

## QUINOXYFEN (222)

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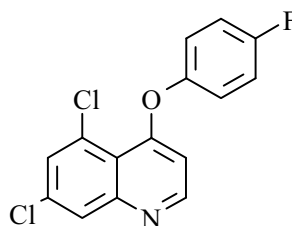
### EXPLANATION

Quinoxifen is a fungicide used for protection against powdery mildew diseases on a variety of crops. At the 36th session of the CCPR (ALINORM 04/27/24), quinoxifen was listed as a candidate for evaluation of a new compound by the 2006 JMPR. It was furthermore identified as a candidate for work sharing.

The sponsor has submitted study reports on the metabolism in lactating goats, wheat, sugar beet, grapes, cucumber, and tomato, on the environmental fate (aerobic soil metabolism, hydrolytic degradation, photochemical degradation, and confined rotational crops), on analytical methods for the determination of quinoxifen in various matrices, and on the storage stability of quinoxifen in stored frozen analytical samples. Crop field trials were supplied for cherries, grapes, strawberries, currants, melons, peppers, lettuce, wheat, barley, hops, sugar beets and sugar beet tops. GAP information (labels) was also supplied. Processing studies were submitted for wheat, barley, and grapes, and dairy cow and laying hen feeding studies were provided. National use information was supplied by Australia, the Netherlands, and the USA. Germany provided field trial data for currants.

### IDENTITY

ISO common name:	Quinoxifen
IUPAC name:	5,7-dichloro-4-(4-fluorophenyl)quinoline
Chemical Abstract name:	5,7-dichloro-4-(4-fluorophenoxy)quinoline
CAS No.:	124495-18-7
CIPAC No.:	566
Synonyms:	XR-795; XDE-795; DE-795
Molecular Formula:	C <sub>15</sub> H <sub>8</sub> Cl <sub>2</sub> FNO
Structural Formula:	



Molecular Weight:	308.14
Minimum purity	97%

### PHYSICAL AND CHEMICAL PROPERTIES

#### Pure Active Ingredient:

Chemical/physical property	Results	Reference
Appearance	Off-white flocculent solid	21129, Cowlyn and Boothroyd, 1994
Melting point	106 – 107.5°C	
Relative density	1.56	
Solvent solubility, 20°C	Hexane 9.64 g/L Methanol 21.5 g/L Toluene 272 g/L	

Chemical/physical property	Results	Reference	
	Dichloromethane 589 g/L Acetone 116 g/L Ethyl acetate 179 g/L		
Water solubility, 20°C	pH	8605, Cowlyn and Boothroyd, 1994	
	6.45		116 ± 5.1
	5		128
	7		47
Vapour pressure	9	36	
	1.2 x 10 <sup>-5</sup> Pa @ 20°C		
	2.0 x 10 <sup>-5</sup> Pa @ 25°C		
Volatility, Henry's Law Constant @ 20°C	Calculation: 3.19 x 10 <sup>-2</sup> Pa.m <sup>3</sup> .mole <sup>-1</sup>		
Partition coefficient, 20°C and pH 6.6	Log P <sub>OW</sub> = 4.66 ± 0.002		

### Technical Material

Chemical/physical property	Results	Reference	
Melting point	100 - 106°C	27304, Cowlyn, 1994	
Relative density	1.49		
Solvent solubility, 20°C	n-heptane		10.2 g/L
	Methanol		24.6 g/L
	Xylene		200 g/L
	Dichloromethane		236 g/L
	Acetone		111 g/L
	Ethyl acetate	138 g/L	
Dissociation constant	Acetonitrile	22.8 g/L	
	n-Octanol	37.9 g/L	
	pKa of protonated DE-795 = 3.63; equivalent Ka = 2.37 × 10 <sup>-4</sup>		

### Formulations

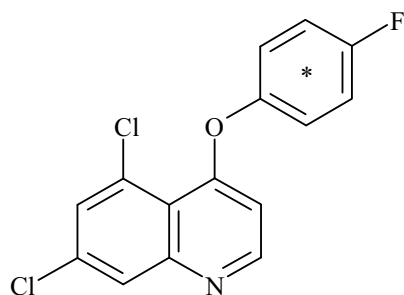
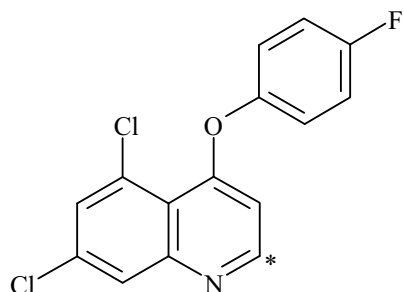
Quinoxifen is a protectant fungicide. In order to provide both protective and curative control, some formulations have been developed consisting of Quinoxifen with a curative fungicide. Quinoxifen is available in the following formulations.

Formulation	Active ingredient content
Suspension concentrate (SC), containing only Quinoxifen as the active ingredient	250 g/L Quinoxifen (EF-1295)
	500 g/L Quinoxifen (EF-1186)
Suspension concentrate (SC), containing a mixture of Quinoxifen and Cyproconazole	200 g/L Quinoxifen + 60 g/L Fenarimol (EF-1303)
	75 g/L Quinoxifen + 80 g/L Cyproconazole (EF-1406)
Emulsion, oil in water (EW), containing a mixture of Quinoxifen and Fenpropimorph	66 g/L Quinoxifen + 250 g/L Fenpropimorph. (EF-1288)

The supervised trials reported to the Meeting used either the EF-1295, EF1186, or EF-1303 formulations.

### METABOLISM AND ENVIRONMENTAL FATE

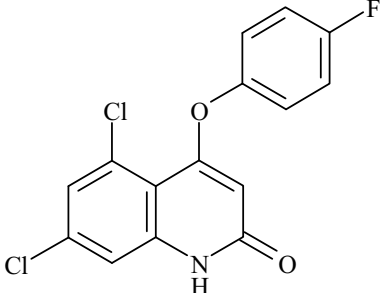
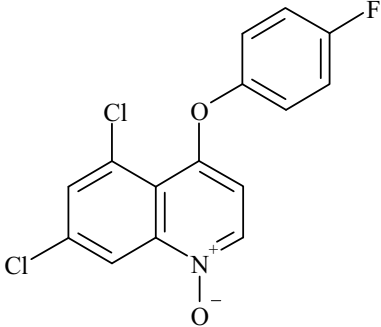
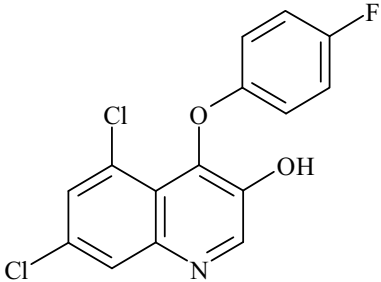
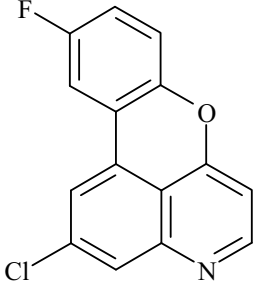
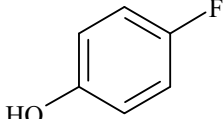
The various metabolism studies were conducted using quinoxifen radio-labelled with the <sup>14</sup>C label in the phenyl ring (phenoxy label) or on the second carbon of the quinoline ring (quinoline label).

**Phenyl-Ring Labelled [<sup>14</sup>C]Quinoxifen****Quinoline-Ring Labelled [<sup>14</sup>C]Quinoxifen [labelled on the second carbon of the quinoline ring]**

The following table summarizes the metabolites identified in the various metabolism and environmental fate studies.

Table 1: Summary of metabolites and degradates.

Common Name/Code	Chemical Name	Structure
Quinoxifen DE-795	5,7-dichloro-4-(4-fluorophenoxy)quinoline	

Common Name/Code	Chemical Name	Structure
2-Oxo DE-795 <sup>1</sup> 2-Oxo Quinoxyfen	5,7-dichloro-4-(4-fluorophenoxy)-2-oxo-quinoline	
DE-795 n-oxide Quinoxyfen n-oxide	5,7-dichloro-4-(4-fluorophenoxy)quinoline-N-oxide	
3-OH DE-795 <sup>1</sup> 3-hydroxy Quinoxyfen	5,7-dichloro-4-(4-fluorophenoxy)-3-hydroxy-quinoline	
CFBPQ	2-chloro-10-fluoro(1)benzopyrano (2,3,4-de)quinoline	
4-Fluorophenol.	4-Fluorophenol	

Common Name/Code	Chemical Name	Structure
DCHQ	5,7-dichloro-4-hydroxyquinoline	

<sup>1</sup> For all radiolabelled studies (plant, livestock, rat and environmental fate) the metabolite identified as 3-hydroxy quinoxifen is in fact 2-oxo quinoxifen.

### ***General for all radiolabelled quinoxifen studies***

The manufacturer has reported that in all studies utilizing radio-labelled quinoxifen, a metabolite has been misidentified (18219, N. R. Pearson and G. L Reeves, 2005). The metabolite identified as 3-hydroxy quinoxifen was subsequently positively identified as 2-oxoquinoxifen by X-ray diffraction. Text and figures have been corrected to reflect this change of structure assignment.

### ***Animal metabolism***

Metabolism in lactating goats- adapted in part from the evaluation of Australia

The Meeting received a report on the metabolism, distribution, and elimination of <sup>14</sup>C-quinoxifen, labelled either in the phenoxy ring or the quinoline ring, in lactating dairy goats (n=5; 51-60 kg bw), (29257, Dunsire and Paul, 1995). Two goats were orally dosed with phenoxy <sup>14</sup>C-quinoxifen (purity > 98%), twice daily for 5 consecutive days, at a rate of 10.7 mg quinoxifen/kg feed (equivalent to 0.20 mg ai/kg bw, 91.16 mg total over 5 days). Similarly, two goats were treated with quinoline <sup>14</sup>C-quinoxifen, twice daily for 5 consecutive days, at a rate of 11.7 mg quinoxifen/kg feed (equivalent to 0.21 mg ai/kg bw, 101.2 mg total over 5 days). The remaining goat was used as the untreated control animal.

Urine and faeces were collected at intervals of 24 hours until sacrifice. The metabolism cages were washed with water at the time of excreta collection and the cage washings were retained for analysis of the TRRs. Milk samples were collected prior to the first treatment with quinoxifen, and then twice daily throughout the study period (at about 8:00 am and 4:00 pm) until animals were sacrificed. The weights of urine, faeces, cage wash and milk samples were recorded and total radioactivity were measured using liquid scintillation counting (LSC). Faecal samples were homogenised with water and subjected to combustion analysis before analysis by LSC.

Goats were sacrificed 16 hours after the final dose, and samples of the following fluids/tissues were collected for TRR analysis: whole blood, plasma, liver, kidney, skeletal muscle, subcutaneous fat, omental fat, perirenal fat, GI tract and contents, and carcass. Tissue samples were analysed for their TRR content using combustion analysis and LSC.

The distribution of quinoxifen TRRs recovered from goats after 10 twice daily oral doses of radio-labelled quinoxifen (approximately 10 mg ai/kg feed/day) are tabulated below. Results are expressed as a percentage of administered dose, and as µg equiv/kg (where applicable).

Table 2. Distribution of the radiolabelled residue in the body fluids and tissues of goats (29257).

Sampling time/period (h)	% Administered ( $\mu\text{g equiv./kg}$ )				
	Control	Phenoxy $^{14}\text{C}$ -quinoxifen			Quinoline $^{14}\text{C}$ -quinoxifen
	Animal 1	Animal 2	Animal 3	Animal 4	Animal 5
<b>Urine</b>					
0-24	0.0	5.8	1.2	1.6	1.20
24-48	0.0	8.3	14.	2.5	2.4
48-72	0.0	7.9	9.1	2.8	0.05
72-96	0.0	9.1	9.8	3.0	5.7
96-120	0.0	9.2	10.	2.8	2.9
<b>Subtotal</b>	<b>NA</b>	<b>40.</b>	<b>44.</b>	<b>13.</b>	<b>12.</b>
<b>Faeces</b>					
0-24	0.0	3.2	0.86	4.5	1.4
24-48	0.02	8.5	6.1	13.	10.
48-72	0.01	7.1	15.	7.0	12.
72-96	0.01	10.	6.8	16.	21.
96-120	0.15	9.5	8.6	16.	20.
<b>Subtotal</b>	<b>NA</b>	<b>39.</b>	<b>38.</b>	<b>56.</b>	<b>65.</b>
<b>Cage wash</b>					
0-24	0.0	0.07	0.03	0.03	0.02
24-48	0.0	0.29	0.20	0.04	0.06
48-72	0.0	0.13	0.29	0.04	0.03
72-96	0.0	0.26	0.28	0.06	0.57
96-120	0.0	0.44	0.61	0.16	0.10
<b>Subtotal</b>	<b>NA</b>	<b>1.2</b>	<b>1.4</b>	<b>0.33</b>	<b>0.78</b>
<b>Milk</b>					
0-8	0.0	0.03 (28.)	0.02 (29.)	0.02 (20.1)	0.01 (26.)
8-24	0.0	0.09 (53.)	0.08 (71.)	0.06 (36.5)	0.06 (56.)
24-32	0.0	0.06 (66.)	0.07 (107.6)	0.04 (46.4)	0.03 (77.)
32-48	0.0	0.11 (68.)	0.11 (96.)	0.06 (44.6)	0.07 (72.)
48-56	0.0	0.06 (76.)	0.07 (120.)	0.04 (50.2)	0.04 (88.)
56-72	0.0	0.10 (74.)	0.12 (109.)	0.06 (48.0)	0.08 (76.)
72-80	0.0	0.10 (90.)	0.09 (140.)	0.05 (59.0)	0.05 (101.)
80-96	0.0	0.12 (75.)	0.13 (110)	0.08 (54.4)	0.07 (74.)
96-104	0.0	0.06 (81.)	0.07 (130.)	0.05 (62.5)	0.06 (120.)
104-120	0.0	0.10 (74.)	0.13 (110.)	0.06 (48.8)	0.06 (64.)
<b>Subtotal</b>	<b>NA</b>	<b>0.83</b>	<b>0.89</b>	<b>0.52</b>	<b>0.53</b>
<b>Tissues</b>					
Liver	0.0	0.92	0.92	0.69	1.3
Kidney	0.0	0.04	0.05	0.03	0.02
GI tract wall	0.0	3.1	3.3	6.9	2.5
GI tract contents	0.0	8.3	11.	11.76	13.
Carcass	0.01	2.1	3.4	1.7	2.3
<b>Subtotal</b>	<b>NA</b>	<b>14.</b>	<b>19.</b>	<b>21.</b>	<b>19.</b>
<b>Total</b>	<b>NA</b>	<b>95.</b>	<b>103</b>	<b>91</b>	<b>98</b>

Concentrations of total radioactivity in tissues for the phenoxy label were liver, 1.03 and 0.93 mg/kg; kidney, 0.29 and 0.34 mg/kg; muscle, 0.022 and 0.032 mg/kg; perirenal fat, 0.18 and 0.19 mg/kg; omental fat, 0.20 and 0.17 mg/kg; and subcutaneous fat, 0.12 and 0.12 mg/kg. Concentrations of total radioactivity in tissues for the quinoline label were liver, 0.94 and 1.5 mg/kg; kidney, 0.22 and 0.17 mg/kg; muscle, 0.015 and 0.032 mg/kg; perirenal fat, 0.13 and 0.32 mg/kg; omental fat, 0.12 and 0.26 mg/kg; and subcutaneous fat, 0.073 and 0.19 mg/kg. TRR levels in milk at 16 hours after the final dose were 0.074 and 0.11 mg/kg for the phenoxy label and 0.049 and 0.064 mg/kg for the quinoline label.

Samples were extracted with methanol. Liver was also subjected to protease digestion (pepsin, 0.1 M HCl, 37°C, overnight), enzyme deconjugation ( $\beta$ -glucuronidase with sulphatase activity) of the methanol extract, mild base hydrolysis, and/or strong base (6 N NaOH) or strong acid (6 N HCl) hydrolysis (reflux, 6 hour). Kidney was subjected to protease digestion. Some extraction efficiencies are summarized in Table 3.

Table 3. Extraction efficiencies of pooled tissue and milk samples (29257).

Matrix	Treatment Step	Extraction Efficiency (% TRR)	
		Phenoxy label	Quinoline label
Milk	Methanol extraction	85	87
Kidney	Methanol extraction	71	45
Kidney	Protease digestion	100	100
Liver	Methanol extraction	42	25
Liver	Protease digestion	100	100
Liver	1M NaOH hydrolysis at 40° C	94	92
Muscle	Methanol extraction	84	76
Omental fat	Methanol extraction	100	100
Subcutaneous fat	Methanol extraction	93	91
Perirenal fat	Methanol extraction	100	100

The TRRs in excreta (urine, faeces), milk and tissues (kidney, liver, fat) from goats were characterized and/or identified. Extracts were analyzed by TLC and HPLC, and some identifications (from urine and faeces only) were confirmed by GC/MS. Available standards (not labelled) included dichlorohydroxyquinoline (DCHQ), N-oxide quinoxifen, 4-fluorophenol, 2-oxo quinoxifen, and 6-hydroxy quinoxifen. Values are expressed as a percentage of the TRR (except as noted) and as mg equiv. /kg (in parenthesis) in Table 4.

Table 4. Characterization/Identification of the radiolabelled residue in excreta, milk, and tissues (29257).

Sample matrix	Extraction method	Percentage TRR (mg equiv./kg) <sup>1</sup>						
		Label	Quinoxifen	Isomeric hydroxy quinoxifens <sup>2</sup>	4-FP	DCHQ	2-oxo	Not identified <sup>4</sup>
Urine	Direct (none)	Phenoxy	ND <sup>3</sup>	ND	3-6	ND	ND	89-92
		Quinoline	ND	ND	ND-21	11-12	ND	67-82
	Acid hydrolysed + methanol	Phenoxy	ND-3.5	ND-5 <sup>7</sup>	35-58	ND	ND	25-55
		Quinoline	ND-3.5	ND-22 <sup>7</sup>	ND-19	38-56	ND	15-38
Faeces	Methanol	Phenoxy	27-31	49-55 <sup>6</sup>	ND-1.1	ND	ND	10-13
		Quinoline	24-26	59-62 <sup>6</sup>	ND	2.5	ND	6-10
Milk	Methanol	Phenoxy	30-42 (0.027-0.038)	ND-0.94 (ND-0.0008)	ND (ND)	ND (ND)	ND-1.4 (ND-0.001)	36-42 (0.032-0.038)
		Quinoline	37-42 (0.021-0.023)	ND (ND)	ND (ND)	ND-3.0 (ND-0.002)	ND (ND)	38-40 (0.021-0.022)
Kidney	Methanol	Phenoxy	1.6-2.3 (0.005-0.008)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	63-66 <sup>5</sup> (0.21-0.22)
		Quinoline	2.4-3.5 (0.005-0.07)	ND (ND)	ND (ND)	ND-1.6 (ND-0.003)	ND (ND)	31-39 <sup>5</sup> (0.59-0.75)
Liver	Methanol	Phenoxy	ND-1.2 (ND-0.012)	ND-2.1 (ND-0.022)	ND-6.7 (ND-0.068)	ND (ND)	ND (ND)	30-34 (0.30-0.35)
		Quinoline	1.8-3.8 (0.022-0.047)	ND (ND)	ND (ND)	ND-3.2 (ND-0.041)	ND (ND)	3.8-20 (0.050-0.25)
	Enzyme deconjugate (of MeOH extract)	Phenoxy	10.5 (0.051)	3.0 (0.015)	13.2 (0.064)	ND (ND)	ND (ND)	60.4 (0.29)
		Quinoline	18.3 (0.054)	10.4 (0.031)	ND (ND)	19.7 (0.058)	ND (ND)	29.0 (0.085)
	Protease digest	Phenoxy	6-7 (0.059-0.070)	ND (ND)	ND-8.3 (ND-0.085)	ND (ND)	ND (ND)	70-74 (0.64-0.71)
		Quinoline	9-15	ND	ND	ND	ND	50-56

Sample matrix	Extraction method	Percentage TRR (mg equiv./kg) <sup>1</sup>						
		Label	Quinoxifen	Isomeric hydroxy quinoxifens <sup>2</sup>	4-FP	DCHQ	2-oxo	Not identified <sup>4</sup>
			(0.12-0.20)	(ND)	(ND)	(ND)	(ND)	(0.62-0.72)
	Protease digest + acid hydrolysis	Phenoxy	5-11 (0.043-0.099)	ND-1.2 (ND-0.011)	ND-22.4 (ND-0.201)	ND (ND)	ND-1.3 (ND-0.012)	59-68 (0.52-0.61)
		Quinoline	2-13.5 (0.019-0.128)	ND (ND)	ND (ND)	ND-15.3 (ND-0.144)	ND (ND)	48-71 (0.45-0.67)
	Protease digest + enzyme deconjugate <sup>6</sup>	Phenoxy	ND-74	ND-8.5	ND	ND	ND-90	ND-22.
		Quinoline	ND-84	ND-4.8	ND	5.5-7.0	ND-81	5.2-8.1
Omental fat	MeOH extract	Phenoxy	51-98 (0.099-0.19)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	1.8-26. (0.004-0.050)
		Quinoline	53-96 (0.100-0.18)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	ND-22 (ND-0.041)
Perirenal fat	MeOH extract	Phenoxy	70-96 (0.13-0.18)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	1.2-14.4 (0.002-0.028)
		Quinoline	90-97 (0.19-0.20)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	ND-3.4 (ND-0.007)
Subcutaneous fat	MeOH extract	Phenoxy	76-83 (0.096-0.10)	ND-1.5 (ND-0.002)	ND (ND)	ND (ND)	ND (ND)	3.7-5.4 (0.005-0.007)
		Quinoline	75-94 (0.061-0.076)	ND (ND)	ND (ND)	ND (ND)	ND (ND)	1.9-6.5 (0.002-0.005)

<sup>1</sup> 4-FP = 4-fluorophenol; DCHQ = 5,7-dichloro-4-hydroxyquinoline; 2-oxo = the 2-oxo derivative of quinoxifen. Calculated on a %TRR basis by the JMPR reviewer using percent of radioactivity in the extract and extraction efficiency.

<sup>2</sup> Radioactive material that co-chromatographed (TLC, HPLC) with the N-Oxide quinoxifen standard in faeces extracts was shown by GC-MS to be comprised of several isomeric hydroxy-quinoxifen metabolites. Other extracts were not subjected to GC/MS/ Thus, identifications of N-oxide in various tissue extracts are not confirmed.

<sup>3</sup> not detected.

<sup>4</sup> Generally characterized as "polar material" by TLC and HPLC.

<sup>5</sup> Deconjugation with mixed glucuronidase/sulphatase treatment did not change the profile.

<sup>6</sup> Percentage of total radioactivity in the final extract.

<sup>7</sup> N-oxide quinoxifen was identified by HPLC in acid-hydrolysed urine but was not confirmed by TLC.

The major component identified in liver was a conjugated form of quinoxifen (approximately 10–15% TRR). The only components identified in kidney were quinoxifen (approximately 3% TRR) and DCHQ (about 2% TRR), with no apparent quinoxifen conjugates present. In both kidney and liver, major portions of the TRR were characterized as polar based on TLC and HPLC behaviour. The major component present in fat was quinoxifen (approximately 90% TRR), while milk contained quinoxifen (about 40% TRR) and some very polar material. Small amounts of radioactivity corresponding to 4-fluorophenol, DCHQ, and several hydroxy-quinoxifen metabolites were also present in the liver. Small amount of radioactivity corresponding to 2-oxo quinoxifen, DCHQ, and isomeric hydroxy quinoxifens were found in the milk. For both labels, hydroxy metabolites and parent compound were the major components present in faeces, while urine contained mainly a polar component which was easily hydrolysed to 4-fluorophenol or DCHQ. A proposed metabolic pathway is presented in Figure 1.



The metabolism in goat and rat (7474, Schumann, 1995) are qualitatively similar. Cleavage of the ether linkage to form 4-fluorophenol and DCHQ is seen in both animals. Isomers of fluorophenyl-ring hydroxylated quinoxifen were found in the rat (bile, faeces), whereas isomers of quinoline-ring hydroxylated quinoxifen (2-oxo) were found in the goat metabolism study. The latter were at very low levels (< 0.1% of the administered dose for the 2-oxo quinoxifen) in the rat.

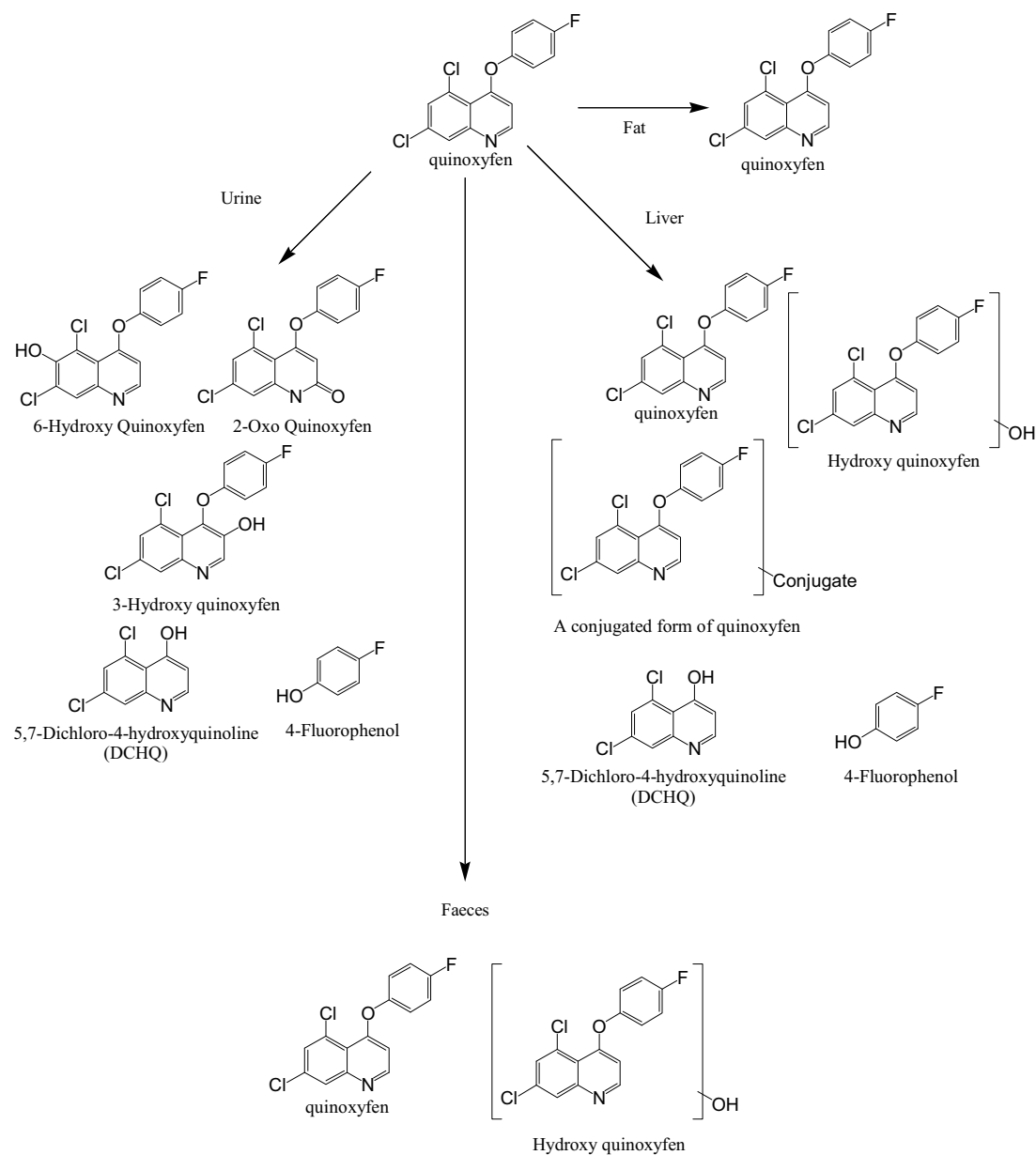


Figure 1: Proposed Metabolic Pathway for Quinoxifen in the Lactating Goat

#### Metabolism in poultry

The Meeting did not receive a poultry metabolism study. Likewise, the evaluations of Australia, the EC, and the USA do not include a poultry metabolism study. However, see the poultry feedings study below, where radiolabelled quinoxifen was utilized.

### Plant metabolism

#### *Wheat – adapted from the Evaluation of the EC (UK)*

The Meeting received two study reports on the metabolism of quinoxifen in wheat (31757, Haq and Brown, 1995a; 31659; Haq, MacDonald, and Brown, 1995). In the first study, which was a probe study, <sup>14</sup>C-quinoxifen was applied to winter wheat plants at growth stage BBCH 32. Another application was made to previously untreated plants at growth stage BBCH 57 (70% of inflorescence emerged). Samples were collected at various time intervals and assayed for total radioactivity.

In the second study, UK trials were carried out in 1993, with [4-fluorophenoxy-U-<sup>14</sup>C]- or [2-quinoline-<sup>14</sup>C]-quinoxifen (radiochemical purities > 98%) formulated as emulsifiable concentrates and applied to winter wheat grown in outdoor pots in single applications of 250 g ai/ha at BBCH 32 (stem elongation phase – 2nd node) or in one application of 250 g ai/ha at BBCH 49 (late booting stage – first awns visible). To aid characterisation of metabolites, applications at 1000 g ai/ha were also made at BBCH 32. Plants receiving an application at BBCH 32 were sampled at days 0, 14, 29 and 105 (harvest) after treatment. Plants receiving an application at BBCH 49 were sampled at days 0 and 78 (harvest) after treatment.

Roots were separated from aerial parts and, for harvest samples, grain separated from straw. A series of solvent washes were used to remove residues from the surface: methanol: water; dichloromethane; methanol. Remaining material was extracted with acidified acetonitrile. Samples were combusted both before and after extraction to determine total radioactivity. Radioactivity remaining in the post-extraction residual material (non-extractable) was determined by combustion/LSC. Radioactive fractions were further characterised by TLC, HPLC, and mass spectrometry. Grain samples from harvest were further separated into grain and chaff. The sequence of washes and extraction procedures employed for grain were similar to those used for straw. Only grain from plants receiving the late season application was used for studying the distribution and characterisation of radioactivity.

The distribution of radioactive residues is presented in Table 5. Total radioactivity in straw at harvest was 3–5 mg/kg for the higher application rate. Total radioactivity in grain was 0.03–0.05 mg/kg.

Table 5. The distribution of radioactivity in winter wheat straw and grain following treatment with phenoxy- and quinoline-labelled [<sup>14</sup>C] quinoxifen (% TRR and mg/kg) (31757; 31659).

Sample <sup>1</sup>	Aqueous wash		dichloromethane wash		methanol wash		Total wash		Acetonitrile extract		Non extractable		Total Activity mg/kg
	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	
STRAW: P-label, , BBCH 32													
Day0 1N	15.7	0.672	25.6	1.10	39.4	1.70	80.7	3.50	15.4	0.66	3.86	0.166	4.3
4N	14.9	3.03	26.8	5.40	35.8	7.30	77.5	15.7	17.0	3.40	5.50	1.12	20.4
Day 14 1N	10.4	0.212	20.8	0.42	23.4	0.48	54.6	1.11	21.3	0.43	24.1	0.49	2.04
4N	10.8	1.16	23.2	2.50	24.8	2.05	58.9	6.28	20.7	2.20	20.4	2.18	10.7
Day 29 1N	8.14	0.070	8.72	0.07	20.7	0.17	37.6	0.30	30.8	0.25	31.5	0.26	0.8
4N	7.93	0.370	11.3	0.54	22.2	1.05	41.5	1.90	25.9	1.22	32.6	1.60	4.7
Harvest1N	8.97	0.090	5.19	0.052	14.4	0.14	28.6	0.28	10.8	0.11	60.6	0.60	1.0
4N	11.7	0.6	10.8	0.52	24.4	1.16	46.9	2.24	11.4	0.55	42.0	2.00	4.8
STRAW: P-label, , BBCH 49													
Day 0 1N	5.10	0.08	23.0	0.35	38.2	0.58	66.4	1.01	30.8	0.47	2.81	0.04	1.53
Harvest1N	7.53	0.16	5.47	0.12	12.8	0.28	25.8	0.56	10.7	0.23	63.5	1.37	2.16
STRAW: Q-label, BBCH 32													
Day 0 1N	15.2	0.804	24.6	1.30	45.7	2.41	85.5	4.52	9.18	0.485	5.33	0.281	5.28
4N	14.4	5.11	34.0	12.0	42.2	15.0	90.6	32.1	6.49	2.30	2.88	1.02	35.4
Day 14 1N	6.61	0.113	16.5	0.283	22.9	0.393	46.0	0.789	17.1	0.294	36.9	0.633	1.72
4N	6.29	0.563	28.2	2.53	24.8	2.22	59.3	5.31	14.8	1.32	26.0	2.33	9.00
Day 29 1N	5.64	0.065	10.0	0.116	19.3	0.223	35.0	0.404	21.1	0.243	43.9	0.507	1.15
4N	7.16	0.323	14.3	0.643	20.4	0.922	41.9	1.89	23.8	1.07	34.3	1.55	4.51
Harvest1N	12.2	0.262	6.43	0.138	14.5	0.311	33.1	0.712	8.77	0.189	58.2	1.25	2.15
4N	10.6	0.555	8.75	0.460	16.5	0.867	35.8	1.88	9.91	0.520	54.2	2.85	5.25

Sample <sup>1</sup>	Aqueous wash		dichloromethane wash		methanol wash		Total wash		Acetonitrile extract		Non extractable		Total Activity mg/kg
	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	
STRAW: Q-label, BBCH 49													
Day 0 1N	8.22	0.290	24.8	0.88	29.5	1.04	62.5	2.21	34.3	1.21	3.18	0.112	3.53
Harvest1N	9.65	0.330	4.54	0.155	10.3	0.353	24.5	0.838	12.0	0.410	63.5	2.17	3.42
GRAIN: P-label, BBCH 49													
Harvest1N	2.48	0.0009	0.92	0.0003	0.82	0.0003	4.22	0.0015	7.91	0.0028	87.9	0.0307	0.0349
GRAIN: Q-label, BBCH 49													
Harvest1N	2.64	0.0014	0.20	0.0001	0.54	0.0003	3.38	0.0018	7.12	0.0038	89.5	0.048	0.0535

<sup>1</sup> 1 N = 250 g ai/ha; 4N = 1000 g ai/ha. Harvest = 105 days after treatment for early application, 78 days after treatment for late application. There were many additional whole plant sample analyses reported, but without sufficient information to calculate TRRs in mg equivalents/kg.

Table 6. Distribution and characterisation of total residues obtained from aqueous and solvent washes and acetonitrile extraction following treatment with [<sup>14</sup>C] quinoxifen. (31757; 31659).

Sample	quinoxifen		Metabolite A <sup>2</sup>		Metabolite B		Metabolite C		Metabolite E		Metabolite F		Metabolite G	
	%	amount	%	amount	%	amount	%	amount	%	amount	%	amount	%	amount
	TRR	mg/kg	TRR	mg/kg	TRR	mg/kg	TRR	mg/kg	TRR	mg/kg	TRR	mg/kg	TRR	mg/kg
STRAW: P-label, BBCH 32														
Day 0 1N <sup>1</sup>	69.	3.0			0.88	0.038			1.2	0.052			1.1	0.047
4N	75.	15.			0.81	0.16			1.5	0.31			0.75	0.15
Day 14 1N	34.	0.68	16.	0.33	15.	0.31	4.5	0.091	2.9	0.060	1.4	0.029	1.9	0.038
4N	39.	4.2	17.	1.8	11.	1.2	6.2	0.66	1.2	0.13	1.2	0.12	1.4	0.15
Day 29 1N	16.	0.13	23.	0.18	4.0	0.033	15.	0.12	4.7	0.039	1.7	0.014	1.7	0.014
4N	16.	0.77	18.	0.83	7.8	0.37	14.	0.67	2.6	0.12	0.91	0.043	7.3	0.35
Harvest 1N	8.3	0.083	23.	0.23			1.9	0.019	4.5	0.045			1.4	0.015
4N	27.	1.3	22.	1.0	0.70	0.034	1.8	0.087	5.5	0.26			1.4	0.067
STRAW: P-label, BBCH 49														
Harvest 1N	11.	0.23	17.	0.36	0.45	0.01	2.0	0.044	4.3	0.093			1.5	0.032
STRAW: Q-label, BBCH 32														
Day 0 1N	75.6	4.0			0.35	0.018			1.5	0.081			1.4	0.074
4N	85.	30.	0.08	0.028					0.96	0.34			0.95	0.34
Day 14 1N	30.	0.52	24.	0.40	1.5	0.026	2.2	0.038	1.7	0.029	2.1	0.037	1.3	0.023
4N	47.	4.2	20.	1.8					1.1	0.101	1.6	0.14	0.85	0.076
Day 29 1N	17.	0.20	27.	0.32	4.4	0.051			4.0	0.046	0.50	0.006	2.1	0.024
4N	33.	1.5	29.	1.3					2.5	0.11	0.57	0.026	1.1	0.051
Harvest 1N	7.9	0.17	27.	0.58	1.8	0.038	1.1	0.025	2.9	0.062			1.2	0.025
4N	20.	1.00	22.	1.2			1.1	0.057	3.3	0.17				
STRAW: Q-label, BBCH 49														
Harvest 1N	5.0	0.17	24.	0.83			1.4	0.049	3.8	0.13			1.8	0.060

Sample	quinoxifen		Metabolite A <sup>2</sup>		Metabolite B		Metabolite C		Metabolite E		Metabolite F		Metabolite G	
	% TRR	amount mg/kg	% TRR	amount mg/kg	% TRR	amount mg/kg	% TRR	amount mg/kg	% TRR	amount mg/kg	% TRR	amount mg/kg	% TRR	amount mg/kg
GRAIN: P-label, BBCH 49														
Harvest 1N	0.11	.00004	8.6	0.003			2.5	.00088	0.68	.00021			0.24	.00007
GRAIN: Q-label, BBCH 49														
Harvest 1N	0.03	.00002	9.0	0.0048			1.23	.00069	0.10	.00006			0.03	.00002

<sup>1</sup> 1N = 0.250 g ai/ha, 4N = 100 g ai/ha

<sup>2</sup> A is 6 or more components, possibly organic acids.

Levels of the quinoxifen in straw declined 4–8 fold from time 0 to harvest. At harvest, 58–63% of total radioactive residue (TRR) was non-extractable, approximately 0.1–0.2 mg/kg quinoxifen were found in day 105 samples following application at BBCH 32 and about 0.2 mg/kg quinoxifen were found in day 78 samples following application at BBCH 49. In grain at harvest, total radioactivity was approximately 0.04–0.05 mg/kg, of which > 90% was unextractable. Less than 0.001 mg/kg quinoxifen was found.

No qualitative differences were found between the metabolite profiles of the phenyl- and quinoline-labelled forms.

The distribution and characterisation of metabolite residues in straw and grain are summarised in Table 7. The extractable fraction (solvent wash and acidified acetonitrile extract) was found to contain 4–6 metabolites (designated A, B, C, E, F, and G) accounting for approximately (A) 0.2–0.8 mg/kg (several components), (C) 0.02–0.1 mg/kg, (E) 0.03–0.1 mg/kg and (G) 0.02–0.06 mg/kg. It was suggested that E and G were formed from quinoxifen by hydroxylation and loss of Cl, respectively, however no structure was given for E. Metabolite G was tentatively identified as a photodegradation product since it exhibited similar chromatographic characteristics to the product of aqueous photolysis of quinoxifen, CFBPQ (see Figure 2). In grain, qualitatively similar metabolites were found to those found in straw, although levels were lower and were < 0.01 mg/kg.

Further experiments to increase the amount of extractable residue were carried out on samples from plants that had received a treatment at BBCH 49. Extraction of the 'non-extractable' straw fraction remaining after acetonitrile extraction involved extraction in 0.1M sodium hydroxide, followed by Soxhlet extraction in 0.2M sodium hydroxide in methanol. Grain was extracted with 0.1M sodium hydroxide. Straw was also subjected to enzyme hydrolysis using either pancreatin (a mixture that includes amylase, trypsin, lipase, ribonuclease, and protease), glucosidase, glucuronidase or cellulase.

The resulting extracts of base hydrolysis were analysed by TLC, LSC and combustion/LSC. Extracts from enzyme hydrolyses were partitioned with methyl t-butyl ether under both acidic and basic conditions. The distribution of the radioactivity between the organic and residual aqueous phases was determined by LSC. The ratio of radioactivity in the organic and aqueous partitions was compared to aliquots of material that had not been incubated in the presence of enzymes.

Alkaline hydrolysis of the straw resulted in up to ca. 82% of the previously unextracted radioactive residue being released (approximately 41% TRR in straw). TLC profiling of the hydrolysed extract indicated that the resulting radiolabelled compounds were polar in nature, as all the radioactivity remained at the origin of the chromatogram.

Alkaline hydrolysis of the grain resulted in up to 38% of the previously unextracted radioactive residue being released (approximately 33% TRR in grain). Due to the gelatinous nature of the extracts the applicant stated that it was not possible to carry out profiling of these extracts.

Enzyme hydrolysis of straw resulted in comparable levels of radioactivity in the organic portion of the resulting extracts compared to samples following the same partitioning process that had not been incubated with enzymes. This indicated that the previously unextracted radioactivity that the

hydrolysis systems released (approximately 70% pancreatin, 94% glucosidase, 89% glucuronidase and 93% cellulase) were polar species.

Potassium permanganate was used as an oxidising agent on straw samples which had been previously extracted with acetonitrile. The agent was buffered with iron nitrate and silver nitrate. The remaining fibre was rinsed with a solution of oxalic acid in ethanol. The radioactivity in the washes and remaining fibre were determined by LSC and combustion/LSC. This system will oxidise lignin but not cellulose and therefore provided an estimate of the partition of 'unextracted' radioactivity between cellulose (direct measurement) and lignin (remainder by mass balance). Of the 64 and 73% of TRR remaining in the acetonitrile extracted tissue, approximately 37 and 40% (about 24 and 29% TRR) have been shown to be associated with cellulose. The balance is considered to be associated with lignin (about 31 and 45% TRR). All values quoted are for phenyl- and quinoline labels, respectively.

Direct measurement of lignin associated radioactivity was made on straw samples which had been previously extracted with acetonitrile. The straw was soaked in dioxane: water and shaken for 4 days at room temperature, then filtered. The process was repeated for a further 2 days at 60°C, it was then centrifuged. The centrifuge pellet was extracted again as before but for 5 days at 50°C. The radioactivity of the supernatants was determined by LSC. This method of estimating lignin associated radioactivity resulted in an estimate of lignin associated radioactivity of 16 and 21% TRR for the phenyl- and quinoline-labels, respectively.

Measurement of the starch related residue of the wheat grain was carried out by finely milling the grain which was then extracted using dimethyl sulphoxide, centrifuged and the starch containing supernatant was decanted. The starch was precipitated from the supernatant with anhydrous ethanol and separated by centrifugation. The radioactivity of the different fractions was determined by combustion/LSC or LSC. These data showed that around 13 and 53% of the TRR in grain was precipitated from the system by the addition of ethanol and is therefore probably incorporated into starch. Approximately 59 and 38% of the residue remained in the supernatant (dimethyl: sulphoxide:ethanol:water) from which the starch was precipitated. All values quoted are for phenoxy and quinoline labels, respectively.

Further characterisation of the polar, origin associated 'metabolite A' in the normal phase TLC system was carried out. Hydrochloric acid was used to hydrolyse the aqueous wash samples at 85°C from the BBCH 49 application. TLC analysis demonstrated that no quinoxyfen or related material was released, by the hydrolysis. Partial hydrolysis of the quinoxyfen was observed but ca. 70% of the parent compound remained unhydrolysed. To better characterise 'metabolite A', derivatization of the aqueous washes of samples from the BBCH 49 application was carried out. Acetylation was used, dried samples were suspended in pyridine: acetic acid at 95°C, to facilitate the partitioning of the 'metabolite' into toluene. This acetylation enabled 42 and 26% of the radioactivity in the washes to be partitioned into toluene for the phenyl- and quinoline-labelled treatments, respectively. The resulting solutions were evaporated to dryness and re-suspended in acetonitrile. Reverse and normal phase TLC of the acetylated extract indicated that 'metabolite A' was (after undergoing an acetylation procedure) made up of several (at least six components).

Reverse phase HPLC analysis of washes and extracts of samples from the BBCH 49 application resulted in a broad peak within 1 minute of the solvent front. When the mobile phase was acidified (2% acetic acid) a broad peak resolved from the solvent front was observed. The applicant suggests this is evidence that 'metabolite A' and the other uncharacterised components are acidic anions. They propose that the acidification of the mobile phase results in the retention of the component on the reverse phase column, but that the multiple components of the metabolite are not resolved by this system. It was noted that in all the chromatograms the UV profile closely mirrored the radio-chromatogram, indicating that the metabolites were very similar to/may be the same as the matrix material. The use of a reverse phase ion exchange column in the chromatographic system resulted in several broad poorly resolved peaks being observed.

Tricapryl methyl ammonium chloride, (a lipophilic quaternary ammonium salt) was used as an ion pair reagent to try to extract the postulated organic acids that are proposed as constituting 'metabolite A' into dichloromethane. This system was used on the aqueous washes of the mature

samples from all the treatment regimes. At pH 2, 30% of the radioactivity was extracted into the dichloromethane. At pH 10, 82% of the radioactivity is extracted into the dichloromethane. This provides further evidence for the acidic anionic nature of the metabolites.

LC-MS studies (electrospray interface) on the ion pair extracts described above identified only one poorly resolved peak when negative ion mode was employed. The retention time of the peak matched a peak in the radioactive trace. A reasonable mass spectrum was produced with a postulated molecular ion at  $m/z$  501, with a strong base peak at  $m/z$  305. However a corresponding peak in the UV trace at the same retention time was proposed by the applicant as indicating that 'metabolites' such as the 'metabolite A' complex and wheat natural products were in fact the same and resulted from natural incorporation.

Aqueous photolysis studies were conducted on aliquots of the parent material and resulted in the production of polar material, demonstrating that polar components were generated on photo-degradation of quinoxifen. Chromatographic analysis of the ion paired product of this polar material showed that it was not the same as the polar material that comprised Metabolite A. This demonstrates that the metabolites produced are not simply photo-degradation products of quinoxifen.

To support the proposal that polar metabolites represented by the 'metabolite A' complex may have arisen by the incorporation of small carbon units (derived from quinoxifen) into natural products, an investigation into the nature of the matrix natural products extracted with surface wash solvents used was carried out. The study demonstrated that the surface washes were relatively inefficient at extracting the dislodgeable matrix material from the plant, (third or fourth extractions still removed material).  $^{13}\text{C}$ -NMR analysis of the aqueous and methanol wash material demonstrated that it comprised largely sugar moieties (either as mono, oligo or polysaccharides). The same analysis of the dichloromethane wash indicated that long chain hydrocarbons were present (waxes).

#### *Metabolism in sugarbeets- adapted in part from the Evaluation of the USA*

The metabolism of  $^{14}\text{C}$ -quinoxifen in sugarbeet roots and leaves following maximum seasonal application (for European use) of 300 g ai/ha applied in two applications, as a suspension concentrate formulation was reported to the Meeting (81925, Graper and Balcer, 2001). The last application was delivered 60 days after the first application and 26 days before the mature harvest. Immature samples were taken between the first and second applications.

Additional higher rate plots (600 g ai/ha) were included to facilitate the characterization and identification of radioactive residues. One application was made and only immature crops were harvested. Half of the plots at either rate were treated with  $^{14}\text{C}$ -quinoxifen labelled in the phenoxy ring and the other half labelled at the quinoline ring.

Sampling intervals for immature leaves and roots were 0, 7, 14, and 28 days after treatment, except that no root and leaf samples were taken from the 600 g ai/ha plot at 0 DAT. The radioactive residues in the samples were isolated and characterized by liquid extraction, partition, and chromatography.

Half of the immature top samples were sequentially surface washed with a dilute surfactant solution (0.1% aqueous solution of Aerosol OT) and dichloromethane. The remaining half of immature tops along with mature tops, and immature and mature root samples were not surface washed. Radioactivity was determined by liquid scintillation counting (LSC) for liquid samples (surface washings) and by combustion/LSC for solid samples (roots and tops). The limit of detection (LOD) and limit of quantitation (LOQ) were reported at 0.002 and 0.007 mg/kg, respectively. TRRs were calculated by summing the radioactivity determined for the surface washings and the respective tissue sample. The TRRs are presented in Table 7.

Table 7. TRRs in /on sugarbeet root and top samples following applications of phenyl- and quinoline-labelled [<sup>14</sup>C]Quinoxyfen. (81925).

Timing and Method of application	Matrix	PHI (days)	TRR (mg/kg) <sup>1</sup>	
			Phenyl-label	Quinoline-label
Two foliar applications for a total application of 0.35-0.36 kg ai/ha	Whole plant	0 after 1 <sup>st</sup> application	6.56 (8.60)	9.00 (10.0)
	Immature sugar beet root	7 after 1 <sup>st</sup> application	0.123	0.077
		14 after 1 <sup>st</sup> application	0.067	0.067
		28 after 1 <sup>st</sup> application	0.014	0.025
	Mature sugar beet root	26 after 2 <sup>nd</sup> application	0.078	0.049
	Mature "split" sugar beet root	26 after 2 <sup>nd</sup> application	0.059	--
	Immature tops	7 after 1 <sup>st</sup> application	3.28 (2.74)	3.08 (4.68)
		14 after 1 <sup>st</sup> application	0.952 (1.15)	1.12 (2.44)
		28 after 1 <sup>st</sup> application	0.503 (0.300)	1.08 (0.345)
Mature tops	26 after 2 <sup>nd</sup> application	1.89	2.20	
Single foliar application at 0.59-0.65 kg ai/ha	Immature sugar beet root	7 after 1 <sup>st</sup> application	0.287	0.124
		14 after 1 <sup>st</sup> application	0.087	0.172
		28 after 1 <sup>st</sup> application	0.063	0.081
	Immature tops	7 after 1 <sup>st</sup> application	18.3 (19.8)	19.0 (16.0)
		14 after 1 <sup>st</sup> application	9.72 (9.13)	7.30 (12.7)
		28 after 1 <sup>st</sup> application	2.75 (3.47)	6.09 (2.60)

<sup>1</sup> TRR of surface-washed top samples are given in parentheses and are sum of the radioactivity determined in surface washings and residual tissue.

For both labels, it was found that the majority of the radioactivity was extractable in 80:20 acetonitrile/water (68–77% TRR root; 55% [quinoline label] –74% TRR leaf).

Chromatographic analyses of the acetonitrile: water extract showed the nature of radioactivity to be similar between the phenyl and quinoline labels. The parent quinoxyfen was identified as the principal residue component accounting for: 26% of TRR in phenyl-labelled roots, 25% of TRR in quinoline-labelled roots, 30% of TRR in phenyl-labelled tops, and 19% of TRR in quinoline-labelled tops. The remainder of radioactivity was characterized as polar residues consisting of multiple metabolites

The organic extracts, partitioning phases, and hydrolysates of sugar beet roots and tops were initially analyzed by HPLC conducted on a YMS ODS-AQ C18 column with a gradient mobile phase of ACN and water each with 0.1% acetic acid, using in-line radioactivity detection and UV detection (225 or 290 nm). Radioactive residues were identified by co-chromatography with the following non-labelled reference standards: quinoxyfen, 2-oxo quinoxyfen, 6-hydroxy quinoxyfen, DCHQ, and 4-fluorophenol.

Thin-layer chromatography (TLC) analysis of the initial aqueous ACN extract was performed to confirm the identity of quinoxyfen. TLC analyses were conducted using silica gel F254 plates and a toluene: acetone (75:25, v:v) solvent system. Reference standards were observed under UV light (254 nm) and radioactive residues were quantitated using phosphor imaging.

Using TLC, the minor peak which co-chromatographed with the 2-oxo metabolite by HPLC analysis, chromatographed near the 6-OH metabolite. This metabolite was not further identified, but is thought to possibly be the CFBPQ [2-chloro-10-fluoro(1)benzopyrano(2,3,4-de)quinoline] metabolite. The CFBPQ metabolite co-chromatographed with the 2-Oxo standard using HPLC analysis in a separate tomato metabolism study (see below). Because CFBPQ was the main metabolite observed in

an aqueous photolysis study (see below), this metabolite is likely formed via photolysis on the surface of the leaves and may have been absorbed and possibly further metabolized.

The aqueous phase of the quinoline-labelled extract was also analyzed by an additional HPLC system with a gradient phase over a longer period and an even more multicomponent profile was observed. The parent and DCHQ metabolite eluted near the standards, but a definitive identification could *not* be made.

Polar metabolites released by acid hydrolysis of the phenyl-labelled aqueous phase were further isolated by C18 SPE. The fraction containing the highest radioactivity was analyzed by HPLC and LC/MS. HPLC analysis was similar to the aqueous phase with 4-fluorophenol identified as the major residue, while LC/MS demonstrated that none of the radioactivity co-eluted with 4-fluorophenol, 2-Oxo, or quinoxifen. It was proposed that the residues were metabolites which had lost the quinoline portion of the quinoxifen molecule and which contain the chlorine atoms, such as conjugates of 4-fluorophenol. The isolated SPE fraction was also acid hydrolysed and partitioned with dichloromethane. HPLC and LC/MS analysis confirmed that the majority of radioactivity was 4-fluorophenol. Because the 4-fluorophenol metabolite was identified by co-chromatography prior to acid hydrolysis in the aqueous phase and was determined from the organic phase following acid hydrolysis, the petitioner stated that the 4-fluorophenol metabolite is present as a conjugate in the SPE fraction. The 4-fluorophenol conjugate(s) was confirmed by LC/MS.

The nonextractable residues, after initial extraction of samples with acetonitrile: water, were 23.2–32.0% of TRR for roots and 17.8–35.9% of TRR for tops. No further attempts were made to characterize bound residues in roots since the TRR was  $\leq 0.02$  mg/kg. To characterize bound residues in tops, sub-samples were subjected to acid detergent fibre, cellulose, and lignin isolation procedures. The results of these procedures showed that most of the radioactivity was associated with lignin.

Table 8. Summary of residue characterization/Identification in mature sugarbeet roots and tops following two foliar applications of phenyl-or quinoline-Label [ $^{14}\text{C}$ ]Quinoxifen (81925).

Metabolite/Fraction	Root		Tops	
	% TRR <sup>a</sup>	mg/kg <sup>a</sup>	% TRR	mg/kg
Phenyl-Label Quinoxifen	TRR = 0.078 mg/kg		TRR = 1.9 mg/kg	
Quinoxifen	26	0.020	30	0.56
4-Fluorophenol	--	--	17	0.32
CFBPQ <sup>b</sup>	--	--	5.0	0.094
Multiple Unknowns, Rt = 6 minutes	37	0.029	--	--
Multiple Unknowns, Rt = 25 minutes	--	--	19	0.36
Other unknowns	7.4	0.008	8.5	0.16
Total Extractable	77	0.060	74	1.4
Total Identified	26	0.020	52	0.98
Total Characterized <sup>c</sup>	44	0.037	28	0.52
Total Unresolved	Not reported (NR)		NR	NR
Total Unextractable <sup>d</sup>	23	0.018	18	0.34
TOTAL	100	0.078	92	1.7
Quinoline-Label Quinoxifen	TRR = 0.049 mg/kg		TRR = 2.2 mg/kg	
Quinoxifen	25	0.012	19	0.43
DCHQ	--	--	6.9	0.15
CFBPQ <sup>b</sup>	--	--	3.0	0.065
Unknown Rt = 6 minutes	18	0.009	--	--
Other unknowns	16	0.007	25.	0.56



Metabolite/Fraction	Root		Tops	
	% TRR <sup>a</sup>	mg/kg <sup>a</sup>	% TRR	mg/kg
Total Extractable	68	0.033	55	1.2
Total Identified	25	0.012	29	0.64
Total Characterized <sup>c</sup>	34	0.016	25	0.56
Total Unresolved	NR	NR	NR	NR
Total Unextractable <sup>d</sup>	32	0.016	36	0.79
TOTAL	100	0.049	91	2.0

<sup>a</sup> Values were normalized in the report to compensate for non-homogeneity problems in roots.

<sup>b</sup> Co-eluted with 2-oxo standard using HPLC, but eluted near the 6-OH standard with TLC; this metabolite was not further identified, but is thought to possibly be the CFBPQ metabolite, (2-chloro-1)-fluoro[1]benzopyrano[2,3,4-de]quinoline.

<sup>c</sup> Total Characterized = sum of all unidentified/characterized metabolites.

<sup>d</sup> Total Unextractable = TRR - Total Extractable, as stated in report. Much of the unextractable residue in tops was characterized as lignin.

### *Metabolism in grapes- adapted from the Evaluation of the USA*

The Meeting received a study report on the metabolism of quinoxifen in/or grape vines (42894, Caley and Kingsley, 1995). <sup>14</sup>C-quinoxifen, labelled in either the phenoxy ring or the quinoline ring, was formulated as a suspension concentrate and applied either at the rate of 375 mg/L or 750 mg/L active ingredient. Both radiolabelled compounds had a radiopurity > 97% (by TLC) and specific activities of 91.45 µCi/mg for the phenoxy label and 82.50 µCi/mg for the quinoline label, as determined by liquid scintillation counting. Applications were made to grape vines grown in a glasshouse, either as a direct spray to berries at approximately 18 days after the end of flowering (1<sup>st</sup> application) or 5 weeks later when fruits were about 70% of mature size (2<sup>nd</sup> application). In addition, at each application time point, part of a whole vine was treated with 375 mg ai/L suspension to investigate translocation into untreated parts of the vine. Fruits treated at the 'early stage' were collected at pre-harvest intervals (PHIs) of 0, 30, and 45 days; fruits treated at the 'late stage' were collected at PHIs of 0 and 10 days.

The harvested fruits were surface washed sequentially with water, dichloromethane, and methanol. Treated vines samples from the translocation studies were not surface washed. Plant tissue (vines and grapes) samples were then frozen in dry ice and homogenized using a blender. Radioactivity was determined by liquid scintillation counting (LSC) for liquid samples (surface washings) and by combustion/LSC for solid samples (vines and grapes). The TRRs were calculated by summing the radioactivity determined for the surface washings and the respective tissue sample.

Table 9. TRRs in /on the fruits and vines of grapes following a single direct spray application of phenyl- and quinoline-labelled [<sup>14</sup>C]Quinoxifen. (42894).

Timing and Method of Application	Grape Matrix	PHI (days)	TRR (mg/kg) <sup>1</sup>	
			Phenyl-label	Quinoline-label
Early application at 375 mg ai/L	Fruit	0	13.3	9.12
		30	2.95	2.21
		45	2.51	1.98
Late application at 375 mg ai/L	Fruit	0	4.86	4.95
		10	2.91	4.24
Early application at an exaggerated rate of 750 mg ai/L	Fruit	45	6.76	5.27
Translocation experiment: Early application to the vine at 375 mg ai/L	Treated fruit	45	1.16	1.50
	Untreated fruit	45	0.008	0.007
	Treated vines (stems/leaves)	45	15.9	23.4
	Untreated vines (stems/leaves)	45	nd <sup>2</sup>	nd

Timing and Method of Application	Grape Matrix	PHI (days)	TRR (mg/kg) <sup>1</sup>	
			Phenyl-label	Quinoline-label
Translocation experiment: Late application to the vine at 375 mg ai/L	Treated grape fruit	10	2.85	1.88
	Untreated grape fruit	10	0.006	0.006
	Treated vines (stems/leaves)	10	18.0	17.4
	Untreated vines (stems/leaves)	10	nd	nd

<sup>1</sup> TRR reported for grapes is the total of radioactivity determined in surface washings and tissue.

<sup>2</sup> Not detected.

The fruit's TRR decreased from the 0-day sampling interval to subsequent sampling intervals. The majority of radioactivity was removed from the grapes by surface washing; > 98% of the TRR was released at 0 day and > 81% TRR was released at maturity. TRR in untreated grapes were 0.002 mg/kg. The TRRs of grapes from the exaggerated rate study were basically proportional to the increase in the application rate.

In the translocation study, low levels (< 0.01 mg/kg) of radioactivity were observed in untreated grapes, and non-detectable residues were observed in the untreated vines (stems/leaves). No translocation of radioactivity from the treated vine and grapes to the untreated vines (stems/leaves) or grapes appeared to have occurred.

Surface washings, extracts, and hydrolysates (0.1 N NaOH) of grape fruit and vines were analyzed by normal-phase TLC and reversed-phase HPLC. HPLC analyses were conducted on Spherisorb ODS 2 (guard and analytical) columns with a gradient mobile phase of ACN and water, using in-flow radio-detection and UV detection (295 nm). TLC analyses were conducted on 60F<sub>254</sub> silica plates using a mobile phase of toluene:isopropyl alcohol:acetic acid (8:2:1, v:v:v). Radioactive residues were identified by co-chromatography with the following non-labelled reference standards: quinoxifen, quinoxifen n-oxide, 4-fluorophenol, and DCHQ (dichloro-hydroxy quinoline). Reference standards were observed under UV light (254 nm), and radioactive residues were quantitated using phosphor imaging.

Table 10. Summary of characterization/identification of residues in mature grapes following a single direct spray application of phenoxy- and quinoline-Labelled [<sup>14</sup>C]Quinoxifen at 375 mg ai/L. (42894).

Metabolite/Fraction	Early application 45-day PHI		Late application 10-day PHI	
	% TRR	mg/kg	% TRR	mg/kg
Phenoxy-label Quinoxifen	TRR = 2.51 mg/kg		TRR = 2.91mg/kg	
Quinoxifen	93.	2.3	97.	2.8
Unknown Peak 1	3.3	0.083	3.0	0.088
Unknown Peak 3	0.7	0.018	--	--
NaOH hydrolysate	2.0	0.049	--	--
Total Extractable	99	2.5	99	4.2
Total Identified	93	2.3	97	2.8
Total Characterized <sup>1</sup>	6.0	0.15	3.0	0.088
Total Unresolved	Not reported (NR)	NR	NR	NR
Total Unextractable <sup>2</sup>	4.2	0.10	1.4	0.041
TOTAL	103.	2.6	101.	2.9

Metabolite/Fraction	Early application 45-day PHI		Late application 10-day PHI	
	% TRR	mg/kg	% TRR	mg/kg
Quinoline-label Quinoxifen	TRR = 1.985 mg/kg		TRR = 4.235 mg/kg	
Quinoxifen	94	1.8	98.	4.1
Unknown Peak 1	2.1	0.042	0.3	0.011
Aqueous	1.5	0.030	0.3	0.011
NaOH hydrolysate	1.2	0.024	--	--
Total Extractable	98	1.9	99.	4.2
Total Identified	94	1.8	98.	4.2
Total Characterized <sup>a</sup>	4.8	0.096	0.6	0.022
Total Unresolved	NR	NR	NR	NR
Total Unextractable <sup>b</sup>	4.6	0.091	1.2	0.051
TOTAL	103	2.04	100.	4.2

<sup>1</sup> Total Characterized = sum of all unidentified/characterized metabolites

<sup>2</sup> Total Unextractable = TRR - Total Extractable; actual value presented in report.

#### *Metabolism in cucumber – adapted from the Evaluation of the USA*

The Meeting received a study report on the metabolism of <sup>14</sup>C-quinoxifen in cucumbers grown in a glasshouse (45725, Chapleo and Caley, 1996). <sup>14</sup>C-quinoxifen, labelled in either the phenoxy ring or the quinoline ring, was formulated as a suspension concentrate containing 75 mg ai/L and was applied with a compressed air sprayer to the fruit and foliage of plants as a spray at the commencement of fruit ripening, 592 mg/plant. Further applications were made to the same plants 10 days and 23 days after the initial treatment. Both radio-labelled forms were applied to separate groups of plants at each application point. Immature fruits and foliage were harvested from a single plant on the day of the first application, and prior to the second and third applications. Mature fruits and foliage were harvested from the remaining two plants 7 days following the third application. Efforts were focused on the characterization of the nature of the residue in mature samples collected from the 3 treatment regime.

In a separate experiment, <sup>14</sup>C-quinoxifen, labelled in either the phenoxy ring or the quinoline ring and formulated as the suspension concentrate, was applied to the foliage only of two plants. Foliage and fruits were harvested 21 days after the single application.

Mature fruits were washed sequentially with water, dichloromethane and methanol and the levels of radioactivity were determined in the washes and fruit. The TRR for each matrix was calculated by summing the radioactivity determined for the surface washings and the respective foliage or fruit tissue sample. Greater than 88% of the total radioactive residue (TRR) was removed by surface washes from samples taken immediately after the initial treatment. Much less was removed at subsequent harvests, and at the final harvest 7 days after last application, 57% TRR (phenyl label) and 36% TRR (quinoline label) were removed by surface washing. The TRR levels at various harvest intervals are summarized in Table 11.

Table 11. TRRs in /on cucumber fruit and foliage following application(s) of phenoxy- and quinoline-Labelled [<sup>14</sup>C]Quinoxifen (45725).

Timing and Method of application	Cucumber Matrix	PHI	TRRs (mg/kg) <sup>1</sup>	
			phenoxy-label	quinoline-label
One to three spray treatments were made to the fruits and foliage of cucumbers beginning at the commencement of fruit ripening at an average rate of 75 mg ai/L per application	Fruit	Just after 1 <sup>st</sup> application	0.12	0.14
		Prior to 2 <sup>nd</sup> application	0.025	0.050
		Prior to 3 <sup>rd</sup> application	0.017	0.017
		7 days (after final application)	0.079	0.076
	Foliage	Just after 1 <sup>st</sup> application	2.7	2.0
		Prior to 2 <sup>nd</sup> application	2.1	1.4
		Prior to 3 <sup>rd</sup> application	3.5	2.9
		7 days (after final application)	4.2	3.4
For the <u>translocation experiment</u> , one spray application was made	Fruit	23 days (coincided with 3 <sup>rd</sup> application above)	0.005	0.014
	Foliage	23 days (coincided with 3 <sup>rd</sup> application above)	0.97	1.1

<sup>1</sup> TRR reported is the total of radioactivity determined in surface washings and tissue.

A sub-sample of treated fruit, that had been surface washed for TRR determination, was extracted (2×) with acetonitrile (ACN): water:1 M HCl (94:5:1, v:v:v) and then centrifuged. The extracts were combined and concentrated for thin-layer chromatography (TLC) analysis. The concentrated extract was re-dissolved in methanol and a precipitate formed. The precipitate was removed by centrifugation and re-dissolved in water.

To investigate the nature of non-extractable ('bound') residues, a sub-sample of fruit which had undergone initial extraction as described above was subjected to acid hydrolysis (refluxed with 1 M HCl for 18 hours). The hydrolysate was partitioned (3×) with hexane, and the hexane fractions were combined. Low levels of radioactivity were partitioned into the hexane phase; therefore, TLC analysis was not performed.

A sub-sample of treated foliage, that had been surface washed for TRR determination, was extracted (2×) with ACN:water:1 M HCl (94:5:1, v:v:v) and then centrifuged. The extracts were combined and concentrated for TLC analysis. Separate sub-samples of the methanol surface washings and extracts were subjected to enzyme hydrolysis to further investigate the nature of polar radioactive components. Residues were re-dissolved in 0.1 M sodium acetate buffer, pH 5. Then β-glucuronidase in sodium acetate buffer was added, and the mixture was incubated at 37°C for 18 hours.

To investigate the nature of non-extractable residues, a sub-sample of non-extractable residues following the initial extraction of residues was subjected to acid hydrolysis (refluxed with 1 M HCl for 18 hours). The hydrolysate was partitioned (3×) with hexane, and the hexane fractions were combined and concentrated for TLC analysis. The aqueous fraction was subjected to solid-phase extraction (SPE) with a phenyl Bond-Elute cartridge; residues were eluted with methanol. Radioactivity was determined in the water fraction (flow-through), methanol fraction, and solid-phase gel. The water fraction was concentrated by freeze-drying, and the methanol fraction was concentrated by rotary evaporation for TLC analysis.

Surface washings, extracts, and hydrolysates of cucumber fruit and foliage were initially analyzed by TLC conducted on 60F<sub>254</sub> silica plates using a mobile phase of toluene:isopropyl alcohol:acetic acid (8:2:1, v:v:v). Radioactive residues were identified by co-chromatography with the following non-labelled reference standards: quinoxifen, 2-oxo quinoxifen, quinoxifen n-oxide and DCHQ (dichloro-hydroxy quinoline). Reference standards were observed under UV light (254 nm) and radioactive residues were quantitated using phosphor imaging.

To confirm results, the surface washings and extracts of phenyl- and quinoline-labelled fruit and foliage samples were also analyzed by high-performance liquid chromatography (HPLC). HPLC analyses were conducted on a Spherisorb ODS 2 (guard and analytical) columns with a gradient mobile phase of ACN and water, using in-flow radio-detection and UV detection (295 nm). Identification of quinoxifen residues was also confirmed by liquid chromatography/mass spectroscopy (LC/MS) analysis. A summary of residue characterization and identification is presented below in Table 12.

Table 12. Summary of residue characterization/identification in cucumber fruit and foliage harvested 7 days following the last of three spray treatments of phenoxy- or quinoline-labelled [<sup>14</sup>C]Quinoxifen at an average rate of 75 mg ai/L per application.(45725).

Metabolite/Fraction	Cucumber Fruit		Cucumber Foliage	
	% TRR	mg/kg	% TRR	mg/kg
Phenoxy-labelled Quinoxifen	TRR = 0.079 mg/kg		TRR = 4.2 mg/kg	
Quinoxifen	74	0.058	74	3.1
Quinoxifen n-oxide	2.8	0.002	1.4	0.057
2-Oxo quinoxifen	--	--	3.7	0.16
Unknown A	4.1	0.003	0.7	0.028
Unknown F	--	--	0.1	0.002
Origin	7.8	0.005	15 <sup>3</sup>	0.64
Water surface wash	3.7	0.003	--	--
Precipitate	1.0	0.001	--	--
SPE gel	--	--	< 0.1	0.002
Total Extractable	93	0.074	< 95	4.0
Total Identified	77	0.060	79	3.3
Total Characterized <sup>1</sup>	17	0.012	< 16	0.67
Total Unresolved	Not reported (NR)	NR	NR	NR
Total Unextractable <sup>2</sup>	13	0.010	13	0.56
TOTAL	107	0.082	108	4.6
Quinoline-Label Quinoxifen	TRR = 0.076 mg/kg		TRR = 3.4 mg/kg	
Quinoxifen	64	0.049	56	1.9
Quinoxifen n-oxide	2.5	0.001	3.3	0.11
Unknown A	1.5	0.001	0.6	0.02
Unknown B	--	--	0.3	0.011
Unknown F	2.1	0.002	0.2	0.006
Origin	10	0.008	27 <sup>3</sup>	0.91
Water surface wash	2.6	0.002	--	--
Precipitate	3.1	0.002	--	--
Acid hydrolysate; hexane phase	0.1	< 0.001	0.1	0.002
Acid hydrolysate; aqueous phase	8.1	0.006	--	--
SPE gel	--	--	0.3	0.010
Total Extractable	95	< 0.072	88	3.0
Total Identified	67	0.050	60	2.0
Total Characterized <sup>1</sup>	28	< 0.022	28	0.96
Total Unresolved	NR	NR	NR	NR
Total Unextractable <sup>2</sup>	17	0.013	11	0.39
TOTAL	111	0.084	99	3.4

<sup>1</sup> Total Characterized = sum of all unidentified/characterized metabolites

<sup>2</sup> Total Unextractable = TRR - Total Extractable.

<sup>3</sup> A polar mixture associated with the baseline of TLC plates. Found in the TLC analysis of the aqueous and methanol surface washes, initial tissue extracts, and various extracts from the acid hydrolysates of the tissue remaining following solvent extractions. Shown not to be glucose conjugates.

*Metabolism in tomato – adapted from the US Evaluation*

The Meeting received a study report on the application of  $^{14}\text{C}$ -quinoxifen labelled either in the phenoxy or quinoline ring to tomatoes at the US maximum seasonal rate of 600 g ai/ha (five weekly applications of 120 g ai/ha), (78962, Byrne *et al.*, 2000). Tomato plants were grown to maturity outdoors in separate plots treated either with  $^{14}\text{C}$ -phenoxy and  $^{14}\text{C}$ -quinoline quinoxifen. Immature fruit was collected at 0, 7, 14, and 28 days after the first application. Mature fruit was collected 14 days after the 5<sup>th</sup> and final application (42 days after the first application). Vines were collected and analyzed 0, 7, and 42 days after the first application.

Treated tomato samples from all sampling intervals were surface washed sequentially with a dilute soap (0.01%) solution and methylene chloride. Treated vines samples, collected prior to the third application and were not analyzed. Surface-washed plant tissue (fruit and foliage) samples were then frozen in dry ice and homogenized using a mill. Radioactivity was determined by liquid scintillation counting (LSC) for liquid samples (surface washings) and by combustion/LSC for solid samples (homogenized fruit and foliage tissue). The limit of detection (LOD) and limit of quantitation (LOQ) were reported as 0.0029 and 0.011 mg/kg, respectively. The TRRs presented in Table 13 below were calculated by summing the radioactivity determined for the surface washings and the respective tissue sample.

Table 13. TRRs in /on tomato fruits and foliage following application(s) of phenoxy- and quinoline-labelled [ $^{14}\text{C}$ ] Quinoxifen (78962).

Timing and Method of application	Matrix	PHI (days)	TRR <sup>1</sup>	
			Phenoxy-label	Quinoline-label
One to five post-emergence foliar applications were made at a nominal rate of 0.12 kg ai/ha per application.	Immature fruit	0 after 1 <sup>st</sup> application	0.057	0.092
		Prior to 2 <sup>nd</sup> application	0.042	0.063
	Immature fruit	Prior to 3 <sup>rd</sup> application	0.083	0.093
		Prior to 5 <sup>th</sup> application	0.13	0.19
	Mature fruit	14 after 5 <sup>th</sup> application	0.19	0.243
	Immature foliage	0 after 1 <sup>st</sup> application	5.4	6.6
		Prior to 2 <sup>nd</sup> application	4.2	3.6
	Mature foliage	14 after 5 <sup>th</sup> application	11	14

The soap (aqueous) and DCM surface-washings of mature fruits contained sufficient radioactivity for chromatographic analysis (HPLC and thin-layer chromatography (TLC)); the DCM surface-washings were concentrated, and residues were re-dissolved in ACN and water prior to analysis.

Sub-samples of post-rinsed samples were extracted (3x) with ACN: water (80:20, v:v) and then centrifuged. The extracts were combined, and an aliquot was concentrated in the aqueous phase and partitioned with DCM: ACN (80:20, v:v). The organic phase was concentrated and diluted with ACN and water for HPLC analysis; the aqueous phase was directly analyzed by HPLC.

To investigate the nature of non-extractable ('bound') residues, a sub-sample of non-extractable residues following the initial extraction was subjected to acid hydrolysis (1 N HCl refluxed for 4 hours) and then vacuum filtered. The acidified pellet was rinsed with water, centrifuged, and filtered. The rinsate was combined with the acid hydrolysate. The nonextractable residues remaining following acid hydrolysis were then extracted with ACN to remove acid-labile, non-water soluble residues.

A separate but larger sub-sample of milled tomato fruit was subjected to a series of fractionation procedures in order to elucidate the nature of bound residues. These sub-samples were extracted and acid hydrolysed as described above, and the nonextractable residues were subjected to ADF isolation, or lignin or cellulose determinations. Briefly, nonextractable residues were refluxed for 1 hour in acid detergent solution (hexadecyltrimethylammonium bromide in 2 N sulfuric acid).

The solids were collected by vacuum filtration and dried in an oven (80° C) overnight. The dried solid acid detergent fibre (ADF) fraction and liquid ADF rinsate were analyzed by LSC or combustion/ISC. To isolate lignin, chilled sulphuric acid was added to nonextractable residues, and the sample was refrigerated overnight. The sample was diluted with water, refluxed for 2 hours, cooled, and vacuum filtered. The solids were dried in an oven (60° C) overnight, and the solid (lignin) fraction was determined by LSC; the liquid filtrate is *assumed* to contain primarily dissolved cellulose. To isolate cellulose, buffered saturated potassium permanganate was added to nonextractable residues, and the sample was filtered. Additional potassium permanganate was added and filtered to ensure complete oxidation/solubilisation of lignin. Excess potassium permanganate was removed from the oxidized solid by the addition of oxalic and hydrochloric acids in ethanol, after which the solids were sequentially washed with ethanol and acetone. The solids were dried in an oven (60°C) overnight, and the solid (cellulose) fraction was determined by LSC; the liquid filtrate is *assumed* to contain primarily oxidized lignin.

Surface washings of phenyl- and quinoline-labelled mature tomatoes contained 57% and 62% TRR, respectively, with the largest amount of radioactivity recovered in the organic surface-washing. The remainder of radioactivity (20–27% TRR) was largely extracted using ACN:water (80:20, v:v). Approximately half of the extract was partitioned into organic solvent. Phenyl- and quinoline-labelled bound residues of mature tomatoes were subjected to sequential acid hydrolysis (1 N HCl at reflux) and ACN extraction, which released an additional 2.4–4% TRR. Bound residues remaining following simple extraction and hydrolysis accounted for 4.0% and 3.9% of TRRs in phenyl- and quinoline-labelled tomatoes, respectively. The levels of radioactivity in the surface washings, extracts, and bound fractions were similar for phenyl- and quinoline-labelled tomato fruit.

Individual surface washings, and the organic and aqueous extracts were subjected to HPLC analysis for characterization/identification of residues. Most of the radioactivity in all of the surface washings was identified as quinoxifen (51–54% TRR). Quinoxifen was also detected as the major residue present at approximately 12% TRR in the organic and aqueous extracts. An unknown peak eluting at approximately 42 minutes and present at < 2% TRR was observed in the organic extract (both labels). This peak had a similar retention time as the 2-oxo metabolite. The remainder of the peaks detected in the aqueous and organic extracts were minor polar unknowns, each present at < 5% TRR. The residue profiles for the phenyl- and quinoline-labelled fruit were similar. An additional 2.4–4% TRR was released from non-extractable residues with acid hydrolysis and subsequent ACN extraction.

A larger sample of surface-washed fruit tissue was extracted and subjected to acid hydrolysis and ACN extraction for further characterization of non-extractable residues. Bound residues were characterized to be associated with ADF (10–12% TRR, 0.020-0.028 mg/kg) containing lignin, cellulose, and hemicellulose.

Tomato foliage samples harvested 14 days following five applications were subjected to extensive investigation. The soap (aqueous) and methylene chloride (DCM) surface-washings contained sufficient radioactivity for chromatographic analysis (HPLC and TLC); the DCM surface-washings were concentrated, and residues were re-dissolved in ACN and water prior to analysis.

A sub-sample of post-rinsed foliage was extracted (3x) with ACN: water (80:20, v:v) and then centrifuged. The extracts were combined, and an aliquot was concentrated in the aqueous phase and partitioned with DCM:ACN (80:20, v:v). The organic phase was concentrated and diluted with ACN and water for HPLC analysis; the aqueous phase was directly analyzed by HPLC.

To investigate the nature of nonextractable residues, a sub-sample of nonextractable residues from the initial extraction was subjected to acid hydrolysis (1 N HCL refluxed for 4 hours) and vacuum filtered. The acidified pellet was rinsed with water, centrifuged, and filtered. The rinsate was combined with the acid hydrolysate. The nonextractable residues remaining following acid hydrolysis were then extracted with ACN to remove acid-labile, non-water soluble residues. The acid hydrolysate was partitioned with DCM: ACN (80:20, v:v). The DCM phase was concentrated, and the organic and aqueous phases were analyzed by HPLC.

A separate but larger sub-sample of milled tomato foliage was subjected to extraction, acid hydrolysis, and ACN extraction. The nonextractable residues following acid hydrolysis and ACN extraction were subjected to ADF isolation, or lignin or cellulose determinations. The similar procedures described for fruits were employed for this purpose.

Non-extractable residues were subjected to sequential acid hydrolysis (1 N HCl at reflux) and ACN extraction, which released an additional 8.4–9.7% TRR. Bound residues remaining following simple extraction and hydrolysis accounted for 5.9% and 6.7% TRR in phenyl- and quinoline-labelled foliage, respectively. Levels of radioactivity in the surface washings, extracts, and bound fractions were similar for phenyl- and quinoline-labelled tomato foliage.

Individual surface washings and the organic and aqueous extracts were subjected to HPLC analysis for characterization/identification of residues. Most of the radioactivity in all of the surface washings was identified as quinoxifen (31.6–34.5% TRR). Quinoxifen was also detected as the major residue present at  $\leq 9$ –12% TRR in the organic extract. 4-fluorophenol was identified as a minor residue (0.9% TRR) in the phenyl-labelled organic extract only. An unknown peak eluting at approximately 42 minutes and present at  $\leq 3.2$ % TRR was observed in the organic extract (both labels). This peak had a similar retention time as the 2-oxo metabolite standard. An additional unknown peak ( $R_t = 35$  minutes) was detected at  $\leq 7$ % TRR, and the remainder of the peaks detected in the organic extracts were minor polar unknowns each present at  $< 1$ % TRR. The aqueous extracts of both phenyl- and quinoline-labelled foliage were comprised of more polar unknown peaks each present at  $\leq 3.3$ % TRR. The residue profiles for the phenyl- and quinoline-labelled foliage were similar.

A larger sample of surface-washed foliage tissue was extracted and subjected to acid hydrolysis and ACN extraction. The majority of the bound residues were associated with ADF (3.7–4.6% TRR) containing lignin, cellulose, and hemicellulose.

The surface washings, extracts, and hydrolysates of tomato fruits and foliage were analyzed by HPLC. HPLC analyses were conducted on a YMC ODS-AQ column with a gradient mobile phase of ACN and water each containing 0.1% acetic acid, using in-flow radiodetector and UV detector (295 nm). Radioactive residues were identified by co-chromatography with the following non-labelled reference standards: quinoxifen, 4-fluorophenol, 2-Oxo (2-oxo quinoxifen), 6-OH (6-hydroxy quinoxifen), and DCHQ (dichloro-hydroxy quinoline).

Residues of quinoxifen were confirmed in the surface-washings and organic phase of the initial extraction by TLC analysis. TLC analyses were conducted on 60F<sub>254</sub> silica plates using a mobile phase of toluene: acetone (75:25, v:v). Reference standards were observed under UV light (254 nm) and radioactive residues were quantitated using a linear detector.

Minor peaks observed by HPLC analysis of the DCM surface-wash of foliage samples eluted with potential photolysis products in the fruit, such as 2-oxo metabolite. However, these peaks did not co-chromatograph with the 2-oxo standard using TLC. These degradates were, therefore, further isolated using an open column system. The phenyl-labelled DCM surface-wash was applied to a medium bore silica column and one-minute fractions were collected for HPLC and LC/MS analysis. In all but the first fraction collected, some radioactivity eluted similar to the 2-oxo metabolite using gradient HPLC; however, multiple components were observed using isocratic HPLC (water: ACN each with 0.1% acetic acid; 4:6, v:v). It is reasonable to conclude that the residue consists of a range of components instead of a single metabolite accounting for  $> 10$ % of the radioactivity present.

The major residue identified by HPLC in fractions 1 and 2 was quinoxifen, and was confirmed by LC/MS. In fraction 3, the major component was analyzed by LC/MS which did not demonstrate fragmentation across the ether linkage; the degradate was proposed to be CFBPQ (2-chloro-10-fluoro[1]benzopyrano[2,3,4-de]quinoline) based on the accurate mass. The spectrum of the degradate, by <sup>1</sup>H NMR analysis, was consistent with CFBPQ. The CFBPQ degradate was the main degradate identified in an aqueous photolysis study; therefore, CFBPQ may be formed via photolysis on the surface of the tomatoes or leaves.



In fraction 4, residues similar to the parent, but more polar and with different fragmentation patterns by LC/MS analysis, were thought to be rearrangement isomers of quinoxifen. The chemical structures could not be conclusively determined with NMR. Analysis of fraction 5 by LC/MS indicated possible structures of a *p*-hydroxyphenoxy degradate and 2-oxo metabolite.

Table 14 lists the summary of residues identified and characterized from this study.

Table 14. Summary of characterization/identification of <sup>14</sup>C-residues in mature tomato fruits and foliage harvested 14 days following the last of five foliar applications of phenyl- or quinoline-Label [<sup>14</sup>C]Quinoxifen for a total rate of 600 g ai/A. (78962).

Metabolite/Fraction	Tomato Fruit 14-day PHI		Tomato Foliage 14-day PHI	
	% TRR	mg/kg	% TRR	mg/kg
Phenoxy-labelled Quinoxifen	TRR = 0.191 mg/kg		TRR = 10.716 mg/kg	
Quinoxifen	63	0.12	43	4.6
4-Fluorophenol	--	--	0.9	0.096
Unknown Rt = 35 minutes	--	--	7.0	0.75
Unknown Rt = 42 minutes	1.9	0.003	3.2	0.34
“Other” unknowns	each ≤ 5.0	each ≤ 0.008	each ≤ 3.3	each ≤ 0.36
Acid hydrolysate	3.6	0.007	7.6	0.81
ACN extract	0.4	0.001	2.1	0.22
Total Extractable	88	0.17	87	9.3
Total Identified	63.	0.12	44	4.7
Total Characterized <sup>1</sup>	> 11 <sup>2</sup>	> 0.019 <sup>2</sup>	> 23.	> 2.5
Total Unresolved	Not reported (NR)	NR	NR	NR
Total Unextractable <sup>3</sup>	4.0	0.008	5.9	0.64
TOTAL <sup>4</sup>	92	0.18	93	10
Quinoline-label Quinoxifen	TRR = 0.24 mg/kg		TRR = 14. mg/kg	
Quinoxifen	65	0.16	43	6.1
Unknown Rt = 35 minutes	--	--	6.5	0.92
Unknown Rt = 42 minutes	1.8	0.004	2.2	0.304
“Other” unknowns	each ≤ 1.6	each ≤ 0.002	each ≤ 2.1	≤ 0.30
Acid hydrolysate	2.1	0.005	6.6	0.93
ACN extract	0.3	0.001	1.8	0.26
Total	84	0.20	85	12
Total Identified	65	0.16	43	6.1
Total Characterized <sup>1</sup>	> 5.8 <sup>2</sup>	> 0.012 <sup>2</sup>	> 19. <sup>2</sup>	> 2.7
Total Unresolved	NR	NR	NR	NR
Total Unextractable <sup>3</sup>	3.9	0.009	6.7	0.9 5
TOTAL <sup>4</sup>	88	0.21	92	13

1 Total Characterized = sum of all unidentified/characterized metabolites

2 Because only the maximum single unknown level was reported; the total identified does not include unknowns below the maximum value.

3 Total Unextractable = TRR - Total Extractable; actual value presented in the report.

4 Total as presented in the report.

*In summary*, quinoxifen was metabolized in plants with portions of the molecule becoming associated with natural plant constituents. The main residue identified in the roots, leaves, and fruits at harvest, was the parent compound, quinoxifen. Hydroxylation of the quinoline or phenoxy rings was

observed. Cleavage of the ether bond was a minor pathway (sugar beet). CFBPQ was formed, perhaps via surface photolysis. There was no evidence of significant translocation from treated foliage to other parts of the plant. The metabolic pathways are indicated in Figure 2.

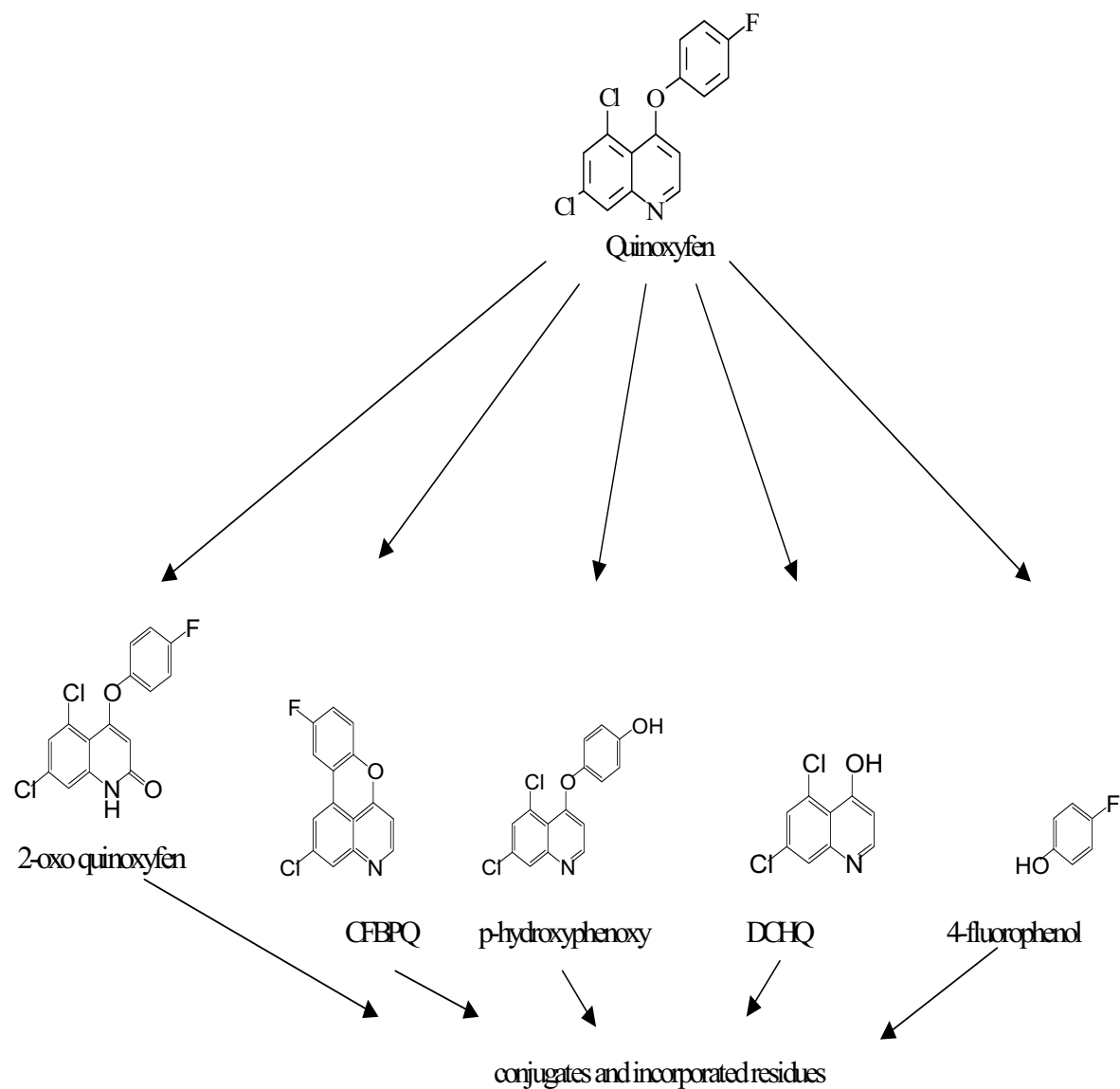


Figure 2. Proposed quinoxifen metabolic pathway in plants.

## Environmental fate

### Aerobic soil metabolism

The Meeting received a study report on the aerobic soil metabolism of quinoxifen (6357, Reeves, 1993; 8411, Ghosh and Portwood, 1994; and 29386, Cracknell *et al.*, 1995). In a laboratory study, one standard (Speyer 2.2) and three UK agricultural soils (Castle Rising, Marcham, and Wereham) were treated with quinoline-labelled [<sup>14</sup>C]-quinoxifen at a rate equivalent to 250 g ai/ha and incubated at 40% moisture content and 20°C in the dark for up to 200 days. Under these conditions parent compound slowly degraded to give 5,7-dichloro-4-(4-fluorophenoxy)-2-oxo-quinoline 2-oxo-DE-795). In the three agricultural soils this did not exceed *ca* 8% of applied radioactivity (AR) at any time, although it did reach 27% AR at 200 days in non-agricultural Speyer 2.2 soil. The pattern of 2-oxo-DE-795 formation was such that no significant plateau and decline could be detected in any soil during the test period. A second metabolite identified as 5,7-dichloro-4-hydroxyquinoline (DCHQ) was also formed as a minor component in Speyer 2.2 soil, and as the only degradation product in acidic Wereham soil (pH4.2), where it reached 6% AR at 100 days. Non-extractable residue (NER; up to 25% AR) and small amounts of CO<sub>2</sub> (< 2% AR) were also seen. The distribution of radioactivity in the four soils is summarized in Table 15.

Table 15. Summary of aerobic soil degradation in various soil types (6357; 8411; 29386).

Matrix	Days After Treatment (% Applied Radioactivity)								
	0	4	8	16	36	64	100	150	200
DE-795	96 - 101	94 - 100	90 - 99	88 - 97	86 - 96	80 - 95	74 - 85	58 - 81	53 - 81
2-OH-quinoxifen <sup>1</sup>	0	0	0	0 - 3	0 - 6	0 - 11	0 - 15	0 - 22	0 - 27
DCHQ	0	0	0	0	0	0	0 - 6	0 - 6	0 - 5
CO <sub>2</sub>	0	trace	trace	trace	< 1	< 1	< 2	< 2	< 2
NER	1 - 5	2 - 6	3 - 10	3 - 11	5 - 14	7 - 16	10 - 18	14 - 25	15 - 25
Total	101 - 103	98 - 103	100 - 102	99 - 101	99 - 102	99 - 102	99 - 102	100 - 102	100 - 102

<sup>1</sup> Misidentified as 3-OH-quinoxifen (18219, N. R. Pearson and G. L. Reeves, 2005)

At 150 days, the NER was further extracted by sonication with methanol at 55°C, and the extracts shown to contain between 34–46% of the NER as DE-795, 2-Oxo-DE-795 and DCHQ (in proportions similar to their content in the original soil extracts) that had become bound to the soil with time.

The proposed route of aerobic soil degradation is shown in Figure 3.

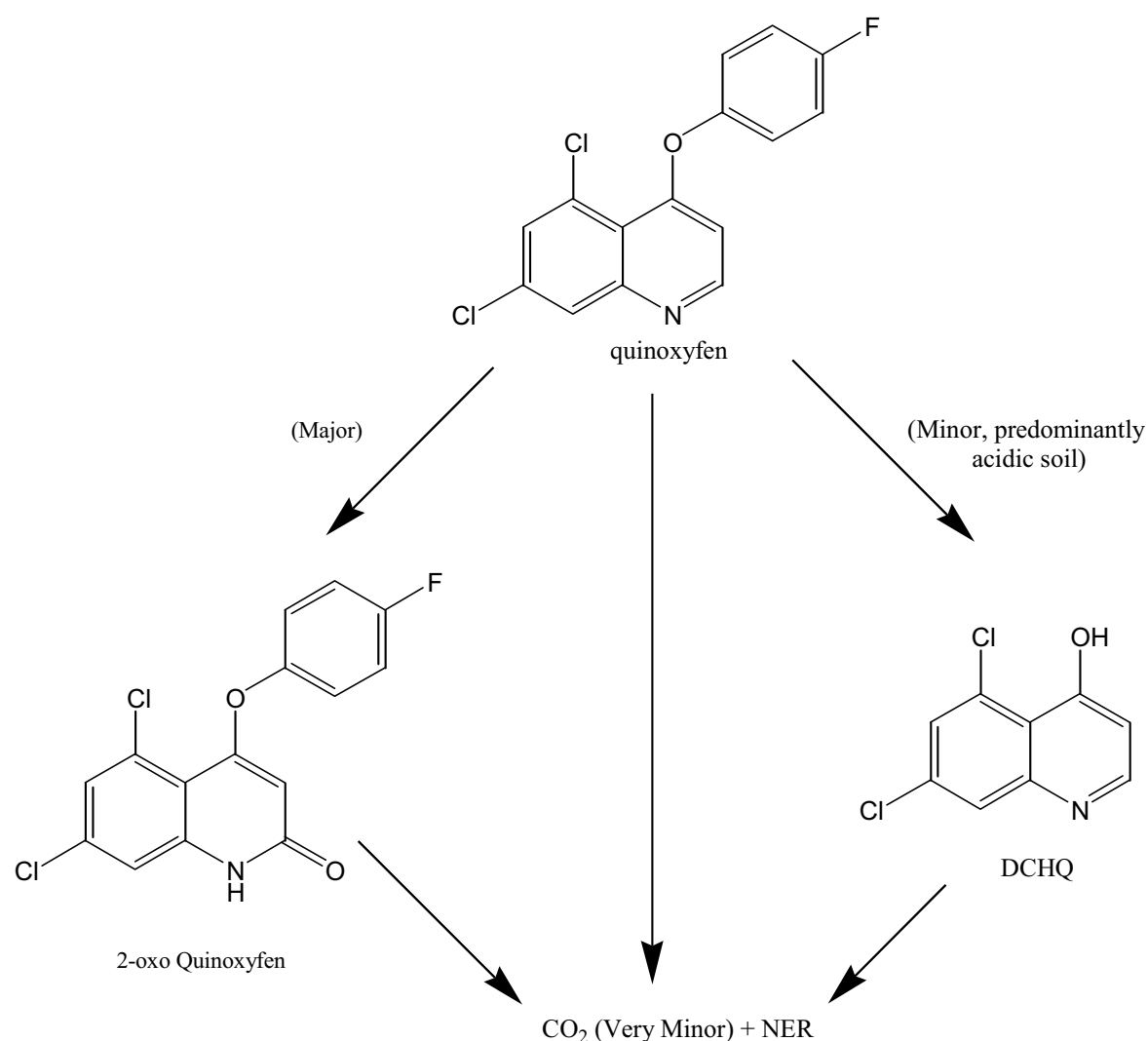


Figure 3. Pathway for the aerobic soil degradation of quinoxifen.

DT<sub>50</sub> and DT<sub>90</sub> values were calculated for the soils from the above study as well as in a second standard soil (Speyer 2.1) as part of the aged residue column leaching study (24033, Reeves, 1994). The application rate was equivalent to 250 g ai/ha (1× rate) throughout. Comparative work was also done to investigate the effect of soil moisture content (Castle Rising at 60%moisture content), temperature (Speyer 2.2 at 10°C and 30°C) and application rate (Speyer 2.2 at 4× and ¼× rate) upon the degradation kinetics (K01). Table 16 shows the kinetic data (calculated assuming first-order kinetics) obtained under the various test regimes.

Table 16. Quinoxifen laboratory aerobic soil degradation half-lives (1× = 250 g ai/ha) (24033).

Soil	Moisture content	Temp.	Application Rate	DT <sub>50</sub> (days)	DT <sub>90</sub> (days)
Speyer 2.2	40%	20°C	1×	220	ca 730
Castle Rising	40%	20°C	1×	510	ca 1700
Marcham	40%	20°C	1×	300	ca 1000
Wereham	40%	20°C	1×	470	ca 1500
Speyer 2.2	40%	20°C	¼×, 4×	220	ca 730-760

Soil	Moisture content	Temp.	Application Rate	DT <sub>50</sub> (days)	DT <sub>90</sub> (days)
Speyer 2.2	40%	10°C	1×	870	-
Speyer 2.2	40%	30°C	1×	87	ca 270
Castle Rising	60%	20°C	1×	450	ca 1500
Speyer 2.1	40%	20°C	1×	300	-

The results showed that quinoxyfen is *slowly* degraded in soil under dark aerobic conditions. There was an apparent decline in the degradation rate in all soils after 100 days, particularly in Marcham soil, suggesting biphasic or non-linear degradation. Therefore, the DT<sub>50</sub> and DT<sub>90</sub> values presented were calculated using only data to 100 days. The rate decline could not be attributed to any significant decrease in microbial biomass.

#### Hydrolytic degradation

The hydrolysis of Quinoxyfen was investigated in sterile buffer solutions (pH 4, 7 and 9) at a nominal concentration of 0.5 µg ai/mL (8557, Reeves, and Ghosh, 1994). Acetone was used as a 1% co-solvent to facilitate solubility. The degradation was studied at 50°C and all pH values, and at pH4 at 25°C and 40°C using [<sup>14</sup>C]-quinoline labelled quinoxyfen. The rates of hydrolytic degradation (t<sub>1/2</sub>) under the various test regimes are summarized in Table 17.

Table 17. Hydrolytic degradation of quinoxyfen (8557).

Temperature	Half-life (t <sub>1/2</sub> )		
	pH4	pH7	pH9
50°C	7 days	Stable	Stable
40°C	16 days	ND	ND
25°C	75 days	ND	ND

Stable = no degradation after 5 days and <1% degradation after 21 days

ND = not determined due to stability seen at 50°C

At a temperature closer to environmental conditions (25°C), quinoxyfen was stable at pH 7 and pH 9 but degraded at pH 4 with a half-life of 75 days. At 25°C, DCHQ reached approximately 41% AR at 46 days (*ca* 33% AR at 30 days). The extent of hydrolysis confirmed that seen in early-stage environmental fate probe studies. The single hydrolysis product (which was seen at all temperatures) was identified as DCHQ by chromatographic analysis and mass spectrometry.

The effect of buffer (phthalate and citrate), quinoxyfen concentration (0.5 and 0.06 µg/mL) and co-solvent (acetone and THF) were further investigated in a hydrolysis study at pH 4 and 50°C (6328, Baloch, R, *et al.*, 1997). The results confirmed the findings of the previous study by Reeves and Ghosh in showing that quinoxyfen was degraded at pH 4 (half-life of approximately 5 days; compared to 7 days from the Reeves study to give DCHQ). This was irrespective of buffer type, quinoxyfen concentration, or co-solvent.

#### Photochemical degradation

The Meeting received several study reports on the photochemical degradation of quinoxyfen. The photolysis quantum yield of quinoxyfen was determined in water/acetonitrile (8:2 v/v) at concentrations of between 4.6–17.9 mg ai/L using artificial light at the absorption maximum (298 nm) at 20°C (4429, Rüdél, 1995). The acetonitrile was shown to have no effect upon light absorption. Quinoxyfen degraded rapidly under these conditions with a quantum yield of  $1.2 (\pm 0.2) \times 10^{-2}$ . This value was then used to calculate photolysis half-lives in dilute aqueous solution at latitude 52°N using the ABIWAS program which is based on the model of Frank and Klopffer (1988). This gave half-lives of 1.7 hours in June and 22.8 hours in December, assuming average light intensities and weather

conditions. The maximal or expected 'worst case' half-lives for March (earliest application) and June (latest application) were 16.4 hours and 6.8 hours, respectively.

Quinoxifen degraded to give two main photoproducts. The main degradate (up to 30% at 8 hours), with a chromatographic polarity between quinoxifen and 5,7-dichloro-4-hydroxy quinoline (DCHQ), was identified by mass spectrometry as 2-chloro-10-fluoro[1]benzopyrano[2,3,4-de]quinoline (CFBPQ) (Portwood, D., 1996; Report GHE-P 4721). A second degradation product (up to 11%) matched DCHQ by HPLC. At 6 hours, a quantitative mass balance was seen in the irradiated solution compared to a dark control, indicating no volatile loss of radioactivity.

In order to investigate the photo degradation of quinoxifen in aqueous solution under sunlight conditions, and to determine the rate and extent of formation of CFBPQ and its subsequent degradation, a non-guideline outdoor photolysis study was carried out (48846, MacDonald., 1997) using quinoxifen radiolabelled [ $^{14}\text{C}$ ] on the C-2 of the quinoline ring. This was performed at Letcombe Regis, UK (latitude around 50°N) using natural lake water, pH 7 buffer, and natural water/sediment, with exposure during August-September, 1996. Favourable conditions existed for photolysis with non-turbid, shallow water being used. The application rate was 0.5  $\mu\text{g}/\text{mL}$ . Further samples without sunlight exposure were used as dark controls.

After 1 day in the light exposed samples, no significant levels of quinoxifen were detected in either the natural water system or the water/sediment system. The water contained only CFBPQ and a very polar, multi-component material. Subsequent analysis of water samples to 28 days after treatment showed that CFBPQ rapidly degraded with a half-life of about 1–2 days in the natural water/buffer test systems, and approximately 4 days in the natural water with sediment present. The degradation of CFBPQ was followed by increasing amounts of very polar, multi-component material (7–27 components). On day 1, the water test system contained 54% of the applied radioactivity as CFBPQ, 27% as polar metabolite(s), and 0% as quinoxifen. On day 14, 0.47% of applied radioactivity was CFBPQ, 73% polar material. The buffered water test system yielded similar results. The dark natural water controls consisted largely of quinoxifen (108% applied radioactivity day 1, 74% day 14, 51% on day 28, with no degradates identified). The dark buffered water controls showed no degradation of quinoxifen over 14 days and about 20% degradation from day 14 to day 28.

The photochemical degradation of quinoxifen on soil was also studied (31076, Reeves, 1995). Speyer 2.2 soil (loamy sand) was surfaced treated with [ $^{14}\text{C}$ ]-quinoxifen labelled at the 2 position of the quinoline ring at a rate of 250 g ai/ha. The soil was maintained in a stainless steel incubation chamber covered with an airtight quartz glass plate. Irradiation was performed in 12 hour cycles of light and dark, using sun simulation lamps. Temperatures during the light and dark cycles were about 25°C and 18°C, respectively. Control samples were maintained under the same conditions, but with no light. At 1, 3, 7, 14, 21, and 30 days after treatment the headspace was purged and analyzed for carbon dioxide and volatiles. Soil samples were taken at the same intervals and immediately after application.

Quinoxifen degraded under the artificial light conditions with a half-life of about 200 days, estimated to be equivalent to > 1 year in natural sunlight in the spring in England. The main degradation product, up to 6.5% of applied radioactivity, remained unidentified. DCHQ was found (2.5% maximum of applied radioactivity). Very little organic volatiles or carbon dioxide was found (< 1% applied radioactivity). Total recovery of radioactivity ranged from 96% to 103%. Greater than 70% of the applied radioactivity was identified as quinoxifen after 30 days. The non-extractable residue in soil increased to a maximum of 11% of applied radioactivity on day 30. No degradation occurred with the dark controls, the non-extractable residue did not exceed 4% of applied radioactivity, and about 94% of applied radioactivity was identified as quinoxifen.

#### *Residues in succeeding crops (Confined rotational crop)*

Uptake of quinoxifen from soil into three succeeding crops was investigated (75502, Haq and Brown, 1995). Two radiolabelled forms of quinoxifen (phenoxy-labelled and quinoline-labelled) were prepared as an emulsifiable concentrate spray solution and applied separately to Mendip loam soil to give an even distribution on the soil surface using a DeVilbiss spray gun. The emulsifiable

concentrate was diluted with water to give a final concentration of 400 g ai/hectare. To assess if the treated tubs received the required amount of quinoxifen, the soil was sampled within 24 hours after application.

The three succeeding crops studied were, turnips (root crop), sunflowers (oilseed crop) and cabbage (leafy crop). The crops were sown into the soil, at the appropriate depth and density for the crop, 30 days after the application. The crops were sampled at harvest (118 days after treatment for cabbage and turnip, 150 days after treatment for sunflower) and separated into above-ground and below-ground portions. The latter were water washed to remove adhering soil. Crop matrix samples were homogenized and the total radioactivity determined by combustion.

Soil samples were extracted sequentially with acetonitrile and acetone. Extraction released about 88% of the radioactivity from day zero soils and about 80% of the radioactivity from harvest day soils. Extracts were analyzed by normal phase TLC and reverse phase HPLC (UV detection 295 nm and radioactivity monitor). Analysis of the soil extracts of Day 0 samples showed only quinoxifen to be present. Analysis of the soil extracts of harvest samples indicated only quinoxifen (> 95% of soil radioactivity) and very low levels of metabolites (< 5%), more polar than the parent. Thus, metabolism of quinoxifen does not occur extensively over the time course of the study (150 days). It is possible that the more polar metabolites were available for uptake into the plants.

The raw agricultural commodity (RAC, i.e. turnip root, cabbage leaves and sunflower head) were homogenized and the total radioactive content of the homogenized fractions determined by combustion. Results are given in Table 18.

Table 18. Total radioactive residue (TRR) content of rotational crops (75502).

Commodity	[ <sup>14</sup> C] Label	µg/kg
Cabbages (leaves)	Phenoxy	0.43
Cabbages (leaves)	Quinoline	0.49
Cabbages (leaves)	Control	-
Sunflowers (Head)	Phenoxy	1.2
Sunflowers (Head)	Quinoline	0.28
Sunflowers (Head)	Control	-
Turnips (Root)	Phenoxy	3.5
Turnips (Root)	Quinoline	3.4
Turnips (Root)	Control	-

The levels of radioactivity taken up from soil treated with <sup>14</sup>C-quinoxifen into the RAC of the three succeeding crops studied (turnip, cabbage and sunflower) were below 4 µg/kg quinoxifen equivalents. The residue levels observed were too low to allow for chromatographic analysis.

## RESIDUE ANALYSIS

### *Analytical Methods*

Analytical methods for determination of residues of quinoxifen have been developed for a wide range of substrates. The methods have been extensively validated with numerous recoveries on a wide range of substrates. The analytical methods for determination of residues of quinoxifen in plant and animal matrices follow similar partitioning, clean-up and quantification procedures. Generally, quinoxifen residues are extracted from plants and animal tissues samples with acidic acetonitrile. After addition of sodium bicarbonate solution to an aliquot of the extract, quinoxifen is partitioned into hexane, which is then evaporated to dryness. The residue is reconstituted in hexane prior to an aminopropyl solid phase extraction using 1% acetone in hexane to elute quinoxifen residues. The eluate is evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane (TMP). Quinoxifen is

quantified either by gas chromatography with mass selective detection (GC-MSD) or by HPLC with UV absorbance. This basic method has been modified and validated for use in various matrices. Validation study results were corrected for control values which were typically < 1% of the lowest fortification level. Matrix-specific methods are summarized below.

The Meeting received several methods for the determination of quinoxifen in grapes and processed grape commodities Method ERC 94.29 – Determination of grapes by reverse phase HPLC using UV absorbance detection at 235 nm (105043, Khoshab, 1995); Independent laboratory validation (41039, Khoshab, 1995) was used in all supervised trials on grapes conducted in various European countries and was used for some supervised trials on grapes conducted in Australia. The method involves extraction of quinoxifen from the crop by macerating with acidic acetone. After addition of sodium bicarbonate solution to an aliquot of the extract, the residue was partitioned into hexane which is then evaporated to dryness. The residue is reconstituted in hexane prior to an aminopropyl solid phase extraction using 1% acetone in hexane to elute the quinoxifen. The eluate is evaporated to dryness and reconstituted in acetonitrile/water. Quinoxifen is quantified by reverse phase HPLC using UV absorbance detection at 235 nm. Confirmation is by GC/MSD (237 and 272 amu ions).

The method was validated by analysis of fortified samples for residues of quinoxifen in grapes over the range of 0.01 – 1.0 mg/kg. The method was independently validated by an external laboratory, where samples were fortified with quinoxifen over the range of 0.01–10 mg/kg. Table 19 summarizes the recovery data.

Table 19. Recovery of quinoxifen from fortified grapes (Method ERC94.29) (105043; 41039).

Fortification levels	% Recovery <sup>1</sup>	
	Original method	Independent validation
Mean control values	0.0000 (n=6)	0.0002 (n=6)
0.01	94, 100 <sup>2</sup>	82, 83 <sup>2</sup>
0.01	98, 86	84, 95
0.01	95, 100	89, 88
0.20	99, 100	100, 93
1.0	98, 99	110, 103
10.0	Not fortified at this level	101, 100
Mean (overall)	97 ± 4.4	94 ± 9
% RSD over validated range (0.01-10.0 mg/kg)	4.5 (n=10)	9.5 (n=12)
% RSD at lowest validated level (0.01 mg/kg)	5.5 (n=6)	5.6 (n=6)
Mean at lowest validated level (0.01 mg/kg)	96 ± 5.3	87 ± 4.9

<sup>1</sup> Corrected for control value and moisture content

<sup>2</sup> Duplicate samples.

**Method ERC 95.26** – Determination of quinoxifen in grapes, must, wine, and pomace by gas chromatography with mass selective detection (GC-MSD) (105334, Khoshab and Roberts, 1996; 83731, Thompson, 2002) was used in processing studies for grapes carried out in European countries and in field trials and processing studies conducted in the US. In this method, quinoxifen residues were extracted from grapes, pomace, and raisins and analyzed as in ERD 94.29. The final residue was reconstituted in 0.1% corn oil in tri-methyl pentane (TMP).

Quinoxifen residues in grape must, grape juice, and wine were extracted by addition of sodium bicarbonate solution followed by partitioning into hexane which was then evaporated to dryness and reconstituted in 0.1% corn oil in TMP.



Quinoxifen was quantified by gas chromatography with mass selective detection (GC-MSD). The m/z 237.0 was used for confirmation, and the m/z 306.9 ion for quantification. The method was validated by fortifying control samples with quinoxifen at levels of 0.01 mg/kg to 2.0 mg/kg. Recovery experiments were performed in 4 batches by two analysts. Table 20 summarizes the recovery data, including the relative standard deviation at the lowest validated level as well as over the validated range.

Table 20. Recovery of quinoxifen from fortified grape wine, must, pomace (Method ERC95.26) (105334).

Matrix	Fortification level (mg/L)	% Recovery <sup>1</sup>	Average % recovery	% RSD
Wine	0.01	88, 90 <sup>2</sup>	87 ± 4	4.6 (n=8)
	0.01	85, 85		
	0.01	93, 88		
	0.01	84, 80		
	0.05	102, 99		
	0.05	107, 111		
	0.05	111, 117		
	0.05	105, 103		
	0.20	108, 107		
	0.20	110, 104		
	0.01 – 0.20	80 - 117	99 ± 11.2	11.3 (n=20)
Must	0.01	87, 76	88 ± 12.5	14.2 (n=6)
	0.01	102, 101		
	0.01	92, 72		
	0.05	99, 100		
	0.05	118, 115		
	0.05	105, 101		
	0.2	99, 112		
	0.5	100, 99		
	0.01 – 0.5	72 - 118	99 ± 12.4	12.5 (n=16)
Pomace	0.05	77, 80	78 ± 2.7	3.4 (n=6)
	0.05	80, 73		
	0.05	79, 79		
	0.20	69, 72		
	0.50	85, 98		
	1.0	75, 75		
	2.0	76, 77		
	0.05 – 2.0	69 - 98	78 ± 6.9	8.9 (n=14)

<sup>1</sup> Corrected for control Mean control values: wine = 0.0000 (n=8); must= 0.0000 (n=6); pomace= 0.0000 (n=6)

<sup>2</sup> Duplicate samples.

Table 21. Recovery of quinoxifen from grapes, juice, and raisins (Method ERC95.26) (83731).

Matrix	Fortification level (mg/L)	% Recovery	Average % recovery	% RSD		
Grapes	0.01	100	99 ± 1	1.5 (n=3)		
	0.01	97				
	0.01	99				
	0.10	0.10	89	92 ± 5	5.6 (n=3)	
		0.10	98			
		0.10	89			
		1.0	1.0	78	89 ± 10	11 (n=3)
			1.0	95		
			1.0	95		
	0.01 – 1.0	78 – 100	93 ± 7	7.5 (n=9)		
Juice	0.01	89	88 ± 2	1.6 (n=3)		
	0.01	87				
	0.01	86				
	0.10	0.10	76	76 ± 0	0 (n=3)	
		0.10	76			
		0.10	76			
	1.0	1.0	73	71 ± 2	3 (n=3)	
		1.0	70			
		1.0	69			
	0.01 – 1.0	69 - 89	78 ± 7.5	9.6 (n=9)		
Raisins	0.01	78	78 ± 1	1(n=3)		
	0.01	77				
	0.01	78				
	0.10	0.10	96	96 ± 1	0 (n=3)	
		0.10	96			
		0.10	97			
	1.0	1.0	89	88 ± 3	0.8 (n=3)	
		1.0	90			
		1.0	85			
	0.01 – 1.0	77 - 97	87 ± 8	9.4 (n=9)		

Method GRM 99.02 – Determination of quinoxifen in grapes and dried grapes by gas chromatography with mass selective detection (GC-MSD) (74780, Teasdale, 2000) Independent laboratory validation (102718, Dobbs, 2001) was used for determination of quinoxifen in supervised trials on grapes in Australia. Sample preparation is similar to that of ERC95.26. Quinoxifen was quantified by gas chromatography with mass selective detection (GC-MSD). The quantitation ion is 237 amu, and the confirmation ion is 272 amu.

At least two samples (in duplicate) were fortified at quinoxifen concentration levels of 0.01 to 0.5 mg/kg. A summary of the recovery data are summarized in Table 22.

The independent laboratory validation (Dobbs, 2001) conducted for the determination of residues of quinoxifen on raisins using Method GRM 99.02 showed average recoveries of 94 ± 8% over the concentration range of 0.01 mg/kg to 0.1 mg/kg. Individual recovery values were within the acceptable range of 70–120%. The results are included in Table 22.

Table 22. Recovery of quinoxyfen from fortified grapes and dried grapes (Method GRM99.02) (74780, 102718).

Fortification level (mg/kg)	n	Recovery range (%)	Mean (%)	Standard deviation	% RSD
<b>GRAPES</b>					
0.01	8	98 - 105	101	2.6	2.6
0.05	3	78 - 104	102	20.5	20.1
0.2	4	91 - 115	103	11.1	10.8
0.5	4	94 - 98	96	1.7	1.8
0.01 - 0.5	19	78 - 115	100	8.8	8.8
<b>DRIED GRAPES</b>					
0.01	4	68 - 95	82	11.9	14.5
0.05	4	84 - 99	92	7.4	8.0
0.2	4	77 - 115	93	15.8	17.0
0.5	4	70 - 95	79	10.8	13.7
0.01 - 0.5	20	68 - 115	86	12.4	14.4
<b>DRIED GRAPES (ILV)</b>					
0.01	5	84 - 86	85	0.84	9.8
0.02	3	98 - 103	101	2.6	2.6
0.10	5	95 - 106	100	4.3	4.3
0.01 - 0.1	13	84 - 106	94	8	8.5

Mean control values: Grapes = 0.0002 mg/kg (n=8); Dried grapes = 0.003 mg/kg (n=8).

Method ERC 95.26 – Validation of method for determination of quinoxyfen in cherries by GC-MSD (102722, Chen, 2002) was validated for use in the supervised trials on cherries conducted in the US. Untreated samples of cherries were fortified at concentration levels of 0.01mg/kg to 1.0 mg/kg. The recovery results are summarized in Table 23.

Table 23. Recovery of quinoxyfen from fortified cherries (102722).

Fortification level (mg/L)	% Recovery <sup>1</sup>	Average % recovery	% RSD
0.01	92	94 ± 2	2.13%
0.01	96		
0.01	94		
0.1	94	96 ± 2	2.16%
0.1	97		
0.1	98		
1.0	79	92 ± 11	11.9%
1.0	98		
1.0	98		
0.01 - 1.0	79 - 98	94 ± 6	6.4% (n=9)

Method ERC 95.26 – Validation of method for the determination of quinoxyfen residues in lettuce by GC-MSD (208698, Barney, 2005)- was validated for use on lettuce samples collected from trials in the US after minor modifications of ERC95.26 such as changes in the filtration procedure or volume of solvent used, which did not affect the performance of the method. Method validation was carried out at fortification levels of 0.01, 0.1, and 1.0 mg/kg of quinoxyfen. The results are summarized in Table 24.

Table 24: Recovery of quinoxifen from fortified leaf lettuce samples (Method ERC95.26) (208698).

Fortification level (mg/L)	% Recovery <sup>1</sup>	Average % recovery	% RSD
0.01	87	88 ± 2.2	2.5
0.01	87		
0.01	89		
0.01	91		
0.01	90		
0.01	85		
0.10	86	88 ± 2.1	2.4
0.10	87		
0.10	90		
1.0	84	89 ± 4.5	5.0
1.0	89		
1.0	93		
0.01 – 1.0	84 - 93	88 ± 2.6	2.9 (n=12)

**Method ERC 96.16** – Independent laboratory validation for the determination of quinoxifen residues in melon peel and pulp by GC-MSD (45724, Khoshab, and Rawle, 1996) was used in the supervised trials on melons conducted in European countries and involved extraction of quinoxifen with acidic acetone and partitioning into hexane after addition of sodium bicarbonate solution. The extract was evaporated to dryness and the residue was reconstituted in hexane prior to an aminopropyl solid phase extraction using 1% acetone in hexane to elute the quinoxifen. The eluate was then evaporated to dryness and reconstituted in tri-methyl pentane containing 1% corn oil and 1,4-dibromonaphthalene as internal standard. Quinoxifen was measured by gas chromatography with mass selective detection using m/z 237 ion. The m/z 286 ion was used for quantification of the internal standard.

Method 96.16 was independently validated by an external laboratory and the results were consistent with recovery data and chromatography generated on the original method (Table 25).

Table 25. Recovery of quinoxifen from fortified melon peel and pulp (Method ERC 96.16) (45724).

Fortification level (mg/kg)	% Recovery	
	Original method	Independent Validation
<b>MELON PEEL</b>		
0.01	82, 82	103, 87
0.01	88, 89	87, 86
0.01	101, 100	92, 95
0.01	93, 92	77, 86
0.05	92, 92	96, 94
0.20	94, 104	84, 93
0.50	100, 97	97, 105
1.0	101, 98	101, 100
Mean Overall	94 ± 6.6	92 ± 7.7
% RSD (0.01-1.0 mg/kg)	7.0 (n=16)	8.4 (n=16)
Mean (0.01 mg/kg)	91 ± 7.2	89 ± 7.7
% RSD (0.01 mg/kg)	7.9 (n=6)	8.6 (n=6)
<b>MELON PULP</b>		
0.01	91, 94	102, 83
0.01	92, 95	89, 89
0.01	92, 100	98, 84
0.01	91, 96	86, 98

Fortification level (mg/kg)	% Recovery	
	Original method	Independent Validation
0.05	92, 98	89, 98
0.20	103, 105	93, 89
0.50	102, 101	102, 101
1.0	99, 99	100, 104
Mean Overall	97 ± 4.6	94 ± 7.0
Mean (0.01 mg/kg)	94 ± 3.1	91 ± 7.2
% RSD (0.01-1.0 mg/kg)	4.7 (n=16)	7.5 (n=16)
% RSD (0.01 mg/kg)	3.3 (n=6)	7.9 (n=6)

Method ERC 96.08 – Validation of method for the determination of quinoxifen residues in peppers (76968, Khoshab and MacMillan, 1996; 08006, Chen, 2003) uses an extraction and clean-up scheme and analysis method similar to ERC 96.16, for use in trials on peppers in the US.

Table 26. Recovery of quinoxifen from fortified samples of peppers (Method ERC 96.08) (76968; 08006).

Fortification level (mg/L)	Range% Recovery	Average % recovery	% RSD
0.01	78 - 120	87.7 ± 10	11.3 (n=18)
0.05	92 - 102	99.1 ± 4.1	4.2 (n=14)
2.0	101 - 107	103.5 ± 2.6	2.6 (n=4)
0.01 – 2.0	78 - 120	93.9 ± 9.8	10.4 (n=36)

Method GRM 99.04 – Determination of residues of quinoxifen in sugar beet roots and tops by GC-MSD (74779, Teasdale, Lyons, Rhodes, and Patel, 2000) was used in trials in European countries. The method uses the extraction, clean-up, and analysis schemes of ERC 96.16. The validation was performed in 4 batches by 2 analysts. The results are summarized in Table 27.

Table 27. Recovery of quinoxifen from fortified sugar beet roots and tops (74779).

Fortification level (mg/kg)	% Recovery <sup>1</sup>	Average % recovery	% RSD
<b>SUGAR BEET ROOTS</b>			
0.01	103, 100	100 ± 9.2	9.2 (n=8)
0.01	92, 98		
0.01	97, 87		
0.01	103, 118		
0.05	98, 96	99 ± 2.6	2.6 (n=4)
0.05	100, 102		
0.2	90, 103	99 ± 61	6.2 (n=4)
0.2	101, 102		
0.5	89, 91	89 ± 2.1	2.4 (n=4)
0.5	89, 86		
0.01 – 0.5	86 - 118	97 ± 7.6	7.8 (n=20)
<b>SUGAR BEET TOPS</b>			
0.1	104, 104	103 ± 7.1	6.9
0.1	101, 105		
0.1	110, 87		
0.1	109, 105		
0.5	99, 100	99 ± 1.4	1.4
0.5	100, 97		
2.0	97, 96	96 ± 3.7	3.8
2.0	92, 101		

Fortification level (mg/kg)	% Recovery <sup>1</sup>	Average % recovery	% RSD
5.0	97, 96	97 ± 0.6	0.6
5.0	98, 96		
0.1 – 5.0	87 - 110	100 ± 5.5	5.5

<sup>1</sup> Corrected for control value and moisture content.

Mean control values: Sugar beet roots = 0.0001 mg/kg (n=8); tops = 0.0002 mg/kg (n=8)

**Method ERC 94.5** – Determination of quinoxifen residues in wheat and barley straw and grain by GC-MSD (63697, Gambie and Nicholson, 1994); Independent laboratory validation (31621, Gambie, Rawle, and Shaw, 1995) was used in supervised trials conducted on wheat and barley in various European countries. After extraction of the residues in acidic acetone, sodium bicarbonate was added and the extract was partitioned into hexane which was evaporated to dryness. The residue was next reconstituted in hexane and the resulting solution cleaned up in an aminopropyl solid phase extractor using 1% acetone in hexane. The eluate was evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane containing 1,4-dibromonaphthalene as internal standard. Quinoxifen was quantified by gas chromatography with mass selective detection. Ions monitored were 237 and 272 m/z for quinoxifen and 286 m/z for the internal standard. This method is very similar to method ERC 96.16.

The method was validated by fortification of samples of wheat and barley grain at quinoxifen concentration levels of 0.01–1.0 mg/kg and samples of straw at levels of 0.05–10 mg/kg. Two independent external laboratories also performed recovery experiments at the same levels of fortification. The results are summarized in Table 28.

Table 28. Summary of recoveries of quinoxifen from fortified wheat and barley grain and straw samples (63697; 31621).

Fortification level (mg/kg)	% Recovery <sup>1</sup>		
	Original method, ERC 94.5	Independent validation lab 1	Independent validation lab 2
<b>WHEAT AND BARLEY GRAIN</b>			
0.01	80, 91 <sup>2</sup>	92, 81 <sup>2</sup>	100, 93
0.01	95, 86	107, 107	98, 93
0.01	92, 86	86, 80	88, 107
0.05	93, 96	119, 119	-
0.10	84, 94	73, 80	97, 110
0.5	-	-	104, 105
1.0	103, 144	-	-
Mean	92 ± 7.2	94 ± 17.2	99.5 ± 7
Mean control values	0.0003 mg/kg (n=6)	0.0002 (n=6)	0.000 (n=3)
% RSD over the validated range	7.9 (n=12)	18.2 (n=10)	7 (n=10)
% RSD at the lowest validated value (0.01 mg/kg)	6.1 (n=6)	13.3 (n=6)	6.9 (n=6)
<b>WHEAT AND BARLEY STRAW</b>			
0.05	87, 88	89, 92	87, 91
0.05	76, 80, 76, 78	88, 83	89, 85
0.05	90, 92, 93	79, 71	94, 87
0.05	82, 86	-	-
0.20	82, 88	-	97, 94
0.20	80, 88	-	-

Fortification level (mg/kg)	% Recovery <sup>1</sup>		
	Original method, ERC 94.5	Independent validation lab 1	Independent validation lab 2
0.50	95, 89	77, 85	103, 95
1.0	90, 96, 98	85, 89	-
5.0	76, 83	-	-
10.0	76, 82	72, 85	88, 86
Mean Overall	85 ± 6.8	82.9 ± 6.8	91.3 ± 5.4
Mean (0.05 mg/kg)			
Mean control values	0.0029 (n=12)	0.0003 (n=6)	0.0096 (n=3)
% RSD over the validated range	7.9 (n=24)	8.2 (n=12)	5.9 (n=12)
% RSD at the lowest validated value (0.05 mg/kg)	7.4 (n=11)	9.2 (n=6)	3.7 (n=6)

1 Corrected for control values.

2 Replicate samples.

Method ERC 95.16 – Determination of quinoxifen residues in flour, bran and bread by GC-MSD (31600, Gambie and Press, 1995) was used in the processing study on wheat and involved extraction and clean-up of quinoxifen residues by the procedure of Method ERC 94.5. Quinoxifen was quantified by gas chromatography with mass selective detection. Ions monitored are 286 amu for the internal standard and 237 amu (quantitation ion) and 272 amu (confirmation) for quinoxifen. Ion 307 is also considered if the ratio of 237/272 is not within ± 10% of the value of the bracketing standard.

The method was validated for each analyte (flour, bran and bread) by fortification with quinoxifen at concentration levels of 0.01 mg/kg to 0.20 mg/kg. The results are summarized in Table 29.

Table 29: Recovery of quinoxifen from fortified wheat flour, bran, and bread (31600).

Fortification level (mg/kg)	% Recovery <sup>1</sup>		
	FLOUR	BRAN	BREAD
0.01	77, 88	75, 73	86, 96
0.01	107, 107	101, 101	98, 98
0.01	90, 87	80, 86	91.90
0.05	86, 77	73, 77	84, 90
0.20	87, 94	86, 89	104, 98
Mean Overall	90 ± 10.4	84 ± 10.4	94 ± 6.3
Mean control values	0.0002 mg/kg (n=6)	0.0004 mg/kg (n=6)	0.000 (n=6)
% RSD over the validated range (0.01-0.20 mg/kg)	11.6 (n=10)	12.4 (n=10)	6.7 (n=10)
% RSD at the lowest validated value (0.01 mg/kg)	12.9 (n=6)	14.3 (n=6)	5.3 (n=6)

<sup>1</sup>Corrected for appropriate control value

Method ERC 95.10 – Determination of quinoxifen residues in beer by GC-MSD (63705, Teasdale and Press, 1995)-was used in the study involving processing of barley into beer. Quinoxifen residues were extracted from beer samples with methyl-tertiary-butyl ether after addition of sodium bicarbonate solution and acetone. The extract was evaporated to dryness and the residue was reconstituted in 0.1% corn oil in tri-methyl pentane. Quinoxifen was quantified by gas chromatography with mass selective detection. The ions monitored are 237 amu and 272 amu for quinoxifen.

The method was validated by recovery experiments carried out in 2 batches by 2 analysts. Beer samples were fortified with quinoxifen at concentration levels of 0.01 mg/kg to 0.5 mg/kg.

Table 30. Recovery of quinoxifen from fortified beer samples (63705).

Fortification level (mg/L)	% Recovery <sup>1</sup>	Average % recovery	% RSD
0.01	75, 72	80.5 ± 9.4	11.6 (n=6)
0.01	80, 72		
0.01	92, 92		
0.05	86, 84	79.8 ± 8.1	10.2 (n=4)
0.05	68, 81		
0.10	90, 92	83 ± 9.6	11.6 (n=4)
0.10	72, 78		
0.50	94, 94	87.3 ± 9	10.3 (n=4)
0.50	75, 86		
0.01 – 0.50	68 - 94	82.4 ± 8.8	10.6 (n=18)

<sup>1</sup> Corrected for control value.

Mean control value = 0.000 mg/kg (n=6)

Method ERC 95.26.S1 – Determination of residues of quinoxifen in hops by gas chromatography with mass selective detection (73994, Oberwalder, 1998; 81400, West, S., 2001); Independent laboratory validation (80416, Eckert, J. and West, S., 2000) was used in trials on hops conducted in the US. It is a modification of Method 95.26 which was originally developed and validated for grapes. The procedure for hops was the same as for grapes, with minor modifications such as increase in volume of extracting solvent and proportionate increase in the volumes of sodium bicarbonate and hexane. Recovery data were generated for hops by an independent laboratory by fortifying untreated control samples with quinoxifen at concentration levels of 0.05 mg/kg and 0.1 mg/kg.

Table 31. Recovery of quinoxifen from fortified samples of hops (73994; 80416; 81400).

Fortification level (mg/L)	% Recovery	Average % recovery	% RSD
0.05	113	106 ± 16	15.4 (n=3)
0.05	117		
0.05	87		
0.10	100	102 ± 2	2 (n=3)
0.10	102		
0.10	104		
0.05 – 0.10	87 - 117	104 ± 10.6	10.6 (n=6)

Method ERC 94.7 – Determination of residues of quinoxifen in skimmed milk, whole milk, and cream by GC-MSD (135047, Class, 2003) was developed for quantitative determination of quinoxifen residues in skimmed milk, whole milk and cream. This method was used in the cattle feeding study. Quinoxifen was extracted from the milk fraction by shaking with methanol. After addition of sodium bicarbonate solution, quinoxifen was partitioned into hexane which was then evaporated to dryness. The residue was reconstituted in 1% acetone in hexane and applied to an aminopropyl SPE cartridge using a further volume of 1% acetone in hexane to elute the residue.

For cream samples, the eluate was evaporated to dryness and reconstituted in 5% methanol in dichloromethane prior to clean-up using gel permeation chromatography. For skimmed milk and whole milk, the residue was reconstituted in hexane and further purified using a silica SPE cartridge using 10% methyl-tertiary-butyl ether in hexane to elute quinoxifen. The eluates were evaporated to dryness and the residue reconstituted in 0.1% corn oil in tri-methyl pentane. Quinoxifen was quantified by gas chromatography with mass selective detection. The 237 m/z fragment ion was used for quantification, and the 272 m/z and 274 m/z fragment ions were used for confirmation.



The method was validated at fortification levels of 0.001 to 0.1 mg/kg quinoxifen.

Table 32. Recovery of quinoxifen from fortified samples of whole milk, skimmed milk, and cream (Method ERC 94.7) (135047).

Fortification level (mg/kg)	% Recovery <sup>1</sup>		
	SKIMMED MILK	WHOLE MILK	CREAM
0.001	87, 93	88, 79	64, 100
0.001	90, 96	83, 78	97, 110
0.001	99, 86	77, 85	90, 83
0.01	86, 85	80, 81	99, 99
0.1	79, 80	78, 84	87, 86
Mean	88 ± 6.5	81 ± 3.6	92 ± 12.6
Mean control values	0.000 mg/kg (n=6)	0.000 mg/kg (n=6)	0.000 (n=6)
% RSD over the validated range (0.001 – 0.1 mg/kg)	7.3 (n=10)	4.4 (n=10)	13.8 (n=10)
% RSD over the lowest validated range	5.6 (n=6)	5.3 (n=6)	17.6 (n=6)

<sup>1</sup>Corrected for appropriate control value

The independent laboratory validation consisted of fortification of skimmed milk and cream samples with quinoxifen at concentration levels of 0.001 mg/kg and 0.1 mg/kg.

Table 33: Summary of ILV results for recovery of quinoxifen from fortified skimmed milk and cream (Method ERC 94.7) (130457)

Matrix	Fortification level (mg/kg)	n	% Recovery (range)	Average % recovery	% RSD
Skimmed milk (1.5% fat)	0.001	5	76 - 113	101	15
	0.1	5	85 - 98	91	5
	Overall fortification	10	76 - 113	96 ± 11.5	12
Cream (30% fat)	0.001	4	69 - 81	75 <sup>1</sup>	9
	0.1	4	70 - 78	74 <sup>2</sup>	4
	Overall fortification	8	69 - 81	74 ± 4.4	6

<sup>1</sup> One result, 39% was identified by Dixon-Test as an outlier and was not included in the calculations.

<sup>2</sup> One result, 55%, was identified by Dixon-Test as an outlier and was not included in the calculations.

**Method ERC 94.20** – Determination of residues of quinoxifen in bovine muscle, kidney, and fat by GC-MSD (63682, Hastings, M. and Gambie, A., 1995); Independent laboratory validation (135044, Class, 2003) is applicable to the quantitative determination of quinoxifen residues in bovine muscle, kidney, and fat down to the lowest validated level of 0.01 mg/kg. Quinoxifen was extracted from the tissue by shaking with methanol. After addition of water, quinoxifen was partitioned into hexane which was then evaporated to dryness. The residue was reconstituted in dichloromethane prior to clean-up using gel permeation chromatography. The eluate was evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane. Quantification was by gas chromatography with mass selective detection. The 237 m/z fragment ion was used for quantification, and the 272 m/z and 274 m/z fragment ions were used for confirmation.

The method has been validated by the analysis of untreated and fortified samples for residues of quinoxifen in muscle, kidney, and fat over the range of 0.01-1.0 mg/kg.

Table 34. Recovery of quinoxifen from fortified samples of bovine muscle, kidney, and fat (Method ERC 94.20) (63682).

Fortification level (mg/kg)	% Recovery <sup>1</sup>		
	MUSCLE	KIDNEY	FAT
0.01	92, 100	91, 91	104, 116
0.01	93, 113	97, 98	108, 100
0.01	102, 112	94, 98	92, 95
0.10	110, 107	78, 86	109, 109
1.0	99, 96	95, 94	80, 93
Overall Mean	102 ± 7.7	92 ± 6.2	101 ± 10.7
Mean at lowest validated value (0.01 mg/kg)	102 ± 9.0	95 ± 3.3	102 ± 8.8
Mean control values	0.0007 mg/kg (n=6)	0.000 mg/kg (n=6)	0.000 (n=6)
% RSD over the validated range (0.01- 1.0 mg/kg)	7.6 (n=10)	6.7 (n=10)	10.6 (n=10)
% RSD over the lowest validated range (0.01 mg/kg)	8.8 (n= 6)	3.5 (n=6)	8.6 (n=6)

<sup>1</sup> Corrected for appropriate control value

For the independent laboratory validation, bovine meat and fat samples were fortified with quinoxifen at levels of 0.01 mg/kg and 1.0 mg/kg.

Table 35. Summary of ILV recovery results for quinoxifen residues in fortified bovine meat and fat (Method ERC 94.20) (135044).

Matrix	Fortification level (mg/kg)	n	% Recovery (range)	Average % recovery	% RSD
Bovine meat	0.01	4 <sup>1</sup>	68 - 93	84	14
	1.0	5	86 - 105	92	9
	0.01- 1.0	8	80 - 105	88 ± 10.6	12
Bovine fat	0.01	5	70 - 96	80	13
	1.0	5	80 - 96	84	8
	0.01 -1.0	10	70 - 96	82 ± 8.2	10

<sup>1</sup> One result, 60% was caused by a partial loss of extract during partition and was not included in the calculation.

**Method ERC 94.30** – Determination of residues of quinoxifen in bovine liver by GC-MSD (63683, Hastings and Gambie, 1995); Independent laboratory validation (135046, Class, 2003) was used in the cattle feeding study. The liver sample was first digested with aqueous hydrochloric acid/pepsin in order to extract quinoxifen residue. After centrifuging, the remaining solid tissue was extracted with methanol and again centrifuged. The methanol was decanted and removed by evaporation. The residue was reconstituted in the original acid/pepsin extract which was then treated with buffer and  $\beta$ -glucuronidase to breakdown any conjugated residues. After addition of water, quinoxifen was partitioned into hexane which was then evaporated to dryness. The residue was reconstituted in dichloromethane prior to clean-up using gel permeation chromatography. The eluate was evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane, and quinoxifen was quantified by gas chromatography with mass selective detection. Ion 237 m/z is used for quantification, and ions 272 m/z and 274 m/z are used for confirmation.

The method has been validated by analysis of untreated and fortified samples for residues of quinoxifen in liver over the range of 0.01 – 1.0 mg/kg. An independent laboratory validation resulted in unacceptable results, while in the repeated tests the recoveries remained poor (Table 37).

Table 36. Recovery of quinoxifen from fortified samples of bovine liver (Method ERC 94.30) (63683).

Fortification level (mg/kg)	% Recovery	Average % Recovery	% RSD
0.01	67, 73	67 ± 3.8	5.6 (n=6)
0.01	61, 67		
0.01	68, 68		
0.10	62, 63		
1.0	62, 64		
0.01 - 1.0	61 - 73	66 ± 3.7	5.7 (n=10)

Mean control value = 0.000 (n=6)

Table 37. Summary of ILV recovery results for quinoxifen residues in fortified bovine Liver, Second Attempt (Method ERC 94.30) (135046).

Fortification level (mg/kg)	% Recovery	Average % Recovery	% RSD
0.01	49	44 ± 4.9	11 (n=5)
0.01	46		
0.01	46		
0.01	36		
0.01	44		
1.0	53	54 ± 2.2	4.1 (n=4)
	56		
	55		
	51		
0.01 - 1.0			

Control values < 0.0005 and 0.0009 mg/kg. One sample at the 1.0 mg/kg fortification level (recovery 41% was excluded because of partial loss of hexane extract on evaporation.

Method ERC 98.05 – Determination of quinoxifen residues in eggs by GC-MSD (64399, Khoshab et.al, 1998); Independent laboratory validation (135045, Class, 2003)-was used in the poultry feeding study. Quinoxifen was extracted from whole egg and egg yolk by macerating and shaking with an acidic acetone solution. After addition of sodium bicarbonate solution, quinoxifen was partitioned into hexane which was then evaporated to dryness. The residue was reconstituted in 2% acetone in hexane and applied to an aminopropyl SPE cartridge using a further volume of 2% acetone in hexane to elute quinoxifen. The eluate was evaporated to dryness and reconstituted in dichloromethane prior to clean-up using gel permeation chromatography. The eluate was evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane containing 1,4-dibromonaphthalene as an internal standard. Quinoxifen was quantified by gas chromatography with mass selective detection. The 1,4-dibromonaphthalene quantification ion is 286 amu; the quinoxifen quantification ion is 272 amu, with confirmation ions 237 amu and 307 amu.

The method has been validated by the analysis of untreated samples and samples of whole eggs and egg yolks fortified with quinoxifen over the range of 0.01 mg/kg to 1.0 mg/kg. Results of the independent laboratory validation were consistent with the initial validation results.

Table 38. Recovery of quinoxifen from fortified samples of eggs (64399).

Fortification level (mg/kg)	% Recovery <sup>1</sup>	Average % Recovery	% RSD
0.01	109, 105 <sup>2</sup>	98 ± 7.3	7.4 (n=8)
0.01	101, 95		
0.01	101, 96		
0.01	85, 95		
0.10	93, 97	97 ± 2.6	2.7 (n=4)
0.10	98, 99		
0.5	92, 90	94 ± 4	4.3 (n=4)
0.5	96, 99		
1.0	93, 87	87 ± 4.5	5.2 (n=4)
1.0	87, 82		
0.01-1.0	82 - 109	95 ± 6.7	7.1 (n=20)

<sup>1</sup> Mean control values: whole eggs = 0.0000 (n=6); yolk = 0.0000 (n=6).

<sup>2</sup> Replicate samples.

Table 39. Summary of ILV recovery results for quinoxifen residues in fortified eggs (135045).

Matrix	Fortification level (mg/kg)	n	% Recovery (range)	Average % recovery	% RSD
Whole eggs	0.01	5	73 - 104	85	15
	1.0	5	79 - 105	92	13
	0.01 - 1.0	8	73 - 105	88 ± 12.3	14
Egg yolk	0.01	5	73 - 78	76	3
	1.0	5	73 - 84	81	6
	0.01 - 1.0	10	73 - 84	78 ± 4.7	6

<sup>1</sup> Corrected from appropriate control value

### Multi-residue Methods

Multi-residue method testing for quinoxifen according to US FDA PAM I, Appendix II, as updated January 1994 was reported to the Meeting (80711, Hackert Anderson and West, S., 2001).

Quinoxifen was analyzed according to the FDA Multiresidue Method Testing guidelines in PAM, Vol. I, Appendix II (1/94). Protocol A. Quinoxifen was evaluated to see if it was naturally fluorescent. With an excitation wavelength of 245 nm and 300 nm, the compound showed no emission response above that of the methanol blank. Therefore, quinoxifen does not naturally fluoresce.

Protocol C. The gas chromatographic behaviour of quinoxifen was evaluated according with three column types (DB-1, DB-17, and DB-225) in combination with electron capture detection (ECD) or nitrogen-phosphorous detection (NPD). Quinoxifen chromatographed within acceptable limits under Level I guidelines using the DB-1, DB-17, and DB-225 with ECD at 200°C and also on the DB-1 with NPD at 200°C.

Protocol D. Testing (without Florisil cleanup) for recovery of quinoxifen from grapes utilizing NPD as a specific detector resulted in an average recovery of 27% at 0.1 mg/kg and 75% at 0.05 mg/kg.

Protocols E and F required Florisil cleanup. For the C1 elution system, the majority of quinoxifen eluted in fraction 2. The majority of quinoxifen eluted in the third fraction for the C2 system.

Protocol E testing with grapes yielded total average quinoxifen recoveries of 37% (low fortification) and 102% (high fortification) for Florisil cleanup C1. The results show incomplete recovery of quinoxifen at low fortification level (0.05 mg/kg) and complete recovery at the high fortification level (0.5 mg/kg). Since quinoxifen is recoverable through the method with the C1 Florisil cleanup, the testing was repeated using the C2 Florisil cleanup. Average recoveries from grapes were 94% (low fortification) and 88% (high fortification) for Florisil cleanup C2, showing complete recovery through the method.

Protocol F testing with ground beef yielded total average quinoxifen recoveries of 12% (low fortification) and 70% (high fortification) for Florisil cleanup C1 and 30% (low fortification) and 93% (high fortification) for Florisil cleanup C2. The results show incomplete or partial recovery at the low fortification level (0.05 mg/kg) and complete recovery at the high fortification level (0.5 mg/kg) with the C1 and C2 Florisil cleanup.

Multi-residue Method DFG S19 – Validation of method for determination of quinoxifen in wheat, barley, grapes, strawberries, melons and other matrices by GC-ECD or GC-MSD (31651, Hastings and Schmidt, 1995)

A multi-residue method, DFG S19 was validated for use in the analysis of quinoxifen in a number of plant matrices. The method involves extraction of plant samples with acetone: water solution (maintained constant at a ratio of 2:1, v/v). The extract was saturated with sodium chloride and diluted with dichloromethane, resulting in separation of excess water. The organic phase was separated and evaporated to dryness. The residue remaining was taken up in dichloromethane and was cleaned up by gel permeation chromatography. The eluate was concentrated and after supplemental clean up on a small silica gel column, quinoxifen residues are determined by gas chromatography using capillary column and electron capture detector or mass selective detector.

Strawberry samples were extracted after adding sodium bicarbonate solution, since the original method resulted in unacceptable recoveries (about 60%).

Control samples of various matrices were each fortified with quinoxifen at levels of 0.01 mg/kg and 0.5 mg/kg. The results are summarized in Table 40.

Table 40. Summary of recoveries of quinoxifen from wheat, barley, melons, strawberries, and grapes at fortification levels of 0.01 and 0.5 mg/kg (MRM DFG S19) (31651).

Analyte	Recovery range (%)	Mean recovery (%)	% RSD
Winter wheat			
Grain	90 – 99	96	4 (n=4)
Straw	87 – 99	93	6 (n=4)
Winter barley			
Grain	84 – 98	91	7 (n=4)
Straw	79 – 100	92	10 (n=4)
Melons			
Peel	90 – 97	94	3 (n=1)
Pulp	95 – 97	96	1 (n=1)
Strawberries	69 – 88	78	10 (n=4)
Grapes	74 – 87	81	7 (n=4)

Method DFG S19 for the determination of residues of quinoxifen on hops by GC-MSD (73994, Oberwalder, 1999), modified, was used for the supervised trials on hops conducted in Germany. The method was validated for hops by fortification of untreated samples with quinoxifen at concentration levels of 0.01 mg/kg to 1.0 mg/kg. Recovery data are summarized in Table 41.

Table 41. Recovery of quinoxifen in fortified samples of fresh and dried hops with MRM DFG S19 (73994).

Matrix	Fortification level (mg/L)	% Recovery
FRESH HOPS CONES	0.01	150 <sup>1</sup>
	0.01	70
	0.02	85
	0.02	70
	0.02	90
	0.50	90
	0.50	73
	1.0	91
	1.0	93
Mean	0.01-1.0	85 ± 11
% RSD over the validated range (0.01-1.0 mg/kg)		12 (n=8)
DRIED HOPS CONES	0.02	105
	0.02	100
	0.50	93
Mean	0.02-0.50	99 ± 6
% RSD over the validated range (0.02 – 0.5 mg/kg)		6.1 (n=3)

<sup>1</sup> Outlier according to Dixon Test; not included in calculation of the mean.

### ***Stability of Pesticide Residues in Stored Analytical Samples***

Frozen storage stability studies were reported to the Meeting for a variety of substrates that include animal tissues and plants. Control samples were fortified with known concentrations of quinoxifen and then placed in frozen storage at approximately -20 C or less. The fortified samples were analyzed periodically for residues of quinoxifen using the same analytical method as that used for the residue field trial or processing samples.

The stability of frozen samples was evaluated as part of the supervised trials on cherries (102721, 102722, Chen, 2002). The maximum storage interval for field-treated samples was 77 days. To evaluate stability of residues during this period, control samples of each matrix were fortified with 1.0 mg/kg quinoxifen and analyzed after 80 days of frozen storage at -18°C. All samples were analyzed within 1 day of extraction. Method ERC 95.26, which was validated and used for the determination of quinoxifen in the supervised trials for cherries, was used for the storage stability test. Concurrent recoveries from samples fortified on the day of analysis were comparable to the test samples.

Table 42. Stability of quinoxifen residues in cherries after frozen storage (102721, 102722).

Matrix	Fortification level (mg/kg)	No. of days in frozen storage	Quinoxifen conc (mg/kg)	% Remaining	% Concurrent recovery <sup>1</sup>	Reference
Cherry fruit	1.0	80	0.908	91	94	Chen, H., 2002a IR-4 Study 07757
	1.0	80	0.926	93	94	
	1.0	80	0.918	92	95	
			Average	92	94	

<sup>1</sup> Concurrent recovery is from samples fortified on the day of analysis. % remaining was not corrected for the concurrent method recovery.

Numerous field trials on grapes were conducted in Europe, Australia, and the US. Throughout these trials, samples of grapes were stored frozen from 5.5 to about 11 months before analysis. A study was undertaken to determine the stability of quinoxifen residues in samples of grapes stored

frozen (47234, Williams, 1996). Untreated samples of macerated grapes from one of the trials conducted in Europe were combined and mixed briefly in a Waring blender. Thirty six aliquots, each being 10 g of the grape sample, were fortified with 0.10 mg/kg quinoxifen. A further 36 aliquots of 10 g each were left unfortified. All samples were stored below -16°C and a proportion of both fortified and untreated samples were analyzed at intervals of 0, 3, 6, 9, and 12 months of storage.

Samples were analyzed according to Method ERC 94.29, which was previously validated over the range of to a lowest validated level of 0.01mg/kg for grapes and was used in the supervised trials. The results are summarized in Table 43.

Untreated samples of grapes (approximately 10 g each) were taken from the trial in the US in which portion of the harvest was processed and fortified with 0.10 mg/kg quinoxifen (Thompson, 2001a; IR-4 Study 07256). Untreated juice and raisin samples were likewise collected after processing and fortified with 0.1 mg/kg quinoxifen. All samples were then frozen at -18°C. Frozen grape samples were analyzed after 206 days of storage, while juice and raisin samples were analyzed after 155 and 254 days of frozen storage, respectively. All samples were analyzed using method ERC 95.26, which had previously been validated for use on grapes and its processed fractions, with a lowest validated level of 0.01 mg/kg. The results are included in Table 43.

Table 43. Residues of quinoxifen in grapes and grape processed fractions during frozen storage (47234).

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent % Recovery <sup>1</sup>	Reference
Grapes	0	0.1	90	93	Khoshab, A. and Williams, M., 1996 (GHE-P-5423)
		0.1	93	93	
		0.1	88		
		0.1	90		
		0.1	102		
		0.1	100		
	Average	93.8	93		
Grapes	90	0.1	110	101	
		0.1	104	97	
		Average	107	99	
Grapes	180	0.1	96	93	
		0.1	96	95	
		Average	96	94	
Grapes	270	0.1	93	90	
		0.1	94	92	
		Average	93.5	91	
Grapes	365	0.1	97	100	
		0.1	98	99	
		Average	97.5	99.5	
Grapes	206	0.10	87	92	Thompson, 2001a (IR-4 Study 07256)
		0.10	86	91	
		0.10	85		
		Average	86	91.5	
Grape juice	255	0.01	93	89	
		0.01	93	93	
		0.01	81		
		Average	89	91	
Raisins	254	0.01	99	99	
		0.01	100	101	
		0.01	98		
		Average	99	100	

<sup>1</sup> Concurrent recovery is from samples fortified on the day of analysis. % remaining was not corrected for concurrent method recovery.

Samples of wheat grain and straw were taken from one of the supervised trials conducted in Europe. These samples were prepared with dry ice in a mill. Aliquots of each substrate (10g for grain

and 5g for straw) were weighed into 57 labelled 150 mL polypropylene pots. Thirty samples of grain were fortified with 0.1 mg/kg quinoxifen, while 30 samples of straw were fortified with 1.0 mg/kg quinoxifen. The remaining 27 samples of each substrate were retained as controls. All samples were then transferred to a freezer and kept frozen at temperatures ranging from -18°C to -24°C during the study with an average temperature of -23°C. The storage intervals were 0, 98, and 267 days for grain and 0, 97, and 280 days for straw (31748, Gambie 1995). Grain samples were kept frozen and analyzed after 534 days. Straw samples were analyzed after 536 days (47586, Gambie, 1996)

Samples were analyzed using method ERC 94.5, which had previously been validated with a lowest validated level of 0.01 mg/kg for grain and 0.05 mg/kg for straw. The results from both studies are summarized in Table 44.

Table 44. Residues of quinoxifen in cereal grain and straw during frozen storage (31748; 47586).

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent% Recovery <sup>1</sup>	Reference	
Grain	0	0.1	92	108	Gambie, A. and Long, T., 1995 (GHE-P-4409)	
		0.1	81	109		
		0.1	97			
		0.1	91			
		0.1	100			
Average	103					
		Average	94	108		
Grain	98	0.1	100	102		
		0.1	99	101		
		0.1	100			
		Average	99	102		
Grain	267	0.1	106	89		
		0.1	92	101		
		0.1	97			
		Average	98	95		
Grain	453	0.1	106	105	Gambie, A., 1996 (GHE-P-5438)	
		0.1	111	107		
		0.1	113			
		Average	110	106		
Grain	534	0.1	75	73		
		0.1	77	75		
		0.1	74			
		Average	75	74		
Straw	0	0.1	91	88		Gambie, A. and Long, T., 1995 (GHE-P-4409)
		0.1	95	87		
		0.1	92			
		0.1	92			
		0.1	97			
		0.1	96			
Average	94	88				
Straw	97	0.1	72	75		
		0.1	79	73		
		0.1	80			
		Average	77	74		
Straw	280	0.1	85	88	Gambie, A. and Long, T., 1995 (GHE-P-4409)	
		0.1	86	87		
		0.1	87			
		Average	86	87		
Straw	456	0.1	87	101		Gambie, A., 1996 (GHE-P-5438)
		0.1	96	94		
		0.1	93			
		Average	92	97		



Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent% Recovery <sup>1</sup>	Reference
Straw	536	0.1	75	78	
		0.1	78		
		0.1	74		
		Average	75		

<sup>1</sup> Concurrent recovery is from samples fortified on the day of analysis. % remaining was not corrected for concurrent method recovery.

The stabilities of frozen samples of hops, lettuce, strawberry, peppers, and cantaloupe (melon) were evaluated as part of the supervised trials (83727, Thompson, 2001; 208698, Barney, W., 2005; 208697, Barney, 2005; 8006, Chen, 2003; 208696, Corley, 2004). To evaluate the stability of residues during this period, control samples of commodity were fortified with quinoxifen and analyzed after some days of frozen storage at -15°C. Samples were generally analyzed on the day of extraction. No samples were analyzed on day 0. Method ERC 95.26 was used for the storage stability tests.

Table 45. Residues of quinoxifen in hops (dried), lettuce, strawberry, peppers, and melon during frozen storage.

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent % Recovery <sup>1</sup>	Reference
Hops	113	0.5	105	109	83727
		0.5	104	107	
		0.5	110	106	
		Average	106	108	
Lettuce (leaf)	280	0.10	93	95	208698
		0.10	94	96	
		0.10	88	95	
		Average	92	95	
Strawberry	162	0.10	92	98	208697
		0.10	97	94	
		0.10	94	97	
		Average	94	96	
Melon (cantaloupe)	251	0.50	89	94	208696
		0.50	95	95	
		0.50	91	93	
		Average	92	94	
Peppers, Bell	318	1.0	98	-	8006
		1.0	104	-	
		1.0	104	-	

<sup>1</sup> Concurrent recovery is from samples fortified on the day of analysis. % remaining was not corrected for concurrent method recovery.

Samples of whole milk from the dairy cow feeding study were stored for up to 87 days prior to analysis. In order to assess the stability of residues of quinoxifen in stored frozen samples, twelve 10-g samples of untreated whole milk were fortified with 0.1 mg/kg and kept frozen until analysis. In order to simulate the conditions in the study, milk was initially stored for 4 days at + 4°C, prior to deep freezing (31599, Gambie and Long, 1995).

Fortified samples, together with untreated samples were analyzed using method ERC 94.7, which has previously been validated with an LOQ of 0.001 mg/kg for milk. Samples were removed from storage and analyzed after 0, 161 and 238 days of frozen storage. Two untreated samples were fortified with 0.1 mg/kg on each day of analysis and analyzed for concurrent recoveries. The results are summarized in Table 46.

Table 46. Residues of quinoxifen in whole milk samples during frozen storage (31599).

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent % Recovery
Milk	0	0.1	93	90
		0.1	90	89
		0.1	91	
		0.1	90	
		0.1	90	
		0.1	89	
		Average	90	90
Milk	161	0.1	82	76
		0.1	81	85
		0.1	83	
		Average	82	80
Milk	238	0.1	86	89
		0.1	91	88
		Average	88	88

The liver, kidney, muscle, subcutaneous and peritoneal fat samples were stored up to 244, 190, 209, and 218 days, respectively during the cow feeding study (31599, Gambie, and Long,1995). In order to evaluate the stability of quinoxifen residues on frozen storage, tissue samples from the control group were fortified with 0.1 mg/kg quinoxifen and frozen at < 20°C until analysis. Liver samples were analyzed using method ERC 94.30, which has been previously validated with an LOQ of 0.01 mg/kg. The rest of the tissues were analyzed with method ERC 94.20, with a lowest validated level of 0.01 mg/kg. Concurrent recoveries were run with control samples fortified with 0.1 mg/kg quinoxifen on the day of analysis. The results are summarized in Table 47.

Table 47. Residues of quinoxifen in animal tissue samples during frozen storage (31599).

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent% Recovery <sup>1</sup>
Liver	242	0.1	64 (107 <sup>1</sup> )	61
		0.1	60 (100 <sup>1</sup> )	61
		0.1	44 (44 <sup>1</sup> )	
		Average	56 (93 <sup>1</sup> )	61
Liver	292	0.1	65	67
		0.1	69	66
		0.1	64	
		Average	66	66.5
Kidney	188	0.1	90	94
		0.1	94	91
		0.1	94	
		Average	93	92.5
Muscle	194	0.1	87	91
		0.1	86	91
		0.1	84	
		Average	86	91

Matrix	Storage Period, Days	Fortification mg/kg	% Remaining	Concurrent% Recovery <sup>1</sup>
Subcutaneous fat	207	0.1	93	90
		0.1	94	89
		0.1	101	
		Average	96	89.5
Peritoneal fat	216	0.1	80	79
		0.1	79	89
		0.1	87	
		Average	82	84

<sup>1</sup> Values in parenthesis are corrected for concurrent recoveries. No other % Remaining values were corrected for concurrent method recoveries.

## USE PATTERN

Quinoxyfen is a protectant fungicide for the control of powdery mildew diseases in a range of crops. Quinoxyfen does not control existing or latent powdery mildew infections and therefore, it must be applied before symptoms of the disease appear, on a protectant schedule. The product is diluted with water and applied as foliar spray or broadcast treatment using conventional spray equipment.

Quinoxyfen is registered for use in a wide range of crops in several countries. Only the registered uses in countries where supervised trials have been conducted or in countries with GAPs similar to where the supervised trials were carried out, are provided and summarized in Table 48. This summary is based on official labels provided by the sponsor and by use information supplied by the governments of Australia, Germany, and the Netherlands.

Table 48. Summary of GAP uses for quinoxyfen.

Crop	Country	Formulation	Application				PHI days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	No. or max (kg ai/ha/season)	
Blueberry	Germany	250 g/L SC	Foliar	0.075		3	14
Cereals (Wheat, barley, oats, rye, triticale)	UK	500 g/L SC	Foliar	0.15	0.0375 – 0.075	2 0.3 kg ai/ha	~60 Zadoks 49 (first awns)
Cereals (Wheat, barley, oats, rye, triticale)	UK	250 g/L SC	Foliar	0.15	0.0375 – 0.075	2 0.3 kg ai/ha	~60 Zadoks 49 (first awns)
Cereals (Wheat, barley, oats, rye, triticale)	UK	66.7 g/L + 250 g/L Fenpropimorph	Foliar	0.1 – 0.2		2	~60 Zadoks 49 (first awns)
Cherry	USA	250 g/L SC (2.08 lbs/gal)	Foliar	0.12		5, maximum 0.63 kg ai/ha/year 7-day intervals	7
Currants	Germany	250 g/L SC	Foliar	0.075		3	14
Gooseberries	Germany	250 g/L SC	Foliar	0.075		3,	14
Grapes	Australia	250 g/L SC	Foliar	0.05 (calculated)	0.0025 at 7-10-day intervals; 0.005 at 10-14-day intervals	3	14

Crop	Country	Formulation	Application				PHI days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	No. or max (kg ai/ha/season)	
Grapes, table and wine	France	250 g/L SC	Foliar	0.05		3, 7-10-day intervals between 2 leaves unfolded and end of bunch closure	21
Grapes, table and wine	Germany	200 g/L + 60 g/L fenarimol	Foliar	0.08	0.005	4, 10-14-day intervals	21
Grapes, table and wine	Italy	250 g/L SC	Foliar		0.0075	5, 8-14-day intervals	28
Grapes, table and wine	Spain	250 g/L SC	Foliar	0.075	0.0075	5, 10-18-day intervals	30 (wine) 21 (table)
Grapes	USA	250 g/L SC	Foliar	0.018 – 0.12 0.036 at 7 day interval 0.072 at 14 day interval 0.12 at 21 day interval		5, 7-21-day intervals; maximum 0.60 kg ai/ha/year	14
Grapes, and wine	France	200 g/L (+ 60 g/L fenarimol) SC	Foliar	0.04		3, 7 – 10 day-intervals	21
Grapes, table and wine	Italy	200 g/L (+ 60 g/L fenarimol) SC	Foliar		0.005 – 0.0075	5, 8 – 10 day intervals	28
Grapes, table and wine	Spain	200 g/L (+ 60 g/L fenarimol) SC	Foliar		0.005 – 0.0075	5, 10-19-day intervals	30 (wine) 21 (table)
Hops	Germany	250 g/L SC	Foliar	0.0675 – 0.15	0.005 – 0.011	4, 10-14-day intervals, maximum 0.5 kg ai/ ha/season	28
Hops	USA	250 g/L SC	Foliar	0.073 – 0.15		4, 7-day intervals; maximum 0.60 kg ai/ha/year	21
Lettuce, head and leaf	USA	250 g/L SC	Foliar	0.073 – 0.11	0.026 -0.039 (calculated)	4, maximum 0.44 kg ai/ha/season. 10 – 14 day intervals	1
Melons	Italy	250 g/L SC	Foliar		0.004 – 0.006	10-12 days intervals	7
Melons	Italy	200 g/L (+ 60 g/L fenarimol) SC	Foliar		0.005 – 0.006	10-12-days interval	7

Crop	Country	Formulation	Application				PHI days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	No. or max (kg ai/ha/season)	
Melons	Spain	250 g/L SC	Foliar	0.075	0.0075	3, 5 – 7 day interval	7
Melons	Spain	200 g/L (+ 60 g/L fenarimol) SC	Foliar		0.005 – 0.0075	3, 10-14 day interval	7
Melons	USA	250 g/L SC	Foliar	0.073 – 0.11	0.039 (calculated)	4, maximum 0.44 kg ai/ha/season	3
Peppers (all)	USA	250 g/L SC	Foliar	0.15	0.02 (calculated)	4, maximum 0.60 kg ai/ha/season 7 day interval	3
Strawberry	Germany	250 g/L SC	Foliar	0.125	0.006	2, 7-21-day intervals. Field and glasshouse	14
Strawberry	USA	250 g/L SC	Foliar	0.073 – 0.11	0.026 – 0.039 (calculated)	4, maximum 0.44 kg ai/ha/season 10 – 14 day interval	1
Sugarbeets	France	500 g/L SC	Broadcast	0.15	0.05 – 0.1	1	28
Sugarbeets	Germany	500 g/L SC	Broadcast	0.12	0.031- 0.062	2	28
Sugarbeets	UK	500 g/L	Broadcast	0.15	0.038 – 0.075	2 0.2 kg ai/ha	28
Sugarbeets	UK	250 g/L	Broadcast	0.15	0.038 – 0.075	2 0.2 kg ai/ha	28
Watermelons	Italy	250 g/L SC	Foliar		0.004 – 0.006	10-12 days intervals	7
Watermelons	Italy	200 g/L (+ 60 g/L Fenarimol) SC	Foliar		0.005 – 0.006	10-12-days interval	7
Watermelons	Spain	250 g/L SC	Foliar	0.075	0.0075	3, 5 – 7 day interval	7
Watermelons	Spain	200 g/L (+ 60 g/L Fenarimol) SC	Foliar		0.005 – 0.0075	3, 10-14 day interval	7
Wheat and Barley	France	500 g/L SC	Foliar	0.15	0.05 – 0.1	1	56
Wheat and Barley	France	200 g/L + (66.7g/L fenpropimorph) SC	Foliar	0.1	0.03 – 0.07	1	56
Wheat and Barley	Germany	500 g/L SC	Foliar	0.15	0.025 – 0.075	2 0.25 kg ai/ha	49 (first awns visible)
Wheat and Barley	Germany	500 g/L SC	Foliar	0.25	-	1	BBCH 25 - 32
Wheat	Netherlands	500 g/L SC	Foliar	0.15	0.025-0.075	1	60

Crop	Country	Formulation	Application				PHI days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	No. or max (kg ai/ha/season)	
Wheat	Netherlands	500 g/L SC	Foliar	0.15	0.025-0.075	1	60

### RESIDUES RESULTING FROM SUPERVISED TRIALS

The results of supervised trials are shown in Tables 50 to 64. Where multiple samples were taken from a single plot or multiple analyses conducted on a single sample, the average value is reported. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot. Results have not been corrected for concurrent method recoveries unless indicated. The following table summarizes information on residues resulting from supervised trials.

Table 49: Field trials.

Group	Commodity	Table No.
Stone fruit	Cherries	50
Berries and other small fruits	Grapes	51
	Strawberries	52
	Currants	53
Fruiting vegetables, cucurbits	Melons	54 - 55
Fruiting vegetables other than cucurbits	Peppers	56
Leafy vegetables	Lettuce	57
Root and tuber vegetables	Sugar Beets	58
Cereal grains	Wheat	59
	Barley	60
Straw, fodder and forage of cereal grains and grasses (straws and fodder dry)	Wheat	61
	Barley	62
Dried herbs	Hops	63
Miscellaneous fodder and forage crops	Sugar beet tops	64

#### *Stone fruit – adapted in part from the Evaluation of the USA*

A total of 13 supervised field trials on cherries were conducted in major cherry growing areas of the USA in 2000 and 2001 (102722; 102721, Chen, 2002). Each treated plot received five foliar-directed applications of a suspension concentrate formulation containing 250 g/L quinoxifen at the rate of approximately 0.12 kg ai/ha (0.11 lbs/acre) per application. There were no adjuvants in the tank mix. The retreatment interval was 6 – 8 days, typically 7 days. The period of time from harvest to analysis ranged from 35 to 77 days. Cherries were pitted prior to analysis.

Table 50. Quinoxyfen residues in cherries (pitted) from foliar directed application in the USA.

Cherries country, year (variety)	Application					PHI days	Residues <sup>1</sup> , mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, USA	250 g/L SC	0.12			5, max 0.63 kg ai/ha/ year	7		
Trial 00-M121 Michigan, USA, 2000 (Montmorency)	250 g/L SC	0.12	0.013	929- 951	5, total = 0.62 kg ai/ha/yr	7	<u>0.13</u>	102722
Trial 00-M122 Michigan, USA, 2000 (Montmorency)	250 g/L SC	0.12	0.013	932- 946	5, total = 0.62 kg ai/ha/yr	7	<u>0.08</u>	102722
Trial 00-M123 Michigan, USA, 2000 (Montmorency)	250 g/L SC	0.12	0.013	930- 948	5, total = 0.62 kg ai/ha/yr	7	<u>0.11</u>	102722
Trial 00-M124 Michigan, USA, 2000 (Montmorency)	250 g/L SC	0.12	0.013	930- 945	5, total = 0.62 kg ai/ha/yr	7	<u>0.14</u>	102722
Trial 00-M125 Michigan, USA, 2000 (Emperor Francis)	250 g/L SC	0.13	0.022	571- 575	5, total = 0.63 kg ai/ha/yr	7	<u>0.12</u>	102722
Trial 00-M126 Michigan, USA, 2000 (Hedelfinger)	250 g/L SC	0.13	0.022	571- 579	5, total = 0.63 kg ai/ha/y	7	<u>0.13</u>	102722
Trial 00-WA39 Washington, USA, 2000 (Bing)	250 g/L SC	0.13	0.009-0.010	1312- 1399	5, total = 0.63 kg ai/ha/yr	7	<u>0.14</u>	102722
Trial 00-WA40 Washington, USA, 2000 (Bing)	250 g/L SC	0.12	0.011	1102- 1159	5, total = 0.61 kg ai/ha/yr	7	<u>0.11</u>	102722
Trial 00-WA41 Washington, USA, 2000 (Montmorency)	250 g/L SC	0.12	0.005-0.006	2144- 2178	5, total = 0.62 kg ai/ha/yr	6	<u>0.05</u>	102722
Trial 00-CO01 Colorado, USA, 2000 (Montmorency)	250 g/L SC	0.11- 0.12	0.006	1765- 1914	5, total = 0.60 kg ai/ha/yr	6	<u>0.15</u>	102722
Trial 00-PA01 Pennsylvania, USA, 2000 (Montmorency)	250 g/L SC	0.12 – 0.13	0.011	1122- 1159	5, total = 0.63 kg ai/ha/yr	6	<u>0.27</u>	102722
Trial 01-CA49 California, USA, 2001 (Brooks)	250 g/L SC	0.12	0.009-0.010	1239- 1360	5, total = 0.61 kg ai/ha/yr	7	<u>0.03</u>	102721
Trial 01-CA50 California, USA, 2001 (Brooks)	250 g/L SC	0.13	0.008-0.009	1469- 1624	5, total = 0.63 kg ai/ha/yr	8	<u>0.08</u>	102721

<sup>1</sup> Average of duplicate field samples from the same plot.

#### Berries and other small fruits

A total of 57 supervised trials were conducted on grapes in the following countries: France (9), Germany (6), Italy (11), Spain (6), US (13), Canada (4), and Australia (8). Results are summarized in Table 51.

A typical residue decline curve from the foliar application to grapes is that from Trial R94-049 in Spain. Six applications were made at 9 – 10 day intervals, and grape samples were taken at intervals of 1 – 62 days after the final treatment. The half-life is 19 days for first-order kinetics.

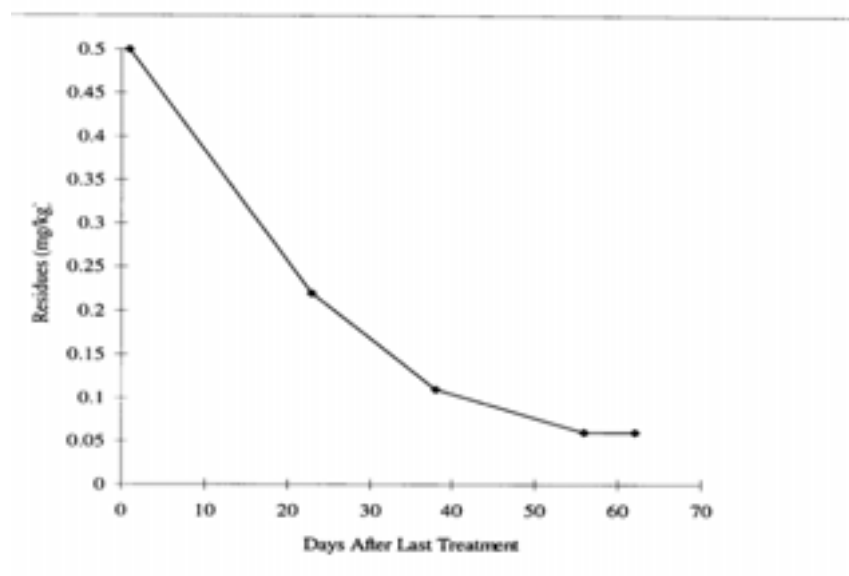


Table 51. Quinoxifen residues in grapes from foliar applications in France, Germany, Italy, Spain, USA, Canada and Australia.

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, France (Table and wine)	250 g/L SC	0.05			3 appl/yr at 7-10-day intervals	21		
Trial D3T6S361 France, 1993 (Cinsault, Wine)	500 g/L SC	0.029 – 0.045	0.0074- 0.0076	390-730	6 at 8-11 days interval	64	0.03	42674
Trial D3T6S361 France, 1993 (Cinsault, Wine)	500 g/L SC	0.031 – 0.058	0.0074- 0.0076	410- 770	8 at 8-11 days interval	43	0.04	
Trial D3T6S361 France, 1993 (Cinsault, Wine)	500 g/L SC	0.031- 0.055	0.0075	410-730	10 at 8-11 days interval	22	<u>0.06</u>	42674
Trial R94-014 France, 1994 (Italia, table)	250 g/L SC	0.05	0.025	200	6 at 6-13 days interval	0 7 15 22 30	0.12 0.06 0.05 <u>0.04</u> 0.04	43622
Trial R94-015 France, 1994 (Gamay, Wine)	250 g/L SC	0.05	0.025	200	6 at 8-13 days interval	0 6 13 20 27	0.39 0.10 0.07 <u>0.13</u> 0.07	43621
Trial R94-016B France, 1994 (Pinot Noir, Wine)	250 g/L SC	0.05	0.027	190	6 at 8-12 days interval	32	0.04	43620



Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial R94-017 France, 1994 (Pinot Meunierr, Wine)	250 g/L SC	0.05	0.024	210	6, at 11-13 days interval	0	0.05	43816
						10	0.04	
						21	0.02	
						28	0.02	
Trial R94-017 France, 1994 (Pinot Noir, Wine)	250 g/L SC	0.05	0.027	190	6, at 8-13 days interval	0	0.12	
						11	0.06	
						18	0.05	
						25	0.04	
Trial R95-037 France, 1995 (Chenin, Wine)	250 g/L SC	0.06	0.047	130	6, at 11-14 days interval	0	0.10	45716
						5	0.08	
						9	0.11	
						15	0.08	
Trial R95-037 France, 1995 (Chenin, Wine)	250 g/L SC	0.06	0.047	130	6, at 11-14 days interval	20	0.09	
GAP, Germany (Table and wine)	250 g/L SC Or 200 g/L + 60 g/L fenarimol SC	0.08	0.005	1600	Max 4, at 10- 14 day interval	21		
Trial R95-038A Germany, 1995 (Silvaner, Wine)	200 g/L SC + 60 g/L fenarimol	0.068- 0.072	0.010- 0.012	610-810	7, at 11-12 days interval	1	0.35	45717
						5	0.24	
						10	0.21	
						15	0.21	
Trial R95-038A Germany, 1995 (Silvaner, Wine)	200 g/L SC + 60 g/L fenarimol	0.020- 0.021	0.003- 0.004	610- 810	7, at 11-12 days interval	21	0.24	
						1	0.05	
						5	0.06	
						10	0.06	
Trial R95-038A Germany, 1995 (Silvaner, Wine)	200 g/L SC + 60 g/L fenarimol	0.020- 0.021	0.003- 0.004	610- 810	7, at 11-12 days interval	15	0.06	
						21	0.04	
						1	0.20	
						5	0.25	
Trial R95-038B Germany, 1995 (Silvaner, Wine)	200 g/L SC + 60 g/L fenarimol	0.020- 0.021	0.003- 0.004	610- 810	7, at 11-12 days interval	10	0.28	45717
						15	0.10	
						21	0.36	
						1	0.04	
Trial R95-038B Germany, 1995 (Silvaner, Wine)	200 g/L SC + 60 g/L fenarimol	0.019- 0.022	0.003- 0.004	600- 840	7, at 11-12 days interval	5	0.06	
						10	0.05	
						15	0.06	
						21	0.05	
Trial R95-039A Germany, 1995 (Riesling, Wine)	200 g/L SC + 60 g/L fenarimol	0.066- 0.077	0.009- 0.012	600-840	7, at 11-13 days interval	21	0.21	45718
Trial R95-039B Germany, 1995 (Riesling, Wine)	200 g/L SC + 60 g/L fenarimol	0.062- 0.068	0.009- 0.012	560-770	7, at 11-12 days interval	21	0.16	
GAP, Italy (Table and wine)	250 g/L SC OR 200 g/L +60 g/L fenarimol		0.008		Max 5/year, at 8 – 14 days interval	28		

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial R94-046A Italy, 1994 (Wine-White Marzemino)	250 g/L SC	0.094	0.008	1200	6 at 11-12 days interval	0	0.50	42673
						6	0.36	
						10	0.20	
						15	0.20	
						20	0.13	
						30	0.17	
Trial R94-046B Italy, 1994 (Wine-White Marzemino)	250 g/L SC	0.125	0.010	1200 - 1300	6 at 10-12 days interval	0	0.65	
						6	0.34	
						10	0.48	
						15	0.43	
						20	0.36	
						30	0.30	
Trial R94-047A Italy, 1994 (Italia, Table)	250 g/L SC	0.96- 0.103	0.008	1300 - 1400	6 at 10-11 days interval	0	0.30	43416
						4	0.24	
						9	0.24	
						14	0.26	
						19	0.24	
						30	0.18	
Trial R94-047B Italy, 1994 (Italia, Table)	250 g/L SC	0.136- 0.138	0.010	1400	6 at 10-11 days interval	0	0.55	
						4	0.25	
						9	0.52	
						14	0.36	
						19	0.34	
						30	0.10	
Trial R94-048A Italy, 1994 (Cardinale, Table)	250 g/L SC	0.083- 0.111	0.01	830-1100	6 at 9-11 days interval	21	0.10	43179
						32	0.06	
Trial R94-048B Italy, 1994 (Cardinale, Table)	250 g/L SC	0.05- 0.083	0.008	670-1100	6 at 9-11 days interval	21	0.07	
						32	0.04	
Trial R95-027 Italy, 1995 (Prosecco, Wine)	250 g/L SC	0.062- 0.065	0.006	1000	7 at 3-13 days interval	20	0.30	44917
Trial R95-028A Italy, 1995 (Garganega, Wine)	200 g/L SC+ 60 g/L fenarimol	0.07-0.072	0.007	1000	7 at 10-12 days interval	21	0.49	45173
Trial R95-028B Italy, 1995 (Prosecco, Wine)	200 g/L SC+ 60 g/L fenarimol	0.07-0.071	0.007	1000	7 at 10-13 days interval	20	0.28	45173
Trial R95-029A Italy, 1995 (Italia, Table)	200 g/L SC+ 60 g/L fenarimol	0.062- 0.065	0.006	1000	7 at 10-13 days interval	20	0.32	45715
Trial R95-029B Italy, 1995 (Italia, Table)	200 g/L SC+ 60 g/L fenarimol	0.069- 0.073	0.007	1000	7 at 10-13 days interval	20	0.25	45715
GAP, Spain (Table and wine)	250 g/L SC	0.075	0.008		Max 5/ season, at 10 - 18 day intervals	30, wine grapes; 21, table grapes		

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial R94-049 Spain, 1994 (Malabeo, Wine)	250 g/L SC	0.042 0.052 0.039 0.047 0.050 0.050	0.008	520- 690	6 at 9-10 days interval	1 23 38 56 62	0.50 <u>0.22</u> 0.11 0.06 0.06	43180
Trial R94-050 Spain, 1994 (Malabeo, Wine)	250 g/L SC	0.038 0.040 0.044 0.040 0.058 0.056	0.0075	510- 780	6 at 9-10 days interval	62	0.04	43181
Trial R95-032 Spain, 1995 (Italia, Table)	200 g/L SC+ 60 g/L fenarimol	0.070	0.007	950	6 at 11-14 days interval	21	<u>0.08</u>	45531
Trial R95-033 Spain, 1995 (Blanca Apireta, Table)	250 g/L SC	0.060- 063	0.01 –0.013	480- 610	5 at 12-14 days interval	0 5 10 15 21	0.15 0.10 0.06 0.10 <u>0.04</u>	45532
Trial R95-034 Spain, 1995 (Palomino Fino, Wine)	250 g/L SC	0.060- 073	0.010	570- 700	6 at 13-15 days interval	21	<u>0.02</u>	45513
Trial R95-035 Spain, 1995 (Macabeo, Wine)	200 g/L SC + 60 g/L fenarimol	0.070- 0.073	0.014	500- 520	7 at 9-15 days interval	20	0.15	45692
GAP, USA	250 g/L SC	0.12 0.036 at 7 day interval 0.072 at 14 day interval 0.12 at 21 day interval			5, Max 0.60 kg ai/ha/year at 7 –21 days interval	14		
Trial 99-NY06 New York, USA, 1999 (Chardonnay)	250 g/L SC	0.094- 0.118	0.006 –0.007	1600	5, at interval of 6-7 days; Total = 0.567 kg ai/season	14	<u>0.22</u>	83731
Trial 99-PA02 Pennsylvania, USA, 1999 (Cayuga)	250 g/L SC	0.118 – 0.123	0.012	1000	5, at interval of 6-7 days; Total = 0.60 kg ai/season	15	<u>0.13</u>	
Trial 99-CA38 California, USA, 1999 (Perlette)	250 g/L SC	0.22 0.22 0.12 0.12	0.009 –0.017	1300- 1400	5, at interval of 6-8 days; Total = 0.8 kg ai/season	14	<u>0.06</u>	
Trial 99-CA39 California, USA, 1999 (Thompson seedless)	250 g/L SC	0.118 – 0.121	0.009	1328- 1400	5, at interval of 6-8 days; Total = 0.598 kg ai/season	14	<u>0.09</u>	

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial 99-CA68 California, USA, 1999 (Thompson seedless)	250 g/L SC	0.120 – 0.121	0.009	1300 - 1400	5, at interval of 6-7 days; Total = 0.612 kg ai/season	14	<u>0.15</u>	
Trial 99-CA69 California, USA, 1999 (Thompson seedless)	250 g/L SC	0.115 – 0.123	0.009	1300 - 1400	5, at interval of 6-7 days; Total = 0.595 kg ai/season	14	<u>0.08</u>	
Trial 99-CA70 California, USA, 1999 (Thompson seedless)	250 g/L SC	0.119 – 0.121	0.009	1300	5, at interval of 6-7 days; Total = 0.598 kg ai/season	14	<u>0.18</u>	
Trial 99-CA71 California, USA, 1999 (Thompson)	250 g/L SC	0.169 – 0.120	0.009	1300	5, at interval of 6-7 days; Total = 0.592 kg ai/season	14	<u>0.24</u>	
Trial 99-CA96 California, 1999 (Sauvignon Blanc)	250 g/L SC	0.23 0.12 0.12 0.12 0.12	0.010- 0.018	1200	5, at interval of 6-8 days; Total = 0.71 kg ai/season	14	<u>0.15</u>	
Trial 99-ID16 Idaho, USA, 1999 (Chardonnay)	250 g/L SC	0.118 – 0.123	0.010	1100 - 1200	5, at interval of 6-7 days; Total = 0.607 kg ai/season	13	<u>0.08</u>	
Trial 99-WA10 Washington, USA, 1999 (Concord)	250 g/L SC	0.120 – 0.122	0.009- 0.012	1000- 1300	5, at interval of 6-7 days; Total = 0.605 kg ai/season	15	<u>0.15</u>	
Trial 99-WA11 Washington, USA, 1999 (Concord)	250 g/L SC	0.120 – 0.121	0.009- 0.012	1000 - 1400	5, at interval of 6-7 days; Total = 0.604 kg ai/season	14	<u>0.13</u>	
Trial 99-FL43 Florida, USA, 1999 (Summit Muscadine)	250 g/L SC	0.123- 0.128	0.013	960- 990	5, at interval of 7-8 days; Total = 0.625 kg ai/season	14	<u>0.44</u>	
GAP, USA (applied to Canadian trials)	250 g/L SC	0.018-0.12 0.036 at 7 day interval 0.072 at 14 day interval 0.12 at 21 day interval			5, Max 0.60 kg ai/ha/year at 7–21days interval	14		
Trial 99-ON06 Ontario, Canada, 1999 (Concord)	250 g/L SC	0.117- 0.121	0.013	880- 920	5 at intervals of 6-7 days; Total = 0.594 kg ai/season	14	<u>0.22</u>	83731
Trial 99-ON06 Ontario, Canada, 1999 (C0ncord)	250 g/L SC	0.058- 0.062	0.007	880-930	5 at intervals of 6-7 days; Total = 0.30	14	0.09	

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial 99-ON07 Ontario, Canada, 1999 (SU-23512)	250 g/L SC	0.115- 0.120	0.013	860- 910	5 at intervals of 6-7 days; Total = 0.594 kg ai/season	14	<u>0.29</u>	
Trial 99-ON07 Ontario, Canada, 1999 (SU-23512)	250 g/L SC	0.058- 0.061	0.007	870- 920	5 at intervals of 6-7 days; Total = 0.297 kg ai/season	14	0.13	
GAP, Australia	250 g/L SC	0.05 (calculated)	0.0025 at 7- 10 day interval;0.005 at 10-14 day interval	1000 (for dilute)	3	14		
Trial 98483-01 Australia, 2000 (Rhine Reisling)	250 g/L SC	0.075 0.15 0.30	0.0025 0.005 0.010	3000 3000 3000	3 3 3	14 14 14	<u>0.15</u> <u>0.45</u> 0.99	1951
Trial 98483-02 Australia, 2000 (Chardonnay)	250 g/L SC		0.0025 0.005 0.010	- - -	3 3 3	14 14 14	<u>0.23</u> <u>0.82</u> 1.32	
Trial 98483-03 Australia, 2000 (Black Shiraz)	250 g/L SC	0.025 0.05 0.10 0.05 0.10	0.0025 0.005 0.010 0.005 0.010	1000 1000 1000 1000 1000	3 3 3 3 3	14 14 14 14 14	< 0.01 <u>0.09</u> < 0.01 <u>0.09</u> < 0.01	
Trial 99050-01 Australia, 1999 (Chardonnay)	250 g/L SC	0.025 0.050 0.10	0.0025 0.005 0.010	1000 1000 1000	7 7 7	14 14 14	<u>0.06</u> <u>0.18</u> 0.39	2148
Trial 99050-02 Australia, 1999 (Verdelho)	250 g/L SC	0.025 0.043 0.083	0.0025 0.005 0.010	1000 850 830	6 6 6	82 82 82	0.02 0.05 0.09	
Trial 99051-01 Australia, 2000 (Cabernet)	250 g/L SC	0.035  0.073  0.15	0.0025  0.005  0.010	1400  1500  1500	3  3  3	0 3 7 14 21 28 0 3 7 14 21 28 0 3 7 14 21 28	0.05 0.05 0.04 0.03 0.03 0.05 0.22 0.27 0.17 <u>0.15</u> 0.10 0.11 0.50 0.43 0.23 0.25 0.18 0.19	2149

Grapes country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial 99051-03 Australia, 2000 (Chardonnay)	250 g/L SC	0.065	0.0025	2600	3	0	0.19	2149
						3	0.21	
						7	< 0.01	
						14	0.17	
						21	0.08	
						28		
	0.13	0.005	2600	3	0	0.60		
					3	0.51		
					7	0.39		
					14	0.54		
					21	0.30		
					28	0.22		
	0.26	0.010	2600	3	1	1.2		
					3	1.0		
					7	0.70		
14					0.65			
21					0.50			
28					0.53			
Trial 99051-04 Australia, 2000 (Thompson seedless)	250 g/L SC	0.17	0.0025	6700	3	1	0.51	2149
						3	0.83	
						7	0.80	
						14	0.41	
						21	0.60	
						28	0.40	
	0.33	0.005	67 00	3	1	1.5		
					3	1.6		
					5	1.7		
					14	1.1		
					21	1.0		
					28	1.0		
	0.67	0.010	6700	3	1	3.2		
					3	4.3		
					7	3.3		
14					3.2			
21					3.1			
28					2.6			

Note: For US trials, residue value is the average of duplicate samples.

A total of eleven supervised trials were conducted on strawberries in Germany from 1999 to 2000 (11110, Kunz, 2001). Eight supervised trials were conducted in strawberry growing areas in the USA (208697, Barney, W., 2005).

Table 52. Quinoxifen residues in strawberries from foliar applications in Germany and the USA.

Strawberry country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, Germany	250 g/L SC	0.12	0.006	2000	2	14		
Trial OR901 (Field) Germany, 1999 (Polka)	500 g/L SC	0.12	0.013	1000	2	21	0.01	11110
Trial B/FO 27/99 (Glasshouse) Germany, 1999 (Polka)	500 g/L SC	0.12	0.013	1000	2	0 7 14 21	0.08 0.04 0.02 0.01	11110

Strawberry country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial RU-F-53 00 RPMZ 1/1 (Plastic tunnel) Germany, 1999 (Elsanta)	250 g/L SC	0.12	0.013	1000	2	0 7 14 21	0.37 0.01 <u>0.05</u> 0.01	11110
Trial RU-L-39 99 MZ (Plastic tunnel) Germany, 1999 (Honeoye Frigo)	500 g/L SC	0.12	0.013	1000	2	7 14 21	0.26 <u>0.07</u> 0.01	11110
Trial PSD-O-19/99 (Glasshouse) Germany, 1999 (Elsanta)	500 g/L SC	0.12	0.013	1000	2	21	0.04	11110
Trial 11312 (Plastic tunnel) Germany, 2000 (Elsanta)	250 g/L SC	0.12	0.013	1000	2	14 21	<u>0.16</u> 0.07	11110
Trial 11312 (plastic tunnel) Germany, 2000 (Elsanta)	500 g/L SC	0.12	0.013	1000	2	14 21	<u>0.09</u> 0.07	11110
Trial PSD-O-26/00 (Glasshouse) Germany, 2000 (Elsanta)	250 g/L SC	0.12	0.013	1000	2	14 21	<u>0.12</u> 0.02	11110
Trial B/FO 36/00 (Glasshouse) Germany, 2000 (Avalon grün)	250 g/L SC	0.12	0.013	1000	2	0 7 14	0.24 0.12 <u>0.04</u>	11110
Trial OR0001 (Field) Germany, 2000 (Elsanta)	250 g/L SC	0.12	0.013	1000	2	21	< 0.01	11110
Trial 00/022 (Field) Germany, 2000 (Elsanta)	250 g/L SC	0.12	0.013	1000	2	14	<u>0.01</u>	11110
GAP, USA	250 g/L SC	0.11		280	4, max 0.44 /kg ai/season	1		
Trial 02-WI12 Wisconsin, USA, 2002 (Honeoye)	250 g/L SC	0.14- 0.15		400 – 440	4, max 0.58 kg ai/ ha/season	1	<u>0.16</u>	208697
Trial 02-NJ25 New Jersey USA, 2002 (Chandler)	250 g/L SC	0.14 - 0.15		500 - 520	4, max 0.58 kg ai/ ha/season	1	<u>0.18</u>	208697
Trial 02-NC16 North Carolina, USA, 2002 (Camarosa)	250 g/L SC	0.14 – 0.15		320 – 330	4, max 0.58 kg ai/ ha/season	1 3 6	<u>0.41</u> 0.25 0.18	208697
Trial 02-FL43, Florida, USA 2002 (Sweet Charlie)	250 g/L SC	0.14 – 0.15		370 - 380	4, max 0.58 kg ai/ ha/ season	1	<u>0.56</u>	208697
Trial 02-WA29 Washington, USA, 2002 (Totem)	250 g/L SC	0.15 - 0.17		390 - 660	4, max 0.65 kg ai/ ha/ season	1	0.05	208697

Strawberry country, year (variety)	Application <sup>1</sup>					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial 02-CA97 California, USA, 2002 (Hecker)	250 g/L SC	0.15		460 - 470	4, max	1	<u>0.46</u>	208697
					0.58 kg ai/ ha/ season	3	0.33	
						7	0.16	
Trial 02-CA98 California, USA, 2002 (Hecker)	250 g/L SC	0.14 - 0.15		460 - 480	4, max	1	<u>0.24</u>	208697
					0.58 kg ai/ ha/ season			
Trial 02-CA99 California, USA, 2002 (Hecker)	250 g/L SC	0.15		470 - 480	4, max 0.60 kg ai/ ha/ season	1	0.53	208697

Supervised trials were conducted on black currants in Germany (20062, Fuchsbichler, 2002; 20061, Fuchsbichler, 2002). The trials were conducted by a government agency in Germany to support the establishment of MRLs in the EU.

Table 53. Quinoxifen residues in currants from foliar application in Germany (20061; 20062)<sup>1</sup>.

Currants (black) Trial No., country, year (variety)	Application					PHI days	Residues <sup>2</sup> mg/kg
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.		
GAP, Germany	250 g/L SC	0.075	0.0075	1000	3	14	
RIP2003-487 (148) Germany, 2001 (Ben Navis)	250 g/L SC	0.075	0.0075	1000	3	14	<u>0.20</u>
RIP2003-490 (244) Germany, 2002 (Tenah)	250 g/L SC	0.075	0.0094	800	3	0	0.30
						7	0.11
						10	0.08
						14	<u>0.06</u>
						21	0.03
RIP2003-492 (246) Germany, 2002 (Titania)	250 g/L SC	0.075	0.017	429	3	14	<u>0.05</u>
RIP2003-449 (147) Germany, 2002 (Titania)	250 g/L SC	0.075	0.01	750	3	0	0.25
						7	0.09
						10	0.04
						14	<u>0.04</u>
						21	0.02
RIP2003-483 (146) Germany, 2002 (Blackdown)	250 g/L SC	0.075	0.0075	1000	3	0	0.63
						7	0.43
						10	0.39
						14	<u>0.40</u>
						21	0.34
RIP2003-489 (243) Germany, 2002 (Titania)	250 g/L SC	0.075	0.0075	1000	3	0	0.60
						7	0.47
						10	0.44
						14	<u>0.30</u>
						21	0.11
RIP2003-491 (245) Germany, 2002 (Ben Tirran)	250 g/L SC	0.075	0.0075	1000	3	14	<u>0.28</u>

<sup>1</sup>Only the report on the analytical phase of the study was available to the Meeting.

<sup>2</sup>All control samples were <LOQ (0.01 or 0.02 mg/kg).



*Fruiting vegetables, Cucurbits*

Sixteen supervised trials on melons were conducted in Spain, Italy, and Greece during 1995 and 1996 (46957; 46958; 46956; 46954, Khoshab, 1995; 48081; 48080; 47141, Khoshab, 1996). Quinoxifen was determined in the peel and the pulp. Residues in the whole fruit were calculated using percentage weight composition of melons from a standard text (The Composition of Foods by Paul, A. and Southgate, D), i.e., 59% pulp and 41% peel.

Table 54. Quinoxifen residues on melons from supervised trials in Italy, Greece and Spain.

Melons country, year (variety)	Application			PHI days	Residues, mg/kg			Reference
	Form	kg ai/hL	no.		Whole fruit	Peel	Pulp	
GAP, Italy	250 g/L OR 200 g/L + 60 g/L fenarimol	0.004- 0.006		7				
Trial R95-025A Italy, 1995 (0328 Numens)	200 g/L + 60 g/L fenarimol	0.0075	3	7	<u>0.03</u>	0.07	< 0.01	46957
Trial R95-025B Italy, 1995 (0328 Numens)	200 g/L + 60 g/L fenarimol	0.0070	3	7	<u>0.02</u>	0.06	< 0.01	
Trial R96-041A Italy, 1996 (vector)	250 g/L	0.0075	3	8	<u>0.03</u>	0.04	0.02	48081
Trial R96-041B Italy, 1996 (vector)	200 g/L + 60 g/L fenarimol	0.0075	3	8	<u>0.02</u>	0.03	0.02	
Trial R96-043A Italy, 1996 (Supermarket)	250 g/L	0.0055	3	7	<u>0.02</u>	0.02	< 0.01	48080
Trial R96-043B Italy, 1996 (Supermarket)	200 g/L + 60 g/L fenarimol	0.0050	3	7	<u>0.01</u>	0.01	< 0.01	
Trial R96-097A Greece, 1996 (Yuppie Hylond)	250 g/L	0.0075	3	7	<u>0.02</u>	0.06	< 0.01	47141
Trial R96-097B Greece, 1996 (Yuppie Hylond)	200 g/L + 60 g/L fenarimol	0.0070	3	7	<u>0.01</u>	0.04	< 0.01	
GAP, Spain	200 g/L + 60 g/L fenarimol	0.005- 0.0075	3	7				
Trial R95-030A Spain, 1995 (Galia-Revigal)	250 g/L	0.0075	3	0 4 7	0.05 0.01 <u>0.02</u>	0.08 0.02 0.06	< 0.01 < 0.01 < 0.01	46958
Trial R95-030A Spain, 1995 (Galia-Revigal)	200 g/L + 60 g/L fenarimol	0.0070	3	7	<u>0.02</u>	0.04	ND	
Trial R95-030B Spain, 1995 (Doral)	250 g/L	0.0074	3	0 4 7	0.03 0.01 <u>0.01</u>	0.07 0.04 0.02	< 0.01 ND ND	

Melons country, year (variety)	Application			PHI days	Residues, mg/kg			Reference
	Form	kg ai/hL	no.		Whole fruit	Peel	Pulp	
Trial R95-030B Spain, 1995 (Doral)	200 g/L + 60 g/L fenarimol	0.0070	3	0	0.02	0.06	ND	
				4	0.02	0.06	ND	
				7	<u>0.01</u>	0.03	ND	
Trial R95-031A Spain, 1995 (Cantaloupe)	250 g/L	0.0077	3	0	0.02	0.06	ND	46956
				4	0.02	0.02	< 0.01	
				7	<u>0.01</u>	0.02	ND	
Trial R95-031B Spain, 1995 (Cantaloupe)	200 g/L + 60 g/L fenarimol	0.0072	3	0	0.02	0.04	ND	46956
				4	< 0.01	0.01	ND	
				7	<u>&lt; 0.01</u>	< 0.01	ND	
Trial R96-045A Spain, 1996 (Regal)	250 g/L	0.0075	3	7	<u>0.02</u>	0.04	< 0.01	46954
Trial R96-045B Spain, 1996 (Regal)	200 g/L + 60 g/L fenarimol	0.0070	3	7	<u>0.02</u>	0.04	< 0.01	

ND = 0.002 mg/kg (20% of LOQ)

A total of 11 supervised field trials on cantaloupes were conducted in major growing areas of the USA and Canada in 2002 and 2003 (208696, Corley, 2004).

Table 55. Summary of quinoxyfen residue data on melons from treatments according to the GAP in the US (208696).

Melons country, year (variety)	Application				PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	water, L/ha	no.		
GAP, USA	250 g/L SC	0.073-0.11	280	4	3	
Trial 01-BC01 BC, Canada, 2001 (Athena)	250 g/L SC	0.14 – 0.15	540 - 560	4, total 0.58 kg ai/ha	4	<u>0.03</u>
Trial 01-ON01 ON, Canada, 2001 (Athena)	250 g/L SC	0.11 – 0.17	520 - 760	4, total 0.57 kg ai/ha	2	<u>0.05</u>
Trial 01-QC03 Quebec, Canada 2001 (Early Dawn)	250 g/L SC	0.14 – 0.15	470 - 490	4, total 0.58 kg ai/ha	4	<u>0.03</u>
Trial 01-CA60 CA, USA, 2001 (Aclaim)	250 g/L SC	0.15	370 - 480	4, total 0.58 kg ai/ ha	3	<u>0.03</u>
Trial 01-CA82 CA, USA, 2001 (Hale's Best)	250 g/L SC	0.15 – 0.16	470 - 480	4, total 0.62 kg ai/ ha	3	0.04
Trial 01-CA83 CA, USA, 2001 (Hearts of Gold)	250 g/L SC	0.15 – 0.16	480 - 490	4, total 0.62 kg ai/ ha	2	0.02
Trial 01-NM09 NM, USA, 2001 (Hale's Best Jumbo)	250 g/L SC	0.15	340 - 370	4, total 0.58 kg ai/ ha	3	<u>0.02</u>
Trial 01-NJ20 NJ, USA, 2001 (Ambrosia)	250 g/L SC	0.15	380 - 390	4, total 0.60 kg ai/ ha	0	0.04
					3	0.03
					7	0.03
Trial 01-TX323 TX, USA, 2001 (Explorer)	250 g/L SC	0.15 - 0.16	320 - 340	4, total 0.61 kg ai/ ha	14	0.02
					0	0.07
					3	0.02
					7	0.02
					14	< 0.01

Melons country, year (variety)	Application				PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	water, L/ha	no.		
Trial 01-TX324 TX, USA, 2001 (Mission)	250 g/L SC	0.15	290 - 300	4, total 0.60kg ai/ ha	2	0.05
Trial 01-GA16 GA, USA, 2001 (Vienna)	250 g/L SC	0.15	280 - 290	5, total 0.75 kg ai/ ha	2	<u>&lt; 0.01</u>

<sup>1</sup> Average of duplicate samples from the same plot.

### *Fruiting vegetables, other than Cucurbits*

#### *Peppers, sweet*

A total of eleven supervised trials were conducted on peppers (six on bell peppers and five on non-bell peppers) in commercial growing areas in the United States during 2001 (8006, Chen, 2003). Samples of marketable pepper were collected by hand from each plot, placed in plastic bags and shipped to the laboratory, where they were kept frozen at about -20°C until analysis (255 days maximum).

Table 56. Quinoxyfen residues in sweet peppers from supervised trials in the USA (8006).

PEPPERS country, year (variety)	Application					PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.		
GAP, USA	250 g/L SC	0.15	0.020	750	4, max 0.60 kg ai/ha/yr	3	
Trial 01-NJ19 NJ, USA, 2001 (Bell- King Arthur)	250 g/L SC	0.14		370 - 390	4, total 0.58 kg ai/ha/yr	2	<u>0.15</u>
Trial 01-FL27 FL, USA, 2001 (Bell- Camelot)	250 g/L SC	0.14		320 - 340	4, total 0.58 kg ai/ha/yr	0 3 7 14	0.41 <u>0.16</u> 0.06 0.02
Trial 01-FL28 FL, USA, 2001 (Bell- Camelot)	250 g/L SC	0.14		320 - 340	4, total 0.58 kg ai/ha/yr	3	<u>0.15</u>
Trial 01-TX20 TX, USA, 2001 (Bell- Jupiter)	250 g/L SC	0.14		360 - 380	4, total 0.58 kg ai/ha/yr	2	<u>0.17</u>
Trial 01-CA58 CA, USA, 2001 (Bell - Jupiter)	250 g/L SC	0.14		460 - 480	4, total 0.58 kg ai/ha/yr	0 3 7 14	0.03 <u>0.01</u> 0.01 0.01
Trial 01-CA59 CA, USA, 2001 (Bell- Jupiter)	250 g/L SC	0.14		480- 490	4, total 0.58 kg ai/ha/yr	3	<u>0.02</u>
Trial 01-OH15 OH, USA, 2001 (Non-bell)	250 g/L SC	0.14		470- 550	4, total 0.58 kg ai/ha/yr	2	<u>0.09</u>
Trial 01-NM07 NM, USA, 2001 (Non-bell- Big Jim)	250 g/L SC	0.14		320 - 370	4, total 0.58 kg ai/ha/yr	4	<u>0.12</u>

PEPPERS country, year (variety)	Application					PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.		
Trial 01-FL29 FL, USA, 2001 (Non-bell -Cheyane)	250 g/L SC	0.14		320 - 330	4, total 0.58 kg ai/ha/yr	3	<u>0.64</u>
Trial 01-TX21 TX, USA, 2001 (Non-bell- Sonora Anaheim)	250 g/L SC	0.14		420 – 590	4, total 0.58 kg ai/ha/yr	2	<u>0.23</u>
Trial 01-GA14 GA, USA, 2001 (Non-bell - Jalapeno)	250 g/L SC	0.14		470 - 480	4, total 0.58 kg ai/ha/yr	5	<u>0.52</u>

<sup>1</sup> Average of duplicate samples in the same plot.

### Leafy vegetables

#### Lettuce

A total of sixteen supervised trials were conducted on lettuce (eight on leaf lettuce and eight on head lettuce) in commercial growing areas in the United States during 2002 (208698, Barney, 2005). A minimum of 4 pounds of head lettuce (with wrapper leaves) or leaf lettuce (with wrapper leaves) was collected per sample. At all of the trials, lettuce samples were harvested randomly across the plots avoiding the ends of the plots. Two samples were collected from each treated plot and one from each untreated plot. Lettuce samples were placed in labelled sample bags and held in frozen storage until analysis (19 to 187 days).

Table 57. Quinoxifen residues on lettuce with wrapper leaves from supervised trials in the USA (208698).

Lettuce (head and leaf) country, year (variety)	Application					PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.		
GAP, USA	250 g/L SC	0.11		280	4, max of 0.44 kg ai/ha/season	1	
Trial 02-CO09 CO, USA, 2002 (Head -Raider)	250 g/L SC	0.14 – 0.15		360 - 400	4, total 0.58 kg ai/ ha/yr	1	<u>1.4</u>
Trial 02-FL40 FL, USA, 2002 (Head - Salinas)	250 g/L SC	0.15		330	4, total 0.58 kg ai/ ha/yr	1	<u>5.3</u>
Trial 02-NC15 NC, USA, 2002 (Head - Maverick)	250 g/L SC	0.14 – 0.15		321	4, total 0.58 kg ai/ ha/yr	1	<u>1.2</u>
Trial 02-CA89 CA, USA, 2002 (Head -Sharp Shooter)	250 g/L SC	0.15 – 0.16		550 - 740	5, total 0.74 kg ai/ ha/yr	1	0.86
Trial 02-CA91 CA, USA, 2002 (Head - Titan)	250 g/L SC	0.14 - 0.15		590 - 650	4, total 0.58 kg ai/ ha/yr	1	<u>1.0</u>

Lettuce (head and leaf) country, year (variety)	Application					PHI days	Residues <sup>1</sup> mg/kg
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.		
Trial 02-CA93 CA, USA, 2002 (Head – Sharp Shooter)	250 g/L SC	0.14 – 0.15		720 - 750	4, total 0.59 kg ai/ ha/yr	1	<u>0.91</u>
Trial 02-CA94 CA, USA, 2003 (Head – Wellton)	250 g/L SC	0.14		380 - 400	4, total 0.58 kg ai/ ha/yr	1	<u>3.1</u>
Trial 02-CA87 CA, USA, 2002 (Head – Empire)	250 g/L SC	0.14 – 0.15		370 - 380	4, total 0.58 kg ai/ ha/yr	1	<u>2.1</u>
Trial 02-CO10 CO, USA, 2002 (Leaf – Capistrano)	250 g/L SC	0.14 – 0.17		360 - 440	4, total 0.62 kg ai/ ha/yr	1	1.8
Trial 02-MD09 MD, USA, 2002 (Leaf – Grand Rapids)	250 g/L SC	0.14 – 0.15		400 - 410	4, total 0.58 kg ai/ ha/yr	1	<u>2.9</u>
Trial 02-CA90 CA, USA, 2002 (Leaf – Green Gene's #1)	250 g/L SC	0.15		450 - 620	4, total 0.74 kg ai/ ha/yr	1 4 7 14	2.2 1.4 0.76 0.29
Trial 02-CA92 CA, USA, 2002 (Leaf – Panther)	250 g/L SC	0.14 – 0.15		660 - 760	4, total 0.58 kg ai/ ha/yr	1	<u>1.3</u>
Trial 02-NM11 NM, USA, 2002 (Leaf – Salad Bowl)	250 g/L SC	0.14		380 - 510	4, total 0.57 kg ai/ ha/yr	1	<u>3.4</u>
Trial 02-CA95 CA, USA, 2002 (Leaf – Marin)	250 g/L SC	0.14 – 0.15		400 - 470	4, total 0.58 kg ai/ ha/yr	1	<u>13</u>
Trial 02-CA88 CA, USA, 2002 (Leaf – Waldemans Green)	250 g/L SC	0.15		370 - 380	4, total 0.58 kg ai/ ha/yr	1	<u>4.3</u>
Trial 02-FL41 FL, USA, 2003 (Leaf – Waldemans Dark Green MTO)	250 g/L SC	0.15		330	4, total 0.58 kg ai/ ha/yr	1 3 7 14	<u>6.9</u> 6.1 5.2 1.8

<sup>1</sup> Average of results from duplicate samples taken for each plot.

### *Root and Tuber vegetables*

#### *Sugar beet roots*

A total of eight supervised trials were conducted on sugar beets in Northern Europe (Germany, Northern France and the UK) 76690, (Jones, 2000; 83187, Kang, 2001,). The first application was made at growth stage BBCH 16–33 and the second at growth stage BBCH 45–49. Samples were immediately frozen and kept in frozen storage at about -18°C up to 4 months (1999 trials) or 179 days (2000 trials), until analysis.

Table 58. Quinoxifen residues in sugar beet roots from supervised trials in Germany, UK, and France.

Sugar Beets country, year (variety)	Application					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, Germany	500 g/L SC	0.12	0.062		2	28		
Trial R99-021C Germany, 1999 (Aries)	500 g/L	0.15 0.15	0.075	200	2	28	<u>&lt; 0.01</u>	76690
Trial CEMS-1348C Germany, 2000 (Beta vulgaris)	500 g/L	0.15 0.15	0.075	200	2	28	<u>0.01</u>	83187
Trial CEMS-1348D Germany, 2000 (Beta vulgaris)	500 g/L	0.16 0.15	0.075	210	2	28	<u>0.01</u>	83187
GAP, UK	500 g/L SC	0.15	0.075	200	2 0.2 kg ai/ha/yr	28		
Trial R99-021A UK, 1999 (Madison)	500 g/L	0.15 0.15	0.075	200	2	28	<u>&lt; 0.01</u>	76690
Trial R99-021B UK, 1999 (Madison)	500 g/L	0.15 0.15	0.075	200	2	28	<u>&lt; 0.01</u>	76690
Trial CEMS-1348A, UK, 2000 (BEA VA/ Chorus)	500 g/L	0.14 0.16	0.075	180-210	2	28	<u>0.02</u>	83187
Trial CEMS-1348B, UK, 2000 (BEA VA/ Jackpot)	500 g/L	0.15 0.14	0.075	190-210	2	28	<u>0.01</u>	83187
GAP, France	500 g/L	0.15	0.10		1	28		
Trial R99-021D France (northern), 1999 (Access)	500 g/L	0.15	0.075	200	2	28	<u>&lt; 0.01</u>	76690

### Cereal grains

#### Wheat

A total of 38 supervised trials were conducted on wheat during 1993 and 1994 (10 in Germany (31265, 31266, 31633, 31262, Gambie, 1995), eight in the UK (24035, 63697, Gambie and Nicholson, 1994; 31080, Gambie, 1995; 29405, Gambie, Nicholson, and Wood, 1995; 31268, Gambie and Wood, 1995), six in northern France (31620, 29912, 31241, Gambie, 1995), 10 in southern France (29406, 31644, 31234, Gambie, 1995), and four in Greece (31231, Gambie, 1995). The trials received either one application of a suspension concentrate formulation containing 500 g/L quinoxifen at the rate of 0.25 kg ai/ha or two applications, one at 0.25 kg ai/ha, the second at 0.15 kg ai/ha. The applications were made around the stem elongation growth stages (BBCH 31-33) with a second one at around the booting stage when first awns are visible (BBCH 47-49). Samples of grain and straw were collected at harvest. Whole plants were cut above ground level by hand with subsequent threshing in a combine harvester. Samples were stored frozen at -18°C until analysis, 9 to 15 months later.

Table 59. Quinoxifen residues on wheat grain from foliar applications in France, Greece, Germany, and UK

Wheat grain	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Grain <sup>1</sup>	
GAP, France	500 g/L SC	0.15	130-300	1	56		
Trial R93-28A S. France, 1993 (Durum, Lloyd)	500 g/L SC	0.25	230	1	79	< 0.01	29406
Trial R93-28A S. France, 1993 (Durum, Llyod)	500 g/L SC	0.15 + 0.25	230-460	2	64	≤ 0.01	
Trial R93-28B S. France, 1993 (Winter, Soissons)	500 g/L SC	0.25	180	1	67	ND	
Trial R93-28B S. France, 1993 (Winter, Soissons)	500 g/L SC	0.15 + 0.25	180	2	55	ND	
Trial R94-018 S. France, 1994 (Winter, Fortal)	500 g/L SC	0.25	300	1	99	ND	31644
Trial R94-018 S. France, 1994 (Winter, Fortal)	500 g/L SC	0.15 + 0.25	300	2	66	ND	31644
Trial R94-019A S. France, 1994 (Durum, Neodor)	500 g/L SC	0.25	200	1	87	ND	31234
Trial R94-019A S. France, 1994 (Durum, Neodor)	500 g/L SC	0.15 + 0.25	200	2	67	ND	
Trial R94-020A S. France, 1994 (Winter, Soisson)	500 g/L SC	0.25	316	1	83	ND	31234
Trial R94-020A S. France, 1994 (Winter, Soisson)	500 g/L SC	0.15 + 0.25	308	2	27	ND	
Trial R93-29A N. France, 1993 (Winter, Sidereal)	500 g/L SC	0.25	333	1	95	ND	29912
Trial R93-29A N. France, 1993 (Winter, Sidereal)	500 g/L SC	0.15 + 0.25	333	2	75	≤ 0.01	
Trial R93-30B N. France, 1993 (Winter, Arche)	500 g/L SC	0.25	200	1	115	ND	31620
Trial R93-30B N. France, 1993 (Winter, Arche)	500 g/L SC	0.15 + 0.25	200	2	87	ND	

Wheat grain	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Grain <sup>1</sup>	
Trial R94-023A N. France, 1994 (Spring, Furio)	500 g/L SC	0.25	200	1	65	ND	31241
Trial R94-023A N. France, 1994 (Spring, Furio)	500 g/L SC	0.15 + 0.25	200	2	50	ND	
GAP, France applied to trials in Greece	500 g/L SC	0.15	130-300	1	56		
Trial R93-36A Greece, 1993 (Hard wheat, Mexicali)	500 g/L SC	0.25	200	1	82	ND	31231
Trial R93-36A Greece, 1993 (Hard wheat, Mexicali)	500 g/L SC	0.15 + 0.25	200	2	60	0.02	
Trial R93-36B Greece, 1993 (Soft wheat, Yecora)	500 g/L SC	0.25	200	1	58	0.02	
Trial R93-36B Greece, 1993 (Soft wheat, Yecora)		0.15 + 0.25	200	2	48	0.09	
GAP, Germany	500 g/L SC	0.15	200-400	2, 0.25 kg ai/ha/yr	49		
	500 g/L SC	0.25	-	1	BBCH 25 – 32		
Trial RF93-31S Germany, 1993 (Winter, Ares)	500 g/L SC	0.25	400	1	84	ND	31266
Trial RF93-31S Germany, 1993 (Winter, Ares)	500 g/L SC	0.15 + 0.25	400	2	70	ND	
Trial RF93-31C Germany, 1993 (Winter, Astron)	500 g/L SC	0.25	400	1	100	ND	31266
Trial RF93-31C Germany, 1993 (Winter, Astron)	500 g/L SC	0.15 + 0.25	400	2	78	≤ 0.01	
Trial RF93-32C Germany, 1993 (Winter, Astron)	500 g/L SC	0.25	400	1	86	ND	31265
Trial RF93-32C Germany, 1993 (Winter, Astron)	500 g/L SC	0.15 + 0.25	400	2	73	ND	



Wheat grain	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Grain <sup>1</sup>	
Trial RF94-038A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.25	400	1	85	<u>ND</u>	31262
Trial RF94-038A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.18 + 0.25	437	2	50	ND	
Trial R94-041A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.25	400	1	84	<u>ND</u>	31633)
Trial R94-041A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.15 + 0.25	400	2	49	<u>ND</u>	
GAP, UK	250 g/L or 500 g/L SC	0.15	200-400	2	~60 Zadoks 49		
Trial R93-34A UK, 1993 (Winter, Mercia)	500 g/L SC	0.25	200	1	113	ND	24035
Trial R93-34A UK, 1993 (Winter, Mercia)	500 g/L SC	0.15 + 0.25	200	2	91	ND	
Trial R93-35A UK, 1993 (Winter, Brock)	500 g/L SC	0.15 + 0.25	200	2	62	<u>ND</u>	24035
Trial R93-35A UK, 1993 (Winter, Clarine)	500 g/L SC	0.15 + 0.25	200	2	69	0.05	
Trial R93-33A UK, 1993 (Winter, Apollo)	500 g/L SC	0.25	200	1	113	ND	29405
Trial R93-33A UK, 1993 (Winter, Apollo)	500 g/L SC	0.15 + 0.25	200	2	70	<u>&lt; 0.01</u>	
Trial R94-002A UK, 1994 (Winter, Spark)	500 g/L SC	0.25	200	1	104	ND	31080
Trial R94-002A UK, 1994 (Winter, Spark)	500 g/L SC	0.15 + 0.25	200	2	71	<u>&lt; 0.01</u>	31080

<sup>1</sup> ND = 0.002 mg/kg for wheat grain (< 20% of LOQ).

### Barley

A total of 22 supervised trials were conducted on barley during 1993 and 1994, eight in Germany (31263, 31261, 31648, 31635, Gambie, 1995); seven in the UK (24035, Gambie and Nicholson, 1994; 31267, Gambie and Wood, 1995; 31235, Gambie, 1995), five in northern France (31620, 29912, 31646, Gambie, 1995) and two in southern France in 1998 (69430, Khoshab and Clements, 1999). The applications were made around the stem elongation growth stages (BBCH 31-33) with a second one at around the booting stage when first awns are visible (BBCH 45-49). Samples of grain and

straw were collected at harvest. Whole plants were cut above ground level by hand with subsequent threshing in a combine harvester. Samples were stored frozen at -18°C until analysis, 8 to 18 months later.

Residues of quinoxifen were determined by gas chromatography with mass selective detection, following method ERC 94.5.

Table 60. Quinoxifen residues in barley grain from supervised trials in Germany, UK, and France.

BARLEY	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Grain <sup>1</sup>	
GAP, France	500 g/L SC	0.15	130-300	1	56		
Trial R98-002A S. France, 1998 (Winter, Majestic)	500 g/L SC	0.15 + 0.16	253	2	65	0.04	69430
Trial R98-002A S. France, 1998 (Winter, Nevada)	500 g/L SC	0.15 + 0.16	246	2	55	< 0.01	
Trial R93-30A N. France, 1993 (Winter, Energy)	500 g/L SC	0.25	200	1	75	0.01	31620
Trial R93-30A N. France, 1993 (Winter, Energy)	500 g/L SC	0.15 + 0.25	200	2	55	0.11	
Trial R93-29B N. France, 1993 (Winter, Plaisant)	500 g/L SC	0.25	300	1	58	< 0.01	29912
Trial R93-29B N. France, 1993 (Winter, Plaisant)	500 g/L SC	0.15 + 0.25	300	2	47	0.12 <sup>2</sup>	
Trial R94-021 N. France, 1994 (Spring, Alexis)	500 g/L SC	0.25	260	1	65	ND	31646
GAP, Germany	500 g/L SC	0.1 - 0.15	200-400	2	49		
	500 g/L SC	0.25	-	1	BBCH 25 – 32		
Trial RF93-114A Germany, 1993 (Winter, Igri)	500 g/L SC	0.25	400	1	66	0.02	31263
Trial RF93-114A Germany, 1993 (Winter, Igri)	500 g/L SC	0.15 + 0.25	400	2	58	0.04	
Trial RF93-115S Germany, 1993 (Winter, Iastrid)	500 g/L SC	0.25	400	1	75	ND	31261
Trial RF93-115S Germany, 1993 (Winter, Iastrid)	500 g/L SC	0.15 + 0.25	400	2	65	ND	
Trial RF94-039A Germany, 1994 (Winter, Grete)	500 g/L SC	0.25	400	1	66	< 0.01	31635

Trial RF94-039A Germany, 1994 (Winter, Grete)	500 g/L SC	0.15 + 0.25	400	2	54	0.05	
Trial RF94-040A Germany, 1994 (Winter, Jana)	500 g/L SC	0.25	400	1	72	<u>&lt; 0.01</u>	31648
Trial RF94-040A Germany, 1994 (Winter, Jana)	500 g/L SC	0.15 + 0.25	400	2	55	0.01	
GAP, UK	250 g/L OR 500 g/L	0.15	200-400	1-2	~60 Zadoks 49		
Trial R93-34A UK, 1993 (Winter, Pasoral)	500 g/L SC	0.25	200	1	96	ND	24035
Trial R93-34A UK, 1993 (Winter, Pasoral)	500 g/L SC	0.15 + 0.25	200	2	82	ND	
Trial R93-85A UK, 1993 (Spring, Alexis)	500 g/L SC	0.25	200	1	76	0.02	31267
Trial R93-85A UK, 1993 (Spring, Alexis)	500 g/L SC	0.15 + 0.25	200	2	64	0.15	
Trial R94-003A UK, 1994 (Winter, Halcyon)	500 g/L SC	0.25	200	1	91	ND	31235
Trial R94-003A UK, 1994 (Winter, Halcyon)	500 g/L SC	0.15 + 0.25	200	2	70	<u>&lt; 0.01</u>	

<sup>1</sup> ND = 0.002 mg/kg for barley grain (< 20% of LOQ).

<sup>2</sup> Trials not included in estimation of MRL due to very late application at growth stage BBCH 58.

*Straw, fodder and forage of cereal grains and grasses (straws and fodders dry)*

*Wheat*

Table 61. Quinoxifen residues on wheat straw from foliar applications in France, Germany, Greece, and UK.

Wheat Straw country, year (variety)	Application <sup>1</sup>				PHI days	Residues, mg/kg Straw <sup>1</sup>	Reference
	Form	kg ai/ha	Water L/ha	no.			
GAP, France (South)	500 g/L SC	0.15	130-300	1	56		
Trial R93-28A S. France, 1993 (Durum, Llyod)	500 g/L SC	0.25	230	1	79	0.10	29406
Trial R93-28A S. France, 1993 (Durum, Llyod)	500 g/L SC	0.15 + 0.25	230-460	2	64	0.24	
Trial R93-28B S. France, 1993 (Winter, Soissons)	500 g/L SC	0.25	180	1	67	0.33	
Trial R93-28B S. France, 1993 (Winter, Soissons)	500 g/L SC	0.15 + 0.25	180	2	55	0.32	

Wheat Straw	Application <sup>1</sup>				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Straw <sup>1</sup>	
Trial R94-018 S. France, 1994 (Winter, Fortal)	500 g/L SC	0.25	300	1	99	< 0.05	31644
Trial R94-018 S. France, 1994 (Winter, Fortal)	500 g/L SC	0.15 + 0.25	300	2	66	0.13	31644
Trial R94-019A S. France, 1994 (Durum, Neodor)	500 g/L SC	0.25	200	1	87	0.07	31234
Trial R94-019A S. France, 1994 (Durum, Neodor)	500 g/L SC	0.15 + 0.25	200	2	67	0.17	
Trial R94-020A S. France, 1994 (Winter, Soisson)	500 g/L SC	0.25	320	1	83	< 0.05	31234
Trial R94-020A S. France, 1994 (Winter, Soisson)	500 g/L SC	0.15 + 0.25	310	2	27	0.06	
Trial R93-29A N. France, 1993 (Winter, Sidereal)	500 g/L SC	0.25	330	1	95	<u>0.19</u>	29912
Trial R93-29A N. France, 1993 (Winter, Sidereal)	500 g/L SC	0.15 + 0.25	330	2	75	<u>0.23</u>	
Trial R93-30B N. France, 1993 (Winter, Arche)	500 g/L SC	0.25	200	1	115	<u>&lt; 0.05</u>	31620
Trial R93-30B N. France, 1993 (Winter, Arche)	500 g/L SC	0.15 + 0.25	200	2	87	<u>0.13</u>	31620
Trial R94-023A N. France, 1994 (Spring, Furio)	500 g/L SC	0.25	200	1	65	0.19	31241
Trial R94-023A N. France, 1994 (Spring, Furio)	500 g/L SC	0.15 + 0.25	200	2	50	0.58	
GAP, France (South) applied to trials in Greece	500 g/L SC	0.15	130-300	1	56		
Trial R93-36A Greece, 1993 (Hard wheat, Mexicali)	500 g/L SC	0.25	200	1	82	0.11	31231
Trial R93-36A Greece, 1993 (Hard wheat, Mexicali)	500 g/L SC	0.15 + 0.25	200	2	60	1.06	
Trial R93-36B Greece, 1993 (Soft wheat, Yecora)	500 g/L SC	0.25	200	1	58	2.99	

Wheat Straw	Application <sup>1</sup>				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Straw <sup>1</sup>	
Trial R93-36B Greece, 1993 (Soft wheat, Yecora)		0.15 + 0.25	200	2	48	7.22	
GAP, Germany	500 g/L SC	0.1 - 0.15	200-400	2	49		
	500 g/L EC	0.25	-	1	BBCH 25- 32		
Trial RF93-31S Germany, 1993 (Winter, Ares)	500 g/L SC	0.25	400	1	84	<u>ND</u>	31266
Trial RF93-31S Germany, 1993 (Winter, Ares)	500 g/L SC	0.15 + 0.25	400	2	70	<u>&lt; 0.05</u>	
Trial RF93-31C Germany, 1993 (Winter, Astron)	500 g/L SC	0.25	400	1	100	<u>0.07</u>	31266
Trial RF93-31C Germany, 1993 (Winter, Astron)	500 g/L SC	0.15 + 0.25	400	2	78	<u>0.11</u>	
Trial RF93-32C Germany, 1993 (Winter, Astron)	500 g/L SC	0.25	400	1	86	<u>0.13</u>	31265
Trial RF93-32C Germany, 1993 (Winter, Astron)	500 g/L SC	0.15 + 0.25	400	2	73	<u>0.36</u>	
Trial RF94-038A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.25	400	1	85	<u>&lt; 0.05</u>	31262
Trial RF94-038A Germany, 1994 (Winter, Kanzler)	500 g/L SC	0.18 + 0.25	440	2	50	0.26	
Trial R94-041A Germany, 1994 (Winter, Kanzler)	500 g/, SC	0.25	400	1	84	<u>&lt; 0.05</u>	31633
Trial R94-041A Germany, 1994 (Winter, Kanzler)	500 g/, SC	0.15 + 0.25	400	2	49	0.12	
GAP, UK	250 g/, or 500 g/L SC	0.15	200-400	1-2	~60 Zadoks 49		
Trial R93-34A UK, 1993 (Winter, Mercia)	500 g/, SC	0.25	200	1	113	<u>0.19</u>	24035
Trial R93-34A UK, 1993 (Winter, Mercia)	500 g/, SC	0.15 + 0.25	200	2	91	<u>0.27</u>	
Trial R93-35A UK, 1993 (Winter, Brock)	500 g/, SC	0.15 + 0.25	200	2	62	0.37	31268

Wheat Straw	Application <sup>1</sup>				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	kg ai/ha	Water L/ha	no.	days	Straw <sup>1</sup>	
Trial R93-35A UK, 1993 (Winter, Clarine)	500 g/, SC	0.15 + 0.25	200	2	69	1.61	
Trial R93-33A UK, 1993 (Winter, Apollo)	500 g/, SC	0.25	200	1	113	<u>0.09</u>	29405
Trial R93-33A UK, 1993 (Winter, Apollo)	500 g/, SC	0.15 + 0.25	200	2	70	0.57	
Trial R94-002A UK, 1994 (Winter, Spark)	500 g/, SC	0.25	200	1	104	<u>0.21</u>	31080
Trial R94-002A UK, 1994 (Winter, Spark)	500 g/, SC	0.15 + 0.25	200	2	71	0.87	31080

<sup>1</sup> ND = 0.01 mg/kg for straw (< 20% of LOQ).

### Barley

Table 62. Quinoxifen residues in barley straw from foliar applications in Germany, UK, and France.

Barley straw	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	Kg ai/ha	Water L/ha	no.	days	Straw <sup>1</sup>	
GAP, France	500 g/L SC	0.15	130-300	1	56		
Trial R98-002A S. France, 1998 (Winter, Majestic)	500 g/L SC	0.15 + 0.16	253	2	65	1.34	69430
Trial R98-002A S. France, 1998 (Winter, Nevada)	500 g/L SC	0.15 + 0.16	246	2	55	1.77	
Trial R93-30A N. France, 1993 (Winter, Energy)	500 g/L SC	0.25	200	1	75	<u>1.23</u>	31620
Trial R93-30A N. France, 1993 (Winter, Energy)	500 g/L SC	0.15 + 0.25	200	2	55	2.10	
Trial R93-29B N. France, 1993 (Winter, Plaisant)	500 g/L SC	0.25	300	1	58	1.13	29912
Trial R93-29B N. France, 1993 (Winter, Plaisant)	500 g/L SC	0.15 + 0.25	300	2	47	1.77	
Trial R94-021 N. France, 1994 (Spring, Alexis)	500 g/L SC	0.25	260	1	65	0.13	31646
GAP, Germany	500 g/L SC	0.15	200-400	2, 0.25 kg ai/ha/season	49		
	500 g/L SC	0.25	-	1	BBCH25 - 32		

Barley straw	Application				PHI	Residues, mg/kg	Reference
country, year (variety)	Form	Kg ai/ha	Water L/ha	no.	days	Straw <sup>1</sup>	
Trial RF93-114A Germany, 1993 (Winter, Igrì)	500 g/L SC	0.25	400	1	66	1.56	31263
Trial RF93-114A Germany, 1993 (Winter, Igrì)	500 g/L SC	0.15 + 0.25	400	2	58	1.76	
Trial RF93-115S Germany, 1993 (Winter, Iastrid)	500 g/L SC	0.25	400	1	75	<u>0.22</u>	31261
Trial RF93-115S Germany, 1993 (Winter, Iastrid)	500 g/L SC	0.15 + 0.25	400	2	65	0.38	
Trial RF94-039A Germany, 1994 (Winter, Grete)	500 g/L SC	0.25	400	1	66	0.29	31635
Trial RF94-039A Germany, 1994 (Winter, Grete)	500 g/L SC	0.15 + 0.25	400	2	54	0.54	
Trial RF94-040A Germany, 1994 (Winter, Jana)	500 g/L SC	0.25	400	1	72	0.20	31648
Trial RF94-040A Germany, 1994 (Winter, Jana)	500 g/L SC	0.15 + 0.25	400	2	55	0.86	
GAP, UK	250 g/L OR 500 g/L	0.15	200-400	1-2	~60 Zadoks 49		
Trial R93-34A UK, 1993 (Winter, Pasoral)	500 g/L SC	0.25	200	1	96	<u>0.30</u>	24035
Trial R93-34A UK, 1993 (Winter, Pasoral)	500 g/L SC	0.15 + 0.25	200	2	82	<u>0.58</u>	
Trial R93-85A UK, 1993 (Spring, Alexis)	500 g/L SC	0.25	200	1	76	<u>2.94</u>	31267
Trial R93-85A UK, 1993 (Spring, Alexis)	500 g/L SC	0.15 + 0.25	200	2	64	5.25	
Trial R94-003A UK, 1994 (Winter, Halcyon)	500 g/L SC	0.25	200	1	91	<u>0.22</u>	31235
Trial R94-003A UK, 1994 (Winter, Halcyon)	500 g/L SC	0.15 + 0.25	200	2	70	1.15	

<sup>1</sup> ND = 0.002 mg/kg for barley grain (< 20% of LOQ).

## Dried herbs

## Hops

Table 63. Quinoxifen residues on dried hops from foliar applications in the US and Germany.

Hops, dry country, year (variety)	Application					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, Germany	250 g/L SC	0.15	0.011		4 or max 0.5 kg ai/ha/season	28		
Trial RF98-200A Germany, 1998 (Hallertauer tradition)	250 g/L SC	0.16 - 0.24	0.007		3, total 0.62 kg ai/ha/season	27 <sup>1</sup>	(0.03)	73994
						35	0.04	
Trial RF98-200B Germany, 1998 (Hallertauer tradition)	250 g/L SC	0.16- 0.24	0.007		3, total 0.63 kg ai/ha/season	27 <sup>1</sup>	(0.02)	73994
						35	< 0.02	
Trial RF98-200C Germany, 1998 (Hallertauer tradition)	250 g/L SC	0.160 - 0.24	0.007		3, total 0.61 kg ai/ha/season	27 <sup>1</sup>	(0.03)	73994
						35	0.04	
Trial RF98-200D Germany, 1998 (Spalter)	250 g/L SC	0.20 - 0.251	0.007		3, total 0.69 kg ai/ha/season	28 <sup>1</sup>	(0.19)	73994
						35	0.05	
Trial G99033R Germany, 1999 (Spalter)	250 g/L SC	0.24- 0.250	0.007		3, total 0.69 kg ai/ha/season	28	0.76	74050
						30	0.28	
Trial G99085R Germany, 1999 (Perle)	250 g/L SC	0.15- 0. 25	0.007		3, total 0.60 kg ai/ha/season	28	0.55	74050
						35	0.34	
Trial G99086R Germany, 1999 (Perle)	250 g/L SC	0.16- 0.25	0.007		3, total 0.62 kg ai/ha/season	28	0.37	74050
						35	0.23	
Trial G99087R Germany, 1999 (Perle)	250 g/L SC	0.16- 0.24	0.007		3, total 0.62 kg ai/ha/season	28	0.41	74050
						35	0.28	
GAP, USA	250 g/L SC	0.15			4 or max 0.6 kg ai/ha/season	21		
Trial 99-WA09 Washington, USA 1999 (Nugget hops)	250 g/L SC	0.15- 0.22	0.018		3, total 0.59 kg ai/ha/season	20	0.39 <sup>2</sup>	83727
Trial 99-OR12 Oregon, USA 1999 (Nugget hops)	250 g/L SC	0.15- 0.23	0.020		4, total 0.75 kg ai/ha/season	21	1.22 <sup>2</sup>	83727
Trial 99-ID03 Idaho, USA, 1999 (Nugget tops)	250 g/L SC	0.15- 0.22	0.021		3, total 0.61 kg ai/ha/season	21	2.17 <sup>2</sup>	83727

<sup>1</sup> Residues in parenthesis were levels on fresh hops as actually determined. The residues in dried hops were estimated assuming fresh hops have a moisture content of 80% and dried hops, about 10%, i.e., a concentration of about 70% in residues after drying.

<sup>2</sup> Average of two replicate samples (from the same plot).



*Miscellaneous Fodder and Forage crops**Sugar beet Tops*

The eight supervised trials conducted on sugar beets in Northern Europe (Germany, Northern France and the UK) were described above. Samples were immediately frozen and kept in frozen storage at about -18°C up to 4 months (1999 trials) or 179 days (2000 trials), until analysis.

Table 64. Quinoxifen residues in sugar beet tops from foliar applications in Germany, the UK, and northern France.

Sugar beet tops country, year (variety)	Application					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
GAP, Germany	500 g/L SC	0.12	0.062	200-400	2	28		
Trial R99-021C Germany, 1999 (Aries)	500 g/L SC	0.15	0.075	200	2	28	<u>0.27</u>	76690
Trial CEMS- 1348C Germany, 2000 (Beta vulgaris)	500 g/L SC	0.153 0.152	0.075	202-204	2	28	<u>0.10</u>	83187
Trial CEMS- 1348D Germany, 2000 (Beta vulgaris)	500 g/L SC	0.155 0.154	0.075	205-207	2	28	<u>0.10</u>	83187
GAP, UK	500 g/L SC	0.15	0.075	200-400	2	28		
Trial R99-021A UK, 1999 (Madison)	500 g/L SC	0.15	0.075	200	2	Whole plant 0 7 14 21  Tops 28	1.0 0.43 0.10 0.06  <u>0.22</u>	76690
Trial R99-021B UK, 1999 (Madison)	500 g/L SC	0.15	0.075	200	2	Whole plant 0 7 14 21  Tops 28	0.71 0.69 0.24 0.14  <u>0.37</u>	76690
Trial CEMS- 1348A, UK 2000 (BEA VA/ Chorus)	500 g/L SC	0.136 0.158	0.075	180-210	2	Whole Plant 0 7 14 21  Tops 28	1.3 0.57 0.41 0.23  <u>0.36</u>	83187

Sugar beet tops country, year (variety)	Application					PHI days	Residues mg/kg	Reference
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
Trial CEMS- 1348B, UK 2000 (BEA VA/ Jackpot)	500 g/L SC	0.154 0.144	0.075	192-205	2	Whole plant		83187
						0	1.4	
						7	0.55	
						14	0.23	
						21	0.14	
Tops								
						28	<u>0.13</u>	
GAP, France	500 g/L SC	0.15	0.10		1	28		
Trial R99-021D France (northern), 1999 (Acces)	500 g/L SC	0.15	0.075	200	2	28	<u>0.07</u>	76690

## FATE OF RESIDUES IN STORAGE AND IN PROCESSING

### *In storage*

No information was provided on the fate of quinoxifen residues under commercial storage conditions.

### *In processing*

Two processing studies were conducted in northern France and the United Kingdom in 1994 to determine the residues in processed fractions of flour and bread from winter wheat samples treated with quinoxifen (31600; 31607, Gambie and Press, 1995).

Grains from foliar application to wheat at GAP rate were first cleaned to remove non-wheat material such as broken kernels and straw. Before milling, samples were conditioned by adding water and again cleaned. The samples were then milled at a feed rate of 5 kg per hour. Each passage and consequent sieving in the milling resulted in flour fractions called respectively the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> reduction flour. In all milling experiments, approximately 200 g of sample material were taken for residue analysis from the 1<sup>st</sup> reduction, the white bread flour and the finished offal. These samples were rapidly deep frozen. The flour fractions were blended by weight and starting with 5 kg of flour, dough's were mixed, dough pieces moulded and placed in greased aluminium-coated tins. Baking was done in a rotary oven at 240°C for 30 minutes for white bread and 15 minutes for wholemeal bread, with steam injection at the start of baking.

All grain samples (RAC) and processed fractions for residue analysis were frozen at -20°C until analysis about 280 days later. Residues of quinoxifen in the RAC were determined by gas chromatography with mass selective detection, following method ERC 94.5, which had a lowest validated level of 0.01 mg/kg for grain. Residues of quinoxifen in flour, bran and bread were determined using gas chromatography with mass selective detection, following method ERC 95.16, which had a lowest validated level of 0.01 mg/kg.

Table 65. Residues in wheat grain and processed fractions.

Processed Fraction	Residues mg/kg	Reference
Wheat grain (RAC)	< 0.01	31600
Flour, 1 <sup>st</sup> reduction	ND	
Flour, 74% extraction	ND	

Processed Fraction	Residues mg/kg	Reference
Wholemeal flour	< 0.01	
Bran	0.01	
White bread	ND	
Wholemeal bread	< 0.01	
Wheat grain (RAC)	ND	31607
Flour, 1 <sup>st</sup> reduction	ND	
Flour, 76% extraction	< 0.01	
Bran	0.01	
White bread	ND	

ND = < 0.002 mg/kg

The residues of quinoxifen after processing barley grain following treatment with quinoxifen into beer was investigated in the UK in 1994 (31624, Gambie and Teasdale, 1995). To ensure that the grain for brewing had sufficient residues, spring barley was treated with two applications of a suspension concentrate formulation containing quinoxifen at 500 g/L, at double the maximum recommended application rate. After collecting about 1 kg of grain for the determination of residues in the RAC, the remaining grain was bulked and sent for processing into beer.

The grain samples were cleaned by sieving prior to processing following commercial practices. Barley malt was prepared. A 200g sample of malt was frozen for residue analysis. The remainder was milled and then mashed and the wort filtered. The spent grains from the filtration process were homogenized and a 1kg sub-sample frozen for analysis. After adjustment of the pH the wort was boiled and the sugar content adjusted prior to fermenting. After storage of the green beer for one month at 0-4°C, the beer was filtered, bottled, and pasteurised. Five litres of beer in bottles were stored at 10°C prior to shipment for residue analysis.

Grain, malt, and spent grain samples were analyzed by method ERC 94.5 using gas chromatography with mass selective detection. The LOQ for the method was 0.01 mg/kg. Procedural recoveries were 88% for grain, 90% for malt, and 88% for spent grains. Residues of quinoxifen in beer were quantified by gas chromatography with mass selective detection according to method ERC 95.19. The LOQ for the method was 0.01 mg/kg. Procedural recovery for beer was 73%.

Table 66. Residues in barley grain and processed fractions (31624).

Matrix	Residues mg/kg	Processing factor
Barley grain (RAC)	0.02	-
Malt	0.01	0.5
Spent grain	0.01	0.5
Beer	ND (< 0.002)	0.1

Several processing studies were carried out in 1995 in Italy, France, and Germany on red and white wine grapes (46975; 47145; Khoshab, 1996 and 47868 Khoshab and Volle, 1996). In the trials in France, vines received seven sequential applications of a suspension concentrate formulation containing 250 g/L quinoxifen, at 11–15 day intervals between post-flowering and 20–21 days before harvest. Grape samples were taken at normal harvest (20–21 days after final application). Samples of the grapes for the RAC were frozen immediately for residue analysis. Additional samples were taken and transported to the processing facility on the same day. Processing was carried out within 48 hours of harvest.

Residue trials on red and white wine grapes were also carried out at two locations in Germany during 1995. The wine grape vines received seven sequential applications of a suspension concentrate formulation containing a mixture of 200 g/L quinoxifen and 60 g/L fenarimol, at a rate of about 0.07 kg ai/ha. Applications were made between post flowering and 22 days before harvest at approximately equal intervals. Grape samples were taken at normal harvest. Samples for the RAC were immediately frozen after harvest. Additional samples taken for wine processing were processed within 8 hours of harvest.

Trials on white wine grapes were conducted in Italy in the same period. The vines were also treated with seven sequential applications of a suspension concentrate formulation containing 250 g/L quinoxifen at the rate of 0.065 kg ai/ha. Applications were made between post flowering and 21 days before harvest at approximately equal intervals. Grape samples were taken at normal harvest (21 days after the last application). Samples for the RAC were frozen immediately for residue analysis. Additional samples were collected and transported the same day for processing into wine. Processing started within 7 hours after arrival at the processing facility.

For the trials in France, processing was carried out according to the VITI R&D methods VINIF/001 and VINIF/002 for white and red grapes, respectively. The processing method used by the German and Italian trials was according to the BBA Guideline Part IV, 3-4. Both these methods follow commercial practices.

In addition to the grapes (RAC), samples of pomace, must and wine were taken in each trial for residue analysis. Grapes were separated from stalks and prepared in a cutter without dry ice. Grape pomace samples were prepared in a homogeniser with dry ice. No preparations were required for must and wine. All prepared samples were stored deep frozen until analysis. Samples were kept frozen at about -20°C for a period of 9 to 12 months before analysis. All samples were analyzed following the methods described below.

Residues of quinoxifen in grape samples were determined using method ERC 94.29 which has a lowest validated level of 0.01 mg/kg. Residues in grape pomace, must and wine samples were determined using method ERC 95.26 which has a lowest validated level of 0.05 mg/kg for pomace and 0.01 mg/kg for must and wine.

Table 67. Residues in grapes and processed fractions.

Matrix	Residues mg/kg	Processing factor	Reference
Red wine grapes (RAC)	0.08		47868
Must	< 0.01	0.13	
Pomace	0.25	3.1	
Wine (2 months)	ND (< 0.002)	0.03	
Wine (6 months)	ND (< 0.002)	0.03	
White wine grapes (RAC)	0.15		47868
Must	< 0.01	0.07	
Pomace	0.78	5.2	
Wine (2 months)	ND (< 0.002)	0.01	
Wine (6 months)	ND (< 0.002)	0.01	
Red wine grapes (RAC)	0.46		46975
Must	0.02	0.04	
Pomace	1.00	2.2	
Young wine	ND (< 0.002)	0.004	
Mature wine	ND (< 0.002)	0.004	
White wine grapes (RAC)	0.14		46975
Must	0.01	0.07	
Pasteurized must	< 0.01	0.07	
Pomace	0.72	5.1	
Young wine	ND (< 0.002)	0.01	

Matrix	Residues mg/kg	Processing factor	Reference
Pasteurized young wine	ND (< 0.002)	0.01	
Mature wine	ND (< 0.002)	0.01	
Pasteurized mature wine	ND (< 0.002)	0.01	
White wine grapes	0.52		47145
Must	0.03	0.06	
Pomace	1.72	3.3	
Wine (2 months)	ND (< 0.002)	0.004	
Wine (6 months)	ND (< 0.002)	0.004	
		AVERAGE (n = 5)	MEDIAN
Grapes (RAC)		-	
Must		0.07	
Pomace		3.8	
Young wine/ 2 months		0.01	0.01
Mature wine/ 6 months		0.01	0.01

One of the trials conducted in California in 1999 to determine the residues of quinoxifen in grapes (RAC) included a determination of the residues on juice and raisins (83731, Thompson, 2001). Mature fruits were harvested 14 days after the last application and sent to the processing laboratory on the day of sampling and kept frozen until processing. A representative sample was taken for RAC residues and the rest of the bulk sample was processed into grape juice and raisins, simulating commercial practices.

Grapes were passed through a crusher/destemmer. The stems were discarded, the crush was transferred to a steam-jacketed kettle, and pectinase enzyme was added. The crush was then heated to 120–130°F for a minimum of 2 hours. The depectinized grape crush slurry was passed through a screw press to extract unclarified juice and wet pomace, which was discarded. The unclarified juice was heated to inactivate the added enzyme and then cooled in a refrigerator for argol settling. After 34 days, the argol-settled juice was filtered using a plate-and frame filter press with depth filter pads and filter aid. The filtered juice was heated to canning temperature, put in jars and sealed. Once cool, the jars were weighed, labelled, bagged, and placed in frozen storage (-10° to -5°F) until shipment to the analytical laboratory for analysis of residues.

Grape bunches were spread on stainless steel drying trays and placed outdoors with adequate protection from birds, insects, and animals. The grapes were turned about once a week during the drying process, which took approximately 1 month. When dry, the moisture content was measured, and the dried grapes were placed in plastic bags and stored at 70°F for approximately 13 days to achieve moisture equilibrium. The dried grapes were frozen, gently rubbed on 4-mesh screen for destemming and cap stem removal, and immersed in 77°F water for approximately 15 minutes for rehydration to raisins. Excess water was drained, and the raisins were placed in plastic bags and returned to storage to achieve moisture equilibrium. After 12 days the moisture content was again measured, and the raisins were weighed, bagged, labelled and placed in frozen storage (-10° to -5°F) until shipment to the analytical laboratory.

Samples were analyzed using method ERC 95.26, which had a lowest validated level of 0.01 mg/kg quinoxifen for grapes and processed fractions. Residues of quinoxifen were quantified by gas chromatography with mass selective detection.

Table 68. Residues in grapes, juice, and raisins (83731).

Matrix	Residues mg/kg	Processing factor
Grapes (RAC)	0.177	
Raisins	0.117	0.66
	(0.109, 0.110, 0.115, 0.132) <sup>1</sup>	
Juice	< 0.01	0.06
	(< 0.01 (4)) <sup>1</sup>	

<sup>1</sup> Replicate sub-samples.

## RESIDUES IN ANIMAL COMMODITIES

### *Farm animal feeding studies*

Two cattle feeding studies were conducted in 1994. One of the studies was conducted using fourteen lactating Friesian cows aged between 4 and 9 years old with weight range of 480 to 644.5 kg and daily milk yield of at least 10 kg/day (31599; Gambie and Long, 1995). The animals were divided into the following treatment groups:

Dose Group	Number of animals	Treatment	
		ppm total diet per day	mg/animal/day
1	3	Untreated	0
2	3	0.2	4
3	3	0.6	12
4	5	2.0	40

The animals received a feed concentrate twice daily. On each occasion, the appropriate amount of quinoxifen was added to the feed concentrate as a corn oil solution, based on a daily food consumption of 20 kg. The untreated group of animals received 20 ml corn oil. The animals were dosed for 28 days. Milk samples were taken throughout the study for residue analysis. In addition whole milk samples from days 14 and 27 were separated into cream and skimmed milk and samples taken for both residue analysis and determination of fat content. Milk samples were stored frozen at about -20°C until analysis in about 51 days. .

After 28 days of dosing, all cows except two from the highest treatment group were sacrificed. The remaining two cows were maintained on a basal diet from day 29 and were sacrificed 7 and 14 days after the end of the dosing period (days 36 and 43, respectively).

At sacrifice, samples of the following tissues were taken for residue analysis: subcutaneous fat, peritoneal fat (perirenal and omental pooled fat), skeletal muscle (pooled from the pectoralis and abductor muscle of the thigh), liver and kidney. The samples were coarsely chopped before freezing and storage at -20°C until analysis in 76-255 days.

A supplementary study (31634; Gambie, Teasdale, and Press, 1995) was undertaken with higher feeding levels of quinoxifen. The study used six lactating Friesian cows aged between 4 and 6 years old with a weight range of 500-620 kg and daily milk yield at least 11 kg/day. Three cows were treated at dose level of 20 ppm total diet/day, equivalent to 400 mg/animal/day. The other three animals received no treatments. The animals were dosed for 28 days and 16 hours after the last dose, they were sacrificed. The same tissue samples as the other study were collected and frozen.

Samples of whole milk, skimmed milk, and cream were analyzed for residues of quinoxifen using method ERC 94.7, which had a lowest validated level of 0.001 mg/kg. Mean procedural recoveries were 81% for whole milk and 80% for cream. The fat content of whole milk and cream samples was determined by the Rose-Gottlieb gravimetric method (BS 1741: Part 3: 1987).

Method ERC 94.30 was used for the determination of residues of quinoxifen in liver, where quantification was done by gas chromatography with mass selective detection. The method had an LOQ of 0.01 mg/kg. Procedural recoveries for liver samples were below 70%.

For analysis of residues of quinoxifen in kidney, muscle and fat, method ERC 94.20, which had a lowest validated level of 0.01 mg/kg, was used. Mean procedural recoveries of up to 94% for kidney, 92% for muscle, and 84% to 92% for fat were obtained from samples fortified at levels of 0.01 mg/kg to 1.0 mg/kg.

In all these methods, quinoxifen residues were quantified by gas chromatography with mass selective detection. All residues equivalent to less than 20% of the lowest validated level were classified as “not detected” (ND).

From the first study (31599), milk sampled on Days 14 and 27/28 was separated into cream and skimmed milk and both the fat content and quinoxifen residues were determined.

During the withdrawal period from day 29 to 42, residues in whole milk decreased from 0.007 to < 0.001 mg/kg within 4 days after dosing ceased. After 14 days depuration period, no residues were detected in milk. Tissue residues were determined after 7 and 14 day depuration period. After 7 and 14 days, residues in peritoneal fat were 0.05 mg/kg and < 0.01 mg/kg, respectively. Residues in other tissues were either < 0.01 mg/kg or not detected during the depuration period.

Table 69. Mean residues of quinoxifen in whole milk over 28 days oral administration of quinoxifen to dairy cows (31599; 31634).

DAY	Concentration of quinoxifen, mg/kg				
	Treatment groups (ppm feed/day)				
	Untreated	0.2	0.6	2.0	20
-1	ND	ND	ND	ND	ND
1	-	-	-	< 0.001	0.017
3	-	-	-	0.006	0.085
5	-	-	-	0.007	-
7	< 0.001	0.001	0.002	0.007	0.37
10	-	-	-	0.009	0.19
14	ND	0.001	0.002	0.009	0.18
18	-	-	-	0.009	-
21	ND	< 0.001	0.002	0.007	0.15
24	-	-	-	0.007	0.16
28*	-	< 0.001	0.002	0.007	-
MEAN	< 0.0005	0.001	0.002	0.007	0.16
30	-	-	-	0.005	0.11
32	-	-	-	< 0.001	-
35	-	-	-	< 0.001	-
37	-	-	-	< 0.001	-
40	-	-	-	< 0.001	-
42	-	-	-	ND	-

\* Final day of dosing;

- No analysis;

ND = not detected (< 0.0002 mg/kg)

Table 70. Residues in whole milk, skim milk, and cream on days 14 and 27/28 following oral administration of quinoxifen to dairy cows (31599; 31634).

Treatment, ppm in feed/day		Quinoxifen residues <sup>1</sup> (mg/kg)			Quinoxifen ratio: cream/whole milk	Fat ratio: cream/whole milk
		Whole milk	Skim milk	Cream		
Day 14						
0.2	Min	< 0.001	ND <sup>2</sup>	< 0.001	-	12.5
	Max	< 0.001	ND	0.007	>7	9.8
	Mean	< 0.001	ND	0.003	>3	10.7
0.6	Min	0.002	ND	0.016	8.0	11.6
	Max	0.002	ND	0.022	11.0	15.2

Treatment, ppm in feed/day		Quinoxifen residues <sup>1</sup> (mg/kg)			Quinoxifen ratio: cream/whole milk	Fat ratio: cream/whole milk
		Whole milk	Skim milk	Cream		
	Mean	0.002	ND	0.018	9.2	12.9
2.0	Min	0.010	0.005	0.046	4.6	3.1
	Max	0.007	< 0.001	0.077	11.0	12.9
	Mean	0.0088	0.0022	0.068	7.9	9.3
Day 27						
0.2	Min	< 0.001	< 0.001	0.006	>6	12.2
	Max	< 0.001	< 0.001	0.007	>7	12.9
	Mean	< 0.001	< 0.001	0.0067	>7	12.0
0.6	Min	0.002	ND	0.011	5.5	12.3
	Max	0.002	ND	0.02	10.0	14.8
	Mean	0.002	ND	0.015	7.3	13.4
2.0	Min	0.009	0.004	0.041	4.6	9.7
	Max	0.007	0.001	0.079	11.3	13.7
	Mean	0.007	0.002	0.059	8.6	11.4

<sup>1</sup>Min and Max refer to the ratio of quinoxifen in cream/quinoxifen in whole milk on a per cow basis within each treatment group.

<sup>2</sup>ND = not detected (< 0.0002)

Table 71. Summary of residues in tissues following 28 days oral administration of quinoxifen to dairy cows (31599; 31634).

Treatment, ppm feed/day (Reference)		Residues, mg/kg				
		Liver	Kidney	Skeletal muscle	Subcutaneous fat	Peritoneal fat
0.2 (GHE-P-4161)	Min	ND	ND	ND	ND	< 0.01
	Max	ND	< 0.01	ND	< 0.01	0.02
	Mean	ND	< 0.01	ND	< 0.01	0.01
0.6 (GHE-P-4161)	Min	ND	ND	ND	< 0.01	< 0.01
	Max	< 0.01	< 0.01	ND	< 0.01	0.02
	Mean	< 0.01	< 0.01	ND	< 0.01	0.012
2.0 (GHE-P-4161)	Min	< 0.01	< 0.01	< 0.01	0.02	0.09
	Max	< 0.01	< 0.01	< 0.01	0.04	0.10
	Mean	< 0.01	< 0.01	< 0.01	0.03	0.09
20.0 GHE-P-4185)	Min	0.04	0.07	0.06	0.78	1.1
	Max	0.21	0.29	0.18	2.0	3.2
	Mean	0.12	0.19	0.11	1.4	2.2

ND = 0.002 mg/kg

A poultry feeding study conducted in 1995 consisted of four groups of 10 Isa Brown laying hens (5-6 months old, weighing *ca* 1-2 kg) fed at the following dose levels: 0.1, 0.3, and 1.0 mg/kg of diet/ day based on the average daily intake of food in the group (31744, Jack. and Dunsire, 1995). The fourth group of hens served as controls and were dosed with empty gelatin capsules. The hens were



fed gelatin capsules containing radiolabelled (mixture of  $^{14}\text{C}$ -quinoline label and  $^{14}\text{C}$ -phenoxy label)  $^{14}\text{C}$ -quinoxifen. Each daily dose was administered in a single capsule at the same time each day for 28 days.

Within each dose group, the ten hens were subdivided into 3 sub-groups of 3 or 4 hens. All samples were pooled by sub-group prior to analysis. Eggs were collected daily from all hens and pooled for residue analysis. On days 14 and 28, the egg samples were separated into whites and yolks, which were analyzed separately.

At the end of the dosing period (approximately 23 hours after last dose on day 28), the hens were sacrificed and the following edible tissues retained for analysis: skin with fat, breast muscle, thigh muscle, liver, kidney, and abdominal fat pad. An approximately equal weight of tissue from each bird in each sub-group was combined and thoroughly mixed.

With the exception of eggs, samples not analyzed immediately were stored frozen at  $-20^{\circ}\text{C}$  until analysis. Eggs were stored at  $4^{\circ}\text{C}$  until analysis. After combustion of the samples, radioactivity was measured by LSC.

Table 72. Residues in eggs over 28 days oral administration of  $^{14}\text{C}$ -quinoxifen to laying hens (31744).

Dose period, Day	Residues (TRR), $\mu\text{g}$ equivalent/g		
	Treatment (ppm feed/day)		
	0.1 ppm	0.3 ppm	1.0 ppm
1	0.000	0.000	0.000
2	0.000	0.001	0.003
3	0.001	0.002	0.006
4	0.001	0.004	0.009
5	0.002	0.005	0.014
6	0.002	0.006	0.018
7	0.002	0.007	0.021
8	0.002	0.007	0.024
9	0.002	0.008	0.023
10	0.002	0.008	0.023
11	0.002	0.008	0.024
12	0.002	0.008	0.023
13	0.002	0.008	0.023
14 (whites)	0.000	0.001	0.002
15 (yolks)	0.008	0.025	0.071
16	0.002	0.008	0.023
17	0.003	0.008	0.025
18	0.003	0.009	0.024
19	0.003	0.009	0.025
20	0.003	0.009	0.023
21	0.003	0.009	0.024
22	0.003	0.009	0.024
23	0.003	0.009	0.024
24	0.003	0.009	0.025
25	0.003	0.010	0.025
26	0.003	0.010	0.025
27	0.003	0.011	0.025

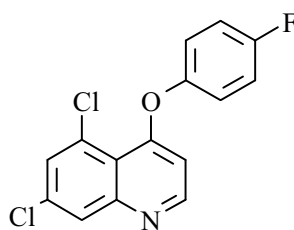
Dose period, Day	Residues (TRR), µg equivalent/g		
	Treatment (ppm feed/day)		
	0.1 ppm	0.3 ppm	1.0 ppm
28 (white)	0.000	0.001	0.002
28 (yolks)	0.010	0.036	0.072

Table 73. Residues in poultry tissues following 28 days oral administration of <sup>14</sup>C-quinoxifen to laying hens (31744).

Treatment, ppm feed/day (Reference)		Residues (TRR), mg equivalent/kg					
		Liver	Kidney	Breast muscle	Thigh muscle	Skin with fat	Abdominal fat pad
0.1 (GHE-P-4394)	Min	0.009	0.003	0.000	0.000	0.003	0.007
	Max	0.009	0.004	0.000	0.000	0.008	0.013
	Mean	0.009	0.003	0.000	0.000	0.005	0.010
0.3 (GHE-P-4394)	Min	0.035	0.016	0.000	0.001	0.012	0.028
	Max	0.040	0.018	0.000	0.001	0.017	0.037
	Mean	0.038	0.017	0.000	0.001	0.014	0.034
1.0 (GHE-P-4394)	Min	0.087	0.039	0.001	0.005	0.034	0.080
	Max	0.097	0.049	0.002	0.009	0.063	0.12
	Mean	0.093	0.045	0.001	0.007	0.051	0.10

## APPRAISAL

**Chemical name:** 5,7-dichloro-4-quinolyl 4 fluorophenyl ether



### Animal metabolism

The Meeting received results of an animal metabolism study in lactating goats. Two goats were orally dosed with phenoxy <sup>14</sup>C-quinoxifen (purity > 98%), twice daily for five consecutive days, at a rate of 10.7 mg quinoxifen/kg feed. Similarly, two goats were treated with quinoline <sup>14</sup>C-quinoxifen, twice daily for five consecutive days, at a rate of 11.7 mg quinoxifen/kg feed.

Urine, faeces and cage wash accounted for 77–80% of the total administered dose. Milk contained 0.5–0.9%, liver 0.9–1.3%, and kidney 0.0–0.05%. The radioactive residue appeared to plateau in milk on day 4. Total radioactive residues (TRRs) in tissues and milk from use of the phenoxy labelled quinoxifen were 0.34 mg/kg in kidney, 1.0 mg/kg in liver, 0.032 mg/kg in muscle, 0.20 mg/kg in omental fat, and 0.11 mg/kg in milk (16 hours after final dose); and from the use of the quinoline labelled quinoxifen, 1.5 mg/kg in liver, 0.22 mg/kg in kidney, 0.032 mg/kg in muscle, 0.32 mg/kg in perirenal fat, and 0.064 mg/kg in milk.

Quinoxifen was identified in milk (30–40% TRR), kidney (2–4% TRR), liver (10–20% TRR), and fat (50–97% TRR). DCHQ (5,7-dichloro-4-hydroxyquinoline) and/or 4-fluorophenol, resulting from cleavage of the ether linkage, was/were found in small amounts (< 5% TRR) in milk, kidney, and liver. Enzyme deconjugation of liver extracts indicated additional substantial quantities of these two compounds (13–20% TRR) present as conjugates. Less than 5% TRR was attributed to isomeric hydroxy quinoxifens in liver, milk, and subcutaneous fat. 2-Oxo-quinoxifen was found in milk at a maximum of 1.4% TRR.

The metabolism in goat and rat are qualitatively similar. Cleavage of the ether linkage to form 4-fluorophenol and DCHQ is seen in both animals. Isomers of fluorophenyl-ring hydroxylated quinoxifen were found in the rat (bile and faeces), whereas isomers of quinoline-ring hydroxylated quinoxifen (2-oxo) were found in the goat metabolism study. The latter were at very low levels (< 0.1% of the administered dose for the 2-oxo quinoxifen) in the rat.

The Meeting concluded that the major metabolite in ruminant commodities from the oral administration of quinoxifen is the parent quinoxifen. Degradation from cleavage of the ether linkage generates free DCHQ and 4-fluorophenol. Another minor pathway involves formation of hydroxy derivatives.

### ***Plant metabolism***

The Meeting received plant metabolism studies for the foliar application of phenoxy- and quinoline-labelled [<sup>14</sup>C] quinoxifen, in separate experiments, to winter wheat, sugar beets, grapes, cucumber and tomato.

In each crop tested, parent quinoxifen was found to be a significant to very major portion of the TRR: 8–27% TRR in wheat straw, 25% TRR in sugar beet root, 19–30% TRR in sugar beet tops, 93–98% TRR in grapes, 64–74% TRR in cucumber fruit, and 63–65% TRR in tomato fruit. DCHQ (7% TRR) and 4-fluorophenol (17% TRR) were found in sugar beet tops, indicative of ether bond cleavage. CFBPQ (2-chloro-10-fluoro(1)benzopyrano (2,3,4-de)quinoline), a product of photolysis, was also found in sugar beet tops (3–5% TRR) and possibly in wheat straw at 2% TRR. The 2-oxo quinoxifen and p-hydroxyphenoxy quinoxifen metabolites were tentatively identified at low concentrations (< 5% TRR) in several crops. Much of the unidentified extractable radioactivity in wheat straw was found to be multicomponent and of an acidic anionic nature (about 20% TRR) not related to conjugates of quinoxifen with natural products.

About  $\geq$  20% of the TRR in mature wheat straw was characterized as lignin, and 25% was associated with cellulose. About 13–53% TRR in wheat grain (100% TRR = 0.03 mg/kg) was associated with starch. About 10% TRR in tomato was associated with lignin, cellulose, and hemicellulose.

Quinoxifen was shown to have no tendency to translocate in grape vines. Radiolabeled material applied only to some vine leaves did not move to the fruit or to untreated leaves.

The Meeting concluded that quinoxifen is a major portion of the residue when applied in a foliar fashion to several crop types (grapes, cucumber and tomato). In wheat quinoxifen was extensively metabolized with portions of the molecule becoming associated with natural plant constituents. Minor metabolic pathways were cleavage of the ether bond, photolysis, and hydroxylation of the quinoline or phenyl rings.

### ***Environmental fate***

The Meeting received information on the aqueous hydrolysis, aerobic soil metabolism, aqueous photolysis, and soil photolysis of quinoxifen. Confined rotational crop studies with radiolabeled quinoxifen were also provided.

Quinoxifen is stable under aqueous hydrolysis at pH 7 and 9, but degrades slowly under acidic hydrolysis conditions. The half-life at pH 4 at 25 °C is about 75 days. The hydrolysis product was identified as DCHQ.

Quinoxifen is relatively stable under conditions of dark aerobic soil metabolism. After 200 days, 53–81% of the quinoxifen applied to various soil types remained. Some 0–27% had been converted to 2-oxo quinoxifen, and 0–5% was present as DCHQ. About 15–25% of the original quinoxifen had become bound to the soil. Less than 2% had been converted to carbon dioxide. Half lives of 90 to 500 days were calculated for the various soil types.

Quinoxifen degraded in aqueous solution under artificial light (298 nm) to yield CFBPQ and DCHQ (minor). Half lives under typical use conditions were calculated to vary from 7 to 16 hours. Other work under natural sunlight conditions in water and water sediment systems showed the rapid loss of quinoxifen, with no quinoxifen remaining after 1 day. CFBPQ formed, but rapidly degraded

In contrast, quinoxifen degraded slowly on the surface of sandy loam soil when exposed to simulated natural light. The half life was estimated to be equivalent to > 2 years in spring in England. DCHQ was identified in minor amounts, but the major metabolite remained unknown.

The uptake of radiolabeled quinoxifen from soil into three succeeding crops (turnips, sunflower and cabbage) was reported. The quinoxifen was applied at a rate equivalent to 400 g ai/ha, typical of the maximum seasonal use rate. Mature crop parts contained very low levels of radioactive residue, 0.4–3.5 µg/kg.

The Meeting concluded that quinoxifen is relatively stable under aerobic conditions in soil and at neutral and alkaline pH in water, it undergoes rapid photolytic degradation in water systems, and that residues of quinoxifen in rotational crops are unlikely.

### ***Methods of Analysis***

The Meeting received information for analytical methods for the quantitative determination of quinoxifen in a variety of crops. The methods were used for data collection in the supervised field trials and livestock feeding studies, and several of the methods were validated by independent laboratories for use as enforcement methods. The methods were typically validated at 0.01 mg quinoxifen/kg matrix for fruits, vegetables, and grains, with some exceptions (sugarbeet tops 0.2 mg/kg; barley and wheat straw and hops, 0.05 mg/kg). The methods were validated at 0.001 mg/kg for milk, and at 0.01 mg/kg for muscle, kidney, fat, and eggs. Bovine liver was problematic, and adequate recoveries were not achieved at levels of 0.01–1.0 mg/kg. Recovery in liver was 40% to 60%.

The various analytical methods for determination of residues of quinoxifen in plant and animal matrices follow similar partitioning, clean-up and quantification procedures. Generally, quinoxifen residues are extracted from plants and animal tissues samples with acidic acetonitrile. After addition of sodium bicarbonate solution to an aliquot of the extract, quinoxifen is partitioned into hexane, which is then evaporated to dryness. The residue is reconstituted in hexane prior to an aminopropyl solid phase extraction using 1% acetone in hexane to elute quinoxifen residues. The eluate is evaporated to dryness and reconstituted in 0.1% corn oil in tri-methyl pentane (TMP). Quinoxifen is quantified either by gas chromatography with mass selective detection (GC-MSD) or by HPLC with UV absorbance. Specific methods differ in the clean-up steps, e.g., the use of gel permeation chromatography for livestock matrices.

The Meeting concluded that adequate analytical methods exist for the determination of quinoxifen in crops and livestock commodities (except liver) both for data collection and MRL enforcement purposes.

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

The Meeting received information on the stability of quinoxifen in a variety of crop and livestock matrices. In all cases, quinoxifen was shown to be stable in the macerated matrices under conditions of frozen storage for an interval at least as great as the storage interval of supervised field trial or livestock feeding samples.

Quinoxifen was stable under conditions of frozen storage for at least 80 days in cherries, 365 days in grapes, 255 days in grape juice and raisins, 530 days in wheat grain and straw, 110 days in dried hops, 280 days in lettuce, 980 days in strawberry, 320 days in bell peppers, 250 days in melons, 240 days in milk, 190 days in kidney and muscle, and 220 days in fat. Quinoxifen appeared to be unstable in liver, 60% remaining at 240 days, but the correction for the average concurrent recovery yields a percent remaining of 93%.

The Meeting concluded that quinoxifen is stable in a variety of analytical crop, processed commodity, and livestock commodity samples under frozen storage conditions.

### ***Residue definition***

The plant and ruminant metabolism studies show that a major portion of the residue is parent quinoxifen. There was no indication that substantial portions of quinoxifen exist as conjugates in the metabolic mixtures. In plant studies, significant degradation with reincorporation of the radiolabel into natural products was indicated.

No metabolism study in poultry was provided. The poultry feeding study utilized radiolabeled quinoxifen, but no attempts were made to identify the radiolabeled residues in eggs and tissues.

The available analytical methods determine only quinoxifen.

The residue definition in Australia, the European Union, and the United States is quinoxifen.

Ruminant feeding studies show that quinoxifen preferentially accumulates in fat as opposed to muscle (10:1). Likewise the quinoxifen ratio between cream and whole milk was about 8 to 1. The goat metabolism study indicated that the TRR in the various fats was about 10× those in muscle. Finally, the octanol/water partition coefficient for quinoxifen is 4.7.

The Meeting concluded that the residue definition for both enforcement and dietary exposure considerations for plant commodities and for farm animal commodities is quinoxifen. The Meeting also decided that quinoxifen is fat-soluble.

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

The Meeting received supervised trials data for the foliar application of quinoxifen as a suspension concentrate formulation (SC) to a variety of crops, including cherries, grapes, strawberries, currants, melons, peppers, lettuce, sugar beets, wheat, barley, and hops.

#### *Cherries*

Field trials are reported from the USA (GAP: 250 g/L SC, 0.12 kg ai/ha, five applications per season, 7 day PHI). The ranked order of residue values on cherries (pitted) for 13 trials conducted at maximum GAP is: 0.03, 0.05, 0.08 (2), 0.11 (2), 0.12, 0.13 (2), 0.14 (2), 0.15, and 0.27 mg/kg. The Meeting estimated an STMR of 0.12 mg/kg, HR of 0.27 mg/kg and a maximum residue level of 0.4 mg/kg.

#### *Grapes*

Field trials are reported from France (GAP: 250 g ai/L SC, 0.05 kg ai/ha, three applications per year at 7–10 day intervals, 21 day PHI), Germany (GAP: 250 g ai/L EC, 0.005 kg ai/hL, four applications maximum at 10–14 day intervals, 21 day PHI, the application volume depends on the growth stage), Italy (GAP: 250 g ai/L SC, 0.008 kg ai/hL, five applications maximum per year at 8–14 day intervals, 28 day PHI), Spain (GAP: 250 g ai/L SC, 0.075 kg ai/ha, 0.008 kg ai/hL, five applications maximum per year at 10–18 day intervals 30 day PHI for wine grapes, 21 day PHI for table grapes), US (GAP: 250 g ai/L SC, 0.12 kg ai/ha, five applications maximum per season or 0.60 kg ai/ha/year at 7–21 day interval, 14 day PHI), Canada (GAP: no label, use USA), and Australia (GAP: 250 g ai/L SC, 0.005 kg ai/hL, three applications maximum at 7–14 day intervals, 14 day PHI).

The trials in France and Germany consisted of 6, 7, or 10 repeat applications. Applications made more than 30 days before harvest will not contribute significantly to the final residue. With the 6–13 day retreatment intervals and a 21 day PHI, only the last three applications will contribute to the residue. The ranked order of residues from trials conducted at the maximum GAP with the additional repeat applications (n=9) in France and Germany is: 0.02, 0.04, 0.04, 0.05, 0.05, 0.06, 0.09, 0.13, and 0.36 mg/kg.

The ranked order of the residue values on grapes for eight trials conducted at the maximum GAP in Italy is: 0.04, 0.06, 0.07, 0.10, 0.17, 0.18, 0.30, 0.49 mg/kg. The ranked order of the residue values on grapes for trials conducted at the maximum GAP in Spain is: 0.02, 0.04, 0.08, 0.22 mg/kg.

The ranked order for 13 trials in the US conducted at the maximum GAP is: 0.06, 0.08 (2), 0.09, 0.13 (2), 0.15 (3), 0.18, 0.22, 0.24, 0.44 mg/kg. The ranked order for two trials in Canada conducted at the maximum GAP of the US is: 0.22, 0.29 mg/kg.

Fifteen trials conducted in Australia comply with the PHI of 14 days, 0.01, 0.05, 0.06, 0.09 (2), 0.15 (2), 0.17, 0.18, 0.23, 0.41, 0.45, 0.54, 0.82, 1.1 mg/kg

The trial residue values from France, Germany, Italy, Spain, Canada, US, and Australia appear to be from the same population and are combined (n = 51) in rank order: 0.01, 0.02 (2), 0.04 (4), 0.05 (3), 0.06 (4), 0.07, 0.08 (3), 0.09 (4), 0.10, 0.13 (3), 0.15 (5), 0.17 (2), 0.18 (3), 0.22 (3), 0.23, 0.24, 0.29, 0.30, 0.36, 0.41, 0.44, 0.45, 0.49, 0.54, 0.82, and 1.1 mg/kg. The Meeting estimated an STMR of 0.13 mg/kg, HR of 1.1 mg/kg and a maximum residue level of 2 mg/kg.

#### *Strawberries*

Field trials were reported to the Meeting from Germany (GAP: 250 g ai/L SC, 0.12 kg ai/ha, 0.006 kg ai/hl, two applications per season, 14 day PHI) and the USA (250 g ai/L SC, 0.11 kg ai/ha, four applications per season (0.44 kg ai/ha/season), 1 day PHI).

The residue values in ranked order from the eight trials in Germany at maximum GAP were: 0.01, 0.02, 0.04, 0.05, 0.07, 0.09, 0.12, and 0.16 mg/kg.

The residue values in ranked order from the six trials in the USA at maximum GAP are: 0.16, 0.18, 0.24, 0.41, 0.46, and 0.56 mg/kg. The values of Germany and the USA are not from the same population.

Using the residue values (n=6) from the USA, the Meeting estimated as STMR of 0.32 mg/kg, HR of 0.56 mg/kg and a maximum residue level of 1 mg/kg.

#### *Currants*

Supervised field trial studies for the foliar application of quinoxifen to black currants in Germany were reported to the Meeting. The GAP is: 240 g ai/L, 0.075 kg ai/ha, 0.0075 kg ai/hL, three applications per year, 14 day PHI.

The residue values in ranked order (n=7) for trials conducted at maximum GAP were: 0.04, 0.05, 0.06, 0.20, 0.28, 0.30, and 0.40 mg/kg.

The Meeting estimated an STMR of 0.20 mg/kg, HR of 0.40 mg/kg and a maximum residue level of 1 mg/kg.

#### *Melons*

Field trials on melons were reported from Spain (GAP: 250 g ai/L SC, 0.0075 kg ai/hL, three applications per year, 7 day PHI), Italy (GAP: 250 g ai/L SC, 0.006 kg ai/hL, 7 day PHI), Greece (No label available, use GAP Italy), and the USA (GAP: 250 g ai/L SC, 0.11 kg ai/ha, four applications per year, 3 day PHI).

The residues in ranked order for whole melons from six trials at maximum GAP in Italy and two trials in Greece are: 0.01 (2), 0.02 (4), and 0.03 (2) mg/kg; and the residues in ranked order for the pulp only were: < 0.01 (6) and 0.02 (2) mg/kg.

The residues in ranked order for whole melons from eight trials at maximum GAP in Spain are: 0.01 (4) and 0.02 (4) mg/kg; and the residues in ranked order for the pulp only are: ND - < 0.01 (8) mg/kg.

The residues in ranked order for whole melons (cantaloupes) from six trials at maximum GAP in the USA (taking into account the permitted maximum total seasonal rate) are: < 0.01, 0.02, 0.03 (3), and 0.05 mg/kg. No data were provided on pulp.

The data from the various countries are from the same population and are combined (n=22) in ranked order, for whole melon: 0.01 (7), 0.02 (9), 0.03 (5), and 0.05 mg/kg; and for pulp (n=16), 0.01 (14) and 0.02 (2) mg/kg.

The Meeting estimated an STMR of 0.01 mg/kg and HR of 0.02 mg/kg for quinoxifen in melon pulp and a maximum residue level of 0.1 mg/kg for quinoxifen in/on whole melon, except watermelon in both cases.

### *Peppers*

A field trial residue study was reported from the USA (GAP: 250 g ai/L SC, 0.15 kg ai/ha, four applications per year, 0.60 kg ai/ha/year, 3 day PHI).

The residues (n=11) in ranked order for quinoxifen residues on peppers from application at maximum GAP were: 0.01, 0.02, 0.09, 0.12, 0.15 (2), 0.16, 0.17, 0.23, 0.52, and 0.64 mg/kg.

The Meeting estimated an STMR of 0.15 mg/kg, HR of 0.64 mg/kg and a maximum residue level of 1 mg/kg for peppers (bell and non-bell).

### *Lettuce*

A field study report was provided for the foliar application of quinoxifen to lettuce (leaf and head) in the USA. The GAP in the USA is: 250 g ai/L SC, 0.11 kg ai/ha, four applications per season and 0.44 kg ai/ha/season, and a PHI of 1 day.

Seven trials on head lettuce were at maximum GAP, with residues in ranked order of: 0.91, 1.0, 1.2, 1.4, 2.1, 3.1, and 5.3 mg/kg. Six trials on leaf lettuce were at maximum GAP, with residues in ranked order of: 1.3, 2.9, 3.4, 4.3, 6.9, and 13 mg/kg.

The Meeting estimated an STMR of 1.4 mg/kg, HR of 5.3 mg/kg and a maximum residue level of 8 mg/kg for lettuce (head).

The Meeting estimated an STMR of 3.8 mg/kg, HR of 13 mg/kg and a maximum residue level of 20 mg/kg for lettuce (leaf).

### *Sugar beet roots*

Field trial data were received from Germany (GAP: 500 g ai/LC SC, 0.12 kg ai/ha, two applications per season, 28 day PHI), UK (GAP: 500 g ai/L SC, 0.15 kg ai/ha, two applications, 28 day PHI), and France (GAP: 500 g ai/L SC, 0.15 kg ai/ha, one application, 28 day PHI).

The residue values for trials conducted in the three European countries at maximum GAP in ranked order are: < 0.01 (4), 0.01 (3), 0.02 mg/kg.

The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.03 mg/kg for sugar beet roots.

### *Wheat grain*

Wheat grain trials were reported from France, Germany, and the UK. The GAPs are: 500 g ai/L SC, 0.15 kg ai/ha, one application in France with a PHI of 56 days; 500 g ai/L SC, 0.25 kg ai/ha, one

application in Germany at growth stages BBCH 25–32 (tillering), and in the UK 500 g ai/L SC, 0.15 kg ai/ha, two applications until growth stage BBCH 49 (about 60 days PHI).

Some trials in Greece were evaluated against the GAP of France. The trials in North France were evaluated against the GAP of Germany.

The trials in Greece were not within the maximum GAP of France. The trials were conducted at rates in excess of the maximum GAP, and they resulted in finite residue values (> LOQ). Some trials (n=21) in France, Germany, and the UK conducted at or in excess of the maximum GAP of the respective countries yielded residue values below the LOQ. The residue values in ranked order were: < 0.01 (21) mg/kg.

The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.01 (\*) mg/kg for wheat grain.

#### *Barley grain*

Barley grain trials were reported from France, Germany, and the UK. The GAPs are: 500 g ai/L SC, 0.15 kg ai/ha, one application in France with a PHI of 56 days; 500 g ai/L SC, 0.25 kg ai/ha, one application in Germany at growth stages BBCH 25–32 (tillering), and in the UK 500 g ai/L SC, 0.15 kg ai/ha, two applications until growth stage BBCH 49 (about 60 days PHI).

All trials in Europe were conducted above the maximum GAP. Eight trials provided residue values below the limit of quantitation. The ranked order of residues is < 0.01 (8) mg/kg.

The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.01 (\*) mg/kg for barley grain.

#### *Wheat straw*

Wheat trials were reported from France, Germany, and the UK. The GAPs are: 500 g ai/L SC, 0.15 kg ai/ha, two applications per season one application in France with a PHI of 56 days; 0.25 kg ai/ha, one application in Germany at growth stages BBCH 25–32 (tillering), and in the UK 500 g ai/L SC, 0.15 kg ai/ha, two applications until growth stage BBCH 49 (about 60 days PHI). Some trials in Greece were evaluated against the GAP of France (South). The trials in the UK and in North France were evaluated against the GAP of Germany.

The residues in rank order in wheat straw (n=16) were: < 0.05 (5), 0.07, 0.09, 0.11, 0.13 (2), 0.19 (2), 0.21, 0.23, 0.27, 0.36 mg/kg. On a dry weight basis (88% DM) the values are: < 0.06 (5), 0.08, 0.10, 0.12, 0.15 (2), 0.22 (2), 0.24, 0.26, 0.31, 0.41 mg/kg. The Meeting estimated a maximum residue level of 0.5 mg/kg and an STMR of 0.14 mg/kg.

#### *Barley straw*

Barley trials were reported from France, Germany, and the UK. The GAPs are: 500 g ai/L SC, 0.15 kg ai/ha, two applications per season one application in France with a PHI of 56 days; 0.25 kg ai/ha, a application in Germany at growth stages BBCH 25–32 (tillering), and 500 g ai/L SC, 0.15 kg ai/ha, two applications until growth stage Zadoks 49 (about 60 days PHI) in the UK. The trials in the UK and in North France were evaluated against the GAP of Germany.

The residues in barley straw in rank order (n=6) are: 0.22 (2), 0.30, 0.58, 1.23, 2.94 mg/kg. On a dry weight basis (89% DM) the values are: 0.25 (2), 0.34, 0.65, 1.38, 3.30 mg/kg. The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 0.50 mg/kg. The highest residue is 3.3 mg/kg.

#### *Hops (dry)*

Hops trials were reported from Germany (GAP: 250 g/L SC, 0.011 kg ai/hL, four applications or 0.5 kg ai/ha/season, PHI 28 days) and from the USA (GAP: 250 g/L SC, 0.15 kg ai/ha, four applications or 0.6 kg ai/ha/season, PHI 21 days).



Six trials in Germany were conducted at the maximum seasonal GAP, but with three applications rather than four. The sum of the three applications was within 30% of the seasonal maximum GAP. The residue values in ranked order were: 0.03, 0.04, 0.07, 0.37, 0.41, and 0.55 mg/kg.

Four trials in the USA were conducted at the maximum season GAP, with three applications rather than four. The residue values in ranked order were: 0.39, 1.2, and 2.2 mg/kg.

The trials in the USA and in Germany are not from the same population. The three trials in the USA provide insufficient data for the estimation of an STMR and maximum residue level.

Using the six trials from Germany, the Meeting estimated an STMR of 0.22 mg/kg and a maximum residue level of 1 mg/kg for residues of quinoxifen in hops (dry).

### *Spices*

Using a default processing (dehydration) factor of 10, the Meeting estimated a maximum residue level of 10 mg/kg and an STMR of 1.5 mg/kg for dried chili peppers based on the maximum residue level and STMR of pepper.

### *Sugar beet tops*

Field trial data were received from Germany (GAP: 500 g ai/LC SC, 0.12 kg ai/ha, two applications per season, 28 day PHI), UK (GAP: 500 g ai/L SC, 0.15 kg ai/ha, two applications, 28 day PHI), and France (GAP: 500 g ai/L SC, 0.15 kg ai/ha, one application, 28 day PHI).

Three trials from Germany and four trials from the UK were conducted at the maximum GAP. The residue values from Germany in ranked order were: 0.10 (2) and 0.27 mg/kg. The residue values from the UK in ranked order are: 0.13, 0.22, 0.36, and 0.37 mg/kg. The combined values (n=7) in ranked order were: 0.10 (2), 0.13, 0.22, 0.27, 0.36, and 0.37 mg/kg.

The Meeting estimated an STMR of 0.22 mg/kg and a highest residue level of 0.37 mg/kg.

### ***Fate of residues in storage***

The effect of storage upon the fate of quinoxifen residues was not reported to the Meeting.

### ***Fate of residues during processing***

Information on the fate of quinoxifen in the processing of wheat, barley, and grapes was reported to the Meeting. No information was supplied on the fate of radiolabeled quinoxifen under general processing conditions.

Winter wheat which had received foliar treatment with quinoxifen was processed into flour and bread in separate studies in France and the UK. The wheat grain contained no residues (< 0.01 mg/kg) and while there was no apparent concentration of residue in bran, flour, or bread, no processing factors could be calculated.

Barley in the UK was treated at an exaggerated rate with quinoxifen, and the grain at normal harvest was processed into malt and beer by a simulated commercial process. The processing factor for malt was 0.5 and that for beer was < 0.1. Using the STMR for barley (0.01 mg/kg), the Meeting estimated an STMR-P of 0.001 mg/kg for beer.

Processing studies for the conversion of grapes to wine were reported from France, Germany, and Italy. In all cases, the grapes had quantifiable field incurred residues of quinoxifen. Three trials were conducted for the preparation of white wine and two for the preparation of red wine. The processing factor varied from 0.004 to 0.03, with a median and average value of 0.01. Applying this processing factor to the STMR of grapes (0.15 mg/kg), the Meeting estimated an STMR-P of 0.015 mg/kg for wine (from grapes).

A processing study for the conversion of grapes to raisins and grape juice was reported from the USA. Grapes with a quantifiable field incurred residue of quinoxifen were processed in separate commercial-type procedures into raisins and pasteurised grape juice. The processing factors for raisins and juice were 0.66 and 0.06, respectively. Using the STMR value for grapes (0.15 mg/kg), the Meeting estimated STMR-Ps of 0.099 mg/kg and 0.009 mg/kg for raisins and grape juice, respectively.

### ***Farm animal dietary burden***

The Meeting estimated the dietary burden of quinoxifen residues in farm animals on the basis of the diets listed in Appendix IX of the *FAO Manual*. Calculation from MRLs, highest residues and STMR-P values provides the levels in feed suitable for estimating MRLs for animal commodities, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage of dry matter is taken as 100% when MRLs and STMR values are already expressed as dry weight.

#### *Estimated maximum dietary burden of farm animals*

Commodity	Group	Residue (mg/kg)	Basis of Residue	Dry matter (%)	Diets			Residue contribution (mg/kg)		
					Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Barley grain	GC	0.01	MRL	88	50	30	80	0.006	0.005	0.009
Sugar beet leaves (tops)	AV	0.37	HR	23	20	10	-	0.32	0.16	-
Barley Straw	AS	3.3	HR	89	10	60	-	0.33	1.98	-
<b>TOTAL</b>					<b>80</b>	<b>100</b>	<b>80</b>	<b>0.66</b>	<b>2.14</b>	<b>0.01</b>

The calculated maximum dietary burdens for beef cattle, dairy cows and poultry are 0.66, 2.1, and 0.01 ppm, respectively.

#### *Estimated STMR dietary burden of farm animals*

Commodity	Group	Residue (mg/kg)	Basis of Residue	Dry matter (%)	Diets			Residue contribution (mg/kg)		
					Beef cattle	Dairy cattle	Poultry	Beef cattle	Dairy cattle	Poultry
Barley grain	GC	0.01	STMR	88	50	30	80	0.006	0.003	0.009
Sugar beet leaves (tops)	AV	0.22	STMR	23	20	10	-	0.19	0.10	-
Barley Straw	AS	0.50	STMR	89	10	60	-	0.05	0.30	-
<b>TOTAL</b>					<b>80</b>	<b>100</b>	<b>80</b>	<b>0.25</b>	<b>0.40</b>	<b>0.01</b>

The calculated STMR dietary burdens for beef cattle, dairy cows and poultry are 0.25, 0.40, and 0.01 ppm, respectively.

### Farm animal feeding studies

The Meeting received two feeding studies for dairy cattle and a radiolabeled quinoxifen feeding study for poultry (chickens). Friesian cows were fed for 28 consecutive days with diets containing 0.2, 0.6, 2.0, or 20 ppm quinoxifen. Residues in whole milk reached a plateau by day 7 of 0.001, 0.002, and 0.007 mg/kg for 0.2, 0.6, and 2.0 ppm dosing levels, respectively. At the 20 ppm dosing level, the quinoxifen residue spiked to 0.37 mg/kg on day 7 and then declined to an apparent plateau of 0.16 ppm by the final day.

At the 0.2 ppm feeding level, the maximum and average (n=3 cows) residue in whole milk (day 27) was < 0.001 mg/kg. In cream, the maximum residue was 0.007 mg/kg and the average residue was 0.003 mg/kg. At the 0.6 ppm feeding level, the maximum and average (n=3 cows) in whole milk (day 27) was 0.002 mg/kg and 0.002 mg/kg, respectively. In cream, the maximum residue was 0.02 mg/kg, and the average residue was 0.015 mg/kg.

At the 0.2 ppm feeding level, the maximum and average residues in liver, kidney, muscle, and fat were ND and ND, < 0.01 and < 0.01 mg/kg, ND and ND, and 0.02 and 0.01 mg/kg, respectively. At the 0.6 feeding level, the maximum and average residues in liver, kidney, muscle, and fat were < 0.01 and < 0.01 mg/kg, < 0.01 and < 0.01 mg/kg, ND and ND, and 0.02 and 0.012 mg/kg, respectively.

At the 0.6 ppm feeding level, the maximum and average residues in milk were 0.002 mg/kg each. The maximum and average values in cream were 0.022 mg/kg and 0.016 mg/kg, respectively. The maximum and average residue values in liver and kidney were < 0.01 mg/kg each. The maximum and average values in muscle were ND (< 0.002 mg/kg). The maximum and average values in fat were 0.02 and 0.12 mg/kg, respectively.

At the 2 ppm feeding level, the maximum and average residues in milk were 0.010 and 0.0088 mg/kg, respectively. The maximum and average residues in cream were 0.077 and 0.068 mg/kg, respectively. The maximum and average residues in liver, kidney, and muscle were < 0.01 mg/kg. The maximum residue in fat was 0.10 mg/kg, and the average was 0.09 mg/kg.

### Quinoxifen total residues, mg/kg

Dietary burden (ppm)	Cream	Milk	Muscle		Liver		Kidney		Fat	
			Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest
MRL, beef cattle	(0.66)			(<0.01)		(<0.01)		(<0.01)		(0.02)
MRL, dairy cattle	[0.6]			[<0.002]		[<0.01]		[<0.01]		[0.02]
STMR, beef cattle	(2.1)	(0.068)								
STMR, dairy cattle	[2]	[0.068]								
MRL, beef cattle	(0.25)				(0.002)		(0.002)		(<0.01)	(0.01)
STMR, beef cattle	[0.2]				[<0.002]		[<0.002]		[<0.01]	[0.01]
MRL, dairy cattle	(0.40)	(0.01)								
STMR, dairy cattle	[0.2/0.6]	[0.003/0.016]								
		[<0.001/0.002]								

A *poultry feeding* study consisted of four groups of 10 Isa Brown laying hens fed at the following dose levels: 0.1, 0.3, and 1.0 ppm of diet/ day. The hens were fed gelatin capsules containing a *radiolabelled* (mixture of <sup>14</sup>C-quinoline label and <sup>14</sup>C-phenoxy label) <sup>14</sup>C-quinoxifen. Each daily dose was administered in a single capsule at the same time each day for 28 days. Only TRR was determined in the eggs and tissues. These levels were very low at a 0.1 ppm diet with maximum values of 0.003 mg/kg in eggs, 0.009 mg/kg in liver, 0.004 mg/kg in kidney, 0.0 mg/kg in muscle, and 0.013 mg/kg in fat. At the 1.0 ppm feeding level, TRR values were 0.025 mg/kg in eggs, 0.097 mg/kg in liver, 0.049 mg/kg in kidney, 0.009 mg/kg in muscle, and 0.063 mg/kg in fat. However, the TRR was not characterized or identified.

*Animal commodity maximum residue levels*

The Meeting estimated the following maximum residue levels for mammalian commodities, based on the cow feeding studies and the calculated dietary intake (see above): muscle, 0.01 (\*) mg/kg; fat, 0.02 mg/kg; edible offal, 0.01 (\*) mg/kg; milk fat, 0.2 mg/kg; milk, 0.01 mg/kg. The Meeting likewise estimated the following STMR values: muscle, 0.002 mg/kg; fat, 0.01 mg/kg; edible offal 0.01 mg/kg; milk fat, 0.02 mg/kg; milk, 0.002 mg/kg. The milk fat estimations assume that cream is 50% fat. Although the metabolic profile in poultry was not determined, the feeding study with radiolabelled quinoxifen demonstrated very low levels of total residue at a feeding level of 0.1 ppm, the estimated dietary burden of poultry. Therefore, the MRLs for poultry commodities are estimated at the LOQs of the analytical method, 0.01 (\*) mg/kg for each of poultry egg and edible offal, and 0.02 mg/kg meat (fat). The STMRs are based on the TRR values and are estimated to be: eggs, 0.003 mg/kg; offal, 0.009 mg/kg; muscle, 0 mg/kg; and fat 0.013 mg/kg.

**RECOMMENDATIONS**

The Meeting estimated the maximum residue levels and STMR values shown below. The maximum residue levels are recommended for use as MRLs.

Definition of the residue: Plant and animal commodities.

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

The residue is fat soluble.

CCN	Commodity Name	MRL, mg/kg		STMR or STMR-P, mg/kg	HR, mg/kg
		New	Previous		
GC0640	Barley	0.01 (*)		0.01	
	Beer			0.001	
FS0013	Cherries	0.4		0.12	0.27
FB0278	Currants, black	1		0.20	0.40
DF0269	Dried grapes (=Currant, Raisins and Sultanas)			0.099	
MO105	Edible offal (mammalian)	0.01 (*)		0.01	
PE0112	Eggs	0.01 (*)		0.003	
FB0269	Grapes	2		0.13	1.1
JF0269	Grape juice			0.009	
DH1100	Hops, dry	1		0.22	
VL0482	Lettuce, head	8		1.4	5.3
VL0483	Lettuce, leaf	20		3.8	13
MM0095	Meat (from mammals other than marine mammals)	0.01 * (muscle) 0.02 (fat)		0.01 fat 0.002 muscle	
VC0046	Melons, except watermelon	0.1		0.01	0.02
ML0106	Milks (excl. processed products)	0.01		0.002	
FM0183	Milk fats	0.2		0.02	
VO0051	Peppers	1		0.15	0.64
?	Peppers, chili, dried	10		1.5	
PO 0111	Poultry, edible offal of	0.01 (*)		0.009	
PM 0110	Poultry meat	0.02		0.013 fat 0.0 muscle	
FB0275	Strawberry	1		0.32	0.56
VR0596	Sugar beet root	0.03		0.01	
AV1051	Sugar beet leaves or tops			0.22	
GC0654	Wheat	0.01 (*)		0.01	
	Wine of grapes			0.015	

## DIETARY RISK ASSESSMENT

### *Long-term intake*

The International Estimated Daily Intakes (IEDI) of quinoxifen, based on the STMRs estimated for 15 commodities for the thirteen GEMS/Food cluster diets were in the range of 0% to 1% of the ADI (Annex 3 of the 2006 JMPR Report). The Meeting concluded that the long-term intake of residues of quinoxifen resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

### *Short-term intake*

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

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Reeves, G. and Ghosh, D.	8557	1994
Cowlyn, T and Boothroyd, S	8605	1994
Kunz, A.	11110	2001
Fuchsbichler, G.	20061	2002
Fuchsbichler, G.	20062	2002a
Cowlyn, T and Boothroyd, S	21129	1994a
Reeves, G.	24033	1994
Gambie, A and Nicholson, A.	24035	1994
Cowlyn, T	27304	1994
Dunsire, J and Paul, H.	29257	1995
Cracknell, M, Duriatti, A, Ghosh, D, Graupner, P and Portwood, D	29386	1995
Gambie, A, Nicholson, A & Wood, S.	29405	1995
Gambie, A.	29406	1995
Gambie, A.	29912	1995a
Reeves, G.	31076	1995
Gambie, A.	31080	1995b
Gambie, A.	31231	1995c
Gambie, A.	31234	1995d
Gambie, A.	31235	1995e
Gambie, A.	31241	1995f
Gambie, A.	31261	1995g
Gambie, A.	31262	1995h
Gambie, A.	31263	1995i
Gambie, A.	31265	1995j
Gambie, A.	31266	1995k
Gambie, A and Wood, S.	31267	1995
Gambie, A, & Wood, S.	31268	1995a
Gambie, A and Long, T.	31599	1995
Gambie, A and Press, A.	31600	1995
Gambie, A and Press, A.	31607	1995a
Gambie, A.	31620	1995l
Gambie, A, Rawle, N., and Shaw, I.	31621	1995
Gambie, A and Teasdale, R.	31624	1995
Gambie, A.	31633	1995m
Gambie, A, Teasdale, R and Press, A.	31634	1995
Gambie, A.	31635	1995n
Gambie, A.	31644	1995o
Gambie, A.	31646	1995p
Gambie, A.	31648	1995r
Hastings, M and Schmidt, F.	31651	1995
Haq, R, MacDonald, A and Brown, G.	31659	1995
Jack, L and Dunsire, J.	31744	1995
Gambie, A.	31748	1995s
Gambie, A.	31753	1995t
Haq, R and Brown, G.	31757	1995
Khoshab, A.	41039	1995
Khoshab, A.	42673	1995a
Khoshab, A.	42674	1995b
Caley, C. and Kingsley, R.	42894	1995
Khoshab, A.	43179	1996
Khoshab, A.	43180	1996a
Khoshab, A.	43181	1996b
Khoshab, A.	43416	1996c
Khoshab, A.	43620	1996d
Khoshab, A.	43621	1996e
Khoshab, A.	43622	1996f
Khoshab, A.	43816	1996g
Portwood, D.	44553	1996
Khoshab, A.	44917	1996h

Khoshab, A.	45173	1996i
Khoshab, A.	45513	1996j
Khoshab, A.	45531	1996k
Khoshab, A.	45532	1996l
Khoshab, A.,	45692	1996
Khoshab, A.	45715	1996m
Khoshab, A.	45716	1996n
Khoshab, A.	45717	1996o
Khoshab, A.	45718	1996p
Khoshab, A. and Rawle, N.	45724	1996
Chapleo, S. and Caley, C	45725	1996
Khoshab, A.	46954	1996r
Khoshab, A.	46956	1996s
Khoshab, A.	46957	1996t
Khoshab, A.	46958	1996u
Khoshab, A.	46975	1996v
Khoshab, A.	47141	1996z
Khoshab, A.	47145	1996x
Williams, M.	47234	1996
Gambie, A.	47586	1996
Khoshab, A and Volle C.	47868	1996
Khoshab, A.	48080	1996y
Khoshab, A.	48081	1996w
MacDonald, A.	48846	1997
Hastings, M and Gambie, A.	63682	1995
Hastings, M and Gambie, A.	63683	1995a
Gambie, A and Nicholson, A.	63697	1994a
Teasdale, R and Press, A.	63705	1995
Khoshab, A, Boothroyd, S, Gale, D and Frewer, N.	64399	1998
Khoshab, A and Clements, B.	69430	1999
Oberwalder, C.	73994	1999
Pollmann, B.	74050	2000
Teasdale, R, Lyons, S, Rhodes, H and Patel, K.	74779	2000
Teasdale, R.	74780	2000
Haq, R and Brown, G.	75502	1995a
Jones, S.	76690	2000
Khoshab, A. and Macmillan, H.	76968	1996
Byrne, S, Balcer, J, Gilbert, J., and Thornburg, S.	78962	2000
Eckert, J and West, S.	80416	2001
Hackert Anderson, Cand West, S.	80711	2001
West, S.	81400	2001
Grafer, L and Balcer, J.	81925	2001
Kang, J., Kingdom, N., and Womack, J.	83187	2001
Thompson, D.	83727	2001
Thompson, D.	83731	2001
Dobbs, L	102718	2001
Chen, H	102721	2002
Chen, H	102722	2002a
Khoshab, A.	105043	1995c
Khoshab, A and Roberts, R.	105334	1996
Khoshab, A. and Macmillan, H.	105351	1996a
Class, T	135044	2003
Class, T	135045	2003a
Class, T	135046	2003b
Class, T	135047	2003c
Corley, J.	208696	2004
Barney, W.	208697	2005
Barney, W.	208698	2005a