DIAZINON (022)

EXPLANATION

Diazinon was first evaluated by the 1965 JMPR and has been reviewed several times since. In 1993 a periodic review was conducted and in 1994 a new MRL was recommended for hops. The 1993 JMPR recommended, among other items, an increase in the CXL for pome fruits from 0.5 to 2 mg/kg and the withdrawal of the CXLs for animal commodities in the absence of animal transfer studies and data from uses as an ectoparasiticide.

The CCPR in 1995 and 1996 endorsed most of the recommendations of the 1993 JMPR with the exception of the proposed MRL for pome fruits and the recommended withdrawal of the CXLs for milks and the meat of cattle, pigs and sheep. The CXLs for animal commodities were retained pending review by the 1996 JMPR of data on new animal feeding trials to be submitted by Australia and the manufacturer. The 1993 proposal for pome fruit was held at step 7C by the 1996 CCPR, mainly owing to concern at the potentially high dietary intake from this source.

The Meeting received (1) data on residues and information on GAP for uses of diazinon as an ectoparasiticide, together with animal transfer studies, from the manufacturer (2) summarized data on residues in pome fruit, plums and carrots from Germany (3) monitoring data and information on GAP and national MRLs from Poland (4) information on GAP for mushrooms in the UK and (5) an Australian submission on residues of diazinon in cattle resulting from ectoparasite control. Summary data on residues and information on GAP for the use of diazinon on rice in Thailand were also received. Summary data were not considered to be an adequate basis for estimating maximum residue levels.

Formulations

EC and WP formulations for crop protection were mentioned in the 1993 Evaluations. EC and WP formulations are also available for the treatment of animals for ectoparasites. The most important, and used in the ectoparasite control trials, were a 250 EC with the formulation code A-7182 (250 g ai/l, trade name Neocidol, a 600 EC with the formulation code A-3695 J (600 g ai/l, trade name Neocidol) and to a lesser extent a 60 EC with the formulation code A-139F (60% w/w, trade name Top Clip Gold Shield). The compositions of these formulations were available to the Meeting. When these three were applied as a spray to sheep at the same nominal (recommended) rate of 600 ppm no differences were found in the resulting residues in blood or fat (Morrison, 1994).

Other code numbers used for diazinon include G 24′480, CGA 31′331, OMS 469 and GNT 19507. Other trade names of formulations for animal health uses include Dimpygal, Nucidol, Sarnicida-Garrapaticida, Vetsarol, Clik, Spike, Protector and Kacador, and for other uses Banosan, Antigal, Galton, Gal-Wash, Galesan, Paragal and Eureka.

METABOLISM AND ENVIRONMENTAL FATE

The fate of diazinon in animals, plants and soil was described in the 1993 JMPR periodic review or in earlier JMPR evaluations, and only those studies not previously reviewed by the FAO Panel or details of which are needed to facilitate the review and understanding of the studies on animal transfer and ectoparasite control will be described in detail.

Animal metabolism

The fate of diazinon in rats, mice, guinea pigs, dogs, goats, sheep, cows and plants was described in the 1993 periodic review and a diagram of the proposed metabolic pathways was presented. Some of these studies were provided to the WHO Expert Group but not to the FAO Panel. For example, the 1993 Expert Group reviewed several animal disposition or metabolism studies which apparently were not provided to either the 1993 or the present FAO Panel. These included a cow metabolism study (Robins *et al*., 1957) the disposition of residues in goats (Simoneaux, 1988a) and chickens Simoneaux, 1988b), the identification of metabolites in hens and goats (Simoneaux *et al*., 1988), a supplementary report on metabolism in hens (Simoneaux *et al*., 1989), and the characterization of diazinon metabolites in chickens (Simoneaux, 1988c). Some studies reviewed by the 1993 JMPR were re-submitted to the present Meeting.

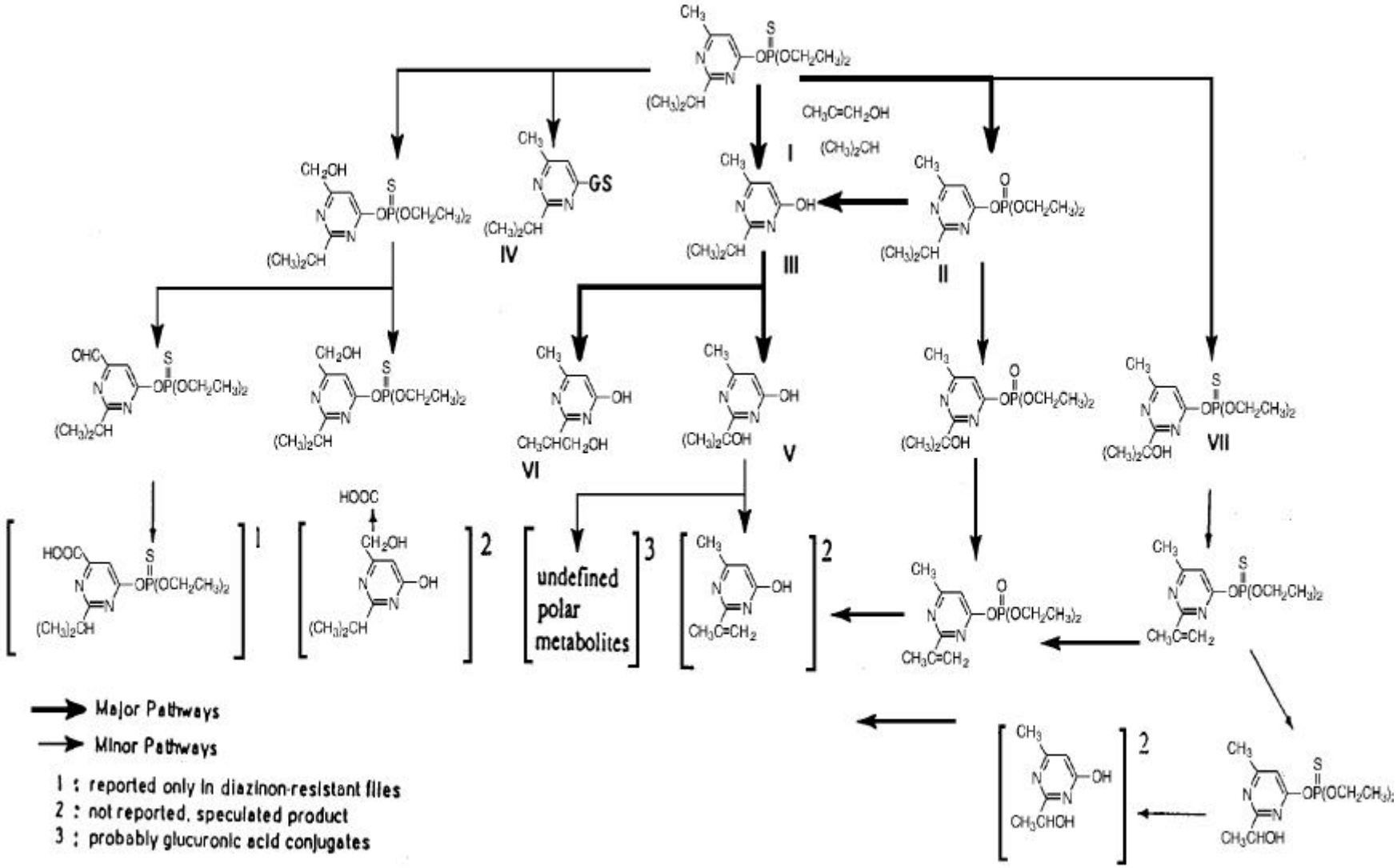
In mammals

In general terms, diazinon was reported in the 1993 Evaluations (Parts I and II) to be almost completely absorbed from the intestinal tract and easily absorbed dermally. Elimination was reported to be rapid in the urine and faeces, mainly the urine. In mammals metabolism was reported to progress primarily via hydrolysis of the ester linkage, yielding 4-hydroxy-2-isopropyl-6-methylpyrimidine (metabolite B1 or G-27550) followed by oxidation of the isopropyl group to give primary and tertiary alcohols, of which the latter may become conjugated. Another primary route is oxidation to diazoxon which may be hydrolysed to B1 or oxidized at the isopropyl group before hydrolysis. Other less important routes include oxidation of the methyl group. Ring cleavage was not reported in rats.

Unchanged diazinon was not a major residue in tissues although low residues of diazinon and diazoxon were reported, especially in fat. Because of the importance of these metabolic routes to the focus of this evaluation on residues in animal products, the proposed metabolic route in mammals presented in the 1993 Evaluations is repeated, slightly modified and expanded, as Figure 1.

In an early study on sheep dosed by stomach tube at 1 g/kg, three cholinesterase-inhibiting metabolites were identified in the urine and fat (Janes *et al.*, 1973). These were hydroxydiazinon (VII in Figure 1), its isomer formed by hydroxylation of the ring methyl group, and dehydro-diazinon, shown in Figure 1 as formed by dehydration of VII. This study was concerned with cholinesterase-inhibiting metabolites, but later studies on metabolism in mammals produced for food have focused on the major routes of metabolism irrespective of cholinesterase inhibition.

Figure 1. Proposed metabolic pathways of diazinon in mammals.



A more recent study (Simoneaux, 1988) was reviewed by the 1993 JMPR (Evaluations Part II - Toxicology). A more detailed description follows. Tissues and milk were analysed after dosing goats by capsule for four consecutive days with [^{14}C]diazinon at a rate equivalent to 100 ppm in the diet. TLC analysis showed that 94% of the radioactivity was extracted from milk. At least 94% of the total ^{14}C was generally extractable from the tissues, but only 79% from liver. Over 80% of the extractable ^{14}C was in the organic phase except that from liver (58%) and kidney (68%). Table 1 indicates the identity and distribution of the residues.

Table 1. Distribution of ^{14}C in tissues and milk of goats dosed for 4 consecutive days with [^{14}C]diazinon at a rate equivalent to 100 ppm in the diet (Simoneaux, 1988).

Sample & total ^{14}C expressed as diazinon	% of organoextractable ^{14}C present as				
	diazinon	diazoxon	hydroxydiazinon	hydroxypyrimidine	Metab. 31144*
Liver 1.6 mg/kg	0.2	0.3	0.2	19.2	19
Kidney 3.0 mg/kg	<0.1	0.3	<0.1	19.8	30.6
Omental fat 0.4 mg/kg	67.8	4.1	12.8	9.3	6.8
Perirenal fat 0.4 mg/kg	64	0.8	12.3	4.3	4.2
Tenderloin 0.4 mg/kg	6.2	1.0	1.4	26	39.4
Leg muscle 0.5 mg/kg	1.6	<0.1	0.4	35.3	40.4
Milk (day 4) 0.7 mg/kg	0.2	0.2	0.1	39.3	37.3

* Metabolite GS-31144 = hydroxy derivative of hydroxypyrimidine
(-OH on tertiary isopropyl carbon, see Figure 1).

The 1993 JMPR also reviewed a study in which residues in tissues were characterized or identified after the dermal treatment of sheep with [^{14}C]diazinon (Capps and Sumner, 1990). The sheep were treated daily for three days with an acetone solution of [^{14}C]diazinon at 40 mg/kg bw approximating the maximum drench treatment, applied to a shaved area of *c*.10% of the back. The sheep were slaughtered 6 hours after the last treatment and tissues were analysed by TLC and HPLC. Over 90% of the ^{14}C was extracted from all the tissues. The distribution of the residues as determined by HPLC is shown in Table 2. Results were similar by TLC for all samples except muscle, which was not analysed by TLC.

Table 2. Distribution of ^{14}C residues in sheep tissues after dermal treatment for three days with 40 mg/kg bw [^{14}C]diazinon as determined by HPLC (Capps and Sumner, 1990)

Sample & total ^{14}C expressed as diazinon[1]	% of organoextractable ^{14}C present as[2]				
	diazinon	Conj. of 3114 and hydroxypyrimidine[3]	Unknown polar compounds	hydroxy-pyrimidine	Metab. 3114*
Liver 4.4 mg/kg	3.7	13.8	10.9	41.4	18
Kidney 9.4 mg/kg	6.2	8.6	28	24.5	22.6
Back fat 7.3 mg/kg	85.2	--	--	1.6	--
Heart 4.4 mg/kg	55.9	--	--	16.4	12
Leg muscle 4.0 mg/kg	59.2	--	--	23.2	13

* Metabolite GS-31144 = hydroxy derivative of hydroxypyrimidine (-OH on isopropyl tertiary carbon, see Figure 1).
[1] Average of sheep 1 & 2
[2] Fat, heart and leg muscle from sheep 1. Kidney and liver average of sheep 1 & 2
[3] Identified as HPLC "region B", mainly conjugates of GS-3114 and hydroxypyrimidine.

In poultry

Poultry feeding (transfer) studies were provided to the Meeting, but poultry metabolism had not been reviewed by the FAO Panel in the 1993 periodic review. Studies of poultry metabolism were therefore provided on request to the present Meeting (Simoneaux, 1988c, 1989; Simoneaux *et al*., 1988, 1989).

Simoneaux (1988c) dosed 4 Leghorn hens with [^{14}C]diazinon by capsule for 7 consecutive days at a rate equivalent to 25 ppm in the diet. Residues were characterized in the excreta, eggs and tissues. More than 78% of the dose was excreted. Simoneaux *et al*. (1988) identified metabolites in goat urine in order to correlate the findings with residues found in the tissues of goats and hens. The identification of G-27550 and GS-31144 by GC-MS and LC-MS after the acid or enzymatic hydrolysis of aqueous fractions gave evidence of their conjugation.

Simoneaux (1989) and Simoneaux *et al*. (1989) provided further clarification of hen metabolism, and demonstrated improved extraction of residues and further identification of metabolites after the treatment of samples with protease. The results of analyses of eggs (day 7) and hen tissues by Simoneaux *et al*. (1989) are summarized in Tables 3-5.

diazinon

Table 3. Distribution and extractability of ^{14}C in eggs and tissues before and after treatment with protease (Simoneaux *et al*., 1989).

Sample	^{14}C		Extractable ^{14}C[1] as % of total		% of extractable ^{14}C in	
	mg/kg as diazinon	% of dose	Before protease	After protease	Organic phase[2]	Aqueous phase
Egg yolk	0.07	<0.01	67	88	88	12
Egg white	0.07	0.01	98		87	13
Liver	0.11	0.02	63	82	49	51
Kidney	0.15	0.01	76	98	48	52
Lean meat	0.03	0.05	64	94	49	51
Skin fat	0.02	0.01	44	100	61	39
Peritoneal fat	0.01	0.01	31	100	62	38

[1]Extracted with 9:1 methanol/water
[2]Methanol/water extract was concentrated and partitioned with hexane

Table 4. Characterization of organo-extractable ^{14}C in 7-day egg yolks and whites by TLC (Simoneaux *et al*., 1989).

Residue	Egg yolks		Egg whites	
	% of ^{14}C in yolk	mg/kg as diazinon	% of ^{14}C in white	mg/kg as diazinon
Diazinon	0.02	<0.001	0.03	<0.001
Hydroxydiazinon (CGA-14128)	0.06	<0.001	0.05	<0.001
Diazoxon (G-24576)	0.42	<0.001	1.3	<0.001
Pyrimidinol metabolite (G-27550)	11.1	0.007	9.4	0.006
Unknown[1]	2.9	0.002	--	--
Hydroxy derivative of G-27550 (GS-31144)[2]	18.6	0.012	33.3	0.022
Metabolite M3[3] + glucuronide & other conjugates	25	0.016	41.3	0.027

[1] Unresolved GS-31144 and G-27550 suspected
[2] 4-hydroxy-2-(1-hydroxy-1-methylethyl)-6-methylpyrimidine (Figure 1, structure V).
[3] 4-hydroxy-2-(2-hydroxy-1-methylethyl)-6-methylpyrimidine (Figure 1, structure VI).

Similar residues were identified by TLC in organic extracts of poultry tissues (Table 5).

Table 5. Distribution of residues in poultry tissues determined by TLC (Simoneaux *et al.*, 1989).

Residue	% of ^{14}C in sample/residue, mg/kg as diazinon				
	Liver	Kidney	Skin	Lean meat	Peritoneal fat
31144	3.5/0.004	3.7/0.006	4.2/0.001	6.5/0.002	3.1/0.001
27550	0.6/<0.001	2.3/0.003	2.6/<0.001	2/<0.001	0.7/<0.001
diazoxon	0.9/0.001	0.18/<0.001	1.3/<0.001	0.24/<0.001	0.77/<0.001
Unknown[1]	-----	-----	-----	-----	1/<0.001
Unknown[2]	-----	-----	6.3/0.001	-----	-----
hydroxydiazinon	<0.01/<0.001	0.11/<0.001	0.02/<0.001	<0.03/<0.001	1.4/<0.001
diazinon	0.03/<0.001	<0.08<0.001	<0.89/<0.001	<0.0.04/<0.001	2/<0.001
Metabolite M3	2/0.002	5.7/0.008	2.3/<0.001	----	-----
Glucuronide & other conjugates	23.5/0.026	24.6/0.04	9.7/0.002	----	-----
Metab. M3 + glucuronide & other conjugates	-----	-----	-----	22.4/0.006	9.7/0.001

[1] Unresolved CGA-14128 suspected
[2] Unresolved GS-31144 and G-27550 suspected

Plant metabolism

The fate of diazinon in plants was described in the 1993 periodic review and a diagram of the proposed metabolic pathways was presented. The metabolic route in plants is summarized briefly here for convenience. Metabolism in plants progresses, as in animals, primarily by hydrolysis of the ester linkage, yielding metabolite B1 (G-27550), followed by oxidation of the isopropyl group to primary and tertiary alcohols and/or oxidation of the methyl group to the alcohol. Glucose or malonylglucose conjugates are formed from the alcohols. Diazoxon was not reported as a significant plant metabolite although low levels were found in mammals.

The major residues reported in various crops in the 1993 evaluation in decreasing order for each crop are were as follows.

Apple	Beans	Maize forage	Lettuce	Potato foliage[1]
diazinon/ G-27550	G-27550 GS-31144 JAK-III-57[2] diazinon	G-27550 JAK-III-57 GS-31144 diazinon	diazinon GS-31144 GS-31144	G-27550 (CL-XIX-29[3]/ conjugate) JAK-III-57 GS-31144 G-27550 diazinon

[1]Diazinon is extensively metabolized in the tuber
[2]G-27550 with the methyl group oxidized to the alcohol, see 1993 evaluation, Figure 2
[3]G-27550 oxidized on the primary carbon of the isopropyl, see 1993 evaluation, Figure 2

Environmental fate in soil

This is described in the 1993 JMPR evaluations.

Environmental fate in water/sediment systems

No information was provided either to the 1993 or the present Meeting.

METHODS OF RESIDUE ANALYSIS

Analytical methods

The 1993 JMPR monograph describes methods which have been used for the residue analysis of samples from crops and animals. The methods summarized in the 1993 monograph and those submitted to the present Meeting are tabulated below. References are given in the text.

Method	Year	Limit of determination, mg/kg	Detector	Substrates
1993 JMPR				
REM 7a/73	1973	0.02	FID	Apple, lettuce, bean leaves
REM 15/82	1982	0.02	NP	Cherry, lettuce, cocoa seed
REM 119.01	1989	0.01	EC or NP	Kiwifruit, maize (whole plant)
AG-550A	1990	0.01-0.02[1] diazinon, diazoxon	FPD	(21 crops, almonds, corn oil, animal tissues
		0.02[1] hydroxydiazinon		
		0.05 ditto		Hops
	Generally 0.02 mg/kg may be a more practical limit of determination for diazinon and metabolites in animal products via AG-550A, although 0.01 mg/kg may be attainable in some cases.			
1996 JMPR				
Method 113	Undated	0.02	Thermionic	Sheep tissues and fat
Method 29/73	1973	0.02-0.05[1]	AFID	Meat and milk
Method 4/74	1974	0.02[1] diazinon	FPD	Animal tissues
		0.05[1] hydroxydiazinon		
		0.2[1] G-27550		
REM 21/86	1987	0.02[1]	NPD	Muscle, liver, kidney, fat
Netherlands Official Methods	1988	0.01-0.05	NPD	Crops
		0.01-0.04		Meat, tissues
		0.001-0.01		Milk
REM 128.02	1991	0.02[1]	NPD	Milk

Method	Year	Limit of determination, mg/kg	Detector	Substrates
Method 132A	1994	0.01	NPD-thermionic	Milk
Method 132B	1992	0.01-0.02[1]	N-P	Butter
Method 135	1994	0.01	thermionic	Muscle, liver, fat

[1] Estimate by the present Meeting (often twice the reported value). In all other cases the reported value could not be confirmed with information provided. LODs apply to diazinon unless otherwise indicated.

Method AG-550A, which has been used extensively for animal products, is discussed below. Other methods summarized by the 1993 JMPR will not be described again.

Method AG-550A (Hubbard *et al.*, 1990) involves extraction of crops and various animal tissues and milk with acetone/water, partitioning into petroleum ether/methylene chloride, concentration, dissolution in acetone and GLC with a flame-photometric detector. It was tested on 21 crops. Some variation is provided for selected samples. For hops the solvent is evaporated and the residue dissolved in hexane and partitioned into acetonitrile before evaporation of the acetonitrile and transfer to acetone for analysis. Corn oil is extracted directly with acetonitrile which is similarly evaporated and the residue transferred to acetone. Beef fat is extracted with hexane before partitioning into acetonitrile, otherwise its treatment is similar to corn oil. An alternative mini-Florisil column clean-up is provided to remove material which interferes with GLC.

Method AG-550A was used in most of the US trials. More importantly, it was the method used in the animal transfer studies reviewed here, in which it was used to determine diazoxon and hydroxydiazinon as well as diazinon. Generally a limit of determination of 0.01 mg/kg (0.05 mg/kg in hops) is reported to be achievable for diazinon and the metabolites with use the preferred capillary columns, and 0.025 mg/kg for diazinon and 0.05 mg/kg for the metabolites with packed columns.

The validations and sample chromatograms provided were generally consistent with the estimated limits of determination, with analytical recoveries generally ≥96% for all three compounds in meat, eggs, fat and milk at a fortification level of 0.01 mg/kg. The exception was 68% for the determination of diazoxon in beef liver. Recoveries were similar in the transfer studies, but again a little lower in liver and kidney. The method was also validated (Hubbard, 1990) for crops and animal tissues with [^{14}C]diazinon in fortified samples and in goat tissues from animal metabolism studies.

Representative chromatograms in the animal transfer study by Selman (1994a) also suggest that 0.01 mg/kg of all three compounds can probably be determined in milk and tissues, although the results were not as convincing with kidney and fat, especially for hydroxydiazinon for which 0.02 mg/kg would appear to be a more reasonable limit of determination. Also on the basis of sample chromatograms in poultry transfer studies (Selman, 1993) 0.02 mg/kg may be a more practical limit of determination, especially for hydroxydiazinon. Measurement with confidence at 0.01 mg/kg may be possible, however, at least for fat and eggs.

Method 113 (Anon., undated) determines diazinon in the fat and tissues of sheep and is based on extraction with hexane, sweep co-distillation and determination by GLC and a thermionic detector. A "method sensitivity" of 0.02 mg/kg was reported, but no information on validation or sample chromatograms were provided.

REM 29/73 (Formica, 1973) for diazinon involves extraction of meat with methanol and milk with acetone, partitioning into chloroform, clean-up on an alumina column and determination by GLC with either flame-photometric or alkali flame-ionisation detectors. The reported limit of detection was 0.01 mg/kg in meat and milk. Recoveries were ≥94% at fortification levels of 0.03 mg/kg in milk and 0.05 mg/kg in meat. Because sample chromatograms of controls showed no really quantifiable residues and since the method was not validated below 0.03 or 0.05 mg/kg, a limit of determination of 0.02-0.05 mg/kg should be achievable.

REM 4/74 (Formica, 1974) was developed for the determination of diazinon, diazoxon, hydroxydiazinon and 4-hydroxy-2-isopropyl-6-methylpyrimidine (G 27550) in animal tissues. For the determination of diazinon, hydroxydiazinon and G 27550, the tissues are macerated or extracted with methanol, the extract is diluted with 1 N HCl and diazinon and hydroxydiazinon are extracted with chloroform. G 27550 is likewise extracted with chloroform after neutralization of the HCl. Diazinon and hydroxydiazinon are cleaned up on an alumina column (or by TLC) before GLC analysis with an FPD. G 27550 is determined with a nitrogen-selective electrolytic conductivity detector. Diazoxon is determined by cholinesterase inhibition, but as this is not a currently acceptable method it will not be further described.

The lowest levels at which analytical recoveries were measured were 0.1 mg/kg of diazinon and hydroxydiazinon and 0.2 mg/kg of G 27550, at which levels recoveries were generally ≥75% from sheep muscle, liver and fat and sow kidney and liver, but only 62% of G 27550 from sheep fat. The limits of detection of diazinon and hydroxydiazinon were reported as 0.01 and 0.02 mg/kg respectively. For G 27550 an interfering GLC peak resulted in a reported limit of detection of 0.1 mg/kg. From sample chromatograms and the validation levels, reasonable limits of determination in muscle would appear to be about 0.02 mg/kg for diazinon, 0.05 mg/kg for hydroxydiazinon and 0.2 mg/kg for G 27550. In the absence of sample chromatograms, the Meeting could make no estimates for other tissues.

In REM 21/86 (Netherlands, 1988) diazinon is extracted from homogenized muscle, liver or kidney with methanol, partitioned into hexane, and cleaned up on a phenyl-coated solid-phase extraction column. Heated fat is extracted with acetonitrile, the extract partitioned with hexane for clean-up, and the acetonitrile rotary-evaporated. The extract is taken up into hexane and cleaned up on a cyano-coated solid-phase extraction column. Determination is by GLC with an NP detector.

Analytical recoveries were ≥85% at a fortification level of 0.02 mg/kg from liver, kidney and fat. The limit of determination was reported to be 0.01 mg/kg. Sample chromatograms suggest that 0.02 mg/kg may be a more practical limit for sheep muscle and fat. Sample chromatograms were not provided for liver or kidney, so the Meeting could not estimate LODs for them.

The Netherlands Official multi-residue GLC Sub-method 1 (1988) for diazinon in fruits and vegetables involves extraction with ethyl acetate and analysis by GLC with a phosphorus-specific detector without further clean-up. For crops recoveries of 80% (fortification level unspecified) and limits of determination of 0.01-0.05 mg/kg are reported. In Sub-method 2 for the determination of diazinon in animal tissues extraction with acetone/acetonitrile is followed by evaporation, partitioning into acetonitrile from hexane and determination by GLC with an NPD. Recoveries of 66-102% and limits of determination of 0.01-0.04 mg/kg are reported. In Sub-method 3 for diazinon in milk, extraction with ethyl acetate is followed by evaporation, dissolution in hexane, partitioning with acetonitrile, evaporation, solution in ethyl acetate and analysis by GLC with a phosphorus-specific detector. Recoveries of 75-100% and limits of determination of 0.001 to 0.01 mg/l are reported. Recoveries and limits of determination were not included in the submission to the JMPR.

REM 128.02 (1991) was developed for the determination of diazinon in blood and milk. The method for milk is based on Method AG-550A, but the initial acetone/water extract is cleaned up on a C-18 solid-phase cartridge before GLC determination with an NPD. The "lower practical level" for milk by this method was reported as 0.008 mg/kg. At the lowest fortification level of 0.02 mg/kg the average recovery from milk was 104%. A sample chromatogram in the report suggested a general practical limit of determination of 0.02 mg/kg, although 0.01 mg/kg might be achievable.

Method 132A (1994) for the determination of diazinon in milk is similar to AG-550A, but residues are extracted with acetone and transferred to methylene chloride, which is evaporated. The residue is taken up into hexane, partitioned into acetonitrile, concentrated into added methanol and finally cleaned up on an alumina column. A recovery of 86% is reported at the lowest fortification level in the report (0.1 mg/kg). The limit of determination is reported to be 0.01 mg/kg, although sample chromatograms of controls and fortified samples were not available for independent confirmation.

Method 132B (1992) determines diazinon in butter. The butter is dissolved in hot hexane and the residues partitioned into acetonitrile, which is evaporated to dryness. Clean-up is on an alumina column and determination by GLC with an NP detector. The average recovery was 90% at the lowest fortification level (0.02 mg/kg). A limit of determination of 0.01 mg/kg is reported and a sample chromatogram indicates that that should be achievable.

Method 135 (1994) determines diazinon in fat and animal tissues. Muscle and liver are macerated with methanol, which is diluted with water and extracted with methylene chloride. This is evaporated and the residue cleaned up on an alumina column. Fat is ground with sodium sulfate, extracted with hot hexane, and cleaned up by partitioning into acetonitrile. The acetonitrile is evaporated and the residue taken up in hexane and further cleaned up on an alumina column. Determination is by GLC with thermionic detection. Analytical recoveries of 84% from fat, 90% from muscle and 82% from liver were reported at the lowest fortification level of 0.1 mg/kg. The limits of detection and determination were reported to be 0.01 mg/kg, but the report did not include sample chromatograms of controls and fortified samples for independent confirmation.

Stability of pesticide residues in stored analytical samples

The studies of storage stability in crops and processed commodities (Beidler and Moore, 1991) and animal tissues (Schnabel and Formica, 1981) reviewed and described by the 1993 JMPR were re-submitted. From the latter study the 1993 JMPR noted that diazinon residues in animal tissues were stable for at least 8 months. The study was on samples from sheep which had been dipped in diazinon and contained initial residues of 0.05-2 mg/kg in muscle, ≤0.1 mg/kg in liver, 0.08-0.5 mg/kg in kidney and 2.8-5 mg/kg in fat. Samples were stored at -20°C. The study did not include information on the storage stability of metabolites in tissues, or of diazinon or metabolites in milk.

USE PATTERN

Information was provided on GAP for uses on both crops animals. Information on crop uses (Netherlands, 1995; Thailand 1995; Norway 1995) is not summarized here, since the emphasis is on residues in animal products.

The most important formulations for ectoparasite control in animals are listed above. WP formulations are also available. All are diluted with water for animal treatment by dipping, spraying,

wash or pour-on, and formulations as dusting powders and ear tags are also available. The most important treatment rates generally recommended are 600 mg/l for dipping cattle and for spraying cattle, sheep and goats, and 250 mg/l for dipping sheep and spraying goats.

Sheep are likely to incur the highest residues because of their wool coat and the high solubility of residues in wool grease (lanolin). Morrison (1994) demonstrated the bioequivalence of different EC formulations in sheep. This led the manufacturer to conclude that similar bioequivalence could be expected for these formulations in other species such as cattle, pigs and goats.

Although information on GAP for the use of diazinon in animal health was provided for over 55 countries and was consulted by the Meeting as needed, the summary in Table 6 below is largely confined to those countries in which supervised trials were conducted, and in some cases neighbouring countries.

Table 6. GAP for the use of diazinon for ectoparasite control on animals.

Animal/ Country	Form.	No. of treatments	Application rate			Pre-slaughter (S) or milking (M) interval	Comments[1]
			mg ai/kg bw (approx.)	l/animal	mg ai/l		
Wound dressings							
CATTLE Australia	Powder 20 g/kg	if needed	not defined	not defined	not defined	S 3	wound dusting S14
SHEEP Australia	Powder 20 g/kg	if needed				S 14	S14
	EC	--	--	--	600-1000	--	saturate wound area
Ear tags							
CATTLE Australia	Ear tags 200 g/kg 15 g/tag	two tags/animal	not defined	not defined	--	"Nil"	S17
Canada	Ear tags 200 g/kg 10.5 g/tag	1-2 tags/animal	2.1-4.2 g ai/animal[2]	not defined	--	"Nil"	S22
Backrubs							
CATTLE Australia	EC	pest-dependent	not defined	--	10 g/L oil	S 3	S16
Dips							
SHEEP Australia	EC	pest-dependent	not defined	not defined	100-200 (plunge/shower dip)	S 14	S15
Egypt[3]	EC	≤3	--	--	250	S 14 M 3	S2
France	EC	1-2/yr	--	--	250	S 14 M 3	S18
Ireland	EC	4-5 wk intervals	--	--	400	S 14 M no inf.	dip at least 1 min. S5
	EC	1-2? at 4-5 wk intervals	--	--	400 (winter dip)	S 14	dip at least 1 min. S5
Morocco	EC	≤3	--	--	250	S 21 M 4	S7
Netherlands	EC	≤3		--	250	S 28	S7

Animal/ Country	Form.	No. of treatments	Application rate			Pre-slaughter (S) or milking (M) interval	Comments[1]
			mg ai/kg bw (approx.)	l/animal	mg ai/l		
						Not for milk	
New Zealand	EC	pest-dependent	--	--	200-400 (shower or plunge dip)	S 21 ewes for milk not treated	S13
Norway	EC	≤3		--	250	S 21 Not for milk	S7
Portugal	EC	≤3		--	250	S 14	S7
Spain	EC	≤3		--	250	S 14 M 3	S7
Switzerland	EC	≤3	--	--	250	S 21 M 4	S7
UK	EC	1-3? (unclear)	--	--	250 dip or shower dip (winter dip)	S 14 ewes for milk not treated	dip at least 1/2 min. S5
CATTLE Austria	EC	≤3	6	--	600	M 5	S6
Egypt[3]	EC 600 g/L	≤3	6	--	600	S 14 M 3	S1
Morocco	EC	≤3	6	--	600	S 21 M 4	S6
Netherlands	EC	≤3	6	--	600	S 28 Not for milk	S6
Norway	EC	≤3	6	--	600	S 21 Not for milk	S6
Portugal	EC	≤3	6	--	600	S 14 M 3	S6
Spain	EC	≤3	6	--	600	S 14-15 M 3	S6
Switzerland	EC	≤3	6	--	600	S 21 M 4	S6
Sprays							
SHEEP Australia	EC	pest-dependent	8-24	1-3	400 jetting	S 14	S15
	spray-on93.3 g/kg	1 off-shear wide-band back spray-on	47	3 ml/kg bw of 1 in 7 dilution	13330	S 21	milk not for human consumption S15
Austria	EC	≤3	36	3	600	S 7 M 5	
Egypt[3]	EC	≤3	36	3	600	S 14 M 3	S2
France	EC	1-2/yr	--	--	550	S 14 M 3	S18
Morocco	EC	≤3	36	3	600	S 21 M 4	S7
Netherlands	EC	≤3	36	3	600	S 28 Not for milk	S7
New Zealand	EC	pest-dependent	500 max./ animal	0.5-1	500 jetting lamb treatment	S 21 Ewes for milk not treated	S13

Animal/ Country	Form.	No. of treatments	Application rate			Pre-slaughter (S) or milking (M) interval	Comments[1]
			mg ai/kg bw (approx.)	l/animal	mg ai/l		
Norway	EC	≤3	36	3	600	S 21 Not for milk	S7
Portugal	EC	≤3		--	600	S 14	S7
Spain	EC	≤3		--	600	S 14 M 3	S7
Switzerland	EC	≤3	36	3	600	S 21 M 4	S7
CATTLE Australia	EC	pest-dependent spray as needed	8	2.3	1000	S 3	Low volume S16
		spray as needed	8	4.5	500	S 3	High volume S16
		spray as needed	1.3	0.5	600-800 Back line spray	S 3	S16
Austria	EC	≤3	6	--	600	S 7	
Egypt[3]	EC	≤3	6	3	600	S 14 M 3	S1
France	EC	≤2/yr	6	--	550	S 14 M 3	S18
Morocco	EC	≤3	6	3	600	S 21 M 5	S6
Netherlands	EC	≤3	6	3	600	S 28 Not for milk	S6
Norway	EC	≤3	6	3	600	S 21 Not for milk	S6
Portugal	EC	≤3	6	3	600	S 14 M 3	S6
Spain	EC	≤3	6	3	600	S 14-15 M 3	S6
Switzerland	EC	≤3	6	3	600	S 21 M 4	S6
GOATS Australia	EC	pest-dependent	30	3	500	S 14	S16
France	EC	≤2/yr	2.5	1	550	S 14	S18
Egypt[3]	EC	≤3	36	3	600	S 14 M 3	S3
Morocco	EC	≤3	6	3	600	S 21 M 4	S8
Norway	EC	≤3	6	3	600	S 21 Not for milk	S8
Spain	EC	≤3	6	3	600	S 14 M 3	S8
Switzerland	EC	≤3	36	3	600	S 21 M 4	S8
PIGS Australia	EC	pest-dependent	5	1	500	S 14	S17
Austria	EC	≤3	6	1	600	S 7	S9
Egypt[3]	EC	≤3	2.5	1	250	S 14	S4
France	EC	2/yr	2.5	1	250	S 14	S19
Morocco	EC	≤3	6	1	600	S 21	S9
Netherlands	EC	≤3	6	1	600	S 28	S9

Animal/ Country	Form.	No. of treatments	Application rate			Pre-slaughter (S) or milking (M) interval	Comments[1]
			mg ai/kg bw (approx.)	l/animal	mg ai/l		
Norway	EC	≤3	6	1	600	S 21	S9
Portugal	EC	≤3	6	1	600	S 14	S9
Spain	EC	≤3	6	1	600	S 14	S9
Switzerland	EC	≤3	2.5	1	250	S 21	S9

[1]S1, S2, ... etc. are cross-references to the Table number of Ectoparasite Vol. 1 GAP Table summary submission from which, along with labels, the information is derived.
[2]Assumes 10.5 g product/tag containing 20% diazinon
[3]And several neighbouring countries

RESIDUES RESULTING FROM SUPERVISED TRIALS

CXLs are currently established at 0.7 mg/kg for the meat (fat) of cattle, goats and pigs and 0.02 mg/kg for milk. The 1993 JMPR reviewed residues resulting from the use of ear tags but not those from other uses on animals. Mainly because of the lack of animal transfer studies the 1993 JMPR recommended withdrawal of these CXLs, noting that data from veterinary uses were also desirable. The 1995 CCPR recommended retention of the limits pending the 1996 JMPR review of promised data on both transfer to animals and treatments against ectoparasites.

Animal feeding studies

The results of studies on cattle and poultry were available.

Cattle. Residues of diazinon, diazoxon (G-24576) and hydroxydiazinon (CGA-14128) were determined in the blood, milk and tissues of Holstein dairy cows dosed with technical diazinon after the evening milking for 28-30 consecutive days by gelatin capsule at rates equivalent to 40 ppm (1X), 120 ppm (3X) and 400 ppm (10X) in the diet (Selman, 1994a,b). Separate reports were provided of the analytical phase (Perez and Wetters, 1994) and the biological phase (Krautter, 1994) of the study, which was based on specified protocols (Selman, 1992a).

Three cows were dosed at each rate and one served as a control. The 1X rate was based on worst-case estimates of residues of 10 mg/kg in bean forage and pea vines each fed at 50% of the diet, converted to a dry-weight basis (34.3 ppm dietary burden) and the dosing took into account the mean dry-weight food consumption by the test animals.

Blood was sampled just before slaughter and composite samples of morning and evening milk were taken from each cow before dosing and 1, 3, 7, 14, 21 and 27 days after the first dose. Liver, kidney, round muscle, tenderloin muscle, and perirenal and omental fat were taken within 18-24 hours after slaughter. All samples were handled and stored satisfactorily (-20°C storage). Storage was for 4-5 months before analysis. As noted earlier, information on storage stability has been provided only for diazinon *per se* and only in tissues, not in milk.

The analytical method used was AG-550A. Results were corrected for procedural recoveries but not for control values. The results of recovery experiments were corrected for control values and diazoxon and hydroxydiazinon were expressed as diazinon (factors of 1.052 and 0.950 respectively). At the 0.01 mg/kg fortification level the percentage recoveries were:

	diazinon	diazoxon	hydroxydiazinon
Liver	101	77	111
Kidney	91	82	104
Muscle[1]	115	107	121
Fat[1]	109	106	113
Milk[1]	108	103	113
Blood	96	35	102

[1] mean recoveries

No residues of diazoxon or hydroxydiazinon were found in milk or any of the tissues at any interval or dosing level with the exception of hydroxydiazinon in omental and perirenal fat, which ranged from 0.01 to 0.06 mg/kg from the 10X dose. The residues of diazinon are shown in Table 7.

Table 7. Residues of diazinon in blood, milk and tissues from dosing diary cows with diazinon for 28-30 consecutive days at rates equivalent to 40, 120 and 400 ppm in the diet (Selman, 1994a,b).

Sample		Diazinon, mg/kg, from equivalent of		
		40 ppm (1X)	120 ppm (3X)	400 ppm (10X)
Liver		<0.01	<0.01	<0.01
Kidney		<0.01	<0.01	<0.01-0.01
Blood		<0.01	<0.01	<0.01
Muscle, round		<0.01	<0.01	<0.01-0.02
Muscle, tenderloin		<0.01	<0.01	0.01-0.02
Fat, perirenal		<0.02-0.03 (0.02)	0.05-0.08 (0.06)	0.15-0.58 (0.4)
Fat, omental		0.02-0.04 (0.03)	0.07-0.1 (0.08)	0.2-0.84 (0.6)
Milk	Days 1	<0.01	<0.01	<0.01-0.05 (0.02)
	3	<0.01	<0.01	0.01-0.06 (0.04)
	7	<0.01	<0.01	0.02-0.08 (0.04)
	14	<0.01	<0.01	<0.01-0.06 (0.03)
	21	<0.01	<0.01-0.01	<0.01-0.03 (0.02)
	27	<0.01	<0.01	<0.01-0.03 (0.02)

Poultry. A study on poultry described by Selman (1992b, 1993) was derived from supporting studies of the biological phase by March and Rezold (1992) and the analytical phase by Perez and Wetters (1992) in accordance with specified protocols (Selman, 1991).

White Leghorn hens (3 groups of five birds at each dose level) were dosed with technical grade diazinon by gelatin capsule at rates equivalent to 0, 0.5 (1X), 1.5 (3X) and 5 ppm (10X) for 28 consecutive days. Feed and water were *ad libitum*. Eggs were collected from all the birds at 0, 3, 7, 14, 21 and 28 days and the hens were killed after 28 days. Composite samples of breast and thigh muscle, skin and attached fat, peritoneal fat and liver were taken on the next day. Samples were transported in dry ice to the laboratory where they were stored at -20°C until analysis within approximately 5 months of sampling. The diazinon content of the capsules was confirmed by analysis.

The samples were analysed by AG-550A for diazinon, diazoxon (G-24576) and hydroxydiazinon (CGA-14128). Procedural recoveries at the 0.01 mg/kg fortification level were respectively 103, 103 and 99% (means) from eggs; 120, 126 and 123% from muscle; 95, 87, and 107% from skin with attached fat; 120, 81 and 117% from fat and 99, 63 and 89% from liver, with all controls <0.01 mg/kg. Sample chromatograms from fat and eggs fortified at 0.01 mg/kg suggest that although 0.01 mg/kg may be attainable, 0.02 mg/kg would be a practical limit of determination. Other sample chromatograms were from fortification levels of 0.1 mg/kg in muscle, 0.05 mg/kg in skin/fat, and 0.5 mg/kg in liver.

No residues (<0.01 mg/kg) of diazinon, diazoxon or hydroxydiazinon were found in any sample at any dose rate.

Uses as an ectoparasiticide

Eight trials were reviewed by the JMPR from 1967 to 1975 and 3 trials with ear tags were reviewed in 1993. All of these were re-submitted to the present Meeting, together with studies not previously reviewed: 9 with sprays (6 on cows, 2 on goats, 1 on pigs), 4 with cattle ear tags, 3 with sheep dips and one trial each on sheep dressing, sheep jetting and cattle backrubbing.

Dust application. In one very old briefly described study 3 cows were hand-dusted from a sprinkler can with 2% w/w diazinon dust (124 g/animal) and milk was analysed by GLC 2, 5, 9 and 24 hours after application (Chilwell *et al.*, 1967). Analytical recoveries averaged 79% at a fortification level of 0.1 mg/kg. The residues (mg/kg) were as shown below.

	2 h	5 h	9 h	24 h
Range	0.01-0.02 0.03-0.05	0.05-0.1	0.05-0.07	
Mean	0.01	0.04	0.09	0.06

No GAP was reported for this use.

Wound dressing. In an old Australian study residues of diazinon were determined in the fat, muscle and liver of fly-struck sheep 10 days after treatment (5 animals at each rate) with a 2% ai powder formulation applied as a wound dressing at 10 and 30 g/animal (Bull, 1974). The lower rate was reported to be according to GAP but this could not be confirmed with the label provided. Residues (mg/kg) were as shown below.

	g/sheep	Liver	Muscle	Omental fat
Range	10	<0.01-0.01	0.01-0.03 0.05-0.08	
Mean		<0.01	0.01	0.06
Range	30	<0.01-0.01	0.01-0.02 0.08-0.1	
Mean		<0.01	0.02	0.09

Backrubs. Two studies were available. The first (Bourne and Arthur, 1967) was a very old published US study in one part of which 56.6 g of 2% diazinon dust formulated on Pyrex ABB with 1% motor oil was hand-rubbed on the backs of 5 cows daily for 4 days. Half a day after the last treatment diazinon residues in the milk ranged from <0.05 to 0.52 mg/kg and after intervals of 1 to 15 days they were <0.05 mg/kg.

In the second part of the study 5 different cows were rubbed several times across the back with a burlap backrubber (1.2 m long X 10.2 cm diameter) impregnated with 0.45 kg of 2% diazinon dust. It was not clear whether the applications were daily but they were probably daily for four consecutive

days as in the other part of the study. Diazinon residues in the milk as determined spectrophotometrically ranged from <0.05 to 0.23 mg/kg 0.5 days after the last treatment to <0.05 mg/kg in all samples from 1 to 15 days after treatment. There was no information on relevant US GAP.

The second study was a recent Australian trial on 2- to 3-year old Brahman male cattle in which the backrubber was charged with 500 ml of 200 g/l diazinon EC per 10l of sump oil (i.e. 10 g ai/l oil). This is reported Australian GAP, which also includes a 3-day withdrawal period (Rose, 1995; Queensland and New South Wales, 1996). Groups of 5 cattle were exposed for 10 days and slaughtered 1 or 2 days after treatment, or for 19 days and slaughtered after 4, 7 or 10 days. Samples of renal and/or loin fat were taken from the 5 cattle in each group at each interval. The residues are shown in Table 8.

Table 8. Residues of diazinon in renal and loin (subcutaneous) fat of groups of 5 cattle 1 to 10 days after backrubber treatment at 10 g ai/l with EC formulation ((Rose, 1995; Queensland and New South Wales, 1996)

Diazinon, mg/kg, at interval, days, after treatment						
1[1]	2[1]	4[2]		7[2]		10[2]
Loin	Loin	Loin	Renal	Loin	Renal	Loin
0.07	0.08	0.66	0.26	0.1	0.08	0.03
0.04	0.05	0.24	0.16	0.05	0.08	0.03
<0.02	0.04	0.07	0.05	0.14	0.06	0.03
0.31	0.12	0.16	0.16	0.15	0.06	0.1
0.04	0.03	0.34	0.17	0.08	0.04	0.07

[1] Exposed for 10 days [2] Exposed for 19 days

Ear tags. Reports of three Canadian and four Australian trials were available. The results are shown in Table 9.

Table 9. Residues of diazinon in milk, milk fat and tissues of cows or calves treated with diazinon ear tags.

Country, year, ref., dose	Sample	Days after tag application	Residue, range and (mean)[1]
Canada 1987 Surgeoner, *et al.*, 1987a Vol 2 of 3 ref. 9 Two tags/cow 11% diazinon	whole milk	5 h through 1 day	ì g/kg this study only ND (= <0.5 ì g/kg) (ND)
		3	ND - 1.4 (0.64)
		7	1.2-1.7 (1.4)
		14	1.1-1.7 (1.4)
		21	ND-1.8 (0.53)
		28	0.73-1.4 (1.1) 3 cows

Country, year, ref., dose	Sample	Days after tag application	Residue, range and (mean)[1]
Canada 1987 Surgeoner *et al.*, 1987b Vol. 2 of 3 ref. 10 Two tags/steer, 9.6% diazinon	back fat (omental)	14 ≥100	0.032, ND (= ≤0.01 mg/kg) ND
	kidney fat (perirenal)	14 ≥100	0.035, ND ND
	muscle or liver	14 to ≥100	ND
	tongue	≥100	ND 3 cows
Canada 1989 Surgeoner *et al.*, 1989 Vol. 2 of 3 ref. 11 Two 20% diazinon tags/steer	back fat (centre, subcutaneous)	7 14	0.01 0.05 0.03, 0.02
	kidney fat (perirenal)	7 14 28	0.03 0.04 0.03, 0.03
	kidney, liver or muscle	7, 14, 28	all ND (= ≤0.01)
	tongue	7 14 28	ND 0.02 ND -0.02 4 steers
Australia, 1989 Bull and Wicker, 1989 Vol. 2 of 3, ref. 19 Two 18% diazinon tags/cow	Milk fat (butter)	1 7 14 28	<0.01-0.02 (<0.01) <0.01-0.01 (<0.01) <0.01-0.01 (<0.01) 0.01-0.02 (0.0125) 4 cows
	Milk (not analysed, but estimate based on the milk fat residue)	1-28	<0.01
Australia, 1990 Mawhinney, 1990 Vol. 2 of 3, ref. 18 One 18% diazinon tag/calf or cow (1/2 max. GAP)	fat (biopsy, subcutaneous tail butt)	calves 7 42 43	 <0.01-0.03 (0.02) 0.01-0.03 (0.02) <0.01-0.01
		cows 7 44	 <0.01-0.01 <0.01
Australia, 1992	milk fat (butter)	1 7 14	0.04-0.08 (0.06) 0.12-0.26 (0.19) 0.06-0.18 (0.13) 5 cows
Bull and Swindale, 1992 Vol. 2 of 3, ref. 15 Two 15 g 20% diazinon tags/cow	whole milk (highest residues assuming 4% fat)[1]	1 7 14	0.003 0.01 0.007
Australia, 1993 Strong and Bull, 1993 Vol. 2 of 3, ref. 16 Two 15 g 20% diazinon tags/cow	fat of milk	1 2 3 7 10 14 28 42 56	<0.01-0.02 (<0.01) <0.01-0.01 (<0.01) <0.01-0.02 (<0.01) 0.01-0.02 (0.02) 0.01-0.02 (0.02) 0.02(4) (0.02) 0.02(4) (0.02) 0.01-0.03 (0.02) 0.01-0.02 (0.02)

Country, year, ref., dose	Sample	Days after tag application	Residue, range and (mean)[1]
		84	<0.01-0.01 (<0.01)

[1] mg/kg unless otherwise indicated

The three Canadian trials were reviewed by the 1993 JMPR and will not be described in detail here. In the first (Surgeoner *et al.*, 1987a) the highest residues in milk during the 28 days of the trial were 0.0018 mg/kg (on day 21) with two 11% diazinon ear tags applied to each of three dairy cows. In the second study (Surgeoner *et al.*, 1987b) with two 9.6% diazinon ear tags on each of three steers, the maximum diazinon residues were 0.035 mg/kg in perirenal fat and 0.032 mg/kg in omental fat 14 days after the application of the tags. No residues (≤0.01 mg/kg) were found in muscle or liver. Residues in the fat decreased to <0.01 mg/kg after 100 days. In the third study (Surgeoner *et. al.*, 1989) with two 20% diazinon tags on each of 4 steers, the highest residues in the 28-day treatment occurred after 14 days with 0.45 mg/kg in back subcutaneous fat, 0.041 mg/kg in perirenal fat and 0.016 mg/kg in tongue. No residues (≤0.01 mg/kg) were reported in muscle, liver or kidney. This study appears to be in accordance with Canadian GAP (see Table 6).

In the first of four Australian trials two ear tags (18% diazinon, 4% Æ-cypermethrin; tag weights unspecified) were applied to each of three Fresian dairy cows and milk samples (two milkings/day) were taken 1, 7, 14 and 28 days after application (Bull and Wicker, 1989). Butter was immediately separated and stored at -15°C until analysis for diazinon by method 132A. The residues were <0.01-0.02 mg/kg on days 1 and 28 and <0.01-0.01 mg/kg on days 7 and 14. Mean procedural recoveries of diazinon from butter of 90% and a limit of determination of 0.01 mg/kg were reported, although sample chromatograms were not included.

In the second trial three *Bos indicus* calves (*c*. 200 kg) and three Brahman cows (400-660 kg) were each treated with a single ear tag impregnated with 18% diazinon and 4% Æ-cypermethrin (tag weights unspecified). Subcutaneous fat was taken by biopsy from fat pads on the side of the tail butt at 7, 42 and 83 days after treatment from the calves and after 7 and 44 days from the cows (Mawhinney, 1990). The highest diazinon residues in the fat from the calves were 0.03 mg/kg after 7 and 42 days and 0.01 mg/kg after 83 days. In the cows the residues were <0.01-0.01 mg/kg at 7 days and <0.01 at 44 days, with controls for both calves and cows <0.01 mg/kg.

The analytical procedure consisted in extraction of the fat with hexane, partitioning with acetonitrile, clean-up on a Florisil column and determination of diazinon by GLC with an NP detector. The reported limit of "detection" was 1 ng/g (0.001 mg/kg at a signal:noise ratio of 5:1). Sample chromatograms suggest that detection at 0.001 mg/kg is possible and that 0.01 mg/kg would probably be a reasonable limit of determination, although controls were not included among the sample chromatograms. At the 0.01 mg/kg fortification level procedural recoveries of diazinon averaged 82%. Diazinon in fat samples from treated animals was confirmed by mass spectrometry.

In the third Australian study two 15 g tags (20% diazinon) were applied to each of 5 Friesian cows and milk was sampled after 1, 7, and 14 days (Bull and Swindale, 1992). Cream was separated from the milk and stored in a refrigerator for 5 days. Butter was then made and stored at -15°C until analysis. The analytical phase was reported to be according to OECD GLP.

The highest residue in the butter of any one cow was 0.26 mg/kg on day 7 with mean residues for

the 5 cows of 0.06 mg/kg on day 1, 0.19 mg/kg on day 7 and 0.13 mg/kg on day 14.

The analytical method was 132B with procedural recoveries from butter ranging from 73 to 103% (n=4, mean 91.5%), excluding one recovery of 58% with fortification at 0.05 mg/kg. No sample chromatograms were provided.

In the fourth Australian trial (Strong and Bull, 1993) diazinon residues were determined in the milk fat of four Friesian cows treated with two 15g, 20% diazinon, ear tags for up to 3 months. Milk was sampled 1, 2, 3, 7, 10, 14, 28, 42, 56 and 84 days after attachment of the tags, immediately separated, and made into butter which was stored at -15°C until analysis. The study was started in October 1992 and the analyses were completed by January 1993: they were reported to be in accordance with OECD GLP.

The residues did not exceed 0.03 mg/kg in any sample. The mean residue for the four cows increased to 0.02 mg/kg by day 7 and remained at that level until day 56, decreasing to <0.01 mg/kg by day 84.

The method of analysis was again 132B with a mean procedural recovery of 87% at 0.02 mg/kg and a reported limit of determination of 0.01 mg/kg. No sample chromatograms were provided.

Dips. Six old trials (1962-1974, 3 on sheep, 3 on cattle) and two more recent trials on sheep (1986, 1989) were available. The results are given in Table 10.

Table 10. Residues of diazinon in the milk, tissues and fat of sheep and cattle following dipping in EC formulations.

Country, ref.	Rate, mg ai/l	No. of dips	Sample	Residues, mg/kg, range and (mean)	Slaughter interval (days)	Comments
SHEEP						
Australia, Hastie & Cavey, 1962a	200	1 for 20 sec	Meat Kidney fat Kidney fat Kidney fat Controls, meat & fat	<0.1 <0.1-1.4 (0.1) 1.1-1.4 (1.2) 0.5-1.4 (0.8) <0.1	1 1 7 14	3 animals per group for fat. Dip period reportedly twice recommended. Rate is GAP according to current label.
Switzerland, Formica, 1973b	200 (0.8 X GAP)	1 plunge dip	Whole milk Trial 1 Trial 2 Controls	Residues at day 6h 1 2 3 4 7 15 30 0.09 0.06 0.02 0.02 0.02 0.02 <0.01<0.01 0.09 0.03 0.01 0.01 0.01 0.01 <0.01<0.01 <0.01		
	400	1 plunge dip	Trial 3 Trial 4 Controls	Residues at day 6h 1 2 3 4 7 15 30 0.18 0.10 0.04 0.03 0.02 0.03 0.01 <0.01 0.16 0.07 0.04 0.02 0.02 0.03 <0.01<0.01 <0.01 Method REM 29/73, reported limit of detection 0.01 mg/kg, 92% recovery at 0.03 mg/kg		
Switzerland	750[1]	1	Muscle	0.21-0.37 (0.28)	10	Applic. rate 3X reported

Country, ref.	Rate, mg ai/l	No. of dips	Sample	Residues, mg/kg, range and (mean)	Slaughter interval (days)	Comments
Formica, 1974c			Liver Omental fat	<0.02 2.2-2.6 (2.3)		GAP Residues of hydroxydiazinon, diazoxon and pyrimidinol below LOD. Method REM 4/74, reported limit of detection 0.02 mg/kg parent; recovery 88% at 0.5 mg/kg
Australia Strong *et al.*, 1986a	250	1 plunge dip		Residues at day 1 3 7 14 21 muscle 0.15 0.08 0.05 0.03 0.01 0.13 0.05 0.04 0.01 0.02 liver 0.01 0.02 <0.01 <0.01 0.01 <0.01 <0.01 <0.01 0.01 0.01 kidney 0.04 0.03 0.02 0.02 0.01 0.03 0.03 0.01 0.01 0.01 kidney fat 2.6 2.2 1.6 0.67 0.29 1.2 2.1 1.0 0.63 0.24 Two sheep/interval. Method 114A, LOD 0.01 mg/kg; recovery ≥87% at 0.1 mg/kg		
UK Roberts and MacDonald, 1989	400 (1.6 X UK GAP, 1 X Ireland & N. Zealand GAP)	1 minute plunge		Residues at day 7 14[1] 21[2] 28 35 Omental fat 1.4 1.1 0.8 0.6 0.2 2.3 1.1 0.7 0.5 0.6 2.8 1.1 0.7 0.7 0.4 1.7 1.3 0.7 0.5 0.4 1.1 1.2 0.5 0.3 0.7 0.8 0.6 0.5 Mean (2.1) (1.1) (0.8) (0.6) (0.4) Subcut. fat --- 1.3 1.4 0.9 0.5 1.4 1.0 0.5 0.7 4.3 1.2 1.2 0.7 Mean (2.3) (1.2) (0.8) (0.6) Controls <0.005 mg/kg; 6 animals/interval (4 at 7 days) [1] Irish GAP PHI [2] New Zealand GAP PHI		
CATTLE						
Australia, Hastie, 1962	500	3	Kidney fat	3.2-3.9 (3.6)	18 h	4 animals. Swiss GAP is 600 mg ai/l and 21-day S.I. Same in Egypt & near countries, but 14 day S.I.
	EC[1]	2-3	Kidney fat	0.0-2.1 (1.5)	90 h	1 animal 3 dips 3 animals 2 dips
		2	Kidney fat	0.6-0.8 (0.7)	7	4 animals

Country, ref.	Rate, mg ai/l	No. of dips	Sample	Residues, mg/kg, range and (mean)	Slaughter interval (days)	Comments
			Control	0.1		
Australia Hastie 1963c	500	1	Kidney fat Subcut. fat Kidney fat Subcut. fat Kidney fat Subcut. fat Controls: Kidney fat Subcut. fat	0.4-1.5 (1) 0.2-0.3 (0.25) 0.4-0.6 (0.5) 0.15-0.2 (0.2) 0.3-0.6 (0.5) 0.4-0.7 (0.5) (0.2) <0.1	1 1 4 4 7 7	4 animals in each group
Australia Hastie 1963b	500	3 at 3 day interval	Kidney fat Subcut. fat Kidney fat Subcut. fat Kidney fat Subcut. fat	1.7-4 (2.7) 0.8-1.5 (1.2) 0.6-1.2 (0.8) <0.2-1.2 (0.7) 0.2-0.8 (0.5) 0.4	1 1 4 4 7 7	2 steers + 1 cow per group

[1] Formulation not stated but presumably EC

Hastie (1963a) reviewed several reports of studies on the dipping and spraying of sheep and cattle (Hastie, 1962, 1963b,c; Hastie and Cavey, 1962a,b, 1963). The reports were essentially brief summaries with little information on sample storage and handling, analytical methods or other details.

The other trials were on sheep dipping. Those by Formica (1973b, 1974c) are fairly well documented in terms of method, sample storage etc. The report by Strong *et al.* (1986) is reasonably detailed (e.g. sample storage at -15°C), although the periods from sampling to analysis are not provided. The trial by Roberts and MacDonald (1989) is the best documented and reported to be in accordance with recognized GLP. Details are given of all aspects of the trial, including sample storage and analysis of dip solutions.

Spraying. Reports of eighteen new or previously reviewed trials were provided: 13 on cattle, 2 on sheep, 2 on goats and 1 on pigs. The results are shown in Tables 11 (cattle) and 12 (sheep, goats and pigs).

Table 11. Residues of diazinon in the milk, fat and tissues of cattle after spraying.

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
Australia Hastie and Cavey, 1962a	Emulsifiable 1500 mg/l (3 X high vol. GAP) 9.5 l/animal (2 X high vol. GAP)	1	 meat kidney fat	1 — 7 — 14 days <0.1 - - 1.1 1.2 0.4 0.9 1.2 0.4 3.2 1.3 0.3 Residues in fat from 3 animals. Residue in meat from single animal. GAP S.I. (pre-slaughter interval) = 3 days
Australia Hastie and Cavey,	Emulsifiable 1000 mg/l	1	kidney fat	1 3 (GAP) days

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
1962b	(1 X low vol. or 2 X high vol. GAP)		(6 animals)	1.8, 1.2 1.0, 0.8 0.9, 1.1 0.7, 0.9 1.5, 1.1 0.9 --
	3.8 l/animal (High vol. GAP is 4.5 l)		subcut. fat (6 animals)	0.2, 0.1 0.3, 0.4 <0.1, 0.2 0.2, 0.7 0.3,<0.1 0.5, --
Australia Hastie and Cavey, 1963	Emulsifiable 1000 mg/l (2 X high vol. GAP) 7.6 l/animal (High vol. GAP)	1	milk (3 cows)	1 2 3 days 0.07 <0.01 Nil 0.05 <0.01 Nil 0.04 <0.01 Nil
	Emulsifiable 500 mg/l (High vol. GAP) 7.6 l/animal (High vol. GAP)	1	milk (3 cows)	0.03 <0.01 Nil 0.04 <0.01 Nil 0.04 <0.01 Nil
USA Claborn,*et al.*, 1963	WP 500 mg/l (1/2 max. low vol. GAP for Australia) 1-1.5 l/animal	16 at weekly intervals	omental fat Spray no.: 1	1 6 7 14 days <0.05, 0.06
			2	<0.05, 0.09
			6	0.2, 0.4 0.2, 0.2 0.5, 0.9 0.8,
			10	0.2, <0.08, 0.7
			11	0.4 <0.05
			16	
	WP 1000 mg/l (max. low vol. GAP for Australia)	16 at weekly intervals	1	0.7 0.5 0.6 0.5 0.5 0.8

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				0.8 0.8 2.3 0.7 <0.05 2 6 10 16
USA Matthysse and Lisk, 1963	EC 600 mg/l 11.4 l/cow (high vol.)	2 10-day interval	Mil k 1st spray 2nd spray	0.5 1 2 3 4 7 days 0.3 0.09 0.03 <0.02 0.3 0.1 0.04 Residue at 4 days is mean of 2 cows. All others are means of 3cows.
UK Chilwell *et al*., 1967	Oil emulsion 200 mg/l 10 l/cow (high vol.)		Milk Cow 1 Cow 2 Cow 3 Mean	2 5 9 24 hours 0.01 0.06 0.07 0.02 0.02 0.06

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				0.08 0.02 0.02 0.05 0.09 0.02 0.02 0.06 0.08 0.02 Each residue is mean of two analyses by GLC/thermionic. Recoveries 79% at 0.1 mg/kg.
Switzerland Blass, 1971	Formulation not stated 500 mg/l (600 mg/l is GAP) 10 l/cow 4 cows	4 (weekly intervals) (Max. 3 is Swiss GAP)	Milk Spray no. 1 Range Mean 2 Range Mean 3 Range Mean 4 Range Mean	0 3 4 (GAP) 6 days 0.2-0.4 <0.02-0.02 <0.02 (0.3) <0.02 (0.02) (<0.02) (<0.02) 0.1-0.2 <0.02-0.04 <0.02-0.02 (0.13) <0.02 (0.03) (0.02) (<0.02) 0.06-0.13 <0.02-0.03 <0.02-0.03 (0.09) <0.02 (0.02) (0.02) (<0.02 0.05-0.14 0.02-0.05 <0.02-0.04 (0.08) <0.02 (0.03)

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				(0.03) (<0.02)
	1000 mg/l (1.7 X GAP) 10 l/cow 4 cows		1 Range Mean 2 Range Mean 3 Range Mean 4 Range Mean	0.2-0.6 <0.02-0.08 <0.02-0.05 <0.02 (0.3) (0.04) (0.04) (<0.02) 0.1-0.2 0.04-0.1 0.02-0.07 <0.02-0.04 (0.2) (0.07) (0.04) (0.02) 0.09-0.1 <0.02-0.08 <0.02-0.05 <0.02-0.02 (0.1) (0.05) (0.03) (0.02) 0.05-0.2 0.03-0.04 <0.02-0.05 <0.02 (0.14) (0.04) (0.03) (<0.02)
Australia Bull and Dougall, 1974	EC?	1	Milk & milk products Pre-treatment Milking Day 1st 1 2nd 1 3rd 2 4th 2 10th 5	Residues from 5 individual cows Whole milk Skim Range Mean milk[1] Butter[1] 0.03 0.02

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				0.08 0.2-0.3 0.2 0.03 5.2 0.03-0.14 0.06 0.02 1.7 0.04-0.08 0.06 - - 0.8 0.02-0.05 0.03 - - 0.3 0.01-0.05 0.02 - - 0.05 [1]Composites Method 132, 0.01 mg/kg limit of detection reported. Recovery ≥97% from milk at 0.13 mg/kg
Bull and Dougall, 1974	500 mg/l (High vol. GAP) 10 l/animal (high vol.)		Milk & milk products	Residues from herd bulk storage Skim Pre-treatment Milk milk Milkings Cream Butter 1st 0.03 0.02 1st & 2nd 0.09 3rd 0.08 3rd & 4th 0.25 0.04 2.4 4.5 0.15 0.03 2.1 2.6 0.06 0.02 0.57 0.60 0.04 0.02 0.26 0.30 Herd size: 60. Method REM 20/71, autoanalyser.

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				Recovery 76% at 0.05 mg/kg
Australia Bull *et al*., 1986a	EC 600 mg/l (1.2 X GAP)	1 10l/cow	Whole milk Pre-treatment MilkingHours 1 7 2 21 3 31 4 45 5 55 6 (GAP)7 7 80	# Range Mean (5 cows) <0.01 <0.01 0.08-0.4 0.2 0.05-0.1 0.08 0.04-0.07 0.06 0.01-0.03 0.02 0.01-0.03 0.02 <0.01-0.01 <0.01 <0.01 <0.01 GLC thermionic detection. Reported LOD 0.01 mg/kg, recovery 91% at 0.1 mg/kg. No corrections made to results.
Australia Strong *et al*., 1986b	EC 600 mg/l	1 10l/steer	 Muscle Liver Kidney Kidney fat Omental fat	1 7 14 21 days 0.06, 0.01, <0.01, NA[1] 0.06 0.01 <0.01 NA <0.01, <0.01, <0.01, NA 0.02 <0.01 <0.01 NA 0.07, 0.01, <0.01, NA 0.06 0.01 <0.01 NA 2.9, 0.4, 0.06, <0.01, 1.3 0.7 0.06 0.01 2.5, -- 0.2, <0.01, 1.4 -- 0.12 0.05

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				GAP withdrawal interval is 3 days. [1]Not analysed. Two steer calves sampled at each time. -15°C storage. Uncorrected for recovery. Method 135. 0.01 mg/kg reported LOD. Recovery ≥88% at 0.1 mg/kg except omental fat 73%.
Egypt Kholif *et al*., 1994	EC 600 mg/l (GAP)	1? (Report not specific, but 1 application presumed) 2l/cow	Milk Hours 2 4 6 8 16 24 36 48	Cows / Buffaloes 0.05 / 0.11 0.2 / 0.2 0.2 / 0.3 0.1 / 0.2 0.05 / 0.02 0.03 / 0.01 ND[1] / 0.005 ND / ND GAP milk withdrawal interval is 3 days [1]Not detected. Method AOAC 1990, GLC/ECD. Total of 20 cows and buffaloes.
Australia, Rose, 1995; Queensland and New South Wales, 1996	EC 800 mg/l nominal 553 mg/l actual (800 is GAP)	1 Back spray 0.5 l/cow (GAP)	Loin Fat Renal fat	Days: 2 / 4 / 7 / 10 / 14 / 16 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 <0.05 0.08 <0.05 <0.05

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				Controls all <0.05 mg/kg 3 cows sampled at 2, 14, and 16 days; 6 cows at 4, 7 and 10 days. All samples except one 4-day loin fat contained <0.05 mg/kg. AOAC method, reported 0.02 mg/kg "limit of detection"

The 13 spray trials on cattle were from 1962 through 1996. One was not reviewed as it was available only in Russian (Leschchev *et al*., 1972). Hastie (1963a) reviewed three of the trials (Hastie and Cavey, 1962a,b, 1963). The first trial (Hastie and Cavey, 1962a) was not according to GAP. The second (Hastie and Cavey, 1962b), which might be interpreted to represent GAP, showed maximum residues of 1 mg/kg and 0.7 mg/kg in kidney fat and subcutaneous fat respectively. Hastie and Cavey (1963) reported residues of <0.01 mg/kg in milk from a GAP application rate after 3 days, the withholding period for milk in several countries. All of the trials were with single sprays whereas GAP allows multiple sprays in most countries.

Another old publication (Mathysse and Lisk, 1963) reports residues in milk up to 0.04 mg/kg with a mean of 0.03 mg/kg 3 days (the Australian withdrawal period) after a spray at 600 mg/l, slightly above the GAP rate for high-volume application, and up to 0.1 mg/kg with a mean of 0.04 mg/kg 4 days after a second spraying. Analysis was based on spectrophotometry.

Another dated publication (Claborn *et al.*, 1963) reported the residues of diazinon in omental fat resulting from 16 spray applications at weekly intervals. Residues 6 days after treatment at half the maximum GAP application rate increased with repeated applications from 0.06 mg/kg after the first application to 0.4 mg/kg after the 6th: they had decreased to <0.08 mg/kg 14 days after the last application. Residues 6 or 7 days after each application at the maximum GAP rate remained between 0.5 and 0.8 mg/kg. They had decreased to <0.05 mg/kg by 14 days after the 16th treatment. Analyses were again by spectrophotometry.

In a UK study Chilwell *et al*. (1967) reported diazinon residues in milk within 24 hours of spray treatments at 200 mg ai/l. The mean residues were 0.02 mg/kg after 2 hours, rose to 0.08 mg/kg after 9 hours and decreased to 0.02 mg/kg after 24 hours. No information on UK GAP for cattle sprays was provided, although the application rate is below most reported GAP rates.

In an old but reasonably well-described study in Switzerland (Blass, 1971) residues of diazinon in milk were determined at various intervals after applying 4 sprays 500 or 1000 mg/l at weekly intervals. The lower rate complies with GAP. After 4 days (the GAP interval for Switzerland) the residues from the lower rate did not exceed a maximum of 0.03 mg/kg or a mean of 0.02 mg/kg after the third spray (the maximum number allowed by Swiss GAP) nor above 0.04 mg/kg maximum (0.03 mg/kg mean) after 3 days, which is the withdrawal interval in other countries. Analyses (presumably colorimetric) were by an autoanalyser.

In another old, but fairly well-described, Australian study residues of diazinon in the milk of cattle were determined after various intervals (Bull and Dougall, 1974). Samples from five individual cows and bulk samples from the whole herd were analysed after one treatment at 500 mg ai/l, the GAP

rate. The cows were milked twice daily. The mean residues from the 5 cows were 0.2 mg/kg (0.3 mg/kg maximum) at the first milking, 0.06 mg/kg at the second, 0.03 at the 4th (day 2) and 0.02 mg/kg at the 10th (the 5th day after treatment). There is no specified Australian withdrawal period for milk but 3 or 4 days is common in other countries with similar GAP. Residues from the first milking were 0.03 mg/kg in skim milk and 5.2 mg/kg in butter, the residue in butter decreasing to 0.05 mg/kg after the 10th milking. Residue levels in the bulk herd samples were similar to the means of the 5 cows.

Two relatively recent studies from Australia were not especially well reported by current standards (e.g. they lacked details of the intervals from sampling to analysis and analytical confirmation of the active ingredient content of the sprayed solutions), but sample storage was at -15°C. In one of these studies diazinon residues were measured in the milk of 5 cows 7 to 80 hours after a single EC spray at 600 mg/l, 1.2 times the high-volume GAP rate (Bull, *et al*., 1986). The residues ranged from a mean of 0.2 mg/kg and a maximum of 0.4 mg/kg 7 hours after application to a mean of ≤0.01 mg/kg after about 3 days (70 hours).

In the other fairly recent Australian study (Strong *et al*., 1986b) a similar application was made to calves, from which tissues were analysed for diazinon. The residues were up to 2.9 mg/kg in fat, about 0.06 mg/kg in muscle and kidney and up to 0.02 mg/kg in liver 1 day after treatment. No results were available for the Australian withdrawal interval of three days, but the residues in muscle, liver and kidneys had decreased to ≤0.01 mg/kg after 7 days, when kidney fat contained up to 0.7 mg/kg. Residues up to 0.2 mg/kg were found in omental fat after 14 days.

In a more recent Egyptian study (Kholif *et al*., 1994) a total of 20 Friesian cows and buffaloes were spray-treated once after the morning milking with an EC formulation at 600 mg/l (the Egyptian GAP rate). The animals were milked twice daily by machine. The residues in the milk of the buffaloes and cows respectively decreased from a maximum of 0.3 and 0.2 mg/kg after 6 hours to 0.005 mg/kg and not detected after 36 hours. The Egyptian withdrawal interval for milk is three days. The trial was generally well described but some desirable details were not included (e.g. sample handling and storage conditions and period of storage.

In a recent Australian trial cattle were back-sprayed once with 0.5l at 553 mg diazinon/l: the nominal rate was 800 mg/l which is the maximum GAP concentration. Loin and renal fat were analysed for residues at intervals from 2 to 16 days after treatment (Rose, 1995; Queensland and New South Wales, 1996). Samples were taken from frozen export packs from the treated cattle. One loin fat sample of six taken four days after treatment contained 0.08 mg/kg; all other residues were below 0.05 mg/kg. Spray solutions were analysed for the active ingredient, but other important information such as sample handling and storage conditions and intervals from sampling to analysis was not reported.

Sheep, goats and pigs

Table 12. Residues of diazinon in the milk, fat or tissues of sheep, goats and pigs following spraying.

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
SHEEP				
Australia	EC	1		14 days (3 sheep)

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
Bull, 1971	800 mg/l	jetting	Muscle Fat	Sheep A B C Mean 0.05 0.05 0.05 0.05 0.15 0.08 0.06 0.13
	WP 800 mg/l	1 jetting	Muscle Fat	Sheep D E F Mean 0.03 0.06 0.09 0.06 Control 0.06 0.16 0.06 0.05 0.09 Control 0.03 Method 113 (sweep-codistillation; GLC thermionic). 0.02 mg/kg limit of detection reported. Recoveries 70% muscle, 92% fat at 0.2 and 0.5 mg/kg respectively. Results corrected.
Switzerland Morrison, 1994	EC 250 600 mg/l (GAP)	1 6 l/sheep (GAP = 3l)	fat (tail base biopsy)	Sheep no. 8 28 days 1 1.8 0.10 2 1.6 0.11 3 3.1 0.13 4 3.3 0.17 5 2.6 0.29 6 3.5 0.11

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				Mean 2.7±0.8 0.15±0.07
	EC A-139 F 600 mg/l (GAP)	1 6 l/sheep	same	1 2.2 0.14 2 2.4 0.17 3 2.1 0.24 4 0.78 0.15 5 2.7 0.08 6 3.2 0.16 Mean 2.2± 0.16±0.05
	EC 600 600 mg/l (GAP)	1 6 l/sheep	same	Sheep no. 8 28 days 1 2.1 0.09 2 2.1 0.06 3 2.1 0.11 4 2.0 0.22 5 1.4 0.10 6 1.9 0.14 Mean 1.9± 0.12±0.12 Method 24480.O. Mean recoveries from fat 95-100% on different days at 0.025 mg/kg. Reported LOD 0.005 mg/kg; chromatograms suggest 0.01 mg/kg more practical.
GOATS				

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
Australia Bull *et al*., 1986b	EC 600 mg/l (GAP is 500 mg/l in Australia, 600 mg/l in other countries)	1 5 l/goat (GAP is 3 l)	Muscle Mean	1 3 7 14 21 days 0.14 0.03 0.01 <0.01 <0.01 0.06 0.04 0.02 <0.01 <0.01 0.1 0.04 0.02 <0.01 <0.01 Controls in all tissues <0.01 mg/kg GAP pre-slaughter interval is 14 days. Two goats sampled at each time.
			Liver Mean	0.04 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.03 <0.01 <0.01 <0.01 <0.01
			Kidney Mean	0.08 <0.01 <0.01 <0.01 <0.01 0.02 0.03 0.01 <0.01 <0.01 0.05 0.03 0.01 <0.01 <0.01
			Kidney fat Mean	3.4 1.0 0.04 <0.01 <0.01 1.1 1.4 0.22 0.02 <0.01 2.3 1.2 0.13 <0.02 <0.01
			Omental fat Mean	3.8 0.39 0.08 0.03 <0.01 0.91 1.2 0.2 0.01 <0.01 2.4 0.8 0.14 0.02 <0.01
Australia Strong *et al*., 1987	EC 600 mg/l	1 5 l/goat	Whole milk (5 goats)	Goat A B C

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval		
						D
						E
						mean
			Pre-treatment	0.01	0.01	<0.01
			Hours			0.01
						0.01
						<0.01
			7			
				0.18	0.25	0.22
						0.18
						0.25
						0.22
				0.07	0.08	0.09
			24			0.06
						0.03
						0.07
				0.08	0.08	0.10
			30			0.08
						0.07
						0.08
				0.03	0.03	0.04
			48			0.02
						0.02
						0.03
				0.04	0.03	0.05
			54			0.03

Country, ref.	Formulation. Application rate, ai	No. of sprays	Sample	Residues, mg/kg, at withdrawal interval
				0.03
				0.04
				0.01 0.01
				0.02
			72	0.01
				0.01
				0.01
				0.02 0.02
				0.02
			78	0.01
				0.01
				0.02
				Method 132A. 0.01 mg/kg limit of "detection" reported. Recovery 81% at 0.1 mg/l.

PIGS						
Switzerland Formica, 1974b	EC 250 mg/l (GAP)	1 5 l/pig (GAP is 1 l)		1		3
			Muscle			—
			Liver			—
			Kidney			—
			Fat			7
			Skin			—
						—
						—
						14
						—
						—
						—
						28
						—
				0.04	0.02	
						0.02
						0.01
						0.01
				All <0.01		
				All <0.01		
				0.22	0.05	
						0.02
						<0.01
						<0.01
				All <0.01		
		2 (GAP is ≤3) 5 l/pig	Muscle	0.02	0.01	<0.01
			Liver			
			Kidney			
			Fat			
			Skin			<0.01
						<0.01
				All <0.01		
				All <0.01		
				0.15	0.06	<0.01
						<0.01
						<0.01
				0.05	0.02	<0.01
						<0.01
						<0.01

	EC 500 mg/l	1 5 l/pig	Muscle Liver Kidney Fat Skin	0.08	0.04		0.01
							0.02
							0.04
				All <0.01			
				0.01	<0.01	<0.01	
							<0.01
							<0.01
				0.5		0.15	
							0.02
							<0.01
							<0.01
				0.13	0.02		
							<0.01
							<0.01
							<0.01
		2 5 l/pig	Muscle Liver Kidney Fat Skin	0.04	0.01		
							<0.01
							<0.01
							<0.01
				All <0.01			
				All <0.01			
				0.21	0.05		
							0.01
							<0.01
							<0.01
				0.01	0.01		<0.01
							<0.01
							<0.01
				Controls <0.01 mg/kg for all samples and times.			

				Method REM 4/74. Recoveries 125, 75 and 90% at 0.1 mg/kg from muscle, liver and fat respectively. 0.01 mg/kg limit of "detection" reported. Results not corrected for recovery
				<u>hydroxydiazinon</u>
			Fat	<0.02 mg/kg in all but two samples (0.02 and 0.03 mg/kg) at 250 and 500 mg/l respectively).
			Other tissues	<0.02 mg/kg in all samples.
				<u>pyrimidinol metabolite G 27 550</u>
			Kidney	<0.1 mg/kg in all samples at 250 mg/l. <0.1, 0.12, 0.12, 0.14, 0.14, 0.16 at 500 mg/l.
			Other tissues	<0.1 mg/kg in all samples.
				<u>diazoxon</u>
			All tissues	<0.01 mg/kg in all samples

Sheep. Two studies were provided. In an Australian study sheep were treated once with a single jet spray with either a WP or an EC formulation, at 800 mg/l (twice the reported GAP concentration for Australia). Muscle and fat samples were analysed after slaughter 14 days later, the GAP interval (Bull, 1971). Although fat was identified as omental, subcutaneous and kidney fat, the data did not specify which residues were in which fat. The residues did not exceed 0.16 mg/kg in fat or 0.09 mg/kg in muscle. Details such as sample handling and storage conditions, intervals from sampling to analysis and confirmation of spray concentrations were not recorded, nor were sample chromatograms supplied.

A more recent and well documented Swiss study (Morrison, 1994) was reported to be in accordance with OECD GLP. Three groups of six sheep were sprayed with different EC formulations, all nominally at the Swiss GAP rate of 600 mg/l, actually 576-592 mg/l, and 6l/animal (twice the GAP volume). Fat samples were taken by biopsy from the base of the tail 8 and 28 days later: the GAP slaughter interval is 21 days in Switzerland, 14 days in some other countries. Samples were stored at -20°C until analysis less than 6 months later. Blood samples were also taken.

Fat samples were extracted with acetonitrile, cleaned up on a solid-phase column and analysed by GLC with an NP detector. Recoveries were near 100% at 0.025 mg/kg. The reported limit of determination was 0.005 mg/kg, but 0.01 mg/kg appears to be more practical from the sample chromatograms.

Eight days after treatment diazinon residues in the fat ranged from 0.8 to 3.5 mg/kg with an overall mean of 2.3 mg/kg after 8 days and 0.06 to 0.3 mg/kg with a mean of 0.14 mg/kg after 28 days, with no significant difference between the three formulations.

Goats. Two Australian trials were reported. In one, each goat was treated once with 5l of an EC at 600 mg ai/l and 5l animal and the goats were slaughtered in pairs 1, 3, 7, 14 and 21 days after treatment (Bull *et al.*, 1986b). GAP in Australia requires 500 mg/l and in other countries up to 600 mg/l. The higher residues of each pair one day after treatment were 0.14 mg/kg in muscle, 0.04 mg/kg in liver, 0.08 mg/kg in kidney, 3.4 mg/kg in kidney fat and 3.8 mg/kg in omental fat. After the Australian GAP slaughter interval of 14 days the only residues above 0.01 mg/kg were 0.02 mg/kg in one sample of kidney fat and 0.03 mg/kg in one of omental fat.

Samples were stored at -15°C until analysis by method 135 for which a limit of determination of 0.01 mg/kg was reported, although no sample chromatograms were presented. Recoveries were ≥87% at the lowest fortification level of 0.1 mg/kg. The interval from sampling to analysis was not reported, nor was confirmation of the actual spray concentration.

In the second study 5 goats were each sprayed once with 5l of EC at 600 mg/l (Strong *et al.*, 1987). Diazinon residues were determined in the whole milk after 7 consecutive milkings by method 132A. Reported recoveries were 81% at 0.1 mg/kg but no sample chromatograms were presented. Samples were stored at -15°C until analysis, but the storage period was not reported nor was confirmation of the spray concentration. Residues decreased from a maximum of 0.25 and a mean of 0.22 mg/kg after 7 hours to 0.01-0.02 mg/kg after 72 and 78 hours. Withholding intervals for milk are 3 to 4 days in other countries.

Pigs. One old but relatively well documented Swiss study (Formica, 1974b) was reported. Pigs were each sprayed once or twice with 5l EC spray (1l is GAP) at either 250 or 500 mg ai/l, the GAP concentration in Switzerland and Egypt respectively. Samples of muscle, liver, kidney, skin and fat taken 1, 3, 7, 14 and 28 days after treatment were analysed for residues of diazinon, diazoxon, hydroxydiazinon and the pyrimidinol metabolite G27550. The Swiss GAP pre-slaughter interval is 21 days.

Although spray concentrations were not confirmed nor chromatograms provided, samples were stored at -20°C until analysis within 7 months of treatment. Residues of diazinon after 14 and 28 days were all ≤0.01 mg/kg except in two muscle samples with 0.02 and 0.04 mg/kg. Residues of hydroxydiazinon were <0.02 mg/kg in all samples except two of fat which contained 0.02 and 0.03 mg/kg. Residues of G 27550 were <0.1 mg/kg except in the kidneys of pigs treated at 500 mg ai/l, where they ranged from <0.1 to 0.16 mg/kg. No residues of diazoxon (<0.01 mg/kg) were detected in any sample.

Summary

For the convenience of a general picture, the residues resulting from treatments according to GAP shown in Tables 8 to 12 above are summarized in Table 13.

Table 13. Summary of diazinon residues found in milk and tissues of cattle, sheep, goats and pigs from treatments against ectoparasites according to GAP.

Sample Type of treatment	Diazinon, mg/kg, maximum and (median) residues in				Maximum residue, mg/kg, from any treatment
	Cattle	Sheep	Goats	Pigs	
Milk Ear tag	0.01 (0.01 mean) 0.3(0.2)fat				Milk 0.02 (mean)[1]
Dip		0.02(0.02)			
Spray	0.05 (0.02 mean)		0.02		
Muscle Ear tag	0.02 (tongue)				Muscle 0.03
Dip		0.03(0.02)			
Spray	0.03[2]		<0.01(<0.01)	0.01	
Liver Ear tag	<0.01				Liver 0.03[2]
Dip		0.01(<0.01)			
Spray	0.03[2]		<0.01(<0.01)	<0.01	

Kidney Ear tag	<0.01				Kidney 0.03[2]
Dip		0.02(0.02)			
Spray	0.03[2]		<0.01(<0.01)	<0.01	
Omental fat Dip		1.3(1.1)			Omental fat 1.3
Spray	0.2(0.2)		0.03(<0.02)		
Renal fat Backrub	0.3(0.2)				Renal fat 0.7
Ear tag	0.04				
Dip		0.7(0.7)			
Spray	0.7(0.6) (low side)		0.02(<0.02)		
Loin (= subcut.?) fat Backrub	0.7(0.2)				Loin fat (subcut.?) 0.7
Spray	0.08(0.05)				
Subcut.fat Ear tag	0.05 "back fat"				Subcutaneous fat 4.3
Dip		4.3(1.3)			
Spray		0.3(0.14) (tail base fat)		<0.01 ("fat")	
Max. mg/kg/ matrix/animal					
milk	0.01	0.02	0.02	--	
muscle	0.03	0.03	<0.01	0.01	
liver	0.03	0.01	<0.01	<0.01	
kidney	0.03	0.02	<0.01	<0.01	
fat -->	0.7	4.3	0.03	<0.01	

[1] Because milk is normally pooled, the highest mean, not the highest individual value, is recorded. This was 0.02 mg/kg from both spray and dip treatments.

[2] Estimated. There were no results at the GAP 3-day pre-slaughter interval, so an estimate was made on the basis of the residues found at 1 and 7 days.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

Information on diazinon residues in commerce or at consumption from The Netherlands for the periods 1991-1993 and for 1994 is shown in Table 14.

Table. 14. Residues of diazinon in foods in commerce in The Netherlands 1991-1993 and 1994 (Netherlands, 1995).

Commodity	No. of samples	No. of samples without residues (<0.02 mg/kg)	No. of samples with residues ≥0.02 mg/kg)[1]
Citrus fruit			
1991-93			
tangerines	523	519	4
oranges	958	948	10
1994			
grapefruit	111	110	1
lemons	102	101	1
tangerines	215	214	1
oranges	348	335	13
Pome fruit			
1991-93			
apples	1698	1692	6
pears	501	498	3
1994			
apples	712	709	3
pears	162	161	1
Stone fruit			
1991-93			
plums	536	534	2
1994			
cherries	68	66	2
nectarines	103	102	1
Berries and small fruit			
1991-93			
grapes	999	995	4
strawberries	2976	2974	2
1994			
grapes	336	335	1
strawberries	913	912	1
other small fruit	103	101	2
Misc. fruit			
1991-93			
kiwifruit	309	294	15
pineapple	93	88	4
1994			
kiwifruit	96	91	5
Root and tuber veg.			
1991-93		561	
carrots	609	762	48
radishes	764		2
1994			
carrots	141	130	11 (mean 0.02 mg/kg)
Bulb veg.			

Commodity	No. of samples	No. of samples without residues (<0.02 mg/kg)	No. of samples with residues ≥0.02 mg/kg)[1]
1991-93			
bulb onions	106	104	2
Fruiting veg.			
1991-93	1129	1125	4
sweet peppers	344	339	5
melons			
1994			
peppers	571	568	3
cucumbers	341	340	1
melons	164	158	6
Brassica veg.			
1991-93			
broccoli	214	208	6
Brussels sprouts	132	128	4
Chinese cabbage	348	345	3
Leafy veg. & fresh herbs			
1991-93			
lettuce	2634	2621	13
endive	1724	1718	6
chives	33	31	32
parsley	563	560	3
1994			
lettuce	1277	1274	3
endive	511	508	3
parsley	158	154	4
Stem veg.			
1991-93			
celery	807	799	8 3 samples ≥0.5 mg/kg (mean 0.04 mg/kg)
1994			
celery	202	201	1
Pulses			
1991-93			
beans	855	853	2

[1] All residues were below 0.5 mg/kg except in the 3 noted samples of celery.

Monitoring data for 1994 were reported from Poland. No diazinon residues were found in 73 samples of apples, 17 of beetroot, 101 of carrots, 30 of cauliflowers, 23 of celery, 62 of greenhouse cucumbers, 20 of field cucumbers, 78 of black currants, 12 of leeks, 47 of bulb onions, 30 of parsley, 10 of sweet peppers (greenhouse), 10 of radishes, 29 of raspberries, 126 of strawberries, and 224 of tomatoes (greenhouse). Residues were found in 20 samples, distributed as shown below.

Commodity	No. of samples	No. positive	Residues, mg/kg	Mean, mg/kg
White cabbage	123	6	0.01-0.2	0.07
Red, white currants	20	13	0.03-0.5	0.15
Lettuce (greenhouse)	9	1	0.5	

NATIONAL MAXIMUM RESIDUE LIMITS

National maximum residue limits reported to the Meeting are listed below. In many cases national authorities have adopted Codex MRLs for animal commodities but several members of the European Union (underlined) will reportedly change to European Union MRLs in 1997.

Commodity	Country	MRL, mg/kg
Products of plant origin		
Cereals	Australia	0.1
	Netherlands, Poland	0.05
Citrus fruits	Australia	0.7
Fruits (except citrus, olives, peach)	Australia	0.5
Kiwifruit	Australia	0.5
Nuts	Australia (tree nuts)	0.1
	Netherlands	0.1
Oilseed	Netherlands	0.1
Olive oil, crude	Australia	2
Olives, unprocessed	Australia	2
"Other foods"	Netherlands	0[1](0.02)
"Other fruits"	Netherlands	0.5
Peach	Australia	0.7
Potato	Netherlands	0.02[1]
Sugar cane	Australia	0.5
Sweet corn (corn-on-the-cob)	Australia	0.7
	Netherlands	0.7
Vegetable oils (except olive oil, crude)	Australia	0.1
Vegetables	Australia	0.7
Products of animal origin		
Edible offal (mammalian)	Australia	0.7
Eggs	Australia	0.05*
Milk	Australia	0.5 (in the fat)
	Canada	0.1 (ear tag uses)

Commodity	Country	MRL, mg/kg
	Austria, Chile, China, Columbia, Egypt, Finland, France, Iraq, Jordan, Kenya, Kuwait, Lebanon, Libya, Morocco, Netherlands, Oman, Poland, Portugal, Saudi Arabia, Spain, Switzerland, Syria, Thailand, Turkey, UK, United Arab Emirates, Vietnam.	0.02
Meat (mammalian)	Canada	0.1 (ear tag uses)
	Switzerland	0.2
	Argentina, Australia, Austria, Chile, China, Columbia, Egypt, Finland, France, Iraq, Ireland, Jordan, Kenya, Kuwait, Lebanon, Libya, Morocco, Netherlands, New Zealand, Oman, Poland, Portugal, Saudi Arabia, Spain, Switzerland, Syria, Thailand, Turkey, UK, United Arab Emirates, USA, Vietnam.	0.7 (fat basis)
Poultry, edible offal of	Australia	0.05*
Poultry meat	Australia	0.05*

[1] Limit of detection
* At or about the limit of determination

APPRAISAL

Diazinon was first evaluated by the 1965 JMPR and has been reviewed several times since. In 1993 a periodic review was conducted and in 1994 a new MRL was recommended for hops. The 1993 JMPR recommended, among other items, an increase in the CXL for pome fruits from 0.5 to 2 mg/kg and the withdrawal of the CXLs for animal commodities in the absence of animal transfer studies and data from uses as an ectoparasiticide.

The CCPR in 1995 and 1996 endorsed most of the recommendations of the 1993 JMPR with the exception of the proposed MRL for pome fruits and the recommended withdrawal of the CXLs for milks and the meat of cattle, pigs and sheep.

Several countries were concerned that the proposed MRL for pome fruit, and to some extent the proposed limits for tomatoes and cabbages, might imply a high dietary intake. Insufficient new data were provided to review the recommendation, which was based on trials in the USA. It was the understanding of the Meeting that US GAP for pome fruits has been revised since 1993, and that additional trials which had been carried out according to the new GAP might support a lower limit. It is desirable that details of these trials be provided to a future JMPR. In order to provide a better estimate of dietary intake, the Meeting estimated STMR levels for pome fruit, tomatoes and cabbages from the data in the 1993 JMPR monograph on trials which complied with GAP at that time. These levels were 0.12, 0.12 and 0.16 mg/kg respectively. The respective proposed MRLs are 2, 0.5 and 2 mg/kg.

The main focus of the present evaluation was the review of submissions in support of MRLs for animal products. The 1993 JMPR considered animal transfer studies and information on veterinary uses to be desirable, and the 1995 CCPR retained the CXLs for animal products pending review by the JMPR of new data on animal feeding trials to be submitted by Australia and the manufacturer. The

Meeting reviewed new submissions on animal transfer studies and supervised trials involving approved uses for ectoparasite control together with reports of additional analytical methods (mainly for animal products) and animal metabolism studies, some of which were provided to the 1993 JMPR, but not to the FAO Panel.

Some studies of animal metabolism were resubmitted at the request of the Meeting, in particular on poultry metabolism which had not been reviewed in 1993. These confirmed that metabolism in hens is essentially similar to that in mammals and that diazinon, diazoxon and hydroxydiazinon generally constitute a small proportion of the total radioactive residue, which consists largely of the pyrimidinol metabolite and hydroxy derivatives of it, together with glucuronide and other conjugates.

The Meeting reviewed nine analytical methods submitted for the first time in addition to re-submissions of methods reviewed in 1993. The new submissions are mainly methods for animal products based on GLC with phosphorus- or NP-selective detectors. Most of them determine only diazinon *per se*, with limits of determination ranging from 0.01 to 0.05 mg/kg. Two methods determine hydroxydiazinon and diazoxon in addition to diazinon, although in most trials only residues of diazinon were reported.

A feeding trial on dairy cows at levels equivalent to 40, 120 and 400 ppm of diazinon in the diet was reported. The manufacturer considered 40 ppm to be a reasonable estimate of intake but the dietary burden based on Codex MRLs for those commodities with the greatest potential for residues in cattle feed, maize forage, sugar beet tops and apple pomace, is likely to be lower. If the maximum percentage of the feed dry weight for dairy and beef cattle is assumed to be 80 and 40% maize forage, 10 and 20% sugar beet tops, and 20 and 40% apple pomace, it can be estimated that the dry weight dietary burden would not exceed about 25 ppm for dairy or 15 ppm for beef cattle. This is based on adjusting the CXLs to a dry weight basis, assuming that they are not already so expressed. Since some countries include other feed items which might contain more diazinon, 40 ppm is a reasonable worst-case assumption, if not needed for estimates based on Codex MRLs.

The study at the 40 ppm level indicated that no residues (<0.01 mg/kg) of diazinon, diazoxon or hydroxydiazinon would be expected in the liver, kidney, muscle, or milk of cattle, but residues of diazinon up to 0.04 mg/kg occurred in omental fat. Intakes calculated from Codex MRLs would be expected to produce residues of ≤0.02 mg/kg in the fat of beef cattle. Diazinon residues in the fat were roughly proportional to the intake of diazinon. Diazinon was detectable in milk only at the tenfold dosing level: the pattern of residues in the milk of individual cows dosed at this rate suggests that residues of diazinon may peak after about 3-7 days and then decrease.

Information on the freezer storage stability of diazinon in milk and of diazoxon and hydroxydiazinon in meat and milk is desirable to confirm the above conclusions.

In a feeding study on poultry no residues (<0.01 mg/kg) of diazinon, diazoxon or hydroxydiazinon were found in any sample from hens fed for 28 consecutive days at rates equivalent to 0.5, 1.5 or 5 ppm in the diet. The basis for considering 0.5 ppm as a likely level in poultry feed was not explained. The only commodity with a Codex MRL which is a significant poultry feed item is maize, which might be up to 80% of a poultry diet. However the CXL for maize is at the limit of determination of 0.02 mg/kg, so a feeding level of 0.5 ppm is more than adequate. A maximum residue level of 0.02 mg/kg (limit of determination) could be supported for poultry meat, fat and eggs.

Eight trials of uses against ectoparasites were reviewed by the JMPR from 1967 to 1975 and 3 ear tag trials were reviewed in 1993. All of these were re-submitted for review by the present Meeting, together

with a number of studies not previously reviewed: 10 spray trials (6 on cows, 2 on goats, 1 on sheep, 1 on pigs), 4 ear tag trials on cattle, 3 sheep dip trials, 1 wound-dressing study on sheep and 1 backrub study on cattle.

Dust applications. Data from one very old study could not be related to GAP. The residues in milk increased from 0.02 mg/kg after two hours to 0.1 mg/kg after 9 hours.
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Wound dressings.In a 1974 Australian study residues of diazinon were determined in the fat, muscle and liver of fly-struck sheep (5 animals/treatment rate) 10 days after treatment with a 2% ai powder formulation applied as a wound dressing at 10 and 30 g/animal. It could not be confirmed with the label provided that 10 g/animal is the GAP rate. The maximum residues from the 10 g treatment after ten days compared to the 14-day Australian GAP slaughter interval were 0.01 mg/kg in liver, 0.03 mg/kg in muscle and 0.08 mg/kg in omental fat. The corresponding median residue levels were <0.01, 0.01 and 0.06 mg/kg.

Backrubber trials. The Meeting could not evaluate the results of a 1967 trial in the USA with both handrubbed and burlap bag applications for which no relevant GAP was available.

In a recent Australian trial on cattle in accordance with Australian GAP the maximum, median and mean diazinon residues were 0.66, 0.24 and 0.29 mg/kg in loin fat and 0.26, 0.16 and 0.16 mg/kg in renal fat 5 days after 19 days of exposure to a typical backrubber application. The GAP withdrawal period is 3 days and the recommended export slaughter interval 10 days. Residues had generally decreased substantially by 7 or more days after exposure ceased. The maximum, median and mean residues of diazinon were 0.3, 0.04 and 0.1 mg/kg in loin fat one day after 10 days of exposure. Residues in renal fat were on average about half those in loin fat. The residues in loin fat were higher after prolonged exposure. The Meeting concluded that residues would not be expected to exceed 0.7 mg/kg in the fat of cattle from applications of EC formulations in backrubbers according to Australian GAP if exposure does not exceed 19 days and a withdrawal interval of 5 days is observed, or 0.1 mg/kg after the 10-day export slaughter interval. The Meeting had no information about exposures greater than 19 days.

Ear tags. Three Canadian and 4 Australian trials were reported. The Canadian reports were rather abbreviated summaries: although most of the essential information was provided, analytical methods were only referenced and details were meagre on intervals from sampling to analysis, sample storage and handling conditions, and confirmation by analysis of the claimed levels of diazinon in the tags. No reference, or confirmation of adherence, to GLP was provided. The Canadian trials are probably according to GAP. The Canadian withdrawal interval is reported to be "Nil" and the label simply refers to removal before slaughter. The Meeting interpreted this to imply essentially a 0-day withholding period.

In the 1987 Canadian trials residues in whole milk were <0.5 ì g/kg 1 day after tag application and reached a maximum, median and mean of 1.7, 1.4 and 1.4 ì g/kg after 7 days. Residues in back fat and kidney fat were respectively 0.03 and 0.035 mg/kg after 14 days. No residues (<0.01 mg/kg) were reported in muscle, liver or tongue. Similar results were reported in the 1989 study, with a maximum of 0.05 mg/kg in back fat. The Meeting concluded that the Canadian trials were not reported in sufficient detail to draw firm conclusions.

Details were also lacking from the first two Australian trials (1989, 1990), although the storage conditions were indicated for the first and sample chromatograms were provided for the second. The

1989 study appears to reflect Australian GAP, but in 1990 only one ear of each animal was tagged whereas two tags conform to GAP. The maximum, median and mean residues in milk fat in 1989 were 0.02, 0.01 and 0.0125 mg/kg after 28 days, and were not significantly different from those after 1 day. The maximum residue would be equivalent to <0.01 mg/kg in whole milk assuming 4% fat. The Meeting placed less reliance on these trials than the better documented 1992/93 Australian trials.

The 1992 and 1993 Australian trials were similar in principle and appear to reflect Australian GAP. Both were reported to comply with OECD GLP. In the 1992 trial diazinon residues in the milk fat peaked after 7 days with maximum, median and mean residues of 0.26, 0.2 and 0.19 mg/kg, corresponding to a maximum of 0.01 mg/kg in whole milk assuming 4% fat. In the 1993 trial residues increased from a maximum, median and mean of 0.02, <0.01 and <0.0125 mg/kg milk fat after 1 day to 0.02, 0.01 and 0.02 mg/kg after 7 days and 0.03, 0.02 and 0.02 mg/kg after 42 days, then decreased to ≤0.01 mg/kg after 84 days of continuous exposure. Maximum and mean residues in whole milk would be ≤0.01 mg/kg assuming 4% milk fat.

Although the Meeting was more confident of the documentation for the 1992/93 Australian trials, there is an apparent inconsistency between the higher residue levels (up to 0.3 mg/kg) found in milk fat in 1992 compared with ≤0.03 mg/kg in 1993 and ≤0.02 mg/kg in the 1989 Australian trials. Before completion of the 1993 study this was attributed to the use of 15 g tags in 1992 compared with 10 g in 1989, but the 1993 tags were also 15 g and the residues were comparable to those in 1989.

After the 1993 study the authors speculated that the inconsistencies were due to differences in the extent of self-grooming by the cattle. This varies according to buffalo fly pressure, which was not recorded. The only other obvious differences between the trials were that in 1992 the cream was stored in a refrigerator for 5 days before the preparation of butter whereas preparation was immediate in 1993, and the ear tags were from different manufacturers. Unfortunately no reference was made to analysing the tags to confirm the diazinon content before the study.

Overall the Meeting gave greater weight to the more recent, better described Australian studies and concluded that diazinon residues from the use of ear tags on cattle according to GAP should not exceed 0.2 mg/kg (mean) in butter, 0.05 mg/kg in back fat or renal fat, 0.01 mg/kg (mean) in milk, or the limits of determination of 0.01 mg/kg in kidney, liver and muscle and 0.02 mg/kg in tongue.

Dipping. Of 8 trials, 3 on cattle and 1 on sheep were very old and insufficiently documented by current standards to provide a basis for estimating maximum residue levels. Only the sheep trial of these four (in 1962) appears to comply approximately with current GAP: it showed maximum and mean residues of 1.4 and 0.8 mg/kg in sheep kidney fat. Even in that study the sheep were dipped for 20 seconds, considered to be twice the recommended time. The Meeting placed little emphasis on these four studies. Since the other three very old trials were the only ones with cattle there are no useful cattle trials and any conclusions on likely residues in dipped cattle must be largely based on sheep dipping, which would normally produce higher residues.

The sheep trials in 1973 and 1974 were fairly well documented. In 1973 the residues in milk from treatments according to GAP were 0.01 and 0.02 mg/kg after the 4-day GAP milking interval. In 1974 the maximum residues were 0.4 mg/kg in muscle, <0.02 mg/kg in liver and 2.6 mg/kg in omental fat, but the dip concentration was 3 times the GAP level. In a reasonably well described Australian trial in 1986 sheep were slaughtered in pairs at intervals after a single dip. The maximum and mean residues after the 14-day GAP pre-slaughter interval were 0.03 and 0.02 mg/kg in muscle, 0.01 and <0.01 mg/kg in liver, 0.02 and 0.02 mg/kg in kidney, and 0.67 and 0.65 mg/kg in kidney fat. The mean residues were also the medians.

The best documented trial was in 1989 in the UK. The dip concentration was 1.6 times the GAP concentration in the UK, but complied with Irish and New Zealand GAP. Pre-slaughter intervals are 14 days in the UK and Ireland, and 21 days in New Zealand. The maximum, median and mean residues after 14 days were 1.3, 1.1 and 1.1 mg/kg in omental fat and 4.3, 1.3 and 2.3 mg/kg in subcutaneous fat, in which the three individual residues were 4.3, 1.4 and 1.3 mg/kg. After 21 days the maximum, median and mean residues were 1.2, 0.75 and 0.8 mg/kg in omental fat and 1.4, 1.0 and 1.2 mg/kg in subcutaneous fat, in which these were also the individual residues.

A comparison of the residues of 4.3, 1.3 and 1.4 mg/kg in subcutaneous fat at 14 days and consideration of the relation between 14- and 21-day residues in both omental and subcutaneous fat led the Meeting to conclude that 4.3 mg/kg was probably aberrant. It is not consistent with the other results, except to the extent that higher residues in subcutaneous fat than in other fats are not unexpected.

In summary, from the available data the maximum and median residues to be expected in sheep from single dipping according to GAP would be as follows.

	Residue, mg/kg	
	Maximum	Median
milk	0.02	0.02
muscle	0.03	0.02
liver	0.01	<0.01
kidney	0.02	0.02
kidney fat	0.7	0.7
omental fat	1.3	1.1
subcutaneous fat	1.4	1.4

From the available information on residues in individual sheep the Meeting concluded that a level of 2 mg/kg would be required to cover residues in sheep fat arising from single dipping according to GAP. Although this is greater than the current CXL of 0.7 mg/kg, several trials according to GAP show that residues above 0.7 mg/kg are likely to occur. A pre-slaughter interval of 35 days would appear to be required to reduce fat residues to the CXL. The Meeting noted that the most reliable sheep dipping trials which complied with GAP were with single dips, although GAP in most countries allows multiple dipping. This emphasises the need for a higher limit than 0.7 mg/kg. Additional trials meeting current standards and including multiple dips according to GAP are highly desirable, as are monitoring data on sheep fat, especially from sheep known to have received dip or spray applications at maximum GAP rates.

Cattle spraying. Thirteen trials were reported, but the Meeting did not review one from 1972 which was available only in Russian. Six of the remaining 12 were very old studies (1962-7), not meeting current reporting standards and often with outdated analytical methods. The Meeting placed little emphasis on these in estimating maximum residue levels in cattle, but considered 5 of the remaining 6 studies to be at least marginally acceptable to varying degrees. It was recognized that they were all with single applications, although GAP generally permits more than one spray. Four of them were concerned with residues in milk and two with residues in fat or tissues.

Residues in milk. A fairly well described 1971 Swiss trial was not fully acceptable to the Meeting, but

was of particular interest because it involved multiple applications in accordance with current GAP. However, because of the obsolete analytical method (autoanalyser) and inadequate reporting of certain details, some uncertainty remains on the validity of the results. The mean diazinon residues in the milk did not exceed 0.02 mg/kg (maximum 0.03 mg/kg) 4 days (the GAP withdrawal interval) after the 3rd spraying (the maximum GAP number). All residues were <0.02 mg/kg after 6 days and mean residues 0.03 mg/kg after 3 days, which is the GAP withdrawal period in other countries.

In a fairly well described Australian study in 1974 the mean diazinon residues in the milk from 5 cows from a herd treated according to GAP were 0.02 mg/kg (maximum 0.05 mg/kg) 5 days after treatment compared to 3- or 4-day GAP withdrawal intervals. This is consistent with the 1971 study. The residues were 0.05 mg/kg in a composite sample of butter and the mean residues in composited skim milk were about 1/3rd to 1/6th of the level in the whole milk, confirming the affinity of diazinon with fat. The study clearly demonstrates that the residues in milk from individual cows are significantly reduced when bulked with milk from other members of a treated herd.

In a 1986 Australian trial the mean diazinon residues in milk were <0.01 mg/kg 70 hours (2.9 days) after a single spray at 1.2 times the GAP concentration compared to the Australian pre-slaughter interval of 3 days and the milk withdrawal intervals of 3 or 4 days in other countries.

A 1994 Egyptian trial was at the concentration of Egyptian GAP, but with a single application whereas 3 are permitted. The highest diazinon residue in the milk was 0.3 mg/kg 6 hours after application, but decreased to <0.005 mg/kg after 36 hours, half the 3-day Egyptian GAP withdrawal interval. Some details were not reported.

Residues in tissues. In a 1986 Australian trial a single spray at 1.2 times the GAP concentration gave maximum and mean/median diazinon residues of 0.7 and 0.6 mg/kg in kidney fat after 7 days, and 0.2 and 0.2 mg/kg in omental fat after 14 days. There were no data at the 3-day GAP pre-slaughter interval. Subcutaneous fat, which would be expected to have higher residues than other fats, was not analysed. After 7 days residues were ≤0.01 mg/kg in muscle, kidney and liver. In a 1996 Australian back spray trial a single GAP application gave diazinon residues in subcutaneous fat of <0.05 mg/kg in 5 animals and 0.08 mg/kg in one after 4 days. The residues in renal fat were <0.05 in 6 animals.

In summary the cattle spraying trials suggest that single spray applications according to GAP might produce the following results.

Sample	Residue, mg/kg			Pre-slaughter interval, days	
	Max.	Median	Mean	In trial	GAP
Milk			0.02	3-5	3-4
Loin (subcutaneous) fat	0.08	<0.05		4	3
Renal fat	0.7	0.6		7	3
Omental fat	0.2	0.2		14	3
Muscle, liver, kidney	0.01			7	3
	0.07			1	3
	0.03[1]			3[1]	3

[1] Estimated residue at GAP pre-slaughter interval. See discussion below.

Some of these residues may be lower than likely maximum levels. In particular, especially in view of the results of the sheep dipping trials, some qualification must attach to the residue in subcutaneous cattle fat in particular because no residues in subcutaneous fat were reported in the GAP trial which gave 0.7 mg/kg in renal fat after 7 days. Residues would have been be expected to be higher in subcutaneous fat, probably above 1 mg/kg. Similarly, even the 0.7 mg/kg in renal fat may be too low as a maximum residue level since it occurred after 7 days whereas the GAP withdrawal interval is 3 days, and residues in renal fat in 2 separate animals of the study after a 1-day withdrawal period were 1.3 and 2.9 mg/kg.

Special attention should also be given to the residues in muscle, kidney and liver since no results were available at the 3-day GAP pre-slaughter interval. The maximum and mean residues after 1 day were 0.06 and 0.06 mg/kg in muscle, 0.02 and <0.02 mg/kg in liver and 0.07 and 0.07 mg/kg in kidney. The Meeting concluded that although the residues would be lower after 3 days they would still exceed the 0.01 mg/kg found after 7 days, and estimated a maximum residue level of 0.03 mg/kg in muscle, liver and kidney from single spray applications to cattle according to GAP.

No conclusion could be drawn with confidence about the results of multiple GAP applications as only very old, inadequately reported, studies were available. Although one of these suggested that residues in omental fat might increase with multiple applications, there were no results at a GAP withdrawal interval, and no analyses of other (e.g. subcutaneous) fat or tissues. The Meeting therefore considered modern spray trials on cattle under maximum GAP conditions (which include multiple sprays) to be highly desirable. Analyses should preferably be for diazinon, diazoxon and hydroxydiazinon in milk, muscle, edible offal and fat (including kidney, omental and especially subcutaneous fat).

Sheep spraying. In a rather poorly reported Australian trial in 1971 with EC and WP formulations applied at twice the GAP concentration, diazinon residues did not exceed 0.16 mg/kg in fat or 0.09 mg/kg in muscle after the GAP pre-slaughter interval of 14 days. In a well-documented Swiss trial in 1994 residues in fat (from the base of the tail) were determined 28 days after a single spray at the GAP concentration. The Swiss withdrawal interval is 21 days. The maximum and median residues from each of three different EC formulations were 0.29 and 0.12 mg/kg, 0.24 and 0.16 mg/kg, and 0.22 and 0.11 mg/kg with an overall maximum and median of 0.29 and 0.14 mg/kg. The Meeting concluded that diazinon residues in sheep fat are unlikely to exceed 0.3 mg/kg after 28 days from a single spray application according to Swiss GAP. There was no information on multiple applications, for which data on residues in milk and tissues are desirable, nor on residues at the GAP withdrawal interval of 21 days.

Goat spraying. In a 1986 Australian trial with a single application approximating the GAP concentration, the residues in two goats after the 14-day Australian GAP pre-slaughter interval were <0.01 mg/kg in the muscle, liver and kidney of both animals, 0.02 and <0.01 mg/kg in kidney fat and 0.03 and 0.01 mg/kg in omental fat. Subcutaneous fat was not analysed. In a 1987 Australian trial the mean residues in milk were 0.02 mg/kg after 78 hours. The GAP withdrawal interval for milk is 3 or 4 days in other countries.

Pig spraying. In a fairly well documented 1974 Swiss trial diazinon residues were ≤0.01 mg/kg in muscle and <0.01 mg/kg in liver, kidney, unspecified fat and skin 28 days after one or two sprays at the GAP concentration. The Swiss pre-slaughter interval is 21 days. Even at twice the GAP concentration the residues were all <0.01 mg/kg except one residue of 0.04 mg/kg in muscle. The samples were also analysed for hydroxydiazinon, the pyrimidinol G 27550 and diazoxon, but the only measurable residue was 0.02 mg/kg of hydroxydiazinon in a single fat sample at the GAP spray concentration. The Meeting concluded that diazinon residues would be unlikely to exceed 0.01 mg/kg in pig tissues from Swiss GAP. For risk assessment purposes the figure would be 0.03 mg/kg.

Estimates of STMR levels

Because the number of trials of ectoparasite treatments were limited and the residues would be from different populations depending on the animal and the type of treatment, the Meeting considered using recommended MRLs for the estimation of dietary intake. However, to conform to the general approach to such estimations, the Meeting estimated STMR levels for animal products.

Poultry. No diazinon (<0.01 mg/kg) was detected in any sample of skin, muscle, eggs, fat or liver after feeding diazinon at a level equivalent to 10 times the expected dietary intake. The Meeting therefore concluded that the effective STMR for poultry meat, poultry edible offal and eggs should be zero.

Milk. Because milk is normally bulked before distribution, the Meeting used mean values of the residues in milk from different animals in individual trials as the basis for STMR estimates. The mean residues in milk from GAP applications were 0.02 mg/kg in cattle and goats from spraying and in sheep from dipping, and 0.01 mg/kg in cattle from ear tags. The Meeting estimated 0.02 mg/kg as a maximum residue level and an STMR level for milk.

Meat (muscle). Although the maximum residue level for use as an MRL for meat is expressed on a fat basis, for dietary intake purposes the Meeting also estimated an STMR for whole muscle. The distribution of maximum residues (mg/kg) in the meat of the animals treated according to GAP, with the types of treatment, were goats <0.01 (spray), pigs 0.01 (spray), cattle 0.02 (ear tags), 0.03 (spray, extrapolated value), and sheep 0.03 (dip). The Meeting estimated an STMR level of 0.02 mg/kg for the meat (whole muscle) of cattle, pigs, sheep and goats.

Edible offal. The residues from applications according to GAP (mg/kg) were as follows. Liver: goats <0.01 (spray), pigs <0.01 (spray), cattle <0.01 (ear tag), sheep 0.01 (dip), cattle 0.03 (spray, extrapolated value). Kidney: goats <0.01 (spray), pigs <0.01 (spray), cattle <0.01 (ear tag), sheep 0.02 (dip), cattle 0.03 (spray, extrapolated value). Liver and kidney combined, in rank order: <0.01 (6), 0.01, 0.02, 0.03, 0.03.

The Meeting estimated an STMR of <0.01 mg/kg for the liver and kidney of cattle, goats, pigs and sheep.

Fat. An STMR was estimated on the basis of the residues in the fat of cattle, goats, pigs and sheep from different uses against ectoparasites according to GAP. Combining the data for these animals gave the following distribution of residues in rank order.

Omental fat: 0.03, 0.2, 1.3 mg/kg.
Renal fat: 0.02, 0.04, 0.3, 0.7, 0.7 mg/kg.
Loin (subcutaneous) fat: <0.01, 0.05 0.08, 0.3, 0.7, 1.4 mg/kg (omitting an aberrant value of 4.3 mg/kg).

All fat: <0.01, 0.02, 0.03, 0.04, 0.05, 0.08, 0.2, 0.3, 0.3, 0.7, 0.7, 0.7, 1.3, 1.4 mg/kg.

The Meeting estimated an STMR of 0.3 mg/kg.

General observations. As has been noted, the trials of diazinon for ectoparasite control range from very old studies, unusable by current standards, to a few relatively recent well-documented trials reported to be in accordance with GLP. The Meeting has tried to make the best use of the available studies that

prudence allows. In many cases even where GAP concentrations have been applied results are lacking at GAP withholding periods. Another common observation is that most of the acceptable studies are with single applications rather than the multiple applications permitted by GAP. In some cases very similar trials have inexplicably produced inconsistent results and in others no data are available on residues in subcutaneous fat, which has been shown to have higher residues than other fat after dermal applications.

These factors have required the Meeting to exercise judgement in estimating maximum residue levels and have lead to some uncertainty as to whether the recommended MRLs are sufficiently high to cover all uses of diazinon as an ectoparasiticide according to GAP. It is also at least possible that in practice some animals might be exposed to more than one type of treatment (e.g. spraying or dipping as well as ear tags or wound dressings). For these reasons the Meeting concluded that additional modern trials with diazinon used for ectoparasite control at maximum GAP concentrations and with multiple dip and spray applications, conducted in accordance with GLP, are desirable in order to confirm the estimated maximum residue levels and STMR levels.

RECOMMENDATIONS

On the basis of the data on residues and information on GAP provided the Meeting estimated the maximum residue levels listed below, which are recommended for use as MRLs. Corresponding STMRs are also listed for estimating dietary intake. For considering long-term dietary intake estimates the Meeting also recommended the use of median residues for pome fruit, tomatoes and cabbages of 0.12, 0.12 and 0.16 mg/kg respectively rather than the respective proposed MRLs of 2, 0.5 and 2 mg/kg.

Definition of the residue for compliance with MRLs and for estimation of dietary intake: diazinon.

The residue is fat-soluble.

CCN	Commodity	Recommended MRL, mg/kg		STMR, mg/kg	Withholding interval, days
		New	Previous		
PO 0840	Chicken, edible offal of	0.02*	--	0	
P 0840	Chicken eggs	0.02*	--	0	
PM 0840	Chicken meat	0.02*		0	
MO 0099	Liver of cattle, goats, pigs and sheep	0.03 V	--	0.01	3
MO 0098	Kidney of cattle, goats, pigs and sheep	0.03 V	--	0.01	3
MM 0097	Meat of cattle, pigs and sheep	2 (fat) V	W[1]	0.3 (fat) 0.02 (whole muscle)	3
MM 0814	Goat meat	2 (fat) V	--	0.3 (fat) 0.02 (whole muscle)	3
ML 0106	Milks	0.02 F V	W[1]	0.02	3
STMRs for fruits and vegetables					

CCN	Commodity	Recommended MRL, mg/kg		STMR, mg/kg	Withholding interval, days
		New	Previous		
FP 0009	Pome fruits			0.12	
VO 0448	Tomato			0.12	
VB 0041	Cabbages, Head			0.16	

* At or about the limit of determination.
[1] Withdrawal of existing CXL proposed by 1993 JMPR.

FURTHER WORK OR INFORMATION

Desirable

1. Studies of the stability of diazinon, diazoxon and hydroxydiazinon in stored analytical samples of meat, fat, edible offal, milk and eggs.

2. Modern dipping and spray trials on sheep and cattle at maximum GAP rates and including multiple dips and sprays. Analyses for diazinon residues in milk, muscle, edible offal and fat (kidney, omental and especially subcutaneous fat) would be desirable, as well as analyses for diazoxon and hydroxydiazinon in addition to diazinon.

3. Data from monitoring analyses of subcutaneous fat of sheep for diazinon, ideally sheep known to have received multiple dip or spray applications at maximum GAP rates.

4. Submission, when the new supervised trials of ectoparasite control are submitted in 1998, of information on current US GAP for pome fruits and cabbages and data from recently completed US supervised trials reflecting that GAP.

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