[a] The most sensitive NOAEL for the primary action the chemical and considered protective of other non-neurotoxic effects from studies of repeated doses.

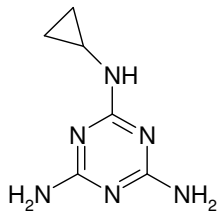
[b] Neurotoxicity occurred a few hours after dosing during the first week of treatment.

5.9 CYROMAZINE (169)

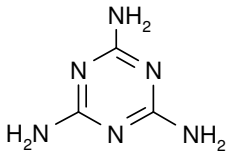
RESIDUE AND ANALYTICAL ASPECTS

Cyromazine was last evaluated by the JMPR in 2006 for toxicology within the Periodic Re-evaluation Programme, where an ADI of 0-0.06 mg/kg bw and an ARfD of 0.1 mg/kg bw were established. The compound was listed at the 38th Session of the CCPR for periodic re-evaluation for residues by the 2007 JMPR. Data submitted by the manufacturer include physical and chemical properties, metabolism in animals and plants, environmental fate in soils, residues in succeeding crops, analytical methods, storage stability, supervised trial on mangos, vegetables and animal commodities and processing studies. Residue and information on good agricultural practices (GAP) was also submitted by the Netherlands.

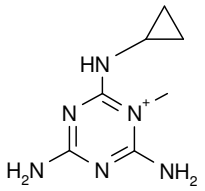
Cyromazine is a selective insecticide that acts by inhibiting the moulting process in insects, particularly in members of the Dipteran family. The figure below shows the compound structure and its main metabolites or degradation products found in animals, plants and/or soils. Metabolism and environmental fate studies submitted to the Meeting were conducted with [triazine-U-^{14}C]cyromazine.



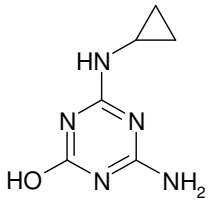
CYROMAZINE



MELAMINE



1-METHYL CYROMAZINE



HYDROXY CYROMAZINE

Animal metabolism

Metabolism studies in rats evaluated by the 2006 JMPR showed that more than 97% of the administered [^{14}C]cyromazine dose was excreted within 24 h, almost exclusively in the urine. Cyromazine was the major compound found in urine (71.5% of the applied radioactivity), with a further 7% attributed to melamine and 8–11% to hydroxy-cyromazine and 1-methyl-cyromazine.

Laying hens that received cyromazine at 5.0 ppm in the feed (equivalent to 0.5 mg/kg body weight/day) for 7 consecutive days had > 99% of the applied radioactivity recovered in the excreta. Egg white and egg yolk had 0.4% and 0.2% of the total applied radioactive dose, respectively; for egg white and egg yolk, an average of 0.15 and 0.12 mg/kg cyromazine equivalents were found in the daily collected eggs of two animals, respectively. Cyromazine represented about 64% TRR in eggs; a metabolite (15.6% TRR) had the same retention volume in an ion exchange column as melamine, but no confirmation of the identity of this compound was performed. Hen tissue residues accounted for 0.1% of the total applied dose, with the highest radioactive levels found in liver, kidney, heart and muscle (0.032, 0.019, 0.10 and 0.09 mg/kg cyromazine equivalents, respectively). The residues in tissues were not characterized. Expired CO_2 and other volatiles accounted for < 0.1% of the applied dose.

Lactating goats dosed with [^{14}C]cyromazine for ten consecutive days at levels of 4.6 ppm (low rate) and 48.4 ppm (high rate) in the feed had most of the administered dose excreted in the urine (86%) and faeces (6.6%). Residues in tissues represented < 2% of the applied dose, mostly found in liver (0.79 and 1.5 mg/kg cyromazine eq. for the low and higher dose, respectively) and kidney (0.043 and 0.44 mg/kg cyromazine eq). About 93% TRR was extracted from the liver, the majority (> 70%) as a non-identified metabolite with cyromazine and melamine representing 2 and 5.6% TRR, respectively. Radioactivity in milk accounted for < 0.4% of the applied dose and plateaued rapidly at both dose levels, with a mean of 0.017 and 0.32 mg/kg cyromazine eq found in the samples collected daily at the low and high dose levels, respectively. The radioactivity in the day 7 milk was mostly associated with the whey fraction, with cyromazine representing about 37% TRR and melamine 9.2 and 4.5% TRR for the low and higher dose, respectively.

In a second study, goats were dosed with cyromazine at 100 ppm in the feed for 4 consecutive days. The TRR was 74% of the applied dose, with 2.7 and 59% eliminated via faeces and urine, respectively; 7.4% of the total dose was found in the gastrointestinal tract. About 6% of the applied dose was recovered in the tissues, mostly in muscle (mean of 2.6%). Highest levels were found in kidney and liver (4.6 and 2.7 mg/kg cyromazine eq, respectively). In liver, the metabolite 1-methylcyromazine was the major compound found (42% TRR), followed by the parent cyromazine (34% TRR). Kidney and muscle had mostly cyromazine (> 70% TRR) and only cyromazine was detected in fat. On average, a total of 0.76% of the applied dose was recovered in the milk, with an average of 0.66 mg/kg cyromazine eq/day. Cyromazine was the major identified compound in milk (68% TRR) followed by melamine (2.9% TRR).

In one study conducted with a mature female sheep fed with [^{14}C]cyromazine for 9 consecutive days at a level of 5 ppm in the diet (equivalent to 0.15 mg/kg bw per day), 94% of the applied radioactivity was recovered, mostly in urine (89%). Tissues represented 0.09% of the applied radioactivity, mostly found in liver (0.17 mg/kg cyromazine eq), kidney (0.048 mg/kg eq) and muscle (0.13 mg/kg eq). While the excreta extracts contained mostly cyromazine, the main compound found in liver extract was melamine (44% total radioactivity), with cyromazine corresponding to 12%.

In summary, animals dosed daily with [^{14}C]cyromazine excreted over 90% of the radioactivity, mainly in urine. Eggs and milk represented < 0.5% and tissues < 2% of the applied or recovered radioactivity. Metabolism of cyromazine involves mainly dealkylation to melamine. Alkylation to 1-methylcyromazine was specific to ruminants; hydroxylation was identified in goats fed at 100 ppm. Cyromazine was the major compound found in hen eggs and milk of goats and sheep. The major compounds found in liver of goat and sheep were the metabolites 1-methylcyromazine and melamine, respectively.

Metabolism in plants

In one greenhouse study conducted at a 0.28 kg ai/ha foliar rate in two phases, celery plants received 2 (1st phase) or 6 applications (2nd phase) and were sampled 7 days after the second application (mature) in the 1st phase or third application (immature) and 14 days after the sixth application (mature) in the 2nd phase. Lettuce received 2 or 4 applications and heads were sampled 7 days after the second application (mature or immature) and 7 days after the fourth application (mature). Radioactivity in the plants was mostly extracted in the aqueous phase (> 74% TRR), with cyromazine representing the major residues (48 to 74% TRR in both plants) and melamine was the only metabolite found (11 to 33% TRR).

In a study conducted with tomatoes in a California field, 6 foliar applications at 0.28 kg ai/ha were made to the crop at 2 weeks intervals. Tomato samples were taken at 0, 7, and 14 days after the 4th or 6th applications and a stalk sample after the last application. TRR in the samples ranged from 64–98% of the applied radioactivity, mostly found in the aqueous extract (56 to 87% TRR) and being characterized as cyromazine (29 to 76% TRR) and melamine (11 to 44% TRR). While the residues ranged from 0.08 to 0.44 mg/kg cyromazine eq. in tomato samples, they reached 37 mg/kg eq in the stalk sample (aerial portion of the plant after removal of the tomato fruits).

Five trials conducted with non-radioactive cyromazine demonstrated that residues did not accumulate significantly in mushrooms under normal use conditions when the crop was grown in amended compost. Cyromazine residues were < 0.05 mg/kg in mushrooms in all trials/flushes with the exception of one trial at a target cyromazine concentration in the compost of 10 mg/kg for which the sample from the third flush contained a residue of 0.08 mg/kg. Residues of melamine were in the range 1.5–6.6 mg/kg at a compost of 5 mg ai/kg, and in the range 3.1–17 mg/kg at a compost of 10 mg/kg.

The results indicated that the major pathway of cyromazine in lettuce, celery and tomato was by dealkylation to form melamine, which can represent about 40% TRR. Melamine was the major compound found in cold treated mushroom.

Environmental fate in soil

Fourteen cyromazine aerobic degradation laboratory studies conducted with a variety of soils were submitted to the Meeting. Soil samples containing from 0.25 to 10.7 mg ai/kg (0.33 to 9.5 kg ai/ha) cyromazine were incubated for up to 12 months in the dark at temperatures ranging from 10 to 25 ˚C. In most studies, TRR was over 90% of the applied radioactivity. Melamine was the only or major degradation product found in the soils. In a 12 months/25 ˚C study conducted with a sandy loam soil (9 mg/kg cyromazine) 15% of the applied dose, at the end of the study, was identified as the carboxylic acid of cyromazine, formed through oxidative opening of the cyclopropane ring. Cyromazine half lives (DT_{50}) varied widely, ranging from 2.9 to 107 days, being lesser at lower temperatures, organic matter content and microbial biomass. In general, the degradation rate of melamine was slower than that of cyromazine.

The photolytic degradation of cyromazine was studied at 20 ˚C under artificial light on soil at a rate of 3.2 µg ai/cm^2 (corresponding to a field rate of 0.32 kg ai/ha). Samples were irradiated for 240 h, equivalent to 30 days natural summer sunlight. In moist irradiated soil, cyromazine degraded rapidly with a calculated DT_{50} of 3.5 days; in dry irradiated soil the level fell rapidly during the first 24 h and the degradation was slow thereafter (DT_{50} > 1 year). In both moist and dry soils, melamine was the major degradation product observed (53 and 15% of applied radioactivity in the moist and dry soil, respectively).

Eleven field soil studies conducted with cyromazine were submitted to the Meeting. In one study cyromazine was applied to bare soil at four different sites in various states in the USA during 1982/83. Plots were treated at an exaggerated rate of 5.6 kg ai/ha as a single application with a second application in Year 2. Residues in the soil at day 0 in both years ranged from 0.39 to 6.6 mg/kg in the 0–15 cm layer, with the highest value occurring from one site in Florida. Cyromazine dissipated at a slow rate at all 4 sites, and could remain unchanged for over 100 days. At the sites in California and Nebraska, essentially no movement of cyromazine was observed below a depth of 15 cm; at the two sites in Florida, cyromazine residues were found to a depth of 30–45 cm in both years. Melamine was detected at all sites down to a depth of 30–45 cm towards the end of each year of the trial.

In four field studies carried out on bare soil plots in potato growing areas of Canada during 1993 and 1994, cyromazine was applied twice at 0.28–0.48 kg ai/ha. Cyromazine residues declined rapidly after the second application and continued to decline over the winter period at a slower rate, with half-lives ranging from 29 to 42 days. The majority of the parent residue was retained in the upper soil layer (0–15 cm) and most of the melamine residues remained in the top 30 cm. Melamine was present from background sources in the three topsoil layers up to 0.011 mg/kg.

In two field studies conducted in Switzerland and France in 2002/2003, soil samples (0–30 cm deep) from plots treated at 0.30 kg ai/ha were taken up to 360 days. In France, no residues were detected in soil below a depth of 20 cm and in Switzerland; no cyromazine residues were found in soil below a depth of below a depth of 10 cm. DT_{50} for cyromazine calculated from the 0–10 cm layer residue data was 17 days and 2.3 days for France and Switzerland, respectively.

In one study conducted in Greece from 2001 to 2003, cyromazine was applied annually 4 times at a rate of 0.30 kg ai/ha at approximately 7 day intervals to bare ground (sandy loam soil type). The plot was cultivated with mustard 1–2 days before the first application in each year. Cyromazine and melamine were found in some occasions at depths of up to 50–70 cm. The degradation of cyromazine was slower during a drought season of the first year (low biological activity) and during the winter.

In a study conducted in Spain, cyromazine was applied yearly to a loamy silt soil in four subsequent early summer applications at 0.30 kg ai/ha (2000–2003). Tomatoes were planted in the second year of the experiment just prior to the cyromazine application. Cyromazine residues were not found in soil layers deeper than 30 cm; melamine could be detected in soil layers up to 100 cm deep in the second and third year of the study, a possible result of higher than average rainfall during this period of the study. DT_{50} for cyromazine, calculated from the first year data, was 51 days.

The proposed metabolic pathway of cyromazine in soil involves the initial cleavage of the cyclopropyl ring moiety to form melamine, with a possible involvement of the carboxylic acid of cyromazine as intermediate. The rate of degradation of cyromazine under laboratory or field conditions vary widely, with estimated half lives ranging from a few days to over 100 days, depending on the soil type and environmental conditions.

Succeeding Crops

Five studies on succeeding crops conducted in USA were submitted to the Meeting. In a greenhouse study conducted in Florida in 1982, celery seedlings were transplanted into a muck soil and [^{14}C]cyromazine mixed with a sample of the soil applied as a top dressing to the crop at 1 kg ai/ha. Celery plants were harvested after 84 days and radishes or sweet corn immediately planted in the same container. About 78% TRR in celery stalks was found the aqueous extract, with cyromazine being the main residue found after 42 and 82 days after treatment (up to 0.45 mg/kg). Radioactivity in radish and mature sweet corn planted 84 days following foliar application of the compound to celery and harvested after 130 or 159 days after planting ranged from 0.01 to 0.02 mg/kg cyromazine eq and were too low for characterization.

In a field study conducted in California, tomatoes were treated in the fall with [^{14}C]cyromazine at 6 × 0.28 kg ai/ha. Tomato plants were harvested 14 days after the last application and winter wheat planted immediately after that. Lettuce, carrot, soy bean and sugar beet were planted the following spring. Two samplings (immature and mature harvest) were taken from each crop for analysis. Radioactive residues in succeeding crops were ≤ 0.05 mg/kg for all crop parts other than half-mature carrot tops (0.19 mg/kg cyromazine eq). Most of the residues in this sample (93%) was partitioned into the aqueous layer and was characterized as 14% cyromazine and 79% melamine.

A study was performed in Georgia to determine the fate of cyromazine in chicken manure amended soil and the uptake and metabolism of cyromazine residues by rotational cops. The soil was prepared by incorporating manure fortified with [^{14}C]cyromazine at 5 mg/kg at a rate of 11.2 t manure/ha and aged for 30 days. Spring wheat, lettuce and sugar beets were planted in buckets containing a 7.6 cm top layer of cyromazine-treated soil and grown to maturity in the greenhouse. TRR ranged from < 0.01 to 0.011 mg/kg cyromazine eq in mature and immature lettuce leaves, sugar beet tops and beets and wheat grain. Immature stalks and mature wheat straw and hulls contained residues between 0.022 to 0.11 (straw) mg/kg eq, greater than the initial soil concentration of 0.064 mg/kg. Cyromazine and melamine accounted for 43% and 28% TRR in wheat straw, respectively.

In a study carried out in Mississippi, tomato crops were treated with 12 applications of cyromazine at 0.14 or 0.28 kg ai/ha, the tomatoes harvested at 14 days after last application and wheat planted 10 weeks after the last application. Cyromazine residues in samples of forage, straw and grain harvested 23 to 43 weeks after planting ranged from < 0.05 to 0.08 mg/kg with the highest value in forage. In California and Florida, 21 field trials were carried with celery treated with 11–15 foliar

applications of cyromazine at rates from 0.14 to 0.28 kg ai/ha. Celery was harvested at 0–14 days after the last application and following a post-harvest interval of 1–6 weeks (Florida) or 8 weeks (California) the field plots were re-planted with sweet corn (eight trials), radishes (eight trials) and lettuce (five trials). Residues of cyromazine were detected in sweet corn forage (0.08 to 0.19 mg/kg), radish roots and tops (0.09 to 0.22 mg/kg) and lettuce leaf (0.05 to 0.08 mg/kg).

In summary, detectable residues of cyromazine and melamine can be found in crops cultivated after cyromazine treated plants have been harvested. Crops planted in cyromazine fortified manure amended aged soil also showed detectable residues.

Analytical methods

Four analytical methods for the analysis of cyromazine and melamine in vegetable crops were provided. In methods developed in the 1980´s, residues can be extracted with water/methanol or pure methanol, cleaned up and partitioned with dichloromethane and hexane, followed by C18 and/or cation exchange columns and additional clean-up with amino column or gel permeation chromatography. The analytes are quantified by HPLC with an amino column and UV detection at 214/215 nm or by GC/NPD. Samples of lettuce, celery, tomato, mushrooms, cucurbits, peppers, grapes, peas and alfalfa, cotton, Sudan grass and/or barley products were fortified at levels that varied from 0.04 to 10 mg/kg level of cyromazine and melamine. In most cases, recoveries were within 70−120% range, however only in few cases replicate samples were analysed.

In a method reported in 2001 (REM 174.02), samples of crops with high water content and fruits with high acid content, are macerated with an acidic solution of potassium dihydrogen phosphate and extracted with methanol. Crops with high fat content, cereals and other dry crops are macerated with water and then extracted with methanol by mechanical shaking. Celite is added, the mixture centrifuged, filtered, and the filtrate acidified. Analysis is by column switching HPLC using two cation exchange columns and detection within the range 215−245 nm depending on crop type and co-extractives. This method was fully validated for sunflower seeds, tomatoes, oranges, beans and potatoes fortified at 0.05 and 0.5 mg/kg (n=5 in each case). Recoveries of cyromazine and melamine ranged from 80 to 110%, with a coefficient of variation (CV) up to 5.2%.

Twelve methods for the analysis of cyromazine and melamine in food of animal origin were provided. The analytes could be extracted with methanol, methanol/water, ethanol or acetone, and the extracts cleaned-up on cation exchange, silica and/or celite column. In some methods, a solvent partitioning step was included before the clean-up, or replaced the clean-up. Quantification was by GC/NPD or MS in most cases, but also by HPLC/UV 214 nm. The methods were validated for eggs, milk and tissues fortified at 0.04 to 1 mg/kg. Recoveries were satisfactory in most cases, and whenever replicate samples were analysed, CV were < 20%. In one method reported in 2003 (RAM 394/01), cyromazine and melamine residues are extracted from liver, kidney, muscle tissue and milk with acetonitrile/water and from eggs with methanol/water. After centrifugation, aliquots are adjusted to pH 4 with glacial acetic acid, subjected to cation exchange clean-up and the compounds quantified by HPLC-MS/MS. This method was fully validated at 0.01 and 0.1 mg/kg levels, with recoveries from 70 to 107% and CV up to 16% (n=5).

Stability of pesticide residues in stored analytical samples

Residues of cyromazine and melamine in crop samples fortified at 0.5 or 1.0 mg/kg levels were stable after being frozen for up to 2 years, with the amount remaining in the range of 80 to 110%. Residues of cyromazine, melamine and 1-methylcyromazine in beef tissues, eggs and milk fortified at 0.5 or 1.0 mg/kg levels were also stable for over 3 years under freezer conditions. Field-incurred residues of cyromazine and melamine in lettuce, celery and tomatoes samples at levels from 0.07 to 21.5 mg/kg increased more than 150% of the initial concentration after stored for up to 23 months under freezer conditions.

Definition of the residue

In 1990, the JMPR defined the residue for cyromazine in food as cyromazine. At the 1992 JMPR, the possibility of including melamine in the definition was discussed, but the Meeting decided to maintain the previous definition in light of melamine was considered to be less toxic than cyromazine, and that melamine may have originated from sources other than from the use of cyromazine. Nevertheless the Meeting recognized that the monitoring of good agricultural practice in growing mushrooms under certain conditions was not possible when melamine was omitted from the residue definition.

Data submitted to the present Meeting have shown that melamine is the main metabolite found in all crops and most animal products. Cyromazine is the major compound found in all crops, with the exception of mushroom, where melamine can be present at levels higher than cyromazine. Most analytical methods analyse cyromazine and melamine and most of the supervised trials submitted to the Meeting contained data for both compounds. It is known that cyromazine is not the only source of melamine in agriculture and in the environment and that melamine can be a component in fertilizers and is used in a variety of manufacturing processes, including plastics. Data provided by the manufacturer have shown that, with the exception of Switzerland, the residue definition in most countries in all foods is cyromazine.

Based on the present knowledge and for practical purposes, the Meeting agreed that the residue definition for cyromazine for enforcement purposes for food of plant and animal origin should continue to be cyromazine.

Toxicological data evaluated by the 2006 JMPR confirmed that melamine is less toxic than the parent compound. The Meeting agreed that the definition for cyromazine in food of plant and animal origin, for dietary intake purposes, is cyromazine.

The octanol-water partition coefficient of cyromazine is < 1 and the compound does not accumulate in fat of animals dosed with cyromazine. The Meeting concluded that cyromazine is not fat soluble.

Definition of residues (for compliance with MRL and for estimation of dietary intake) for plants and animal commodities: *cyromazine.*

Results of supervised trials on crops

Metabolism studies conducted in plants and plant residue data for melamine (not included in this evaluation) indicate that cyromazine is always present at a higher concentration than melamine in the treated crops considered in this evaluation. Cyromazine might be absent or present at lower concentration than melamine in treated mushrooms.

Mango

Mango is registered in Mexico to be used as a foliar application in the field at rates from 0.07 to 0.10 kg ai/ha. The maximum number of application is not specified on the label and the PHI is 0 day. Six trials were conducted with cyromazine in mango in Mexico from 1984 to 1993. The compound was applied 5 times at 0.09 kg ai/ha and samples harvested from day 0 to day 28 after the last application. Residues of cyromazine in the whole fruit at 0 day PHI were: 0.06, 0.10, 0.11, 0.14(2) and 0.25 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg, an STMR of 0.125 mg/kg and an HR of 0.25 mg/kg for cyromazine in mango.

Onions

The registered use of cyromazine in bulb vegetables in the USA recommends up to 6 foliar applications at 0.14 kg ai/ha rate with a 7 day PHI. A seed treatment at 5 g ai/100 g seed is also recommended, but with no PHI specified. Eight trials were conducted in 1993 with bulb onions using

the seed treatment at the GAP rate and resulted in residues in the onion bulbs at 98 to 207 days PHI of < 0.05 (7) and 0.06 mg/kg. Residues in the whole plant at 60–75 days PHI were 0.09, 0.16, 0.27, 0.34, 0.35, 0.44, 0.83 and 1.7 mg/kg. Dried onion bulb samples (fresh bulbs dried in the field) from all trials gave residues of < 0.05 and 0.06 mg/kg. In nine trials conducted in 1999, using foliar application within US GAP, residues found in onion bulbs were: < 0.05 (7) and 0.07 (2) mg/kg.

The Meeting agreed that trials conducted at GAP using foliar and seed application gave residues in onion bulbs at the same level and could be combined. Residues in ranked order (median underlined) were: < 0.05 (14), 0.06 and 0.07 (2) mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.07 mg/kg for cyromazine in bulb onions.

Four trials were conducted with cyromazine in spring (green) onions in USA in 1999 using 6 foliar applications at 0.14 to 0.17 kg ai/ha. Residues in the whole plant within 7 days PHI were 0.26, 0.30, 0.75 and 0.78 mg/kg. Data from immature plant from the bulb onion trials can be considered for the estimation for spring onion and the results from the trials can be combined. Residues in ranked order (median underlined) were: 0.09, 0.16, 0.26, 0.27, 0.30, 0.34, 0.35, 0.44, 0.75, 0.78, 0.83 and 1.7 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg, a STMR of 0.35 mg/kg and a HR of 1.7 mg/kg for cyromazine in spring onion.

Broccoli and cabbage

In the USA, cyromazine is registered for the brassica leafy vegetable group to be applied 6 times as a foliar application in the field at 0.41 kg ai/ha and 7 days PHI. In six trials conducted in broccoli at GAP, residues found in flower head and stem at 7 days PHI were: < 0.05, 0.05, 0.09, 0.21, 0.26 and 0.51 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.15 mg/kg and an HR of 0.51 mg/kg for cyromazine in broccoli.

In six trials conducted at GAP rate in USA, residues in cabbage head (with wrapper leaves) were: 0.06, 0.10, 0.24, 0.28, 0.50 and 6.1 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR of 0.26 mg/kg and an HR of 6.1 mg/kg for cyromazine in cabbage, head.

The IESTI calculation indicates that the consumption of cabbage at the HR level of 6.1 mg/kg will lead to an exceedance of the ARfD, but no residue data was available from an alternative GAP to estimate a lower maximum residue level.

Fruiting vegetables, cucurbits

Cyromazine is registered for use in cucumber, melon and summer squash in many European countries at similar rates, with the PHI ranging from 3 to 14 days. In France, the maximum GAP rate is 0.3 kg ai/ha (field and protected), with a PHI of 3 days for cucumber and summer squash. Fifteen protected cropping or field trials were conducted in cucumber from 1999 to 2001 in France (6), Greece (2), Italy (5), Spain (1) and Switzerland (1) using 3 to 4 applications at 0.30−0.34 kg ai/ha rate. Residues found at 3 days PHI, in ranked order were: 0.30, 0.32, 0.33, 0.40, 0.43, 0.46, 0.50, 0.52(2), 0.62, 0.71, 0.74, 0.79, 0.88 and 1.3 mg/kg.

In USA, cyromazine is registered for the Cucurbits crop group with a recommendation of a maximum of 6 foliar applications at 0.14 kg ai/ha at 7 day intervals with a 0 day PHI. Due to the rapid rate of growth exhibited by cucurbits, it was considered unlikely that early applications would contribute significantly to the final residues. As a result, trials conducted with a higher number of applications were considered to comply with the US GAP. In five trials conducted in the USA on cucumbers in 1986 and 1990 where 6 or 8 applications, at the GAP rate were made, residues at 0 days

PHI were: 0.16 (2), 0.20, 0.22 and 0.56 mg/kg. In four trials conducted at the double rate, residues found were within the same range.

The Meeting considered that the data from the 20 trials conducted in cucumbers according to the GAPs of Europe and the USA belonged to the same population and could be combined. Residues in ranked order (median underlined) were: 0.16 (2), 0.20, 0.22, 0.30, 0.32, 0.33, 0.40, 0.43, 0.46, 0.50, 0.52(2), 0.56, 0.62, 0.71, 0.74, 0.79, 0.88 and 1.3 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.048 mg/kg and an HR of 1.3 mg/kg for cyromazine in cucumbers.

The Meeting recommended withdrawing the previous recommendation of 0.2 mg/kg for cyromazine in cucumbers.

In eight field trials conducted in summer squash in France, Italy and Spain, between 2000 and 2003, using 3 applications of 0.3 to 0.35 kg ai/ha (0.03 kg ai/hL) with a 3 day PHI, residues found in ranked order were: 0.11, 0.14, 0.15, 0.16, 0.18, 0.21 and 0.27 (2) mg/kg.

In seven trials conducted in the USA from 1986 to 1990 based on the cucurbits GAP rate (6 or 8 applications), residues at 0 days PHI were 0.07 (2), 0.11(2), 0.18, 0.22 and 1.0 mg/kg. In five trials conducted at double rate, residues were within the same range.

The Meeting considered that the residues from 15 trials conducted in summer squash according to European GAP at 3 days or 14 days PHI and in USA according to US GAP belonged to the same population and could be combined. Residues in ranked order (median underlined) were: 0.07 (2), 0.11 (3), 0.14, 0.15, 0.16, 0.18(2), 0.21, 0.22, 0.27 (2) and 1.0 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.16 mg/kg and an HR of 1 mg/kg for cyromazine in summer squash.

GAP for melons in Spain is 0.3 kg ai/ha (14–30 days interval) with a PHI of 3 days. In France, the rate is also 0.3 kg ai/ha (10–15 days interval) and a PHI of 7 days. A total of fourteen trials (field and glasshouse) matching French GAP were conducted in melons in France, Italy and Spain from 1998 to 2001 using 3 applications of 0.28 to 0.33 kg ai/ha (7 days interval). Residues in the whole fruit were: < 0.05, 0.06 (3), 0.07, 0.08, 0.09(2), 0.11, 0.12, 0.13, 0.16, 0.18 and 0.25 mg/kg.

In seven trials conducted in the USA in 1986 in melons and cantaloupe using 8 applications at the GAP rate, residues at 0 days PHI were: < 0.05, 0.08, 0.09, 0.11(2), 0.13 and 0.45 mg/kg. In one trial conducted in watermelon at the same rate, residues found were 0.13 mg/kg.

The Meeting considered that residues from trials conducted in melons according to GAP in Europe and USA appeared to be from similar populations and could be combined. Residues in melons from the 21 trials, in ranked order (median underlined), were: < 0.05 (2), 0.06 (3), 0.07, 0.08 (2), 0.09 (3), 0.11 (3), 0.12, 0.13 (2), 0.16, 0.18, 0.25 and 0.45 mg/kg.

In some of 3 day PHI trials conducted in melons in Europe, residues in fruit were calculated from the levels found in the pulp and in the peel; residues in the pulp were < 0.05(4) mg/kg. The residue ratio fruit/pulp calculated from these and other trials was 1.1, > 1.6, > 2.4, > 2.6, > 3 and > 3.2, with an estimated mean of > 2.3. A fruit/pulp ratio of 2.3 was applied to the median and highest residues for melons (0.09 and 0.45 mg/kg), estimating the median and the highest residue in melon pulp as 0.04 and 0.19 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg for cyromazine in melons, except watermelons, an STMR of 0.04 mg/kg and an HR of 0.19 mg/kg for cyromazine in melons (pulp).

The Meeting recommends withdrawing of the previous recommendation of 0.2 mg/kg for cyromazine in melons, except watermelons.

Fruiting vegetables, other than cucurbits

Cyromazine is registered in tomato and eggplant in many European countries for either in the field or under protected cropping. In France (F&P) and Italy (F) the maximum application rate is 0.3 mg/kg ai/ha. The recommended PHI is 3 days in France and 14 days in Italy. Eighteen foliar trials complying with French GAP were conducted in France, Greece, Italy and Spain under field or glasshouse conditions with 4 foliar applications at 0.3 to 0.34 kg ai/ha. Residues at 3 days PHI were: 0.05, 0.09, 0.11(3), 0.13 (2), 0.14, 0.15, 0.16, 0.18, 0.21, 0.22, 0.23, 0.29, 0.34, 0.42 and 0.58 mg/kg.

Application through irrigation is also recommended in Italy and Greece, at rates of 0.75 and 0.98 kg ai/ha with a PHI of 14 days. Only one of the four trials conducted in Greece, Italy and Spain using either drip or soil drench irrigation matched the GAP of Italian and Greece, giving residues of cyromazine at 14 days PHI of < 0.05 mg/kg.

In the USA, cyromazine can be applied to tomatoes up to 6 times at a rate of 0.14 kg ai/ha with a 0 day PHI. In 13 trials conducted according to GAP, residues at day 0 were: 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.18, 0.21(2), 0.22, 0.26, 0.28 and 0.30 mg/kg. Five trials conducted at double rate gave residues in the same range.

The Meeting considered that residues in tomatoes from 31 foliar trials conducted in Europe and USA matching GAP belonged to the same population and could be combined. Residues found, in ranked order (median underlined) were: 0.05, 0.09(2), 0.10, 0.11 (4), 0.12, 0.13(3), 0.14 (2), 0.15, 0.16, 0.18 (2), 0.21(3), 0.22(2), 0.23, 0.26, 0.28, 0.29, 0.30, 0.34, 0.42 and 0.58 mg/kg.

In four field trials conducted with eggplant in France and Switzerland 3 applications were made at 0.30 to 0.36 kg ai/ha, residues found at a 3 day PHI were: 0.05, 0.14, 0.23 and 0.26 mg/kg.

The Meeting considered that the residues of cyromazine found in tomatoes and eggplant belonged to the same population and could be combined. Residues from the trials, in ranked order (median underlined) were: 0.05 (2), 0.09 (2), 0.10, 0.11(4), 0.12, 0.13(3), 0.14(3), 0.15, 0.16, 0.18 (2), 0.21(3), 0.22(2), 0.23(2), 0.26(2), 0.28, 0.29, 0.30, 0.34, 0.42 and 0.58 mg/kg.

In the USA cyromazine may be applied to peppers at up to 6 applications at a rate of 0.14 kg ai/ha with a PHI of 0 days. Data from 12 US trials on chilli and bell pepper in 1984/1985 did not comply with GAP as 12 applications were made at 0.14 or 0.28 kg ai/ha, residues found at 0 day ranged from 0.10 to 0.95 mg/kg. Although these trials were conducted with a higher number of applications, residues found at 0 days PHI were within the same range as residues found in tomato and eggplants. The Meeting decided that data from trials on tomato and eggplants, conducted according to GAP, supported the residues found in peppers.

Based on the residues found in tomato and eggplant, the Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.16 mg/kg and an HR of 0.58 mg/kg for cyromazine in fruiting vegetables, other than cucurbits, except sweet corn (on-the-cob) and mushrooms.

The Meeting recommends withdrawing the previous recommendations of 0.5 mg/kg for cyromazine in tomato and of 1 mg/kg for cyromazine in peppers.

Mushrooms

Spanish GAP allows cyromazine application to mushrooms at rates up to 0.75 g ai/m^2; Swiss GAP allows treatment at 1 g/m^2 to the casing layer or compost with a PHI of 14/15 days. In France, the application rate is 0.4 g/m^2 with a 14 day PHI. In the USA, cyromazine can be used as a coarse drenching spray at a maximum rate of 0.57 g ai/ m^2, with no specified PHI. Nine mushroom-house trials were conducted in France, Italy and Switzerland from 1986 to 2001 using 1 or 2 applications of cyromazine at 0.4 to 0.8 g ai/m^2. In four trials conducted according to French GAP, residues of cyromazine were 0.37, 1.3, 2.4 and 4.2 mg/kg. Samples collected at a higher PHI in three other trials giving residues of 0.75, 2.2 and 2.8 mg/kg were also considered for MRL estimation. Two trials

conducted at double rate gave residues in the same range. Residues considered for the estimation of an MRL and STMR level were: 0.37, 0.75, 1.3, 2.2, 2.4, 2.8 and 4.2 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg, an STMR of 2.2 mg/kg and an HR of 4.2 mg/kg for cyromazine in mushrooms.

The Meeting recommends withdrawing of the previous recommendations of 5 mg/kg for cyromazine in mushroom.

Lettuce

Cyromazine is approved for use on lettuce in a number of European countries. French and Italian GAP for field grown lettuce allows a maximum rate of 0.3 kg ai/ha with a PHI of 21 days and 14 days, respectively. In Spain and Switzerland, GAP comprises a maximum rate of 0.03 kg ai/hL or 0.3 kg ai/ha with a PHI of 7 days in the production of either field grown or protected lettuce. Between 1993 and 2002, 40 trials were conducted in Europe in head and leaf lettuce in both field and greenhouse situations using 3 applications at 0.19 to 0.30 kg ai/ha (0.03 to 0.1 kg ai/hL). These trials were evaluated against either the GAP of Italy (PHI of 14 days) or of Spain/Switzerland (PHI of 7 days).

In three field trials conducted in France in head lettuce complying with the Spanish GAP rate, residues at 14 days PHI were: < 0.03, 0.34 and 1.7 mg/kg. In four protected cropping trials (plastic tunnels), residues were: 2.2, 2.9, 3.0 and 4.9 mg/kg.

In 14 field trials conducted in France, Italy, Spain and Switzerland in Cos lettuce (leaf) complying with the Italian GAP rate, residues at 7 days PHI were: 0.15, 0.18, 0.19, 0.22, 0.24, 0.27, 0.28, 0.34, 0.45, 1.3, 1.5, 1.8(2) and 2.0 mg/kg. Residues in trials according to Spanish or Italian GAP with PHIs of 7 or 14 days in 17 protected trials were: 0.13, 0.55, 1.5, 2.4, 2.8, 3.3, 4.7, 5.2(2), 5.8(2), 6.2, 6.5, 7.9, 11, 14, 15 and 18 mg/kg.

On the basis of the European trials, the Meeting concluded that residues conducted with head and Cos lettuce using the same rate gave residues in the same range. Residues from 17 field trials conducted in lettuce in Europe in ranked order (median underlined), were: < 0.03, 0.15, 0.18, 0.19, 0.22, 0.24, 0.27, 0.28, 0.34(2), 0.45, 1.3, 1.5, 1.7, 1.8(2) and 2.0 mg/kg. Residues from 22 protected trials were: 0.13, 0.55, 1.5, 2.2, 2.4, 2.8, 2.9, 3.0, 3.3, 4.7, 4.9, 5.2(2), 5.8(2), 6.2, 6.5, 7.9, 11, 14, 15 and 18 mg/kg.

In the USA, GAP for leafy vegetables, including brassica leafy vegetables, is a maximum of 5 or 6 applications (6 for head lettuce 5 for all other leafy vegetables) at 0.14 kg ai/ha with a 7 days PHI. In nine trials conducted with head lettuce using 8 applications at 0.14 or 0.28 kg ai/ha rate, residues 7 days after the final application ranged from < 0.05 to 3.8 mg/kg. In nine field trials conducted with leaf lettuce using 5 applications at 0.14 kg ai/ha, residues at 7 days after the final application were: 0.58, 1.5, 1.6, 2.0, 2.8(2), 3.9, 4.4, 5.2 mg/kg.

The Meeting considered the field and protected cropping trials conducted in Europe and the field trials conducted in USA were from different populations and could not be combined. The Meeting considered that the 22 protected trials, conducted in Europe, reflected the most critical use in lettuce.

The Meeting estimated a maximum residue level of 25 mg/kg, an STMR of 2.8 mg/kg and an HR of 18 mg/kg for cyromazine in head lettuce and leaf lettuce.

The IESTI calculation indicates that the consumption of lettuce, at the HR level of 18 mg/kg coming from protected trials, would lead to an exceedance of the ARfD. Consequently, the Meeting used the prospective alternative GAP approach and selected the USA residue data for the maximum residue level estimation.

The Meeting estimated a maximum residue level of 10 mg/kg, an STMR of 2.8 mg/kg and an HR of 5.2 mg/kg for cyromazine in head lettuce and leaf lettuce.

The IESTI calculation indicates that the consumption of lettuce at the HR level of 5.2 mg/kg, coming from the USA field trials, would lead to an exceedance of the ARfD for children. The Meeting once again used the prospective alternative GAP approach and selected the EU residue data population, coming from field trials, for the recommendations.

The Meeting estimated a maximum residue level of 4 mg/kg, an STMR of 0.34 mg/kg and an HR of 2 mg/kg for cyromazine in head lettuce and leaf lettuce.

Mustard greens

Five trials were conducted in the USA according to the GAP for brassicas leafy vegetables (maximum of 5 applications at 0.14 kg ai/ha with a 7 days PHI). Residues in mustard greens (leaves) were: 1.1, 1.6, 2.7, 6.5 and 7.4 mg/kg.

The Meeting estimated a maximum residue level, an STMR value and an HR value for cyromazine in mustard greens of 10, 2.7 and 7.4 mg/kg.

Spinach

From 16 trials conducted with spinach in the USA, eight were conducted according to GAP for leafy vegetables. Residues at 7 days PHI were: 0.4, 1.1, 1.2, 1.8, 2.3, 4.2, 5.4 and 6.1 mg/kg. The Meeting estimated a maximum residue level of 10 mg/kg, an STMR value of 2.0 mg/kg and an HR value of 6.1 mg/kg for cyromazine in spinach.

The IEST calculation indicates that the consumption of spinach at the HR level of 6.1 mg/kg will lead to an exceedance of the ARfD, however no data was available for an alternative GAP review to estimate a lower maximum residue level.

Beans

US GAP allow 6 applications of cyromazine in lima bean and dry beans at a rate of 0.14 kg ai/ha with a PHI of 7 days. In nine trials conducted in lima beans complying with GAP from the USA, residues found in ranked order (median underlined), were: < 0.05, 0.11, 0.17, 0.19, 0.23(2), 0.32, 0.38 and 0.58 mg/kg. Trials conducted with 8 applications at 0.14 kg ai/ha or 6 applications at 0.28 kg ai/ha gave residues in the range of 0.23 to 1.0 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg, an STMR of 0.23 mg/kg and an HR of 0.58 mg/kg for cyromazine in lima beans.

In nine trials in dry beans from the USA complying with that countries GAP, residues found in ranked order (median underlined), were: 0.23, 0.68, 0.84, 0.97, 1.0, 1.1(2), 1.2 and 1.8 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg and an STMR of 1 mg/kg for cyromazine in beans (dry).

Potato

In Spain cyromazine may be applied to potatoes at a maximum rate of 0.24 kg ai/ha (0.02 kg ai/hL) with a PHI of 21 days. In Italy, field and greenhouse GAP consists of an application rate of 0.3 kg ai/ha with a PHI of 35 days. In eight potato trials conducted in Spain using 3 applications at 0.17 to 0.33 kg ai/ha with samples harvested at 21 or 35 days post application. Four trials could be evaluated against Spanish or Italian GAP, with residues of < 0.05, 0.06, 0.11, and 0.12 mg/kg.

The Meeting decided that there were insufficient trials submitted, complying with GAP, and did not estimate a maximum residue level.

Stalk and stem vegetables

In Spain, cyromazine can be used in artichoke at 0.03 kg ai/hL with a PHI of 7 days. In four Spanish trials conducted complying with that countries GAP, residues were: 0.85, 0.95, 1.1 and 1.3 mg/kg.

The Meeting estimated a maximum residue level of 3 mg/kg, an STMR of 1 mg/kg and an HR of 1.3 mg/kg for cyromazine in artichoke.

In France, cyromazine can be applied to celery in the field or in greenhouses at an application rate of 0.3 kg ai/ha with a PHI of 14 days. In 11 trials conducted in France and Spain from 1998 to 2003 using 3 or 4 applications at 0.3–0.36 kg ai/ha, residues, in ranked order (median underlined), were: 0.27(3), 0.36, 0.57, 0.58, 0.60, 0.68, 1.6, 1.8 and 2.3 mg/kg. The commodity description in the trials specified whole plant or stems and was interpreted by the Meeting as matching the Codex description for celery (whole commodity).

Fourteen trials were conducted in the USA in celery at a greater than GAP application frequency (maximum of 6 applications at 0.14 kg ai/ha with a 7 days PHI). Residues 7 days after the last application ranged from 0.05 to 13 mg/kg.

Based on the European trials, the Meeting estimated a maximum residue level of 4 mg/kg, an STMR value of 0.58 mg/kg and an HR value of 2.3 mg/kg for cyromazine in celery.

Fate of residues in processing

Hydrolysis studies representing food processing procedures of pasteurization, baking, boiling, brewing and sterilization were conducted with [^{14}C]cyromazine in buffer solution at pH 4, 5 and 6, incubated for 20 or 60 minutes at 90–120 ˚C, showed that cyromazine was the only compound found at the end of the incubation period.

In a tomato processing study in the USA, tomatoes were harvested 7 days after the last of 6 applications at 0.140 or 0.250 kg ai/ha. Treated samples were pooled and subject to treatment simulating normal commercial processing. Residues decreased after washing, in canned tomato, tomato juice and in ketchup, with mean processing factors (PF) of 0.71, 0.53, 0.75 and 0.84. Residues in wet pomace remained unchanged, but increased in dry pomace (PF=2.8), puree (PF=1.2) and paste (PF=2.1).

Based on the estimated PFs and STMR for tomato of 0.16 mg/kg, the Meeting estimated an STMR-P of 0.11 mg/kg for washed tomato, 0.09 mg/kg for canned tomato, 0.12 for tomato juice, 0.13 mg/kg for ketchup, 0.19 mg/kg for puree and 0.34 mg/kg for tomato paste.

In one study conducted with potatoes, samples from six trials conducted in USA in 1996 were processed according to commercial practices. Mean cyromazine residues in the raw potato was 0.71 mg/kg, which decreased in peeled/rinsed potatoes with a mean PF of 0.9, but increased in potato chips (PF=1.3) and potato granules (PF=2.8). As no recommendation was made for the raw commodity potato, the Meeting did not make a recommendation for processed potato products.

Residues in animal commodities

Direct treatment of poultry (in-feed use)

In four feeding trials, conducted in Australia, hens were fed at rates of 1.5 mg ai/kg for 35 days, 3 mg ai/kg for 4 days, 5 mg ai/kg for 7 days and 9 mg ai/kg for 4 days, samples were taken of muscle, liver and/or eggs. Muscle and liver samples from hens, treated at the GAP rate of 5 mg ai/kg feed, were taken immediately after treatment and up to 2 days post-treatment. Cyromazine residues in muscle were found to decrease from 0.03 to < 0.02 mg/kg in muscle and from 0.12 to < 0.05 mg/kg in liver.

In two trials conducted in France in 1985/1986, hens were fed cyromazine at 5 mg ai/kg feed for up to 38 days. Residues in eggs (egg white/yolk) sampled from 0 to 22 days, following 15 to 38

days of feeding were: 0.15/0.16, 0.15/0.11, 0.12/0.05, 0.08/0.11, 0.12/0.05, 0.04/0.08, 0.08/0.06, 0.08/0.04, < 0.02/0.04, < 0.02/0.03(3) and < 0.02/0.02(9) mg/kg. As the egg white comprises approximately 66% and the yolk 33% of a typical poultry egg, the levels found in egg white/yolk can be expressed on a whole egg basis, in ranked order, as: < 0.02(12), 0.04, 0.05, 0.07(2), 0.09, 0.10(2), 0.14 and 0.15 mg/kg.

In a trial conducted in Israel in 1987, hens were fed cyromazine at 5 and 50 mg/kg feed for 31 days with the animals sacrificed 4 h after removal of the feed. Residues of cyromazine in muscle and liver ranged from 0.04 to 0.10 mg/kg at the 5 mg/kg treatment level and from 0.36 to 0.76 mg/kg at the higher feeding level. Eggs were not analysed.

In a study conducted in the Philippines in 1982 hens were fed for 60 days, at a rate of 1.6 mg ai/kg of feed, no residues were detected in muscle (< 0.025 mg/kg) and liver (< 0.04 mg/kg) in animals slaughtered 2 to 9 days after cessation of feeding. Residues in eggs collected from animals fed cyromazine from 29 to 60 days, 0 to 9 days after feeding ceased were 0.02, < 0.02 and 0.04 mg/kg.

In ten studies conducted in the USA from 1979 to 1986, hens were fed cyromazine for up to 56 days at levels of 2.5, 5.0, 25 and 50 mg ai/kg of feed. In one trial where hens were fed cyromazine at 5 mg/kg from 14 to 27 days, residues in egg white/yolk at day 0 were: 0.09/0.08, 0.11/0.06 and 0.11/0.07 mg/kg, or 0.09 (2) and 0.10 mg/kg in the whole egg. In three trials conducted at 5.0 mg ai/kg feed, egg samples were collected 0 to 7 days after feeding from animals fed 14 to 56 days. Residues in eggs in ranked order, were: < 0.05(4), 0.11(2), 0.07, 0.09(3), 0.10(7), 0.12(4) and 0.16 mg/kg. In one feeding study conducted at a 2.5 mg/kg feeding level for 14 days, residues at 0 days were < 0.05 mg/kg in muscle, skin and fat and 0.08 mg/kg in liver. The levels found after the animals had been fed for 27 days were 0.05 mg/kg in meat and < 0.05 mg/kg in the other tissues. In all cases, residues in fat were < 0.05 mg/kg.

In one study conducted in Japan in 2000, hens were fed cyromazine for 28 days at the level of 5 mg ai/kg. Residues in egg white/yolk collected from 0 to 2 days after treatment were < 0.02/0.03, < 0.02/0.05 and 0.04/0.07 mg/kg, or < 0.02, 0.04 and 0.05 mg/kg expressed on a whole egg basis. Residues at 0 day were 0.05 mg/kg in muscle, 0.07 mg/kg in liver and 0.09 mg/kg in kidney. Cyromazine levels in all tissues after 1 to 3 days were < 0.02 mg/kg.

In summary, residues of cyromazine in eggs from trials conducted according to GAP were: < 0.02 (13), 0.02, 0.04 (3), < 0.05 (4), 0.05 (2), 0.07(3), 0.09 (4), 0.10(9), 0.11(2), 0.12(4), 0.14, 0.15 and 0.16 mg/kg. Residues at 0 day at 2.5 mg/kg level were < 0.05 and 0.05 mg/kg in muscle, < 0.05 and 0.08 mg/kg in liver and < 0.05 mg/kg in fat.

Lactating dairy cows

In two feeding studies conducted in the USA in 1983 and 1992, Holstein dairy cows were dosed at 5.0, 10, 25, 50 or 100 mg ai/kg diet for up to 28 days. Animals were sacrificed on test days 14, 21 and 28 with tissue samples taken. Milk samples consisted of pooled aliquots from the evening and the following morning's milk. Residues in milk plateaued rapidly on the commencement of dosing with the mean levels, after 28 days treatment, increasing proportionally with the dose, ranging from 0.02 mg/kg at the 5 mg/kg to 0.42 mg/kg at the 100 mg/kg level. In one study, the highest residues in tissues, at the lower dose, were found in the animals sacrificed following 14 days of feeding with 0.13 mg/kg in kidney and 0.12 mg/kg in meat; these levels increased to 1.9 and 0.59 mg/kg, respectively in the animals dosed at 50 mg/kg. In the second study, no residues (< 0.05 mg/kg) were found in tissues from animals dosed at 10 mg/kg level. No residues were found in fat samples from any animal at any dosing level in either study.

Livestock Dietary burden

Dietary burden calculations for beef and dairy cattle and broilers and laying poultry are provided in Annex 6. The calculations were made according to the animal diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report). A summary of the results are shown on the Table below.

Animal (feed items)	Livestock dietary burden, cyromazine, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	0.31	0.17	8.54	0.57	1.02	0.57
Dairy cattle	0.31	0.17	8.54	0.57	0.31	0.17
Poultry - broiler and layer	0.41	0.06	2.4	0.14	1.4	0.21

Residues in animal commodities

The high and the mean estimated dietary burden for cattle were 8.5 and 0.57 ppm. The estimations were done by interpolation of residues at the 5 ppm feeding level.

Dietary burden (mg/kg)[1] Feeding level [ppm][2]		Cyromazine residues, mg/kg[3]				
		Milk Mean	Muscle High	Liver High	Kidney High	Fat High
MRL cattle beef and dairy	(8.5) [5] high		*(0.204)* 0.12	*(0.153)* 0.09	*(0.221)* 0.13	*(< 0.05)* 0
STMR cattle beef and dairy	(0.57) [5] av		*(0.01)* 0.06	*(0.01)* 0.06	*(0.01)* 0.08	*(< 0.05)* *0*
STMR cattle beef and dairy	0.57) [5] av	*(0.005)* 0.045				

[1] Values in parentheses are the estimated dietary burdens

[2] Values in square brackets are the actual feeding levels in the transfer study

[3] Residue values in parentheses in italics are interpolated from the dietary burden, feeding levels in the transfer study and the residues found in the transfer study. High is the highest individual animal tissue residue in the relevant feeding group. Mean is mean animal tissue (or milk) residue in the relevant feeding group.

The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.01 and an HR of 0.20 mg/kg for cyromazine in meat (from mammals other than marine mammals).

The Meeting estimated a maximum residue level of 0.3 mg/kg, an STMR of 0.01 and an HR of 0.187 mg/kg for cyromazine in edible offal (mammalian).

The Meeting estimated a maximum residue level of 0.01 mg/kg and an STMR of 0.005 mg/kg for cyromazine in milks. The Meeting also estimated a median and a highest residue level of 0 mg/kg in mammalian fat.

The high and the mean estimated dietary burden for poultry were 2.4 and 0.14 ppm. The direct treatment for poultry (in-feed use) conducted at 2.5 mg/kg feeding level can be used for estimating residues in poultry tissues.

The Meeting estimated a maximum residue level of 0.1 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.05 mg/kg for cyromazine in poultry meat.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.065 mg/kg and an HR of 0.08 mg/kg for cyromazine in poultry edible offal. The Meeting also estimated a median and a highest residue level of 0 mg/kg in poultry fat.

The Meeting agreed that for the residue estimation in eggs, the residues coming from the direct use of cyromazine in the feed at 5 mg/kg level, according to GAP (0 day withholding period) represents a better estimation of the likely residues.

The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.07 mg/kg and an HR of 0.16 mg/kg for cyromazine in eggs.

The Meeting recommends the withdrawal of the current recommendation of 0.2* mg/kg for cyromazine in eggs, of 0.01* mg/kg in milks, and of 0.05* mg/kg in poultry meat and sheep meat.

DIETARY RISK ASSESSMENT

Long-term intake

The ADI for cyromazine is 0-0.06 mg/kg bw. The International Estimated Daily Intakes (IEDI) for cyromazine was estimated for the 13 GEMS/Food cluster diets using the STMR or STMR-P values estimated by the current Meeting for 35 commodities. The results are shown in Annex 3. The IEDI ranged from 0–2% of the maximum ADI. The Meeting concluded that the long-term intake of residues of cyromazine from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for cyromazine is 0.1 mg/kg bw. The International Estimated Short Term Intake (IESTI) for cyromazine was calculated for the plant commodities for which STMRs and HRs were estimated and for which consumption data were available. The results are shown in Annex 4. For the general population, the IESTI was higher than the ARfD for cabbage (120%) and spinach (130% ARfD). For children, the IESTI was higher than the ARfD for cabbage (280%) and spinach (390%). For all the other commodities, the intakes ranged from 0–40%.

The Meeting concluded that the short-term intake of residues of cyromazine from uses other than cabbage and spinach that had been considered by the JMPR is unlikely to present a public concern. The information provided to the JMPR precludes an estimate that the short-term intake of residues of cyromazine from the consumption of cabbage and spinach will be below the ARfD.

The ARfD established by the Meeting in 2006 was based on body-weight loss and decrease in food consumption in dams in developmental toxicity studies. The reason for these effects was unknown and there is a rapid recovery on cessation of administration. The Meeting noted that this ARfD may be conservative. Furthermore, it is possible that the short-term risk assessment conducted by the Meeting may also be conservative.

The Meeting noted that no residue data was available from an alternative GAP to estimate a lower maximum residue level for cyromazine in cabbage and spinach.