instance, clofentezine degraded slightly (by approximately 10%) to form metabolite 2-chlorobenzoic (2-chlorobenzylidene) hydrazide (AEC 593600). The parent clofentezine was rapidly hydrolysed at pH 6 and 120 °C and it was not detected after 20 minutes. The major reaction products as a percentage of the applied radioactivity were 2-chlorobenzoic (2-chlorobenzylidene) hydrazide (78%), 2-chlorobenzonitrile (4.9%) and 2-chlorobenzamide (17%).

The processing was carried out to produce apple sauce from samples spiked with clofentezine in the laboratory. The time of cooking and pasteurizing was approximately 15 minutes at a temperature of over 97 °C. The treated apples, the apple sauce and the processing by-products (washed apple, apple cores, peeled apples, wash water), were analysed for the potential degradation products of clofentezine (AEC 593600, 2-chlorobenzonitrile and 2-chlorobenzamide), but none of the compounds was present in quantifiable concentration in any of the samples. One uncooked apple peel sample contained 0.02 mg/kg for 2-chlorobenzonitrile. The clofentezine residue in the pasteurized apple sauce was reduced from 0.40 mg/kg in the apple in one study, and from 0.41 mg/kg to < 0.02 mg/kg in three samples in a follow up test, where the three degradation products were not detectable. The Meeting noted that the 3 degradation products found in the above hydrolysis study, performed at pH 6 and 120 °C, were not present in apple sauce prepared following a normal processing procedure.

Processing studies for the conversion of oranges, apples, grapes and strawberries to various processed products were reported from Germany, Italy, Spain and USA. In most cases, the raw agricultural commodities had quantifiable field incurred clofentezine residue. Calculated processing factors and the mean or best estimate for the processing factors are summarized in the following table.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors. [1/]	Median or best estimate
Orange	Juice	< 0.08, < 0.11, < 0.14, 0.14, < 0.17(3), < 0.20, < 0.25(2), < 0.33(2)	0.14
Apples	Wet pomace	< 0.50, 1.20, 1.50 (2), 2.00 (4), 2.11, 2.40, 3.00, 3.44, 5.50, 5.69, 5.79, 6.00	2.06
	Juice	0.016, 0.11, 0.20, < 0.5 (3)	0.11
Grapes	Raisins	0.22, 0.28, 0.64, < 0.67, 1.09, 1.12, 1.70, 2.33, 2.92	1.11
	Juice	nd	0
	Wet pomace	1.88, 1.89	1.89
	White wine making	< 0.042, < 0.50 (2)	< 0.042

[1/] 'Less-than' (<) values are derived from cases where residues were not detected in the processed commodity. The 'less-than' processing factor is then calculated from the LOQ of the analyte in the processed commodity and the residue in the raw agricultural commodity.

The processing factor for orange juice (0.14) was applied to the estimated STMR for orange (0.10 mg/kg) to produce STMR-P values for orange juice (0.014 mg/kg).

The processing factors for wet apple pomace (2.06) and apple juice (0.11) were applied to the estimated STMR for apple (0.05 mg/kg) to produce STMR-P values for wet apple pomace (0.103 mg/kg) and apple juice (0.0055 mg/kg).

The processing factors for grapes to raisins (1.11), grape juice (0), white wine (0.042) and wet pomace (1.89) were applied to the estimated STMR for grapes (0.25 mg/kg) to produce an STMR-P value for dried grapes (0.28 mg/kg), grape juice (0), white wine (0.011 mg/kg) and wet pomace (0.47 mg/kg). The processing factors for raisins (1.09) were applied to the grape residue data (highest value 0.89 mg/kg) to produce estimated highest values for dried grapes (0.99 mg/kg).

The Meeting estimated a maximum residue level for clofentezine in dried grapes of 2 mg/kg.

Residues in animal commodities

Farm animal feeding studies

The Meeting received feeding studies on lactating dairy cows, calves and laying hens, which provided information on likely residues appearing in animal tissues, milk and eggs from residues in the animals' diet.

Lactating Friesian cows were dosed with clofentezine at the equivalent of 10 (1), 30 (3 ×) and 100 (10 ×) ppm in the dry-weight diet using an average feed consumption of 20 kg for 28 consecutive days. Milk was collected twice daily for analysis. Animals were sacrificed at 1 or 3 days after the final dosing.

No residues (total clofentezine=clofentezine and metabolites hydrolysable to 2-chlorbenzoic acid and expressed as clofentezine) were detected in milk samples taken from the control and the 1 × dose groups. From day 7, total residues between < 0.05 and 0.14 mg/kg were detected in the milk of cows from the 3 × dose group. In the 10 × dose group, residues occurred regularly from day 7 in the concentration range of 0.11 to 0.27 mg/kg.

The total residue was below the LOQ (0.05 mg/kg) in all tissue samples except liver from the treatment rate of 1 ×. No residue was detectable in heart, muscle and fat samples at any dose level. The average residues were present in liver (0.26, 1.15, 2.20 mg/kg) and in kidney (< 0.05, 0.18, 0.40 mg/kg) at the dose rates of 1 ×, 3 × and 10 ×, respectively.

Calves were dosed at a rate equivalent to 0.5 ppm feed (dry weight) using an average feed consumption of 3.5 kg for 28 days. Animals were sacrificed at 19 h after the final dosing. The total

clofentezine residues were below the limit of quantification (0.05 mg/kg clofentezine equivalents) in the liver and kidney samples.

Laying hens were fed clofentezine at 0.05, 0.15, 0.50 and 6.0 ppm in the diet (dry weight) for 28 days. Egg samples were taken daily during the study and kept frozen. Birds were sacrificed 1 day after the final dosing. Only one egg sample obtained from the highest dose rate group contained quantifiable residues (0.06 mg/kg). From the dose groups of 0.05, 0.15, 0.50 ppm, no residue was present above the LOQ (0.05 mg/kg) in any tissue samples. Quantifiable residues were only present at the exaggerated 6.0 ppm dosage rate: liver (0.08 mg/kg), kidney (0.06 mg/kg) and abdominal and subcutaneous fat (0.13, 0.09 mg/kg).

Livestock dietary burden

The Meeting estimated the dietary burden of clofentezine in farm animals on the basis of the diets listed in the Annex 6 of the 2006 JMPR Report. Calculation from highest residue and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle and turkey are provided in Annex 6. The calculations were made according to the animal diets from USA, Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

The calculations are then summarized and the highest dietary burdens (underlined) are selected for MRL and STMR estimates on animal commodities.

	Animal dietary burden, clofentezine, ppm of dry matter diet					
	USA-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.35	0.15	0.05	0.05	<u>0.98</u> [1/]	<u>0.78</u> [2/]
Dairy cattle	0.33	0.13	0.03	0.03	<u>0.95</u> [3/]	<u>0.75</u> [4/]
Poultry - layer	0	0	0	0	0	0
Poultry - layer	0	0	0	0	0	0

[1/] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat.

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

[3/] Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk.

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

The dietary burden for both beef and dairy cattle was 0.93 mg/kg, below the lowest feeding level (10 ppm in the feed). Therefore, the resulting residues in milk and cattle tissues were calculated by applying the respective transfer factors (transfer factor=residue level in tissue or milk ÷ residue level in feed) to the estimated dietary burden. In the feeding study the highest residue levels in tissues were used to calculate the highest likely mammal commodity residue levels and mean residue levels in milk and tissues were used to estimate the mammal commodity STMRs. In the table below, dietary burdens and the corresponding estimated residues in brackets are indicated with Italic fonts.

	Feeding level (mg/kg) actual	Clofentezine residues, mg/kg									
		Milk		Muscle		Fat		Liver		Kidney	
		Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL beef cattle	*0.98*			*(< 0.005)*		*(< 0.005)*		*(0.031)*		*(< 0.005)*	
	10			< 0.05		< 0.05		0.33		< 0.05	

MRL	*0.95*		*(< 0.005)*								
dairy cow	10		< 0.05								
STMR	*0.78*				*(< 0.004)*		*(< 0.004)*		*(0.019)*		*(< 0.004)*
beef cattle	10				< 0.05		< 0.05		0.26		< 0.05
STMR	*0.75*		*(< 0.004)*								
dairy cow	10		< 0.05								

The dietary burden for laying hens was 0 mg/kg, therefore the table of calculation of MRLs and STMRs for poultry meat and eggs is not necessary.

The Meeting estimated maximum residue levels of 0.05 (*) mg/kg for mammalian meat (fat), mammalian edible offal, and milks to replace the present recommendations of 0.05 (*) mg/kg for cattle meat, 0.01 (*) mg/kg and 0.1 mg/kg for edible offal of cattle. The Meeting also estimated the following STMR values: muscle 0 mg/kg, fat 0 mg/kg, edible offal 0.05 mg/kg, and whole milk 0 mg/kg.

The Meeting estimated maximum residue levels of 0.05 (*) mg/kg for eggs, poultry meat (fat), and poultry edible offal, based on the limit of quantification for poultry commodities to confirm the present recommendation of 0.05 (*) mg/kg. Also estimated were STMRs of 0 mg/kg for eggs, meat, and edible offal of poultry.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of clofentezine, based on the STMRs estimated for sixteen commodities, were 0–3% of the maximum ADI of 0.02 mg/kg bw for the thirteen GEMS/Food regional diets. The Meeting concluded that the long-term intake of residues of clofentezine resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2005 JMPR decided that an ARfD was unnecessary. The Meeting therefore concluded that the short-term intake of clofentezine residues is unlikely to present a public health concern.

5.7 CYFLUTHRIN (157)/ BETA-CYFLUTHRIN (228)

RESIDUE AND ANALYTICAL ASPECTS

Cyfluthrin was identified as a priority compound under the Periodic Re-evaluation Programme at the 37th Session of the CCPR. The Meeting received information on cyfluthrin metabolism and environmental fate, methods of residue analysis, freezer storage stability, national registered use patterns, supervised residue trials, farm animal feeding studies, fate of residues in processing and national MRLs. The Meeting also received information on beta-cyfluthrin methods of residue analysis, freezer storage stability, national registered use patterns and supervised residue trials. The metabolism and environmental fate, transfer from feeds to farm animals and fate of residues in processing provided for cyfluthrin are used to support both pesticides.