

**COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD,
CONSUMER PRODUCTS AND THE ENVIRONMENT**

**CHEMICALS USE AND PARA-OCCUPATIONAL EXPOSURE IN THE UK.
INFORMATION PROVIDED BY CHEMICALS REGULATION
DIRECTORATE (CRD)**

Chemicals Use

1. The Pesticide Usage Survey Group, at The Food and Environment Research Agency (Fera formerly known as the Central Science Laboratory, CSL), produce reports which give information on the use of plant protection product pesticides. Individual reports can be down loaded from:

<http://www.fera.defra.gov.uk/plants/pesticideUsage/fullReports.cfm>

2. These report aggregate uses on individual farms. It is possible for Fera to examine the data on individual substances at a farm level, to get figures on the amount used, duration and the frequency of use. However, this generates a large amount of information. As a step to provide more detail in a manageable form, regional data for the top 50 actives substances (determined by area treated) are shown separately for arable, vegetable orchard crops below. Tables 1-3 below show for arable, vegetable and orchard crops the time of application and the amounts applied for the survey regions recording the most use. Estimating the duration of use from these data, may still over estimate duration of use on individual farms.

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Table 1. Sum of amount applied to arable crops in Eastern Survey Region (Bedfordshire, Cambridgeshire, Essex, Hertfordshire, Norfolk, and Suffolk, total arable crop area 1, 017,084 ha)

Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
2-chloroethylphosphonic acid				887	13504	1609							16001
Alpha-cypermethrin		5	11	57	111	23			56	109	24	3	398
Azoxystrobin			2136	3962	16259	14192	42			23		118	36732
Boscalid				15361	10544	261							26167
Carbendazim				1034	15020	916	220	841	171	428	548	243	19421
Chlormequat			34793	587203	82670	6325	366						711356
Chlormequat chloride				6798	20751	2338							29887
Chlorothalonil			3882	142896	174642	96830	875					314	419439
Chlorpyrifos	2704	1046	278		1312	17172			166	373			23050
Cymoxanil			12	59	1482	5413	4637	2623	639	38			14903
Cypermethrin	92	198	436	1118	646	164	339	151	866	4192	4711	787	13701
Cyproconazole			105	4501	1872	1254	222	197					8152
Diflufenican	198	247	170	220					128	3504	4197	508	9171
Epoxiconazole				10416	22105	11629		134	11				44295
Ethofumesate			41	6422	14009	4260	14						24746
Fenpropimorph				6474	20919	7311							34704
Florasulam			1	85	60	14							159
Fluazinam					1109	5733	1903	4609	3424	170			16947
Flufenacet	307		14		196				9252	15700	3580	97	29145
Fluoxastrobin				2798	2802	1506				159			7266
Fluroxypyr			24	7526	16108	4899							28557
Flusilazole				267	979	394	1277	2838	277	1857	2748	631	11267
Glyphosate	2958	14393	15119	17894	18799	25118	104917	35541	102971	41697	10624	1514	391545
Imazaquin				49	3								52
Iodosulfuron-methyl-sodium	17	8	136	206	23					11	56	21	478

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Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Isoproturon	8880	11880	6885	12469					5429	201804	254050	21091	522488
Kresoxim-methyl				254	1581	817							2652
Lambda-cyhalothrin				63	263	515	130	12	36	66	65	4	1153
Mancozeb			58	1792	27109	89564	93191	47859	10451	575			270600
Mecoprop-P	38	583	1127	19226	15159	207	72	753	609	13616	14061	668	66119
Mesosulfuron-methyl	86	38	673	967	63					56	279	106	2267
Metaldehyde		145	147	1903	773	156	1111	12173	26549	18915	2710	535	65116
Metazachlor				4517	1659			11047	19865	6008			43097
Metconazole			208	1816	220	416			20	490	208	57	3434
Metrafenone			52	2216	1756	879							4905
Metsulfuron-methyl		0	10	290	478	92	1			3			874
Pendimethalin	2801	10496	8970	6219	1111	788			49490	89776	48592	5288	223531
Phenmedipham				12123	18049	6146	25						36342
Prochloraz				3603	2703	6100				708	318		13432
Propaquizafop	11		79	64	345	323		103	1202	913	383	103	3527
Prothioconazole			157	11412	14115	8191				216	414		34506
Pyraclostrobin				365	10264	5694		357	30				16710
Spiroxamine			125	4111	1774	2482							8491
Tau-fluvalinate			4	232	507	841			15	347	336	5	2288
Tebuconazole			438	4621	8206	19187	134		4	328	311		33228
Thifensulfuron-methyl		5	3	494	1216	35	6			7	11	10	1788
Tribenuron-methyl			1	178	319	46				8	5		555
Trifloxystrobin				280	862	425							1567
Trifluralin	1634	4616	3768	5952	109	57		20723	34204	93842	68531	11152	244588
Trinexapac-ethyl			160	5049	599								5808
Zeta-cypermethrin	19	2		98	195	196			9	76	150	21	765

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Table 2. Sum of amount applied to outdoor vegetable crops in Eastern Survey Region (Bedfordshire, Cambridgeshire, Essex, Hertfordshire, Norfolk, and Suffolk, total vegetable crop area 31,217 ha)

Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Azoxystrobin			6	77	151	481	1802	1047	293	118	12		3987
Bentazone			12	705	816	915	1016	24					3487
Bifenthrin					1	1		1	1	1			5
Boscalid			18	91		38	133	242	198	36	8		763
Chloridazon			80	326	510	32	1	1		17			967
Chlorothalonil			5	134	750	5707	10355	3764	299	32	45		21090
Chlorpropham		90	1695	1358	337	360	227	282	27		14		4391
Chlorpyrifos			10	36	2	19	23	47	6	4			147
Clomazone	15	8	31	25	81	30	25						216
Copper oxychloride			10	177	800	2735	6524	4154	760	35			15195
Cyanazine			5	182	1437	1948	341	32					3945
Cypermethrin			<1	2	26	32	33	23	15	2	<1		133
Deltamethrin			<1	2	4	11	14	19	20	10	<1		81
Difenoconazole						2	10	81	44	21	12		170
Dimethoate					39	28	103	23	24	23	19		260
Dimethomorph				44	92	807	1640	862	132				3577
Fenpropimorph								464	282	225	34		1004
Fluroxypyr	<1		1	41	161	153	18	7					381
Glyphosate	96	2028	6284	2064	2010	623	389	943	2881	2742	686	231	20977
loxynil			24	364	673	525	204	21		11			1822
Iprodione			34	47	47	15	20	44					206
Isoxaben		2	13	53	14	28							111
Lambda-cyhalothrin				7	18	29	56	72	26	1			209
Linuron	121	135	271	809	648	781	863	291	22		13	14	3970

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Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Mancozeb			30	1102	3574	15316	24287	13425	2026	97	17		59876
MCPB				453	1107	1309	190						3060
Metalaxyl-M			<1	17	49	186	645	336	51	4	1		1291
Metaldehyde		11	41	96	63	267	238	48	56	24	22		867
Metamitron		15	274	1014	395	474	85	11	266				2534
Metazachlor			119	121	89	160	205	85	11	4			794
Metoxuron					1071	1200	1441	1047	35				4793
Nicotine			<1	13	165	169	93	164	297	57			958
Oxamyl	473	144	648	145	365	289	20			16		81	2182
Paraquat			248	89	61	122			14	9			544
Pendimethalin	393	438	2297	3539	1360	939	722	4	14	59	72	36	9874
Pirimicarb				54	1057	895	577	506	586	133	1		3810
Prometryn			19	179	251	307	308	51		31			1147
Propachlor	485	638	18791	3576	1454	1715	902	928	405	279	92		29266
Propaquizafop			<1	66	126	58	48	41	5				344
Pymetrozine				24	7	17	24	95	105	16	26		313
Pyraclostrobin			4	23		10	33	61	50	9	2		191
Sulphur				117	853	2046	4673	2122	5445	919			16174
Tebuconazole				1	14	60	249	448	308	239	86		1405
Tepraloxym				25	120	131	44	31		1			352
Terbutylazine			580	333	297	125	90		19				1444
Terbutryn			1353	499	693	225			44				2815
Thiacloprid				4		1		4	17	7	<1		33
Trifloxystrobin						1	1	24	53	70	5		154
Trifluralin			371	434	310	155	249	98	45	8			1671

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Table 3. Sum of amount applied to orchard crops in London & South East Survey Region (bershire, Buckinghamshire, Hampshire, Isle of Wight, London, Kent, Oxfordshire, Surrey, E Sussex, and W Sussex, total area approximately 10,000 ha)

Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
2,4-D			408	877	100	492	73			9			1961
Amitraz					1	175		1					176
Amitrole			85	1	146	67	91			7	214	42	652
Bupirimate	1			<1	255	604	1182	584					2626
Captan	7		391	5195	9201	13118	7521	2864					38296
Carbendazim		98	1357	2092	1425	1311	679	243		56	73		7334
Chlorpyrifos	<1		136	1540	2133	3604	2554	995					10962
Copper oxychloride		580	2477	68	47	37	62	37	229	1054	864	15	5470
Cypermethrin			24	5	3	13	8	6		4			63
Dicamba			17	27	34	17	4	8		5	13	<1	124
Dichlorprop-P				21	17	2	43			1			84
Diflubenzuron					12	57	22	20					112
Dinocap					10	21	148	60					239
Diquat					11	2	13	<1		<1	28		55
Dithianon		4	5028	7235	2825	1807	1102	12					18014
Diuron	143		532	595	39					47	58	52	1466
Dodine			77	404	4	5							490
Fenbuconazole			12	72	45	37	39	3					207
Fenhexamid				1	98	138	63	64		14			378
Fenoxycarb			3	179	100	47	<1						328
Fenpyroximate				<1	<1	<1	8	4					12
Gibberellins	<1		<1	8	24	9	<1						41
Glufosinate-ammonium	<1			<1	83	511	105	69					768
Glyphosate	249	60	1100	2319	658	32	5		1	12	30	1170	5636
Kresoxim-methyl				146	634	132	<1						912

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Amount applied kg a.s.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Lambda-cyhalothrin		<1	2	1		<1				<1			3
Mancozeb			39	991	1423	3919	680	12					7063
MCPA			242	453	480	293	96	109		68	182	3	1926
Mecoprop-P			41	96	99	43	62	18		13	30	1	402
Methoxyfenozide	1			81	96	547	224	42					991
Myclobutanil	<1		5	509	871	440	246	77					2147
Paclobutrazol	38	<1	6	89	399	666	391	101	3			6	1698
Paraquat			5	1	57	176	19	<1		1	43		300
Penconazole	<1			52	103	425	251	75					906
Pendimethalin	1160	<1	164	79							36	56	1496
Pirimicarb				54	79	246	3	<1					382
Potassium hydrogen carbonate					218	537	287	556					1598
Propyzamide	404		9							35	10		458
Pyrimethanil			93	527	732	52	7						1411
Simazine	79		30	175	30						119	65	498
Sulphur			3485	5481	8806	10094	9310	2184		107			39466
Tar oil	18970	4867									415	27333	51585
Thiacloprid				406	233	164							804
Thiram						194	717	298					1209
Tolyfluanid			99	78	753	408	244	2772	80				4434
Triazamate				73	25	116	14						229
Urea				941	1148	1957	931	224	593	5913	1336		13044
Vinclozolin				32									32
2,4-D			408	877	100	492	73			9			1961
Amitraz					1	175		1					176
Amitrole			85	1	146	67	91			7	214	42	652

Chemicals Exposure

3. Information on para-occupational exposures has been collected in a number of published biomonitoring studies done in the USA. The following abstracts are from papers that have been identified as relevant by a review of the published literature currently being done by the Chemicals Regulation Directorate (CRD). Comments from CRD are included below each extract.

1 Acquavella *et al* 2004

Environ Health Perspect. 2004 Mar;112(3):321-6.

Comment in:

Environ Health Perspect. 2006 Nov;114(11):A633; author reply A633-4.

Glyphosate biomonitoring for farmers and their families: results from the Farm Family Exposure Study.

Acquavella JF, Alexander BH, Mandel JS, Gustin C, Baker B, Chapman P, Bleeke M.

Epidemiology, Monsanto Company, mail stop A2NE, 800 North Lindbergh Boulevard, St. Louis, MO 63167, USA. john.f.acquavella@monsanto.com

Glyphosate is the active ingredient in Roundup agricultural herbicides and other herbicide formulations that are widely used for agricultural, forestry, and residential weed control. As part of the Farm Family Exposure Study, we evaluated urinary glyphosate concentrations for 48 farmers, their spouses, and their 79 children (4-18 years of age). We evaluated 24-hr composite urine samples for each family member the day before, the day of, and for 3 days after a glyphosate application. Sixty percent of farmers had detectable levels of glyphosate in their urine on the day of application. The geometric mean (GM) concentration was 3 ppb, the maximum value was 233 ppb, and the highest estimated systemic dose was 0.004 mg/kg. Farmers who did not use rubber gloves had higher GM urinary concentrations than did other farmers (10 ppb vs. 2.0 ppb). For spouses, 4% had detectable levels in their urine on the day of application. Their maximum value was 3 ppb. For children, 12% had detectable glyphosate in their urine on the day of application, with a maximum concentration of 29 ppb. All but one of the children with detectable concentrations had helped with the application or were present during herbicide mixing, loading, or application. None of the systemic doses estimated in this study approached the U.S. Environmental Protection Agency reference dose for glyphosate of 2 mg/kg/day. Nonetheless, it is advisable to minimize exposure to pesticides, and this study did identify specific practices that could be modified to reduce the potential for exposure.

CRD Comments: The study subjects were 48 families living and working on agricultural holdings, where pesticides containing glyphosate were applied

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routinely. The families farmed at least 4 ha within 1 mile of the family home. The family members collected all urine voids in 500 ml HDPE containers. In this way, 5 consecutive 24h samples were taken from the day before to 3 days after application. Samples were stored in coolers and collected daily.

Pharmacokinetic data suggests that absorbed glyphosate is excreted unchanged, predominantly in the urine. The method of Cowell *et al.*, 1986 was used to extract and analyse the a.s. (quantification by HPLC). The method has an LOD of 1 µg/l. A value of 0.5 x LOD was assigned to results <LOD. The results were corrected for laboratory recovery results (69% for samples fortified at 10 ppb and 78% for 100 ppb.)

Systemic dose was calculated by taking into account the daily amount excreted during the study period, adjusted for incomplete excretion and pharmacokinetic recovery and individual bodyweight. The pharmacokinetic recovery corrections were based on a 95% recovery from an intravenous dosing study carried out on monkeys.

Fourteen farmers applied glyphosate post day₀, during the sampling period. Corrections were not made for this to present a conservative evaluation. 14 farmers had also applied the a.s. in the 7 days prior to the study. 29 operators had closed cabs. 34 used gloves for mixing and loading. The area treated was between 3.65 and 160 ha. A significant percentage of operators were observed to spill chemical, have skin contact with chemical and repair contaminated equipment during application.

Systemic doses were not presented in any great detail (only the GM and maximum for operators and maximum for spouses and children).

2 Alexander et al 2006

J Expo Sci Environ Epidemiol. 2006 Sep;16(5):447-56. Epub 2006 Mar 29.

Chlorpyrifos exposure in farm families: results from the farm family exposure study.

Alexander BH, Burns CJ, Bartels MJ, Acquavella JF, Mandel JS, Gustin C, Baker BA.

Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, Minnesota 55455, USA. balex@umn.edu

We used urinary biological monitoring to characterize chlorpyrifos (O,O-diethyl-O-(3,5,6-trichloro-2-pyridinyl) phosphorothioate) exposure to farm family members from Minnesota and South Carolina who participated in the Farm Family Exposure Study. Five consecutive 24-h urine samples were obtained from 34 families of licensed pesticide applicators 1 day before through 3 days after a chlorpyrifos application. Daily 3,5,6-trichloro-2-pyridinol (TCP) urinary concentrations characterized exposure profiles of the applicator, the spouse, and children aged 4-17 years. Self-reported and observed determinants of exposure were compared to the maximum postapplication TCP concentration. All participants had detectable (> or = 1 microg/l) urinary TCP concentrations at baseline. Applicators' peak TCP levels occurred the day after the application (geometric mean (GM) = 19.0 microg/l). Postapplication TCP change from baseline in the spouses and children was negligible, and the only reliable predictor of exposure was assisting with the application for children aged 12 years and older. The applicators' exposure was primarily influenced by the chemical formulation (GM = 11.3 microg/l for granular and 30.9 microg/l for liquid), and the number of loads applied. Repairing equipment, observed skin contact, and eating during the application were moderately associated TCP levels for those who applied liquid formulations. Estimated absorbed doses (microg chlorpyrifos/kg bodyweight) were calculated based on TCP excretion summed over the 4 postapplication days and corrected for pharmacokinetic recovery. The GM doses were 2.1, 0.7, and 1.0 microg/kg bodyweight for applicators, spouses, and children, respectively. Chlorpyrifos exposure to farm family members from the observed application was largely determined by the extent of contact with the mixing, loading, and application process.

CRD Comments: The study subjects were 34 families living and working on agricultural holdings, where pesticides (in this instance containing chlorpyrifos) were applied routinely. The treated crops were at least partly within 1 mile of the family home. The family members collected all urine voids in 500 ml HDPE containers. In this way, 5 consecutive 24h samples were taken from the day before to 3 days after application. Samples were stored in coolers and collected daily.

Urinary concentrations of 3,5,6-trichlorochlorpyrifos (TCP), the main metabolite of chlorpyrifos, were measured by GC/MS with an LOQ of 1 µg/l. No corrections for recovery were made, as the results from spikes were just >100% on average.

Systemic dose estimates were made based on total TCP excretion over the post-application period. The mean elimination rate for TCP was calculated from the operator's urinary TCP data using the sigma-minus method (Gibaldi and Perrier, 1975¹). The GM, GSD, 75th and 90th percentiles were presented for operators, spouses and children. A sensitivity analysis was conducted to evaluate the impact of incomplete 24-h collections.

Determinants of exposure for operators were related to application practices, e.g. formulation, area treated, loads, observed skin contact, mishaps, PPE, repairs and smoking/eating. 24 operators applied an EC by boom sprayer and 10 applied a granule in furrow treatment. The median area treated was 11ha (POEM assumes 50ha/d) and 20 operators wore gloves (14 did not). The ratio of closed cabs to open was 19:15. Observed covariates for spouses and children were proximity to treated crops, area treated, number of loads, presence of the individual and observed opportunities for direct contact with the chemical.

3 Alexander *et al* 2007

Environ Health Perspect. 2007 Mar;115(3):370-6. Epub 2006 Dec 14.

Biomonitoring of 2,4-dichlorophenoxyacetic acid exposure and dose in farm families.

Alexander BH, Mandel JS, Baker BA, Burns CJ, Bartels MJ, Acquavella JF, Gustin C.

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OBJECTIVE: We estimated 2,4-dichlorophenoxyacetic acid (2,4-D) exposure and systemic dose in farm family members following an application of 2,4-D on their farm. **METHODS:** Farm families were recruited from licensed applicators in Minnesota and South Carolina. Eligible family members collected all urine during five 24-hr intervals, 1 day before through 3 days after an application of 2,4-D. Exposure profiles were characterized with 24-hr urine 2,4-D concentrations, which then were related to potential predictors of exposure. Systemic dose was estimated using the urine collections from the application day through the third day after application. **RESULTS:** Median urine 2,4-D concentrations at baseline and day after application were 2.1 and 73.1 microg/L for applicators, below the limit of detection, and 1.2 microg/L for spouses, and 1.5 and 2.9 microg/L for children. The younger children (4-11 years of age) had higher median post-application concentrations than the older children (> or = 12 years of age) (6.5 vs. 1.9 microg/L). The geometric mean systemic doses (micrograms per kilogram body weight) were 2.46 (applicators), 0.8 (spouses), 0.22 (all children), 0.32 (children 4-11 years of age), and 0.12 (children > or = 12 years of age). Exposure to the spouses and children was primarily determined by direct contact with the application process and the number of acres treated. Multivariate models identified glove use, repairing equipment, and number of acres treated as predictors of exposure in the applicators. **CONCLUSIONS:** We observed considerable heterogeneity of 2,4-D exposure among farm family members, primarily

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attributable to level of contact with the application process. Awareness of this variability and the actual magnitude of exposures are important for developing exposure and risk characterizations in 2,4-D-exposed agricultural populations.

CRD Comments: The target population was families living and working on farms where 2,4-D was to be used as part of the normal operation on at least 3.6 ha of cropland, some of which was within 1 mile of the family home. The family members collected all urine voids in 500 ml HDPE containers. In this way, 5 consecutive 24h samples were taken from the day before to 3 days after application. Samples were stored in coolers and collected daily.

2,4-D is excreted in the urine as 2,4-D or a conjugate. The urine samples were analysed by GC/MS. The intraday analysis of relative recovery (range 1 – 500 µg/l) was 85-90%. The LOQ was 1 µg/l.

Creatinine was measured and the exposure was corrected accordingly (2,4-D per gram creatinine.) Systemic dose was estimated by the following procedure. Daily total volumes were multiplied by the 2,4-D concentration to estimate daily exposure on days 0 to 3. A mean elimination rate was calculated from the operator's urinary 2,4-D data using the sigma-minus method. It was assumed that 93% clearance of 2,4-D is achieved (Sauerhoff *et al.*, 1977) and a final correction for incomplete urine collection was made.

Indicators of exposure for children and spouses were proximity of the house to treated fields, the area treated, number of loads, presence as a bystander and observation of opportunity for direct contact with the chemical. Determinants for operators included area treated, number of loads, observed skin contact/ spills etc., use of PPE and smoking/eating.

4 Bernard *et al* 2001

Arch Environ Contam Toxicol. 2001 Aug;41(2):237-40.

Environmental residues and biomonitoring estimates of human insecticide exposure from treated residential turf.

Bernard CE, Nuygen H, Truong D, Krieger RI.

Personal Chemical Exposure Program, Department of Entomology, University of California, Riverside, California 92521, USA.

Intentional and unavoidable human exposure is a consequence of using pesticides to nurture and protect residential turf. Limited exposure studies have been conducted for assessing potential human exposure of turf residues. Exposure was measured in persons who performed a 20-minute structured activity (Jazzercise) on chlorpyrifos (CP)-treated Kentucky bluegrass (12 +/- 4 microg CP/cm(2)). CP exposure was measured by determining urine clearance of the 3,5,6-trichloro-2-pyridinol (TCP). Study participants wore either 100% cotton whole body dosimeters (union suit, gloves, and socks) or exercise suits (shorts and a sports top or one-piece suit with similar amounts of exposed skin). An average of 1.6 mg CP/person was extracted from whole body dosimeters worn by study participants. The measured residue

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transfer was well below the 35 mg CP/person estimated using the US EPA standard operating procedures. Biomonitoring based on urine clearance of TCP indicated that an average of 1.3 microg CP/kg was absorbed. Absorbed dosages (0.5 to 2 microg CP/kg) derived from transferable residue on cotton cloths pressed to the turf with a weighted roller were similar to estimates from biomonitoring. A very limited amount of CP applied to turf is available for transfer and absorption during intensive human contact.

CRD Comment: Exposure was measured in twenty two persons performing a 20 minute structured activity (Jazzercise) on chlorpyrifos treated turf. A 22% chlorpyrifos spray solution was applied to the turf at a rate of 1.12 kg a.s./ha. The exposure period began when the treated turf was touch dry, approximately 3 hours after application. The participants (all female) wore either 100% cotton whole body clothing (body suit, gloves and socks) or an exercise suit (shorts and sports top).

Urine (seven consecutive morning voids) was collected from all participants and analysed for TCP to estimate chlorpyrifos equivalents. Urine collection commenced the day before the exercise activity and continued for 5 days after the exposure event. Daily TCP clearance was estimated using a creatinine correction of 1 g/day for female adults (Synder 1994). Complete clearance of chlorpyrifos was assumed in estimates of absorbed dose based on the 27 hour half life and approximately 72% clearance of chlorpyrifos in urine (Nolan et al 1984). A method of analysis for analysis of the urine samples is described in the paper but no details of laboratory for field recovery are given.

The author comments that use of TCP potentially overestimates exposure to chlorpyrifos as TCP may result from other exposures, notably TCP as a food residue and a trace environmental contaminant

5 Fenske *et al* 2000

Environ Health Perspect. 2000 Jun;108(6):515-20.

Biologically based pesticide dose estimates for children in an agricultural community.

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Current pesticide health risk assessments in the United States require the characterization of aggregate exposure and cumulative risk in the setting of food tolerances. Biologic monitoring can aggregate exposures from all sources and routes, and can integrate exposures for chemicals with a common mechanism of action. Its value was demonstrated in a recent study of organophosphorus (OP) pesticide exposure among 109 children in an agricultural community in Washington State; 91

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of the children had parents working in agriculture. We estimated individual OP pesticide doses from urinary metabolite concentrations with a deterministic steady state model, and compared them to toxicologic reference values. We evaluated doses by assuming that metabolites were attributable entirely to either azinphos-methyl or phosmet, the two OP pesticides used most frequently in the region. Creatinine-adjusted average dose estimates during the 6- to 8-week spraying season ranged from 0 to 36 microg/kg/day. For children whose parents worked in agriculture as either orchard applicators or as fieldworkers, 56% of the doses estimated for the spray season exceeded the U.S. Environmental Protection Agency (EPA) chronic dietary reference dose, and 19% exceeded the World Health Organization acceptable daily intake values for azinphos-methyl. The corresponding values for children whose parents did not work in agriculture were 44 and 22%, respectively. The percentage of children exceeding the relevant reference values for phosmet was substantially lower (< 10%). Single-day dose estimates ranged from 0 to 72 microg/kg/day, and 26% of these exceeded the EPA acute reference dose for azinphos-methyl. We also generated dose estimates by adjustment for total daily urine volume, and these estimates were consistently higher than the creatinine-adjusted estimates. None of the dose estimates exceeded the empirically derived no-observable-adverse-effect levels for these compounds. The study took place in an agricultural region during a period of active spraying, so the dose estimates for this population should not be considered representative of exposures in the general population. The findings indicate that children living in agricultural regions represent an important subpopulation for public health evaluation, and that their exposures fall within a range of regulatory concern. They also demonstrate that biologically based exposure measures can provide data for health risk evaluations in such populations.

CRD comments: The study involved 109 children. 91 were from households with at least one adult engaged in field based agriculture. The other 18 were from non-agricultural backgrounds and lived at least 402m from treated farmland. The May to June study period coincided with spraying against codling moth with phosmet and azinphos methyl. Single voids were taken from children on two occasions at their convenience. The second sample was taken 3-7 days after the first and all within the 6-8 week spraying season.

The dialkylphosphate metabolites DMP, DMTP and DMDTP were analysed by GC. However, the DMP results were unreliable and gave recoveries of <50%. The LOQs were 0.015-0.030 µg/l and values of 0.5 x LOQ were assigned to samples <LOQ.

A deterministic approach to systemic dose estimation was taken, allowing direct back-calculation from metabolite concentrations. The 2 samples for each child were averaged. (In a few cases only a single sample was available). The samples were corrected for extraction efficiency, then metabolite concentrations were converted to molar equivalents and summed to produce a single dialkyl-phosphate concentration for each sample. These were then converted to OP concentrations assuming a m. wt. of 317 g/l for azinphos-methyl and phosmet. Lastly, the OP concentrations were converted by taking into account age related creatinine excretion or urinary excretion volume and bodyweight.

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The results were presented as systemic dose estimates (for children of operators (n=49), children of farm workers (n=13) and control children.

6 Krieger and Dinoff 2000

Arch Environ Contam Toxicol. 2000 May;38(4):546-53.

Malathion deposition, metabolite clearance, and cholinesterase status of date dusters and harvesters in California.

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Date gardens in the Coachella Valley in California typically receive multiple treatments of malathion to control major insect pests. Variable amounts of malathion dust retention by skin and clothing and individual work behaviors limit the usefulness of clothing as an exposure dosimeter in date dusters and harvesters. To determine malathion absorption in workers, urine clearance of dimethyl phosphates (alkyl phosphates; AP) and malathion mono- (MCA) and di- (DCA) acids were estimated from date dusters (loaders/applicators) and harvesters (both on ground and high in trees). A series of self-administered doses of malathion were either ingested in gelatin capsules or applied to the volar surface of the forearm to guide biomonitoring. Each of the dimethyl phosphates (dimethylthio > dimethyldithio > dimethyl-) and both malathion mono- and diacids were present in urine as soon as 2-3 h of work. On a micromole basis dimethylthiophosphate and the malathion acids (MCA > DCA) were the most prominent metabolites in urine. Applicator exposures ranged from 95-210 mg equivalents per day (1-3 mg/kg-day). Harvester exposures ranged from 1-270 microg/kg-day. Mid-season Monday morning urine specimens before work contained low or unmeasurable levels of malathion acids, indicating that malathion is rapidly metabolized and cleared from the body in the urine. Saliva was not useful for biomonitoring. No inhibition of cholinesterase activity was measured in any members of two separate crews of harvesters who had previous prolonged dust exposure (1 and 2 months).

CRD comment: A biomonitoring study of date dusters and harvesters exposed to malathion is reported. Whilst there are no equivalent UK uses for this use of malathion, as a separate part of the study, the exposure of a family (weeder, spouse, daughter and son) who lived within a date garden was monitored to evaluate their exposure. Spot measurements on two children (aged 9 and 4) and their other family members (duster and spouse) were made along with two other workers (duster and a weeder) who lived with them. The dusters provided pre and post shift urine specimens for 4 consecutive days.

Urine was analysed for dimethyl phosphates (alkyl phosphates; AP) and malathion mono-(MCA) and diacids (DCA) to estimate the absorbed dose of malathion. Results were expressed as mole equivalents malathion /g creatinine when measurements of all metabolites were available. In other cases the amounts of MCA and DCA ($\mu\text{g/g}$ creatinine; 1.5 l urine per day) were summed, multiplied by 2 to account for the AP's and by daily creatinine (1.7 g

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for adult male, 1.0 for adult female and 0.08 g/year of age for children to age 10) (Synder 1994).

These samples were normalised to 24 hour specimens using either a volume or creatinine correction. The study reports both methodologies gave similar results.

4. The data from the above papers are summarised in Table 3 below.

Table 3. Comparison of systemic exposure based on urinary metabolites biomonitoring for farm families

Study	Active substance(s)	Exposure group	n	Systemic exposure (mg/kg bw/d)
Acquavella <i>et al</i> , 2004	Glyphosate	Spouses	48	0.00004 maximum
		Children	79	0.0008 maximum
Alexander <i>et al</i> , 2006	Chlorpyrifos	Spouses (GM)	34	0.0007 geometric mean 0.0041 maximum
		Children (GM)	50	0.001 geometric mean 0.0063 maximum
Alexander <i>et al</i> , 2007.	2,4-D	Spouses	34	0.00008 geometric mean 0.00016 75 th percentile 0.00025 90 th percentile 0.00114 maximum
		Children	53	0.00022 geometric mean 0.00046 75 th percentile 0.000107 90 th percentile 0.03107 maximum
Bernard <i>et al</i> (2001)	Chlorpyrifos	Female (Jazzercise activity) (mean)	5 (whole body covered)	0.0011 mean
			6 (1 piece dance suit)	0.0015 mean
			11 (2 piece dance suit)	0.0014 mean
Fenske <i>et al</i> , 2000	Azinphos-methyl/phosmet	Children (of operators)	49	0.0054 ± 0.0062 mean ± SD 0.0078 75 th percentile 0.0153 ^a max*
		Children (of workers)	13	0.0038 ± 0.0044 mean ± SD 0.0045 75 th percentile 0.0153 maximum
		Children (control)	14	0.0035 ± 0.0050 mean ± SD

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				0.0073 75 th percentile 0.015 maximum
Krieger and Dinoff (2000)	Malathion	Girl aged 9	1	0.0006
		Boy aged 4	1	0.005
		Spouse	1	0.004

* spray season estimates calculated by volume adjusted presented here as these were highest

^a there appears to be an error in the paper and this value should be 0.029 mg/kg bw/d. In addition, higher maximum values were observed in siblings of the study focus children up to 0.036 mg/kg bw/d, and up to 0.072 mg/kg bw/d for single day samples.