Dicamba (human health related, incl. rodent studies)
20110909

1. Kimura O, Tsukagoshi K, Hayasaka M, Endo T. 2011 Jul 16. Uptake of triclopyr (3,5,6-trichloro-2-pyridinyloxyacetic acid) and dicamba (3,6-dichloro-2-methoxybenzoic acid) from the apical membranes of the human intestinal Caco-2 cells. Arch Toxicol .Abstract: We investigated whether the uptake of triclopyr (3, 5, 6-trichloro-2-pyridinyloxyacetic acid) and dicamba (3,6-dichloro-2-methoxybenzoic acid) across the apical membrane of Caco-2 cells was mediated via proton-linked monocarboxylic acid transporters (MCTs). The uptake of triclopyr from the apical membranes was fast, pH-, temperature-, and concentration dependent, required metabolic energy to proceed, and was competitively inhibited by monocarboxylic acids such as benzoic acid and ferulic acid (substrates of L: -lactic acid-insensitive MCTs), but not by L: -lactic acid. Thus, the uptake of triclopyr in Caco-2 cells appears to be mediated mainly via L: -lactic acid-insensitive MCTs. In contrast, the uptake of dicamba (a benzoic acid derivative) was slow, and it was both pH- and temperature dependent. Coincubation with ferulic acid did not decrease the uptake of dicamba, although coincubation with benzoic acid moderately decreased it. The uptake of dicamba appears to be mediated mainly via passive diffusion, which is in contrast to the uptake of benzoic acid via MCTs. We speculate that the substituted groups in dicamba may inhibit uptake via MCTs.

2. Band PR, Abanto Z, Bert J, Lang B, Fang R, Gallagher RP, Le ND. 2011 Feb 1. Prostate cancer risk and exposure to pesticides in British Columbia farmers. Prostate 71(2):168-83.Abstract: BACKGROUND: Several epidemiologic studies have reported an increased risk of prostate cancer among farmers. Our aim was to assess the risk of developing prostate cancer in relation to exposure to specific active compounds in pesticides. METHOD: A case-control approach was used with 1,516 prostate cancer patients and 4,994 age-matched internal controls consisting of all other cancer sites excluding lung cancer and cancers of unknown primary site. Lifetime occupational history was obtained through a self-administered questionnaire and used in conjunction with a job exposure matrix to estimate the participants' lifetime cumulative exposure to approximately 180 active compounds in pesticides. Conditional logistic regression was used to assess prostate cancer risk, adjusting for potential confounding variables and effect modifiers. These include age, ethnicity, alcohol consumption, smoking, education, and proxy respondent. RESULTS AND CONCLUSIONS: The significant association between prostate cancer risk and exposure to DDT (OR = 1.68; 95% CI: 1.04-2.70 for high exposure), simazine (OR = 1.89; 95% CI: 1.08-3.33 for high exposure), and lindane (OR = 2.02; 95% CI: 1.15-3.55 for high exposure) is in keeping with those previously reported in the literature. We also observed a significant excess risk for several active ingredients that have not been previously reported in the literature such as dichlone, dinoseb amine, malathion, endosulfan, 2,4-D, 2,4-DB, and carbaryl. Some findings in our study were not consistent with those reported in the literature, including captan, dicamba, and diazinon. It is possible that these findings showed a real association and the inconsistencies reflected differences of characteristics between study populations.

3. Greco L, Pellerin J, Capri E, Garnerot F, Louis S, Fournier M , Sacchi A, Fusi M, Lapointe D, Couture P. 2011 Jan. Physiological effects of temperature and a herbicide mixture on the soft-shell clam Mya arenaria (Mollusca, Bivalvia). Environ Toxicol Chem 30(1):132-41.Abstract: The aim of the current study was to investigate effects of temperature and a mixture of herbicides on the physiological status of the bivalve Mya arenaria. Bivalves acclimated to two temperatures (7 and 18 degrees C) were exposed for 28 d to 0.01 mg/L of a pesticide formulation containing dichlorophenoxyacetic acid (2,4-D), 2-(2-methyl-4-chlorophenoxy) propionic acid (mecoprop), and 3,6-dichloro-2-methoxybenzoic acid (dicamba). At days 7, 14, and 28, mortality, immune parameters (hemocyte number, phagocytic activity, and efficiency), biomarkers of oxidative stress (catalase [CAT] and superoxide dismutase [SOD] activities and malondialdehyde [MDA] content), the metabolic enzyme cytochrome C oxidase (CCO), a biomarker of pesticide exposure (acetylcholinesterase [AChE]), and the activity of an enzyme related to gametogenesis (aspartate transcarbamylase [ATCase]) were monitored in clam tissues. Gonadosomatic index (GSI), condition factor (CF), and sex were also assessed. In clams acclimated to 7 degrees C, exposure to pesticide enhanced CCO activity and CF and decreased MDA content, hemocyte number, CAT, and SOD

activities. In clams kept at 18 degrees C, pesticide effects appeared minor compared with samples kept at 7 degrees C. In bivalves acclimated to 18 degrees C, CCO, SOD, and ATCase activity and MDA content were enhanced, and hemocyte number, CAT, and AchE activities and phagocytosis were suppressed. In samples exposed to pesticides, increased temperature enhanced MDA content and CCO and SOD activity and suppressed hemocyte number and CAT and AchE activity. A gradual sexual maturation was observed in both sexes through experimental time, but females had a higher sensitivity to temperature and pesticides compared to males. Increased temperature altered the ability of the sentinel species Mya arenaria to respond to pesticide exposures. Further work is needed to understand the impacts of increasing temperature on the whole St. Lawrence estuary ecosystem.

4. Brkic D, Gasic S, Radivojevic L, Szakonyne-Pasics I, Karan V, Neskovic N. 2011 . Avalon (R) (bentazon plus dicamba) herbicide: Subchronic toxicity to rats. Toxicol Lett 205 Suppl 1:S228-S229.

5. Harris SA, Villeneuve PJ, Crawley CD, Mays JE, Yeary RA, Hurto KA, Meeker JD. 2010 Sep 22. National study of exposure to pesticides among professional applicators: an investigation based on urinary biomarkers. J Agric Food Chem 58(18):10253-61. Abstract: Epidemiologic studies of pesticides have been subject to important biases arising from exposure misclassification. Although turf applicators are exposed to a variety of pesticides, these exposures have not been well characterized. This paper describes a repeated measures study of 135 TruGreen applicators over three spraying seasons via the collection of 1028 urine samples. These applicators were employed in six cities across the United States. Twenty-four-hour estimates (mug) were calculated for the parent compounds 2,4-D, MCPA, mecoprop, dicamba, and imidacloprid and for the insecticide metabolites MPA and 6-CNA. Descriptive statistics were used to characterize the urinary levels of these pesticides, whereas mixed models were applied to describe the variance apportionment with respect to city, season, individual, and day of sampling. The contributions to the overall variance explained by each of these factors varied considerably by the type of pesticide. The implications for characterizing exposures in these workers within the context of a cohort study are discussed.

6. Weichenthal S, Moase C, Chan P. 2010 Aug. A review of pesticide exposure and cancer incidence in the Agricultural Health Study cohort. Environ Health Perspect 118(8):1117-25. Abstract: OBJECTIVE: We reviewed epidemiologic evidence related to occupational pesticide exposures and cancer incidence in the Agricultural Health Study (AHS) cohort. DATA SOURCES: Studies were identified from the AHS publication list available at http://aghealth.nci.nih.gov as well as through a Medline/PubMed database search in March 2009. We also examined citation lists. Findings related to lifetime-days and/or intensity-weighted lifetime-days of pesticide use are the primary focus of this review, because these measures allow for the evaluation of potential exposure-response relationships. DATA SYNTHESIS: We reviewed 28 studies; most of the 32 pesticides examined were not strongly associated with cancer incidence in pesticide applicators. Increased rate ratios (or odds ratios) and positive exposure-response patterns were reported for 12 pesticides currently registered in Canada and/or the United States (alachlor, aldicarb, carbaryl, chlorpyrifos, diazinon, dicamba, S-ethyl-N,N-dipropylthiocarbamate, imazethapyr, metolachlor, pendimethalin, permethrin, trifluralin). However, estimates of association for specific cancers were often imprecise because of small numbers of exposed cases, and clear monotonic exposure-response patterns were not always apparent. Exposure misclassification is also a concern in the AHS and may limit the analysis of exposure-response patterns. Epidemiologic evidence outside the AHS remains limited with respect to most of the observed associations, but animal toxicity data support the biological plausibility of relationships observed for alachlor, carbaryl, metolachlor, pendimethalin, permethrin, and trifluralin. CONCLUSIONS: Continued follow-up is needed to clarify associations reported to date. In particular, further evaluation of registered pesticides is warranted.

7. Mukherjee M, Muraleedharannair P, Karmakar UK, Datta BK, Sar TK, Chakraborty AK, Bhattacharya A, Choudhury A, Mandal TK. 2010 Jan 30. Toxicokinetics and recovery studies of dicamba dimethyl amine salt in goats following single oral administration. J Sci Food Agric 90(2):257-66. Abstract: BACKGROUND: Toxicokinetics and recovery studies of dicamba dimethyl amine salt (DDAS) were conducted to obtain more information about its toxicity and tissue retention in farm animals. RESULTS: The minimum oral toxic dose level of DDAS was determined as 1400 mg kg(-1) body

weight. In the toxicokinetic study, blood DDAS concentration of 55.6 +/- 0.59 microg mL(-1) (mean +/- standard error) was detected at 0.08 h, which peaked to 102.3 +/- 5.03 microg mL(-1) at 0.25 h, and declined to a minimum of 4.1 +/- 0.06 microg mL(-1) at 36 h. In recovery studies, DDAS concentration in urine began to increase significantly ($P < 0.05$) from 12 h, peaked at 24 h and declined from 48 h onwards. Maximum excretion through faeces was at 24 h and was complete by 144 h. The residual level in tissues decreased significantly ($P < 0.05$) on day 7 as compared to day 4. In histopathological studies, cellular alterations in lungs, liver, kidney, adrenal gland and spleen were found. CONCLUSION: DDAS persists in the body for a shorter period and its major excretory route is through urine. DDAS has lower affinity to accumulate in tissues, and intensity of cellular alterations is not severe after single-dose oral administration.

8. Vitali M, Protano C, Del Monte A, Ensabella F, Guidotti M. 2009 Jul. Operative modalities and exposure to pesticides during open field treatments among a group of agricultural subcontractors. Arch Environ Contam Toxicol 57(1):193-202.[1]Abstract: This paper reports the results of a field study of occupational pesticide exposure (respiratory and dermal) among a group of Italian agricultural subcontractors. These workers consistently use pesticides during much of the year, thus resulting in a high exposure risk. Ten complete treatments were monitored during spring/summer. Pesticides that were applied included azinphos-methyl, dicamba, dimethoate, terbuthylazine, and alachlor. Several observations were made on worker operative modalities and the use of personal protective equipment (PPE) during work. Total potential and actual exposure ranged from 14 to 5700 microg and from 0.04 to 4600 microg, respectively. Dermal exposure contributed substantially more than inhalation to the total exposure (93.9-100%). Hand contamination ranged from 0.04 to 4600 microg and was the major contributor to dermal exposure. Penetration through specific protective garments was less than 2.4% in all cases, although penetration through general work clothing was as high as 26.8%. The risk evaluation, based on comparison between acceptable daily intake and total absorbed doses, demonstrates that it is presumable to expect possible health effects for workers regularly operating without PPE and improper tractors. Comparisons between exposure levels and operative modalities highlighted that complete PPE and properly equipped tractors contributed to a significant reduction in total exposure to pesticides during agricultural activities. In conclusion, monitored agricultural subcontractors presented very different levels of pesticide exposure due to the high variability of operative modalities and use of PPE. These results indicate the need to critically evaluate the efficacy of training programs required for obtaining a pesticide license in Italy.

9. Protano C, Guidotti M, Vitali M. 2009 Jul. Performance of different work clothing types for reducing skin exposure to pesticides during open field treatment. Bull Environ Contam Toxicol 83(1):115-9.[1]Abstract: The aim of this study was to estimate the performance of different work clothing types for reducing skin exposure to five pesticides (azinphos-methyl, terbutylazine, alachlor, dimethoate, and dicamba) in field distribution by tractor equipped with boom sprayer. Performance was assessed by measuring the penetration factors of different types of work clothing. The results show that the protection offered by personal protective equipment (PPE) was always >97%, whereas the performance of cotton garments ranged from 84.1% to 92.5%. The different cotton garments differed significantly in their permeability, and the upper part of the body was the anatomical region showing the greatest values of the penetration factors. These results confirm the necessity of using PPE properly to minimise dermal exposure to pesticides.

10. Yang YJ, Haught RC, Goodrich JA. 2009 Jun. Real-time contaminant detection and classification in a drinking water pipe using conventional water quality sensors: techniques and experimental results. J Environ Manage 90(8):2494-506.[1]Abstract: Accurate detection and identification of natural or intentional contamination events in a drinking water pipe is critical to drinking water supply security and health risk management. To use conventional water quality sensors for the purpose, we have explored a real-time event adaptive detection, identification and warning (READiw) methodology and examined it using pilot-scale pipe flow experiments of 11 chemical and biological contaminants each at three concentration levels. The tested contaminants include pesticide and herbicides (aldicarb, glyphosate and dicamba), alkaloids (nicotine and colchicine), E. coli in terrific broth, biological growth media (nutrient broth, terrific broth, tryptic soy broth), and inorganic chemical compounds (mercuric chloride and potassium ferricyanide). First, through adaptive transformation of

the sensor outputs, contaminant signals were enhanced and background noise was reduced in time-series plots leading to detection and identification of all simulated contamination events. The improved sensor detection threshold was 0.1% of the background for pH and oxidation-reduction potential (ORP), 0.9% for free chlorine, 1.6% for total chlorine, and 0.9% for chloride. Second, the relative changes calculated from adaptively transformed residual chlorine measurements were quantitatively related to contaminant-chlorine reactivity in drinking water. We have shown that based on these kinetic and chemical differences, the tested contaminants were distinguishable in forensic discrimination diagrams made of adaptively transformed sensor measurements.

11. Gonzalez NV, Soloneski S, Larramendy ML. 2009 Apr 15. Dicamba-induced genotoxicity in Chinese hamster ovary (CHO) cells is prevented by vitamin E. J Hazard Mater 163(1):337-43. Abstract: In the present study the cytogenetic and genotoxic effect of benzoic herbicide dicamba and its Argentinean commercial formulation banvel (57.71% dicamba) was evaluated and whether this effect is mediated through oxidative damage or not. The protective role of vitamin E was also studied. Sister chromatid exchange (SCE) frequency, cell-cycle progression, and cell viability analyses in CHO cells were used as in vitro end-points. Treatments with the test compounds were performed either during 24h (Protocol A) or 12h (Protocol B) before harvesting. Protocol A showed that vitamin E decreased pesticide SCE induction, corrected the cell-cycle delay and partially protected cell-death only in 500 microg/ml dicamba-treated cultures. A similar trend was found in banvel-treated cultures. Protocol B revealed similar protective role of vitamin E only for dicamba-induced geno- and cytotoxicity. Based on these observations it could be suggested that dicamba injures DNA by delivering reactive oxygen species rather than by another type of mechanism/s. Although banvel mimics the effect observed by dicamba, its formulation contains other xenobiotic/s agents able to induce cellular and DNA damage by a different mechanism/s. Further investigations are needed to acquire a comprehensive knowledge of the possible mechanism/s through dicamba and banvel exert their toxic effects.

12. Yarpuz-Bozdogan N. 2009. Assessing the environment and human health risk of herbicide application in wheat cultivation. Journal of Food Agriculture & Environment 7(3-4):775-781. Abstract: In Turkey, herbicide active ingredient (a.i.) was used approximately 25% in pesticide applications in 2007. In Adana province, Turkey, 10 numbers of active ingredients were used for weed control in wheat cultivation areas in 2007. These are: fenoxaprop-p-ethyl, clodinafop-propargyl, mesosulfuronmethyl, iodosulfuron-methyl-sodium, florasulam, flumetsulam, 2,4-D acid dimethylamin, tribenuron-methyl, triasulfuron and dicamba. In this study, total risk of herbicide on human health and environment were assessed by POCER (The Pesticide Occupational and Environmental Risk) indicator. In this study, it was obtained that clodinafop-propargyl a.i. has high potential risk for worker (1.000) and operator (0.909) due to 1.000 of maximum EF values. Flumetsulam a.i, and triasulfuron a.i. have no total risk for human health and environment due to 0 EF values in all risk indicators. In this study, it was shown that human health has been affected higher than environment in herbicide applications. It was determined that risk for human health contains 88.7% of total risk values in herbicide application for wheat cultivation areas. It was shown that, in this study, some factors affecting proper application of herbicides such as application techniques and equipment, meteorological conditions and application doses should be taken into account for protecting of human health and environment.

13. Weselak M, Arbuckle TE, Wigle DT, Walker MC, Krewski D. 2008 Aug. Pre- and post-conception pesticide exposure and the risk of birth defects in an Ontario farm population. Reprod Toxicol 25(4):472-80. Abstract: The use of pesticides has enhanced the health and economies of nations around the world by improving crop production. However, pesticides may pose health risks, particularly to the fetus and young children. In a secondary analysis of the Ontario Farm Family Health Study, we explored the relationship between birth defects and parental pesticide exposure during the 3 months prior to conception and the first trimester of pregnancy. A total of 3412 pregnancies were included in the study. Logistic regression fit by maximum likelihood was used in the analysis. The results showed that pre-conception exposure to both cyanazine (odds ratio=4.99, 95% confidence interval: 1.63-15.27) and dicamba (OR=2.42, 95% CI: 1.06-5.53) were associated with increased risk of birth defects in male offspring. Nevertheless, given the self-reported nature of the exposure and outcomes

in this study, the present findings should be considered primarily as hypothesis generating, requiring verification in subsequent investigations.

14. Gonzalez NV, Soloneski S, Larramendy ML. 2007 Dec 1. The chlorophenoxy herbicide dicamba and its commercial formulation Banvel induce genotoxicity and cytotoxicity in Chinese hamster ovary (CHO) cells. Mutat Res 634(1-2):60-8.Abstract: The sister chromatid exchange (SCE) frequency, the cell-cycle progression analysis, and the single cell gel electrophoresis technique (SCGE, comet assay) were employed as genetic end-points to investigate the geno- and citotoxicity exerted by dicamba and one of its commercial formulation banvel (dicamba 57.71%) on Chinese hamster ovary (CHO) cells. Log-phase cells were treated with 1.0-500.0 microg/ml of the herbicides and harvested 24 h later for SCE and cell-cycle progression analyses. All concentrations assessed of both test compounds induced higher SCE frequencies over control values. SCEs increased in a non-dose-dependent manner neither for the pure compound (r=0.48; P>0.05) nor for the commercial formulation (r=0.58, P>0.05). For the 200.0 microg/ml and 500.0 microg/ml dicamba doses and the 500.0 microg/ml banvel dose, a significant delay in the cell-cycle progression was found. A regression test showed that the proliferation rate index decreased as a function of either the concentration of dicamba (r=-0.98, P<0.05) or banvel (r=-0.88, P<0.01) titrated into cultures in the 1.0-500.0 microg/ml dose-range. SCGE performed on CHO cells after a 90 min pulse-treatment of dicamba and banvel within a 50.0-500.0 microg/ml dose-range revealed a clear increase in dicamba-induced DNA damage as an enhancement of the proportion of slightly damaged and damaged cells for all concentrations used (P<0.01); concomitantly, a decrease of undamaged cells was found over control values (P<0.01). In banvel-treated cells, a similar overall result was registered. Dicamba induced a significant increase both in comet length and width over control values (P<0.01) regardless of its concentration whereas banvel induced the same effect only within 100.0-500.0 microg/ml dose range (P<0.01). As detected by three highly sensitive bioassays, the present results clearly showed the capability of dicamba and banvel to induce DNA and cellular damage on CHO cells.

15. Bushek D, Heidenreich M, Porter D. 2007 Oct. The effects of several common anthropogenic contaminants on proliferation of the parasitic oyster pathogen Perkinsus marinus. Mar Environ Res 64(4):535-40.Abstract: Estuarine contaminants have varying effects on estuarine inhabitants and host-parasite interactions. Some field collected contaminant mixtures have been shown to increase oyster susceptibility to parasitism by Perkinsus marinus, but little is known about contaminant effects on the parasite itself. This study examined the effects of ammonium, nitrate, phosphate, fluoranthene, phenanthrene and a common herbicide mixture (Weed-B-Gone) on in vitro proliferation of P. marinus. Only the herbicide had a significant effect, but not at or below the manufacture's recommended application rate (7.81 microl ml(-1)). The herbicide's active ingredients (3.1% 2,4-dichlorophenoxyacetic acid, 10.6% mecoprop and 1.3% dicamba) mimic growth hormones of broadleaf plants; over stimulation of growth results in death. The mode of action of these compounds on P. marinus warrants further investigation which may provide insight towards the identification of biocides to control P. marinus.

16. Donald DB, Cessna AJ, Sverko E, Glozier NE. 2007 Aug. Pesticides in surface drinking-water supplies of the northern Great Plains. Environ Health Perspect 115(8):1183-91.Abstract: BACKGROUND: Human health anomalies have been associated with pesticide exposure for people living in rural landscapes in the northern Great Plains of North America. OBJECTIVE: The objective of this study was to investigate the occurrence of 45 pesticides in drinking water from reservoirs in this area that received water primarily from snowmelt and rainfall runoff from agricultural crop lands. METHODS: Water from 15 reservoirs was sampled frequently during the spring pesticide application period (early May to mid-August) and less frequently for the remainder of the year. Drinking water was sampled in early July. Sample extracts were analyzed for pesticide content using mass spectrometric detection. RESULTS: We detected two insecticides and 27 herbicides in reservoir water. Consistent detection of a subset of 7 herbicides suggested that atmospheric deposition, either directly or in rain, was the principal pathway from fields to the reservoirs. However, the highest concentrations and number of herbicides in drinking water were associated with runoff from a localized 133-mm rainfall over 15 days toward the end of spring herbicide

application. Water treatment removed from 14 to 86% of individual herbicides. Drinking water contained 3-15 herbicides (average, 6.4). CONCLUSIONS: We estimated the mean annual calculated concentration of herbicides in drinking water to be 75 ng/L (2,4-dichlorophenoxy)acetic acid, 31 ng/L (2-chloro-4-methylphenoxy)acetic acid, 24 ng/L clopyralid, 11 ng/L dichlorprop, 4 ng/L dicamba, 3 ng/L mecoprop, and 1 ng/L bromoxynil. The maximum total concentration of herbicides in drinking water was 2,423 ng/L. For the seven herbicides with established drinking water guidelines, all concentrations of the individual chemicals were well below their respective guideline. However, guidelines have not been established for the majority of the herbicides found in drinking water or for mixtures of pesticides.

17. Chu S, Henny CJ, Kaiser JL, Drouillard KG, Haffner GD, Letcher RJ. 2007 Jan. Dacthal and chlorophenoxy herbicides and chlorothalonil fungicide in eggs of osprey (Pandion haliaetus) from the Duwamish-Lake Washington-Puget Sound area of Washington state, USA. Environ Pollut 145(1):374-81. Abstract: Current-use chlorophenoxy herbicides including 2,4-dichlorophenoxyacetic acid, dicamba, triclopyr, dicamba, dimethyl tetrachloroterephthalate (DCPA or dacthal), and the metabolite of pyrethroids, 3-phenoxybenzoic acid (3-PBA), and the fungicide, chlorothalonil, were investigated in the eggs of osprey (Pandion haliaetus) that were collected from 15 sites from five study areas Puget Sound/Seattle area of Washington State, USA. DCPA differs from acidic chlorophenoxy herbicides, and is not readily hydrolyzed to free acid or acid metabolites, and thus we developed a new method. Of the 12 chlorophenoxy herbicides and chlorothalonil analyzed only DCPA could be quantified at six of these sites (2.0 to 10.3 pg/g fresh weight). However, higher levels (6.9 to 85.5 pg/g fresh weight) of the unexpected DCPA structural isomer, dimethyl tetrachlorophthalate (diMe-TCP) were quantified in eggs from all sites. diMe-TCP concentrations tended to be higher in eggs from the Everett Harbor area. As diMe-TCP is not an industrial product, and not commercially available, the source of diMe-TCP is unclear. Regardless, these findings indicate that DCPA and diMe-TCP can be accumulated in the food chain of fish-eating osprey, and transferred in ovo to eggs, and thus may be of concern to the health of the developing chick and the general reproductive health of this osprey population.

18. Weselak M, Arbuckle TE, Wigle DT, Krewski D. 2007. In utero pesticide exposure and childhood morbidity. Environ Res 103(1):79-86. Abstract: In humans. immune development begins early in embryonic life and continues throughout the early postnatal period. Although a number of pesticides have been observed to induce developmental immunotoxicity in mice, few human studies have examined the long term effects of in utero pesticide exposure on childhood morbidity. Empirical evidence suggests that the vulnerable period for toxic insults to the developing immune system extends from early gestation to adolescence in humans and animals. Using data from the Ontario Farm Family Health Study, we examined the relationship between farm couple exposures to pesticides during pregnancy and subsequent health outcomes in their offspring, including: persistent cough or bronchitis, asthma, and allergies or hayfever. No strong associations between pesticide exposures during pregnancy and persistent cough or bronchitis, or asthma were found. There was suggestive evidence that allergies and hayfever appeared to be more common in offspring, especially male offspring, exposed to certain specific pesticides* during the period of pregnancy. Nevertheless, given the indirect indicators of pesticide exposure used in this study, and the scarcity of human studies on in utero exposure to pesticides and the development of allergies and other child health outcomes, these findings serve primarlily to generate hypotheses for future research. *2,4-D

19. Gonzalez NV, Soloneski S, Larramendy ML. 2006 Dec. Genotoxicity analysis of the phenoxy herbicide dicamba in mammalian cells in vitro. Toxicol In Vitro 20(8):1481-7. Abstract: The cytogenetic effects exerted by the phenoxy herbicide dicamba and one of its commercial formulations banvel (57.71% dicamba) were studied in in vitro whole blood human lymphocyte cultures. The genotoxicity of herbicides was measured by analysis of the frequency of sister chromatid exchanges (SCEs) and cell-cycle progression assays. Both dicamba and banvel activities were tested within 10.0-500.0 microg/ml doses range. Only concentrations of 200.0 microg/ml of dicamba and 500.0 microg/ml of banvel induced a significant increase in SCE frequency over control values. The highest dose of dicamba tested (500.0 microg/ml) resulted in cell culture cytotoxicity. The cell-cycle kinetics was affected by both test compounds since a significant delay in cell-cycle progression and

a significant reduction of the proliferative rate index were observed after the treatment with 100.0 and 200.0 microg/ml of dicamba and 200.0 and 500.0 microg/ml of banvel. For both chemicals, a progressive dose-related inhibition of the mitotic activity of cultures was observed. Moreover, only the mitotic activity statistically differed from control values when doses of both chemicals higher than 100.0 microg/ml were employed. On the basis of our results, the herbicide dicamba is a DNA damage agent and should be considered as a potentially hazardous compound to humans.

20. Samanic C, Rusiecki J, Dosemeci M, Hou L, Hoppin JA, Sandler DP, Lubin J, Blair A, Alavanja MC. 2006 Oct. Cancer incidence among pesticide applicators exposed to dicamba in the agricultural health study. Environ Health Perspect 114(10):1521-6.Abstract: BACKGROUND: Dicamba is an herbicide commonly applied to crops in the United States and abroad. We evaluated cancer incidence among pesticide applicators exposed to dicamba in the Agricultural Health Study, a prospective cohort of licensed pesticide applicators in North Carolina and Iowa. METHODS: Detailed pesticide exposure information was obtained through a self-administered questionnaire completed from 1993 to 1997. Cancer incidence was followed through 31 December 2002 by linkage to state cancer registries. We used Poisson regression to estimate rate ratios and 95% confidence intervals for cancer subtypes by tertiles of dicamba exposure. Two dicamba exposure metrics were used: lifetime exposure days and intensity-weighted lifetime exposure days (lifetime days x intensity score). RESULTS: A total of 41,969 applicators were included in the analysis, and 22,036 (52.5%) reported ever using dicamba. Exposure was not associated with overall cancer incidence nor were there strong associations with any specific type of cancer. When the reference group comprised low-exposed applicators, we observed a positive trend in risk between lifetime exposure days and lung cancer ($p = 0.02$), but none of the individual point estimates was significantly elevated. We also observed significant trends of increasing risk for colon cancer for both lifetime exposure days and intensity-weighted lifetime days, although these results are largely due to elevated risk at the highest exposure level. There was no apparent risk for non-Hodgkin lymphoma. CONCLUSIONS: Although associations between exposure and lung and colon cancer were observed, we did not find clear evidence for an association between dicamba exposure and cancer risk.

21. Bukowska B, Kopka A, Michalowicz J, Duda W. 2006 Sep. Comparison of the effect of Aminopielik D pesticide and its active components on human erythrocytes. Environ Toxicol Pharmacol 22(2):189-93.Abstract: In the present work, the effect of Aminopielik D [417.5g/l of dimethylamino salts of 2,4-dichlorophenoxyacetic acid (2,4-D) and 32.5g/l of 3,6-dichloro-2-metoxybenzoic acid (Dicamba)] and its active components (used separately and in mixture) on human erythrocytes was examined. The parameters studied were: lipid peroxidation, metHb formation and catalase activity. Aminopielik D used at doses of 100-1000ppm was found to increase lipid peroxidation, decrease of catalase activity and oxidation of haemoglobin. 2,4-D and Dicamba are present in Aminopielik D in the dimethylamino form; their sodium salts in solution (separately and as a mixture) did not cause such strong effects. A synergistic action of 2,4-D and Dicamba was excluded as the individual compounds caused the same effects as their mixture. Aminopielik D provoked slightly higher changes in the lipid peroxidation and catalase activity than its active components alone and in mixture, which was probably a result of the properties of the additives and interaction of tested systems with the dimethylamino group.

22. Pahwa P, McDuffie HH, Dosman JA, McLaughlin JR, Spinelli JJ, Robson D, Fincham S. 2006 Mar. Hodgkin lymphoma, multiple myeloma, soft tissue sarcomas, insect repellents, and phenoxyherbicides. J Occup Environ Med 48(3):264-74.Abstract: OBJECTIVE: The objective of this study was to determine if there is an additional risk of developing Hodgkin lymphoma, multiple myeloma, or soft tissue sarcoma as a consequence of exposure to a combination of phenoxyherbicides, rubber gloves, DEET (N, N-diethyl-m-toluamide), and sunlight compared with each of the individual chemicals. METHODS: This was a population-based study of men with specific cancers and age, province-matched control subjects. RESULTS: No additional risk from these combinations of exposures of developing these three types of tumor was found in contrast to non-Hodgkin lymphoma. CONCLUSIONS: The mechanisms by which phenoxyherbicides contribute to the risk of multiple myeloma and non-Hodgkin lymphoma may be different.

23. Obendorf SK, Lemley AT, Hedge A, Kline AA, Tan K, Dokuchayeva T. 2006. Distribution of pesticide residues within homes in central New York State. Arch Environ Contam Toxicol 50(1):31-44.Abstract: Residues for 17 pesticides were analyzed in 41 households in central New York State that represented farm, rural, and urban houses. Samples were taken in both summer and winter of 2000-2001 from the same households from four locations; family room carpet; adjacent smooth floor; flat tabletop surface; and settled dust collected in a Petri dish on a tabletop. Pesticide residues were analyzed to identity factors that influence both the transport into and the redistribution of pesticides in the indoor environment. Differences were observed between the various pesticides and pesticide classifications relative to location within and between households as well as by season. Variations in the pesticide residues were related to a number of factors. Higher residues were observed in the farm households, particularly in summer, with the highest amount observed for chloropyrifos in carpet (33 mu g/ m(2')). For many pesticides, the frequency of detection and the amount of residues were higher in summer, which relates to usage patterns in agriculture and horticulture; however, larger amounts of insecticides such as mecoprop, resmethrin, and tetramethrin were found on flat surfaces in winter, indicating household use and possible redistribution within the home. Distribution patterns suggest that routines within a household may cause high variation in residues; these practices include indoor pets and treatment for fleas and ticks, use of termiticides, and fastidiousness of occupants. Frequency of pesticide detection was highest in carpet for both summer and winter for all households. indicating that carpets hold pesticides over time. Adsorbent fibrous materials such as textiles hold pesticides by macro- and micro-occlusion in their complex structures. Amounts of pesticide residue were higher in carpets than on smooth floors, particularly for rural farm households where the farmer was a certified pesticide applicator. The maximum amount of pesticide residue on a smooth floor surface was 13.6 mu g/m(2) malathion while the maxima on wiped surfaces and in settled dust were 1.8 mu g/m(2) 2, 4 D and 3 mu g/m(2) pendimethalin, respectively. Physical properties of individual pesticides such as vapor pressure influenced the distribution of the pesticide within the households. Evidence of volatilization of pesticides and redeposition on surfaces was observed, indicating that this is a mechanism for contamination of surfaces in addition to adsorption on airborne particles and tracking. High residues in winter are evidence that closure of households in winter that reduces ventilation results in redistribution of pesticides within households.

24. McDuffie HH, Pahwa P, Robson D, Dosman JA, Fincham S, Spinelli JJ, McLaughlin JR. 2005 Aug. Insect repellents, phenoxyherbicide exposure, and non-Hodgkin's lymphoma. J Occup Environ Med 47(8):806-16.Abstract: OBJECTIVE: We sought to test a hypothetical explanation of contradictory results in studies of phenoxyherbicides and NHL, that the exposure of rubber gloves recommended for use by farmers when mixing or applying pesticides simultaneously to 2,4-D (2,4-dichlorophenoxyacetic acid), DEET (N,N-diethyl-m-toluamide), and ultraviolet rays increased their permeability to 2,4-D. METHODS: We conducted a case (NHL n = 513)/control (n = 1506) study among men using age; province of residence; exposure to insect repellents containing DEET, phenoxy-herbicides, or dicamba; and gloves when handling pesticides. RESULTS: Using conditional logistic regression, the stratum with reported exposure to mecoprop, to DEET and the use of rubber gloves had higher odds ratios (3.86; 95% confidence interval = 1.57-9.49) compared with strata with other combinations. CONCLUSIONS: In conclusion, the etiologic complexity of NHL was demonstrated.

25. Hartge P, Colt JS, Severson RK, Cerhan JR, Cozen W, Camann D, Zahm SH, Davis S. 2005 Apr. Residential herbicide use and risk of non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev 14(4):934-7.Abstract: CONTEXT: Environmental exposure to herbicides has been hypothesized to contribute to the long-term increase in non-Hodgkin lymphoma (NHL). OBJECTIVE: To estimate the effects of residential herbicide exposure on NHL risk. DESIGN: Population-based case-control study. SETTING: Iowa and metropolitan Detroit, Los Angeles, and Seattle, 1998 to 2000. PARTICIPANTS: NHL patients ages 20 to 74 years and unaffected residents identified by random digit dialing and Medicare eligibility files. MAIN OUTCOME MEASURES: Computer-assisted personal interviews (1,321 cases, 1,057 controls) elicited data on herbicide use at each home occupied since 1970. Levels of 2,4-dichlorophenoxy-acetic acid and dicamba were measured in dust taken from used vacuum cleaner bags in the current home (679 cases, 510 controls who had owned

at least half of their carpets for > or = 5 years). RESULTS: Herbicide use on the lawn or garden was similar among cases and controls (adjusted relative risk, 1.02; 95% confidence interval, 0.84-1.23). Estimated risk did not increase with greater duration, frequency, or total number of applications of herbicides to the lawn, the garden, or to both combined. Risk was not elevated for respondents who applied the herbicides themselves and not for those exposed during the 1970s, 1980s, or 1990s. We detected 2,4-dichlorophenoxy-acetic acid equally often in homes of cases and controls (78%). We found dicamba in homes of 15% of cases and 20% of controls. We also found no elevation in risk among the respondents who had the highest dust levels and highest self-reported exposures. We found no consistent patterns for specific histologies. CONCLUSIONS: We found no detectable excess associated with residential exposures. Residential herbicide exposures are unlikely to explain the long-term increase in NHL.

26. Berube VE, Boily MH, DeBlois C, Dassylva N, Spear PA. 2005 Jan 26. Plasma retinoid profile in bullfrogs, Rana catesbeiana, in relation to agricultural intensity of sub-watersheds in the Yamaska River drainage basin, Quebec, Canada. Aquat Toxicol 71(2):109-20.Abstract: Amphibian populations are decreasing globally and the causes are presently unclear. Retinoids have been extensively studied in other vertebrate classes where they are associated with pleiotropic effects such as susceptibility to disease (including cancer and parasitic infections), deformities and reproduction. To investigate the hypothesis that retinoid homeostasis is influenced by agricultural activities, blood samples were collected from adult bullfrogs, Rana catesbeiana, at each of six sub-watersheds chosen to represent a gradient of agricultural intensity within the Yamaska River drainage basin. Samples of surface water were collected at each of the study sites approximately 1 month after spraying and analyzed for 53 pesticides. Male body weight was significantly different ($p<0.001$) between study sites with the smallest bullfrogs captured from the Riviere a la Barbue sub-watershed associated with high agricultural intensity. A significant linear regression ($p<0.001$; $R2=0.176$) was obtained between plasma retinol and body weight. Plasma retinol concentrations were significantly different between study sites ($p<0.001$) being lowest at both Riviere Noire and Riviere a la Barbue. More than 60% of the land area in these sub-watersheds is under intensive corn-soya cultivation and surface water contained the highest concentrations of the herbicides atrazine, deethyl-atrazine, simazine, metolachlor, dimethenamide, chlopyralide, dicamba and bentazone. Plasma 13-cis-4-oxo-retinoic acid was significantly different ($p<0.001$) between sub-watersheds, however this effect was apparently unrelated to agricultural intensity. Plasma retinol was negatively correlated ($p=0.026$; $r=-0.237$) with plasma 13-cis-4-oxo-retinoic acid. These results suggest that retinoid homeostasis in bullfrogs may be influenced by agricultural practices.

27. Bureau of Land Management (BLM). 2005. Vegetation Treatments Using Herbicides on Bureau of Land Management Lands in 17 Western States [Draft].Abstract: **Overview [bolding from TC's notes in PEIS and PER Executive Summaries, and LEC's notes from other parts of the documents]**An important facet of the BLM's multiple-use mission is the management and control of vegetation on public lands. To meet that responsibility, in 2001 the BLM launched a multi-year effort to develop a programmatic environmental impact statement that contains national guidance for using herbicides and other treatments to manage vegetation on BLM-administered public lands in 17 western states. This effort also responds to directions from the President and Congress to implement the *National Fire Plan* and the *Healthy Forests Restoration Act of 2003* by taking more aggressive actions to reduce catastrophic wildfire risk on public lands. The BLM started this Programmatic EIS project to replace analyses contained in four existing EISs completed between 1986 and 1992 for 14 western states, and to analyze vegetation treatments in two additional western states and Alaska. This Programmatic EIS will provide a comprehensive NEPA (National Environmental Policy Act) document that can be used by BLM field-level staffs for local land-use planning. The BLM's *Draft Vegetation Treatments Using Herbicides on Bureau of Land Management Lands in 17 Western States Programmatic EIS* (PEIS) has two primary objectives: To determine which herbicide active ingredients are approved for use on public lands in the western U.S., including Alaska, to improve the agency's ability to control hazardous fuels and unwanted vegetation.

To develop a multi-agency, state-of-the-science human health and ecological risk assessment methodology that will serve as the initial standard for assessing human health and ecological risk for herbicides that may become available for use in the future. This PEIS is accompanied by a Draft

Vegetation Treatments on Bureau of Land Management Lands in 17 Western States Programmatic Environmental Report (PER), which describes the environmental impacts of using non-herbicide vegetation treatment methods on public lands. Supporting reports and documentation are also available on links listed below. **The final PEIS will guide the BLM's actions through its proposed treatment of vegetation on approximately 932,000 acres annually in 17 western states in the United States, including Alaska, using 14 currently approved and four new herbicide active ingredients [according to the Executive Summary: imazapic, diquat, diflufenzopyr (in formulation with dicamba), fluridone; in addition BLM "would approve diflufenzopyr for use in the future as a stand-alone active ingredient if it becomes registered for herbicidal use."]. [App B lists as "new" the following 6: dicamba (with diflufenzopyr in Overdrive), diflufenzopyr (with dicamba in Overdrive), diquat (Reward), fluridone (Sonar), imazapic (Plateau), sulfometuron methyl (Oust)]** The final PER will guide the treatment of 5.1 million acres by other means, including prescribed fire and manual, mechanical, and biological methods. The proposed actions would reduce the risk of catastrophic wildfires by reducing hazardous fuels and restoring fire-damaged lands, and would improve ecosystem health by controlling weeds and invasive plant species and managing vegetation to benefit fish and wildlife habitat, improve riparian and wetlands areas, and improve water quality in priority watersheds. The public has been involved throughout the scoping process for this project, and the BLM now invites you to read these documents, attend scheduled public meetings if possible, and send constructive comments to the BLM during the public comment period, Nov. 10, 2005, through January 9, 2006. Details for sending comments are in the Frequently Asked Questions. · News Release · FAQs (Frequently Asked Questions) · Public Meetings Schedule (27KB PDF) · **Draft PEIS, Volume 1 - DOWNLOADED** · **Draft PEIS, Volume 2 - DOWNLOADED** · **Draft PER** · Human Health Risk Assessment - DOWNLOADED main, App A, App B "(Dicamba. in progress)"[?]; Appendix B printed · Ecological Risk Assessment Protocol and Assessments · Draft Biological Assessment · Air Quality Modeling for BLM Vegetation Treatment Methods (644KB PDF) · Annual Emissions Inventory for BLM Vegetation Treatment Methods (609KB PDF) · Air Quality Policies summary for the Vegetation Treatments PEIS & PER (2.4MB PDF) · Paleontological Overview for the Western United States (130KB PDF) · *Federal Register* Notice of Availability (42KB PDF) - DOWNLOADED a version; have hardcopy email also. [for dicamba/ diflufenzopyr/ diquat/ fluridone/ imazapic/ sulfometuron methyl/ : see Human Health Risk Assessment] [for bromacil/ chlorsulfuron/ diflufenzopyr/ diquat/ diuron/ fluridone/ imazapic/ Overdrive/ sulfometuron methyl/ tebuthiuron/ : see Ecological Risk Assessment] [Herbicide formulation labels in the HHRA Appendix A: **Overdrive (R)** =Diflufenzopyr and Dicamba (no sample label supplied); **Reward (R)** =Diquat (see annotated text on controlling spray drift); **Sonar (R)** =Fluridone; **Plateau (R)** =Imazapic; **Oust (R)** =Sulfometuron Methyl [+] **TC's other notes from the PEIS Executive Summary:** At present the BLM treats about **300,000 acres annually using 20 approved herbicides.** The Proposed action would reduce the risk of .. wildfires, by reducing hazardous fuels, restoring fire-damaged lands, and improving ecosystem health by 1) **controlling weeds and invasive species**; and 2) **manipulating vegetation to benefit fish and wildlife habitat, improve riparian and wetlands areas, and improve water quality in priority watersheds. ... Invasive vegetation and noxious weeds are the dominant vegetation on an estimated 35 million acres of public lands. ... .. the President and Congress have directed the USDI and BLM, through implementation of the National Fire Plan, and the Healthy FOrests Restoration Act of 2003, to take more aggressive actions to reduce catastrophic wildfire risk on public lands. ... In addition to the herbicides currently approved for use, additional active ingredients are being considered for use by the BLM in order to address emerging weed problems associated with public lands, such as downy brome (cheatgrass)** and invasive aquatic species **Several herbicides used, or proposed for use by the BLM, are known groundwater contaminants. Herbicides pose risks to terrestrial and aquatic vegetation.** Most aquatic herbicides and several terestrial herbicides, are on-selective and could adversely impact **non-target vegetation. ...including croplands nad other vegetation found on privately-owned lands near treatment areas. Many of the herbicides currently available for use by the BLM pose risks to fish and wildlife...** All of the herbicides pose **some risk to non-target terrestrial and aquatic vegetation, and damage to these plants could adversely impact**

haabitats used by fish and wildlife. Acetolactate synthase-inhibitine herbicides are highly potent and can damage plants at low application rates....Livestock and wild horses and burros could be impacted by herbicides. ... While herbicde treatmens could affect cultural or paleontological resources near or on the surface, they would be **more likely to affect traditional cultural practices of gathering plants and the health of Native peoples. ...Herbicide treatments could affect visual, wilderness, and recreation resources. ...Treatments could harm the health of workers and the public. ...Treatments could result in short-term irreversible loss of some resources, including soil, vegetation, wildlife, and livestock forage opporunities. ..."** **<u>TC's other notes from the PER Executive Summary:</u>** BLM ...manages vegetation on nearly 262 million acres of public lands in 17 states in the western U.S., including Alaska. Management and control... is accomplished using a variety of treatment methods, including, but not limited to: **herbicides, prescribed fire and wildland fire use for resource benefit (collectively termed "fire use"), manual and mechanical methods, and biological controls such as insects, pathogens, and domestic grazing animals. ...**BLM is planning to increase the number of acres of vegetation treated **annually from approximately 2 million to 6 million. ...** by 1) **controlling weeds and invasive species**; and 2) **manipulating vegetation to benefit fish and wildlife habitat, improve riparian and wetlands areas, and improve water quality in priority watersheds. ...**Concurrently, public lands must be administered under the **principles of multiple use and sustained yield** in accordance with the intent of Congress as stated in the Federal Land Policy and Management Act of 1976 (FLPMA)**When developing treatment objectives on the national and local level, the BLM will 1) take actions to prevent or minimize the need for vegetation controls, were feasible; 2) use effective non-chemical methods of vegetation control, where feasible; and use herbicides only after considering the effectiveness of all potential methods. ...**Acres to be treated by the BLM and assessed in this PER were estimated based on **information provided by BLM field offices. ...**Based on this estimate, approximately **3.5 million acres would be treated annually to reduce hazardous fuels, 1.5 million acres to restore and revegetate lands burned by wildfires or damaged by weed and other invasive species, and 1 million acres to meet other agency objectives, including iproving fish and wildlife habitat and watershed processes. Mechanical treatments would be used on approximately 2.2 million acres, fire use on 2.1 million acres, herbicides on 932,000 acres, biological control on 454,000 acres, and manual treatmens on 271,000 acres annually. ...**The BLM would foster **collaborative relationships with stakeholders,** including individuals, communities, and governments

28. Semchuk K, McDuffie H, Senthilselvan A, Cessna A, Irvine D. 2004 Sep 10. Body mass index and bromoxynil exposure in a sample of rural residents during spring herbicide application. J Toxicol Environ Health A 67(17):1321-52.Abstract: Bromoxynil (3,5-dibromo-4-hydroxybenzonitrile), a phenolic herbicide, is widely used in production of cereals and other crops. Little is known, however, about bromoxynil exposure in humans. Results of previous research suggest a longer residence time in the body for bromoxynil compared to phenoxy herbicides [e.g., (2,4-dichlorophenoxy)acetic acid (2,4-D), 4-chloro-2-methylphenoxyacetic acid (MCPA)] and that bromoxynil would tend to partition into fatty tissue more so than 2,4-D. In previous research, body mass index (BMI) was found to be an independent predictor of plasma concentrations of 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), the persistent lipophilic metabolite of the chlorinated pesticide bis(4-chlorophenyl)-1,1,1-trichloroethane (DDT). As part of the Prairie Ecosystem Study, gas chromatography/mass spectrometry analysis was used to measure concentrations of bromoxynil and seven other herbicides (2,4-D, dicamba, fenoxaprop, MCPA, ethalfluralin, triallate, and trifluralin) in plasma from residents (104 men, 88 women, 24 youths age 12-17 yr) of a cereal-producing region in Saskatchewan, Canada, during spring herbicide application, 1996. Multiple logistic regression analysis was used to explore whether BMI predicted detection of bromoxynil in plasma from the adults. The prevalence of detection (detection limits: 2-50 microg/L) was markedly higher for bromoxynil (men, 44.2%; women, 14.8%; youths, 20.8%) compared to each of the other herbicides including 2,4-D (men, 16.5%; women, 3.4%; youths, 12.5%) and MCPA (men, 6.8%; women, 1.1%; youths, 4.2%), although bromoxynil is commonly formulated or tank mixed with these herbicides. In the multiple logistic regression analysis, the variables BMI, exposure group [bromoxynil applicators, non-applicator family members of bromoxynil applicators, all others (reference group)], and days elapsed since the last use of

bromoxynil were found to be independent predictors of detection of bromoxynil, while age, gender, and farm residency were not statistically significant. With adjustment for exposure group [bromoxynil applicators: odds ratio (OR = 24.30, 95% confidence interval (CI) = 9.59-61.58; nonapplicator family members of bromoxynil applicators: OR = 3.53, 95% CI = 1.19-10.44; all others (reference group)], the OR for detection of bromoxynil was 2.35 (95% CI = 0.87-6.33) for participants in the middle (25.53-29.00 kg/m2) tertile (men: OR = 2.85, 95% CI = 0.75-10.82; women: OR = 1.63, 95% CI = 0.36-7.40) of BMI and 4.01 (95% CI = 1.46-11.03) for participants in the highest (> 29.00 kg/m2) tertile (men: OR = 4.67, 95% CI = 1.17-18.58; women: OR = 2.20, 95% CI = 0.44-10.99) with participants in the lowest (< 25.53 kg/m2) tertile as the reference group. Similar ORs were observed for BMI with adjustment for days elapsed since the last use of bromoxynil. In conclusion, further research is needed to investigate whether adiposity is an important modifying factor for persistence of bromoxynil in the body.

29. Campbell B. 2004 Aug 22. Re: 2,4-D Risk Assessment; Docket ID No. OPP-2004-0167 (Parts 1 and 2). Letters to: Environmental Protection Agency, Public Information and Records Integrity Branch (7502C), Office of Pesticide Programs, 1200 Pennsylvania Ave., NW, Washington, D.C. 20460-0001 :5+9 pp.

30. Greenlee AR, Ellis TM, Berg RL. 2004 May. Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos. Environ Health Perspect 112(6):703-9.Abstract: Occupational exposures to pesticides may increase parental risk of infertility and adverse pregnancy outcomes such as spontaneous abortion, preterm delivery, and congenital anomalies. Less is known about residential use of pesticides and the risks they pose to reproduction and development. In the present study we evaluate environmentally relevant, low-dose exposures to agrochemicals and lawn-care pesticides for their direct effects on mouse preimplantation embryo development, a period corresponding to the first 5-7 days after human conception. Agents tested were those commonly used in the upper midwestern United States, including six herbicides [atrazine, dicamba, metolachlor, 2,4-dichlorophenoxyacetic acid (2,4-D)], pendimethalin, and mecoprop), three insecticides (chlorpyrifos, terbufos, and permethrin), two fungicides (chlorothalonil and mancozeb), a desiccant (diquat), and a fertilizer (ammonium nitrate). Groups of 20-25 embryos were incubated 96 hr in vitro with either individual chemicals or mixtures of chemicals simulating exposures encountered by handling pesticides, inhaling drift, or ingesting contaminated groundwater. Incubating embryos with individual pesticides increased the percentage of apoptosis (cell death) for 11 of 13 chemicals (p <or= 0.05) and reduced development to blastocyst and mean cell number per embryo for 3 of 13 agents (p <or= 0.05). Mixtures simulating preemergent herbicides, postemergent herbicides, and fungicides increased the percentage of apoptosis in exposed embryos (p <or= 0.05). Mixtures simulating groundwater contaminants, insecticide formulation, and lawn-care herbicides reduced development to blastocyst and mean cell number per embryo (p <or= 0.05). Our data demonstrate that pesticide-induced injury can occur very early in development, with a variety of agents, and at concentrations assumed to be without adverse health consequences for humans.

31. Colt JS, Lubin J, Camann D, Davis S, Cerhan J, Severson RK, Cozen W, Hartge P. 2004 Jan. Comparison of pesticide levels in carpet dust and self-reported pest treatment practices in four US sites. J Expo Anal Environ Epidemiol 14(1):74-83.Abstract: Epidemiologic studies have used both questionnaires and carpet dust sampling to assess residential exposure to pesticides. The consistency of the information provided by these two approaches has not been explored. In a population-based case-control study of non-Hodgkin's lymphoma, carpet dust samples were collected from the homes of 513 control subjects in Detroit, Iowa, Los Angeles, and Seattle. The samples were taken from used vacuum cleaner bags and analyzed for 30 pesticides. Interviewers queried subjects about the types of pests treated in their home using a detailed questionnaire accompanied by visual aids. Geographic variations in pesticide levels were generally consistent with geographic differences in pest treatment practices. Los Angeles residents reported the most treatment for crawling insects, fleas/ticks, and termites, and Los Angeles dust samples had the highest levels of propoxur, chlorpyrifos, diazinon, permethrin, and chlordane. Iowa had the most treatment for lawn/garden weeds, and also the highest levels of 2,4-dichlorophenoxyacetic acid and dicamba. Although Seattle had the highest proportion

of subjects treating for lawn/garden insects, the lawn/garden insecticides were higher in other sites. Multivariate linear regression revealed several significant associations between the type of pest treated and dust levels of specific pesticides. The strongest associations were between termite treatment and chlordane, and flea/tick treatment and permethrin. Most of the significant associations were consistent with known uses of the pesticides; few expected associations were absent. The consistency between the questionnaire data and pesticide residues measured in dust lends credibility to both methods for assessing residential exposure to pesticides. The combined techniques appear promising for epidemiologic studies. Interviewing is the only way to assess pesticide exposures before current carpets were in place. Dust sampling provides an objective measure of specific compounds to which a person may have been exposed through personal use of a pesticide or by drift-in or track-in from outside, and avoids recall bias.

32. Peterson RKD, Hulting ANG. 2004. A comparative ecological risk assessment for herbicides used on spring wheat: the effect of glyphosate when used within a glyphosate-tolerant wheat system. Weed Science 52(5):834-844. Abstract: Glyphosate-tolerant spring wheat currently is being developed and most likely will be the first major genetically engineered crop to be marketed and grown in several areas of the northern Great Plains of the United States. The public has expressed concerns about environmental risks from glyphosate-tolerant wheat. Replacement of traditional herbicide active ingredients with glyphosate in a glyphosate-tolerant spring wheat system may alter ecological risks associated with weed management. The objective of this study was to use a Tier 1 quantitative risk assessment methodology to compare ecological risks for 16 herbicide active ingredients used in spring wheat. The herbicide active ingredients included 2,4-D, bromoxynil, clodinafop, clopyralid, dicamba, fenoxaprop, flucarbazone, glyphosate, MCPA, metsulfuron, thifensulfuron, tralkoxydim, triallate, triasulfuron, tribenuron, and trifluralin. We compared the relative risks of these herbicides to glyphosate to provide an indication of the effect of glyphosate when it is used in a glyphosate-tolerant spring wheat system. Ecological receptors and effects evaluated were avian (acute dietary risk), wild mammal (acute dietary risk), aquatic vertebrates (acute risk), aquatic invertebrates (acute risk), aquatic plants (acute risk), nontarget terrestrial plants (seedling emergence and vegetative vigor), and groundwater exposure. Ecological risks were assessed by integrating toxicity and exposure, primarily using the risk quotient method. Ecological risks for the 15 herbicides relative to glyphosate were highly variable. For risks to duckweed, green algae, groundwater, and nontarget plant seedling emergence, glyphosate had less relative risk than most other active ingredients. The differences in relative risks were most pronounced when glyphosate was compared with herbicides currently widely used on spring wheat.

33. Peixoto F, Vicente JA, Madeira VM. 2003 Jul. The herbicide dicamba (2-methoxy-3,6-dichlorobenzoic acid) interacts with mitochondrial bioenergetic functions. Arch Toxicol 77(7):403-9. Abstract: The effects of dicamba, a widely used broad-leaf herbicide, on rat liver mitochondrial bioenergetic activities were examined. The results obtained for state 4 respiration indicate not only an uncoupling effect, the result of an increase on the permeability of inner mitochondria membrane to protons, but also a strong inhibitory effect on the redox complexes. State 3 and respiration uncoupled by FCCP (carbonylcyanide p-trifluoromethoxyphenylhydrazone) were inhibited to approximately the same extent, i.e. by about 70%. Depression of respiratory activity is essentially mediated through partial inhibition of mitochondrial complexes II and III. ATPase activity was much less depressed by dicamba than ATP synthase activity. Therefore, a considerable part of the inhibition observed on ATP synthase is the result of an inhibition on the redox complexes. The loss of phosphorylation capacity, induced by dicamba, was in the last analysis not only the result of a direct effect of dicamba on the enzymatic complex (F(0)-F(1) ATPase) but also the result of a deleterious effect on the integrity of the mitochondrial membrane, which can promote an inhibition of the respiratory complexes and an increase of the proton permeability of the inner membrane.

34. George TK, Waite D, Liber K, Sproull J. 2003 Jul. Toxicity of a complex mixture of atmospherically transported pesticides to Ceriodaphnia dubia. Environ Monit Assess 85(3):309-26. Abstract: The presence of several anthropogenic chemicals has been documented in the atmosphere of the Canadian prairies. The deposition of these chemicals as a mixture is of importance since little is known of the combined effects of these chemicals on aquatic organisms. This study was designed to

evaluate the acute and chronic toxicity of a complex mixture of nine atmospherically transported pesticides to Ceriodaphnia dubia. The nine selected pesticides (bromoxynil, dicamba, 2,4-D, MCPA, triallate, trifluralin, pentachlorophenol, lindane, and 4,4'-DDT) were detected in appreciable quantities in dry atmospheric deposits. The concentration of each pesticide in the mixture was based on maximum measured daily dry deposition rates for central Canada, except for pentachlorophenol, which was estimated based on atmospheric concentrations. The 48-h LC50 estimate for C. dubia exposed to the pesticide mixture was 174.60 microg L(-1) (340 times the measured total dry deposition concentration). The estimated NOEC and LOEC for both survival and reproduction, as determined in the 7-d chronic toxicity test, were 51.3 (100 times) and 154 microg/L(-1) (300 times), respectively. A basic risk assessment, using the toxic unit approach, suggested that the toxicity of the pesticide mixture was mainly due to 4,4'-DDT. Overall, this atmospherically transported complex mixture of pesticides appears to pose a negligible toxicological risk to non-target aquatic invertebrates such as zooplankton.

35. Semchuk KM, McDuffie HH, Senthilselvan A, Dosman JA, Cessna AJ, Irvine DG. 2003 Jan 24. Factors associated with detection of bromoxynil in a sample of rural residents. J Toxicol Environ Health A 66(2):103-32. Abstract: In regions of intensive crop production residents may be exposed to herbicides through direct contact or environmental sources. The environmental herbicide exposures of rural populations and resultant potential health effects are not well understood. Epidemiologic studies or herbicides have focused on occupational exposures using, primarily, self-reported data (e.g., information on occupational and non-occupational herbicide use, agricultural practices and exposures, farm residence). Herbicide exposure characterization in epidemiologic research would be strengthened by the use of self-reported data and biological monitoring (e.g. measuring the herbicide parent compound or its metabolites in blood or urine specimens) to classify individual exposures, identify factors associated with exposure, and obtain integrated estimates of exposure. As both exposure metrics are susceptible to measurement error and some self-reported and biological monitoring data might not be correlated, a worthwhile first step is to identify self-reported data that are statistically associated with biological measures or exposure. This study use gas chromatography/mass spectrometry analysis to measure blood plasma concentrations of target herbicides in a sample of rural residents (men, women, and youths) of Saskatchewan, Canada, and identified factors, based on self-reported data, associated with detection. The questionnaire data and blood specimens were collected in February/March 1996 during winter (frozen soil and water and snow cover) conditions. Sixty-four of the 332 study participants (19.3%) had detectable levels of the herbicide bromoxynil although herbicide application in the region had not occurred for approximately 5 mo and bromoxynil has a relatively short environmental half-life. **The prevalence of detection of other target herbicides (2,4-D, triallate, trifluralin, dicamba, fenoxaprop, MCPA, and ethalfluralin) varied from 0.3% to 2.7%**. Self reported factors identified in the multiple-variable analysis as statistically significant predictors of bromoxynil detection included recent exposure to grain production as the main farming operation (statistically significant for producers and for non-farming family members of producers), a history of bromoxynil use, a history of having felt ill with a pesticide exposure and a history of pesticide spill on skin or clothing, with apparent gender differences in the relative importance of these factors. Detection of bromoxynil in this rural sample, 3-4 mo after freeze-up and winter snow cover, suggests either that bromoxynil is very slowly metabolized/excreted from the body or study participants were environmentally or occupationally exposed tothe herbicide during this period. Further research is needed to elucidate the pathways of exposure, biological half-life, and potential human health effects of bromoxynil.

36. Wargo J, Alderman N, Wargo L. 2003. Risks from lawn-care pesticides.Connecticut: Environment and Human Health, Inc. Abstract: EHHI's report reveals that the scientific community clearly supports the conclusion that pesticides pose a special risk to fetuses, infants, and children. The report recommends immediate changes in laws at the federal, state and local levels of government. It also recommends precautionary measures that may be taken immediately by stores and consumers to limit health and environmental hazards.

37. Alavanja MC, Samanic C, Dosemeci M, Lubin J, Tarone R, Lynch CF, Knott C, Thomas K, Hoppin JA, Barker J, Coble J, Sandler DP, Blair A. 2003. Use of agricultural pesticides and prostate cancer risk

in the agricultural health study cohort. Am J Epidemiol 157(9):800-814.Abstract: The authors examined the relation between 45 common agricultural pesticides and prostate cancer incidence in a prospective cohort study of 55,332 male pesticide applicators from Iowa and North Carolina with no prior history of prostate cancer. Data were collected by means of self-administered questionnaires completed at enrollment (1993-1997). Cancer incidence was determined through population-based cancer registries from enrollment through December 31, 1999. A prostate cancer standardized incidence ratio was computed for the cohort. Odds ratios were computed for individual pesticides and for pesticide use patterns identified by means of factor analysis. A prostate cancer standardized incidence ratio of 1.14 (95% confidence interval: 1.05, 1.24) was observed for the Agricultural Health Study cohort. Use of chlorinated pesticides among applicators over 50 years of age and methyl bromide use were significantly associated with prostate cancer risk. Several other pesticides showed a significantly increased risk of prostate cancer among study subjects with a family history of prostate cancer but not among those with no family history. Important family history- pesticide interactions were observed.

38. Cavieres MF, Jaeger J, Porter W. 2002 Nov. Developmental toxicity of a commercial herbicide mixture in mice: I. Effects on embryo implantation and litter size. Environ Health Perspect 110(11):1081-5.Abstract: We investigated the developmental toxicity in mice of a common commercial formulation of herbicide containing a mixture of 2,4-dichlorophenoxyacetic acid (2,4-D), mecoprop, dicamba, and inactive ingredients. Pregnant mice were exposed to one of four different doses of the herbicide mixture diluted in their drinking water, either during preimplantation and organogenesis or only during organogenesis. Litter size, birth weight, and crown-rump length were determined at birth, and pups were allowed to lactate and grow without additional herbicide exposure so that they could be subjected to additional immune, endocrine, and behavioral studies, the results of which will be reported in a separate article. At weaning, dams were sacrificed, and the number of implantation sites was determined. The data, although apparently influenced by season, showed an inverted or U-shaped dose-response pattern for reduced litter size, with the low end of the dose range producing the greatest decrease in the number of live pups born. The decrease in litter size was associated with a decrease in the number of implantation sites, but only at very low and low environmentally relevant doses. Fetotoxicity, as evidenced by a decrease in weight and crown-rump length of the newborn pups or embryo resorption, was not significantly different in the herbicide-treated litters.

39. Harris SA, Sass-Kortsak AM, Corey PN, Purdham JT. 2002 Mar. Development of models to predict dose of pesticides in professional turf applicators. J Expo Anal Environ Epidemiol 12(2):130-44.Abstract: Epidemiologic studies designed to assess the chronic effects of pesticides are limited by inadequate measurements of exposures. Although cohort studies have been initiated to evaluate the effects of 2,4-dichlorophenoxyacetic acid (2,4-D) and other pesticides in professional turf applicators, they may have limited power to detect significant health risks and may be subject to bias from exposure measurement error. In this study, the doses of 2,4-D, mecoprop [2-(4-chloro-2 methylphenoxy) propionic acid, MCPP] and dicamba (3,6-dichloro-o-anisic acid) were evaluated in a group of 98 professional turf applicators from 20 companies across southwestern Ontario. During a 1-week period (Saturday to Thursday), the volume of pesticide (active ingredient) applied was only weakly related to the total dose of 2,4-D absorbed (R(2)=0.21). Two additional factors explained a large proportion of variation in dose: the type of spray nozzle used and the use of gloves while spraying. Individuals who used a fan-type nozzle had significantly higher doses than those who used a gun-type nozzle. Glove use was associated with significantly lower doses. Job satisfaction and current smoking influenced the dose but were not highly predictive. In the final multiple regression models predicting total absorbed dose of 2,4-D and mecoprop, approximately 63-68% of the variation was explained. The future application of these models for epidemiologic research will depend on the availability of information and records from employers, the feasibility of contacting study subjects and cost.

40. Perry MJ, Marbella A, Layde PM. 2002 Jan. Compliance with required pesticide-specific protective equipment use. Am J Ind Med 41(1):70-3.Abstract: BACKGROUND: This study measured compliance with pesticide-specific protective gear use requirements practiced by farmers applying pesticides to field crops. MATERIALS AND METHODS: Two hundred and twenty randomly

selected dairy farmers were interviewed 1 week after pesticide application to determine use of personal protective equipment while applying at least 1 of 15 possible restricted use pesticides (response rate = 82.4%). RESULTS: Among the three most common pesticides used (dicamba, atrazine, and cyanazine), the proportions of farmers fully complying with gear use requirements were 8.8, 8.6, and 2.5%, respectively. For those same pesticides, the proportions (and 95% CI) using none of the required gear were 56.9% (47.3-66.5%), 38.6% (27.2-50.0%), and 47.5%(32.0-63.0%), respectively. CONCLUSIONS: Both full and partial compliance with required personal protective equipment was low for each of the 15 chemicals applied by the applicators in this sample.

41. McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, Dosman JA, Robson D, Skinnider LF, Choi NW. 2001 Nov. Non-Hodgkin's lymphoma and specific pesticide exposures in men: cross-Canada study of pesticides and health. Cancer Epidemiol Biomarkers Prev 10(11):1155-63.Abstract: Our objective in the study was to investigate the putative associations of specific pesticides with non-Hodgkin's Lymphoma [NHL; International Classification of Diseases, version 9 (ICD-9) 200, 202]. We conducted a Canadian multicenter population-based incident, case (n = 517)-control (n = 1506) study among men in a diversity of occupations using an initial postal questionnaire followed by a telephone interview for those reporting pesticide exposure of 10 h/year or more, and a 15% random sample of the remainder. Adjusted odds ratios (ORs) were computed using conditional logistic regression stratified by the matching variables of age and province of residence, and subsequently adjusted for statistically significant medical variables (history of measles, mumps, cancer, allergy desensitization treatment, and a positive history of cancer in first-degree relatives). We found that among major chemical classes of herbicides, the risk of NHL was statistically significantly increased by exposure to phenoxyherbicides [OR, 1.38; 95% confidence interval (CI), 1.06-1.81] and to dicamba (OR, 1.88; 95% CI, 1.32-2.68). Exposure to carbamate (OR, 1.92; 95% CI, 1.22-3.04) and to organophosphorus insecticides (OR, 1.73; 95% CI, 1.27-2.36), amide fungicides, and the fumigant carbon tetrachloride (OR, 2.42; 95% CI, 1.19-5.14) statistically significantly increased risk. Among individual compounds, in multivariate analyses, the risk of NHL was statistically significantly increased by exposure to the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D; OR, 1.32; 95% CI, 1.01-1.73), mecoprop (OR, 2.33; 95% CI, 1.58-3.44), and dicamba (OR, 1.68; 95% CI, 1.00-2.81); to the insecticides malathion (OR, 1.83; 95% CI, 1.31-2.55), 1,1,1-trichloro-2,2-bis (4-chlorophenyl) ethane (DDT), carbaryl (OR, 2.11; 95% CI, 1.21-3.69), aldrin, and lindane; and to the fungicides captan and sulfur compounds. In additional multivariate models, which included exposure to other major chemical classes or individual pesticides, personal antecedent cancer, a history of cancer among first-degree relatives, and exposure to mixtures containing dicamba (OR, 1.96; 95% CI, 1.40-2.75) or to mecoprop (OR, 2.22; 95% CI, 1.49-3.29) and to aldrin (OR, 3.42; 95% CI, 1.18-9.95) were significant independent predictors of an increased risk for NHL, whereas a personal history of measles and of allergy desensitization treatments lowered the risk. We concluded that NHL was associated with specific pesticides after adjustment for other independent predictors.

42. Eleff RM, Pesticide Project Director. 2001. The Pesticide Report. Inaction Speaks Louder Than Words: The Minnesota Department of Agriculture's Failure to Protect Minnesota From Pesticide Contamination.Minnesota: Minnesota Center for Environmental Advocacy. Abstract: This report is the culmination of more than two years of investigation by the Minnesota Center for Environmental Advocacy (MCEA) to assess the environmental and health impacts of pesticide use in Minnesota and the efficiacy of state programs to reduce and limit those impacts. Two major findings emerged: A growing body of scientific research is investigating the health risks of exposure to low levels of pesticides which are ubiquitous in Minnesota and the Minnesota Department of Agriculture has failed to effectively carry out its statutory duties to collect pesticide use information, to monitor the extent of pesticide contamination of Minnesota's water resources, to take action to reduce contamination when it is detected, and to provide leadership in developing the state's program fostering non-chemical pest management methods. Appendix C shows pesticides sold that are toxic to wildlife and Appendix D shows pesticides sold that are associated with human health effects. Appendix E is a review of epidemiological studies showing adverse health effects, esp. cancers. Appendix F is a review of pesticide use reporting programs in 9 states (CA, OR, Massachusetts, WI, NY, NH, NJ, AZ, CT).

43. Arbuckle TE, Lin Z, Mery LS. 2001. An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population. Environ Health Perspect 109(8):851-857. Abstract: The toxicity of pesticides on human reproduction is largely unknown-- particularly how mixtures of pesticide products might affect fetal toxicity. The Ontario Farm Family Health Study collected data by questionnaire on the identity and timing of pesticide use on the farm, lifestyle factors, and a complete reproductive history from the farm operator and eligible couples living on the farm. A total of 2,110 women provided information on 3,936 pregnancies, including 395 spontaneous abortions. To explore critical windows of exposure and target sites for toxicity, we examined exposures separately for preconception (3 months before and up to month of conception) and postconception (first trimester) windows and for early (< 12 weeks) and late (12-19 weeks) spontaneous abortions. We observed moderate increases in risk of early abortions for preconception exposures to phenoxy acetic acid herbicides [odds ratio (OR) = 1.5; 95% confidence interval (CI), 1.1-2.1], triazines (OR = 1.4; 95% CI, 1.0-2.0), and any herbicide (OR = 1.4; 95% CI, 1.1-1.9). For late abortions, preconception exposure to glyphosate (OR = 1.7; 95% CI, 1.0-2.9), thiocarbamates (OR = 1.8; 95% CI, 1.1-3.0), and the miscellaneous class of pesticides (OR = 1.5; 95% CI, 1.0-2.4) was associated with elevated risks. Postconception exposures were generally associated with late spontaneous abortions. Older maternal age (> 34 years of age) was the strongest risk factor for spontaneous abortions, and we observed several interactions between pesticides in the older age group using Classification and Regression Tree analysis. This study shows that timing of exposure and restricting analyses to more homogeneous endpoints are important in characterizing the reproductive toxicity of pesticides.

44. Espandiari P, Glauert HP, Lee EY, Robertson LW. 1999 Jan. Promoting activity of the herbicide dicamba (2-methoxy-3, 6-dichlorobenzoic acid) in two stage hepatocarcinogenesis. Int J Oncol 14(1):79-84. Abstract: Our goal was to examine whether dicamba, a widely-used broad leaf herbicide, has promoting activity in two-stage hepatocarcinogenesis. Female Sprague Dawley rats were given a single dose of diethylnitrosamine and then diets containing dicamba, or phenobarbital, or both for six months. The number and volume of placental glutathione-S-transferase-positive, glucose-6-phosphatase-negative or ATPase-negative foci were quantified in the liver. Dicamba alone did not increase the number or volume of these altered hepatic foci. Dicamba did, however, show a significant effect on the number or volume of certain markers in animals also treated with phenobarbital. These data show that dicamba in combination with other promoters may have weak promoting activity in two-stage hepatocarcinogenesis in the rat.

45. Vogel A. 1998. Methodology and determination of 2,4-D and triclopyr residues employing the GC-ITD in the analysis of lettuce plants cultivated in the Tala Valley, Republic of South Africa. Bull Environ Contam Toxicol 60(3):371-378. Abstract: Hormone herbicides used on sugar cane plantations may be linked to growth abnormalites seen in other crops grown in the Tala Valley. In tha lab growth abnormalites were seen in lettuce plants exposed to 2,4-D iso-octyl ester. Therefore the next step was to ascertain whether lettuce plants grown in the Tala Valley, exhibiting growth abnormalities, would be found to contain residues of 2,4-D. This would constitue and important part of the continued monitoring of 2,4-D,dicamba, MCPA, 2,4,5-T, triclopyr, MCPB, and 2,4-DB occuring in rain,water, air, and dew. Preliminary analysis of lettuce plants randomly sampled in the Tala Valley revealed that the 05/12/89 samples contained 5.54 ug/ 2,4-D per kg while 2,4-D could not be detected in the 30/01/90 and 19/03/90 samples.

46. Holovska K, Lenartova V, Rosival I, Kicinkova M, Majerciakova A, Legath J. 1998. Antioxidant and detoxifying enzymes in the liver and kidney of pheasants after intoxication by herbicides MCPA and ANITEN I. J Biochem Mol Toxicol 12(4):235-44. Abstract: The activity of antioxidant and detoxifying enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSHPx), glutathione reductase, glutathione-S-transferase (GST), the contents of thiobarbituric acid reactive substances, and the superoxide dismutase and glutathione-S-transferase isoenzyme patterns, were determined in the liver and kidney of pheasants after acute intoxication by herbicides MCPA and ANITEN I. In the liver, the activity of antioxidant enzymes was significantly decreased in the group given ANITEN I. New superoxide dismutase isoforms (pI 6.30, 6.85, 7.00) and higher intensity of isoform with pI 6.60 were observed after isoelectrofocusing in all experimental groups.

In the kidney, the activity of superoxide dismutase was significantly decreased, and a higher intensity of superoxide dismutase isoforms (pI 6.00 and 6.60) was observed in all experimental groups. The contents of thiobarbituric acid reactive substances were significantly increased in the group with ANITEN I. The glutathione-S-transferase isoenzyme pattern was studied by using subunit-specific substrates and by Western blotting. The activity of glutathione-S-transferase with ethacrynic acid and cross-reactivity with rat subunit 7 was lower in all experimental groups in the kidney and liver, except in the liver of the group given a higher dose of ANITEN I. In this group, we have found a 2.10-fold higher activity to ethacrynic acid and a strong induction of subunit 7.

47. Espandiari P, Ludewig G, Glauert HP, Robertson LW. 1998. Activation of hepatic NF-kappaB by the herbicide Dicamba (2-methoxy-3,6-dichlorobenzoic acid) in female and male rats. J Biochem Mol Toxicol 12(6):339-44. Abstract: Nuclear factor-kappaB is a transcription factor that is activated in many different cell types by pathologic stimuli, such as reactive oxygen intermediates. One class of hepatocarcinogens, the peroxisome proliferators, may produce reactive oxygen intermediates, and one potent peroxisome proliferator, ciprofibrate, was recently reported to activate nuclear factor-kappaB. In this study, we investigated whether Dicamba, a broad leaf herbicide and peroxisome proliferator, could activate nuclear factor-KB in the livers of rats. Female and male Sprague Dawley rats (n = 4) were fed diets containing either 0, 1, or 3% Dicamba or 0.01% ciprofibrate for 7 days. As expected, the potent peroxisome proliferator, ciprofibrate, significantly increased fatty acyl CoA oxidase, peroxisomal beta-oxidation, and catalase activities in male rats and, except for catalase, also in female rats. Dicamba significantly increased peroxisomal fatty acyl CoA oxidase, peroxisomal beta-oxidation, and catalase activities, but decreased the activity of the cytosolic antioxidant enzyme, Se-dependent glutathione peroxidase, in both female and male rats. Dicamba increased nuclear factor-kappaB binding in the nuclear protein of livers from male rats fed both the 1 and 3% Dicamba diets. However, the highest binding was seen in nuclear protein from female rats fed 3% Dicamba. Both supershift and cold competition assays confirmed that this DNA binding activity was specific for nuclear factor-kappaB. Our results in this study suggest that the herbicide and peroxisome proliferator Dicamba has the ability to activate nuclear factor-kappaB.

48. Vacco DC. 1996. Pesticides in schools: *Reducing the risks*. New York State Department of Law Report . Abstract: Attorney General's Office in the Fall of 1991 initiated the first state-wide study of pesticide use in New York State in the public schools. This report describes the state-wide survey, provides information about some of the potential dangers of these chemicals, and recommends steps that schools and communities can take to minimize pesticide use. We found that 87% of schools use pesticides, and that all of the pesticides used contained substances which may causes immediate or long-term health problems. Only 21 percent of schools outside New York City reported posting warning signs around indoor areas that have been treated with pesticides, and less than 43 percent posted signs for outdoor applications. At least 50 different active pesticidal ingredients are being applied to the buildings and grounds of the schools in New York State. The pesticides most commonly used by the responding schools include the insecticides chlorpyrios and bendiocarb and the herbicides 2, 4-D and dicamba.

49. Shealy DB, Bonin MA, Wooten JV, Ashley DL, Needham LL, Bond AE. 1996. Application of an improved method for the analysis of pesticides and their metabolites in the urine of farmer applicators and their families. Environment International 22(6):661-675. Abstract: As the annual use of pesticides in the United States has escalated, public health agencies have become increasingly concerned about chronic pesticide exposure. However, without reliable, accurate analytical methods for biological monitoring, low-level chronic exposures are often difficult to assess. A method for measuring simultaneously the urinary residues of as many as 20 pesticides has been significantly improved. The method uses a sample preparation which includes enzyme digestion, extraction, and chemical derivatization of the analytes. The derivatized analytes are measured by using gas chromatography coupled with isotope-dilution tandem mass spectrometry. The limits of detection of the modified method are in the high pg/L - low mu g/L range, and the average coefficient of variation (CV) of the method was below 20% for most analytes, with approximately 100% accuracy in quantification. This method was used to measure the internal doses of pesticides among selected farmer applicators and their families. Definite exposure and elimination patterns (i.e., an increase in urinary analyte

levels following application and then a gradual decrease to background levels) were observed among the farmer applicators and many of the family members whose crops were treated with carbaryl, dicamba, and 2,4-D esters and amines. Although the spouses of farm workers sometimes exhibited the same elimination pattern, the levels of the targeted pesticides or metabolites found in their urine were not outside the ranges found in the general U.S. population (reference range). The farmer applicators who applied the pesticides and some of their children appeared to have higher pesticide or metabolite levels in their urine than those found in the general U.S. population, but their levels were generally comparable to or lower than reported levels in other occupationally exposed individuals. These results, however, were obtained from a nonrandom sampling of farm residents specifically targeted to particular exposures who may have altered their practices because they were being observed; therefore, further study is required to determine if these results are representative of pesticide levels among residents on all farms where these pesticides are applied using the same application techniques. Using this method to measure exposure in a small nonrandom farm population allowed differentiation between overt and background exposure. In addition, the important role of reference-range information in distinguishing between various levels of environmental exposure was reaffirmed. Copyright (C) 1996 Elsevier Science Ltd

50. Nishioka MG, Burkholder HM, Brinkman MC, Gordon SM, Lewis RG. 1996. Measuring transport of lawn-applied herbicide acids from turf to home: Correlation of dislodgeable 2,4-D tuff residues with carpet dust and carpet surface residues. Environ Sci Technol 30(11):3313-3320.[SEP]Abstract: Transport of lawn-applied herbicides into the home via walking over treated turf, defined here as track-in, was measured at five different times out to 1 week after application. Residues of turf-applied 2,4-D and dicamba were measured in carpet dust and on the carpet surface after track-in. Both carpet dust levels and carpet surface dislodgeable residue levels were highly correlated with turf dislodgeable residue levels. Turf dislodgeable residues were 0.1-0.2% of turf application levels. Transfer of herbicides from turf to carpet dust was 3% of the turf dislodgeable residues. Transfer from turf to carpet surface was 0.3% of the turf dislodgeable residues. Herbicide 2,4-D was measured in the carpet dust of suburban homes at the 0.1-5 mu g/g levels that are predicted by this efficiency of mass transfer. New tools used to collect these samples included the polyurethane foam roller dislodgeable residue sampler and the high-volume solid surface sampler.

51. Hoppin P. 1996. Impact of pesticides in the Great Lakes Basin.[SEP]Abstract: Includes: The top 25 (by weight) and other important pesticides used in the Great Lakes Basin; Endocrine disrupting pesticides in the Great Lakes Basin; Carcinogenicity classification; Pesticides that pose a high acute risk to birds, mammals, or aquatic organisms; Hazard characteristics of the 25 most heavily used pesticides and other important pesticides; Exposure characteristics of the 25 most heavily used pesticides and other important pesticides.

52. Garry VF, Schreinemachers D, Harkins ME, Griffith J. 1996. Pesticide appliers, biocides, and birth defects in rural Minnesota. Environ Health Perspect 104(4):394-399.[SEP]Abstract: Earlier studies by our group suggested the possibility that offspring of pesticide appliers might have increased risks of birth anomalies. To evaluate this hypothesis, 4,935 births to 34,772 state-licensed, private pesticide appliers in Minnesota occurring between 1989 and 1992 were linked to the Minnesota state birth registry containing 210,723 live births in this timeframe. The birth defect rate for all birth anomalies was significantly increased in children horn to private appliers. Specific birth defect categories, circulatory/respiratory, urogenital, and musculoskeletal/integumental, showed significant increases. For the general population and for appliers, the birth anomaly rate differed by crop-growing region. Western Minnesota, a major wheat, sugar beet, and potato growing region, showed the highest rate of birth anomalies per/1000 live births: 30.0 for private appliers versus 26.9 for the general population of the same region. The lowest rates, 23.7/1000 for private appliers versus 18.3/1000 for the general population, occurred in noncrop regions. The highest frequency of use of chlorophenoxy herbicides and fungicides also occurred in western Minnesota. Births in the general population of western Minnesota showed a significant increase in birth anomalies in the same three birth anomaly categories as appliers and for central nervous system anomalies. This increase was most pronounced For infants conceived in the spring. The seasonal effect did not occur in other regions. The male/female sex ratio for the four birth anomaly categories of interest in areas of high phenoxy

herbicide/fungicide use is 2.8 for appliers versus 1.5 for the general population of the same region (p = 0.05). in minimal use regions, this ratio is 2.1 for appliers versus 1.7 for the general population. The pattern of excess frequency of birth anomalies by pesticide use, season, and alteration of sex ratio suggests exposure-related effects in appliers and the general population of the crop-growing region of western Minnesota.

53. Espandiari P, Thomas VA, Glauert HP, O'Brien M, Noonan D, Robertson LW. 1995 Jun. The herbicide dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a peroxisome proliferator in rats. Fundam Appl Toxicol 26 (1):85-90.[1] Abstract: The widely used broad leaf herbicide, dicamba, or Banvel, is similar in structure to xenobiotics which induce hepatic drug metabolism or proliferation of hepatic peroxisomes in rodents. The ability of xenobiotics to effect these hepatic changes often portends their positive outcomes in chronic bioassays. Dicamba's ability to induce hepatomegaly and peroxisome proliferation was studied in male and female Sprague-Dawley rats. Rats were placed on feed containing 0, 0.001, 0.01, 0.1, or 1% dicamba or 0.01% ciprofibrate for 3 weeks. Dicamba had no effect on relative liver weights or feed efficiency in either female or male rats at all doses tested. Dicamba, however, caused a statistically significant increase in peroxisomal beta-oxidation activity in liver homogenates from rats of both sexes fed 1% dicamba. Fatty acyl CoA-oxidase activity was increased in male rats fed 1% dicamba. A protein of M(r) 80 kDa was visible when liver homogenates of female or male rats fed 1% dicamba were subjected to SDS-PAGE. Lauric acid hydroxylase activity and CYP4A-reactive protein were increased in microsomes from male rats fed the highest level of dicamba. Moreover, dicamba was observed to transcriptionally upregulate the peroxisome proliferator-activated receptor (PPAR), a peroxisome proliferator sensitive receptor previously shown to be linked to the transcriptional regulation of a variety of peroxisome-specific enzymes. These studies show that dicamba is a peroxisome proliferator in rats. Although dicamba was not an efficacious inducer of peroxisomal enzymes in these rats, dicamba's ability to transcriptionally activate the PPAR and induce peroxisomal and related enzymes must be considered in the safety evaluation of this herbicide.

54. Cork DJ, Khalil A. 1995. Detection, isolation, and stability of megaplasmid-encoded chloroaromatic herbicide-degrading genes within Pseudomonas species. Adv Appl Microbiol 40:289-321.[1] Abstract: Dicamba is used as a model system for microbial degradation of chloroaromatic benzoic acids. The detection, isolation, and stability of a megaplasmid within a Pseudomonas sp. is described as the first step in optimizing the growth of this microorganism and other microorganisms similar to it. A large plasmid, pDK1, consisting of approximately 250 kb, was purified from dicamba-degrading Pseudomonas sp. PXM. This plasmid was purified by the method of Allen (personal communication, 1994), which is a modified version of several that have been attempted for the isolation of large plasmids (Lee and Rasheed, 1990). The restriction analysis of this plasmid (pDK1) from PXM. revealed many distinctive bands on agarose gel electrophoresis. Based on the preliminary restriction enzyme analysis, the estimated size of this plasmid is 250 kb, which could make it one of the largest procaryotic plasmids encoding for chloroaromatic degrading enzymes. Allen's methodology results in very high purity and reproducibility compared to the other methods used in this study. As described in this work, the method of Kado and Liu (1981) is easier to perform and results in a more reproducible plasmid preparation than the method of Casse et al. (1979). Casse's protocol requires the use of a highly alkaline SDS solution (pH 12.45) in order to eliminate the chromosomal DNA. However, only incomplete removal of the chromosomal DNA results. Compared to the Casse et al. protocol, the Kado and Liu protocol requires the use of a highly alkaline solution (pH 12.6) and a high temperature (55-65 degrees C) to eliminate the chromosomal DNA. This results in a nearly complete removal of the chromosomal DNA. The high temperature treatment also quickly eliminates the RNA. Another advantage of the protocol of Kado and Liu over the protocol of Casse et al. is that the former uses phenol-chloroform extraction while the latter uses only phenol extraction. The phenol-chloroform extraction step denatures the DNA along with the proteins. In addition to this, the phenol-chloroform mixture minimizes the formation of a brown oxidation pigment that usually occurs with phenol extraction alone. Finally, the time needed to complete the Kado and Liu protocol is much shorter (2 hr) than the time needed to complete the Casse protocol (8 hr). As described previously, a highly purified plasmid preparation with minimal chromosomal DNA was prepared by following the suggestions of L. Allen.(ABSTRACT

TRUNCATED AT 400 WORDS)

55. Hrelia P, Vigagni F, Maffei F, Morotti M, Colacci A, Perocco P, Grilli S, Cantelli-Forti G. 1994 Jun. Genetic safety evaluation of pesticides in different short-term tests. Mutat Res 321(4):219-28. Abstract: Cyanazine, cyhexatin, dicamba and DNOC are pesticides commonly and broadly used in agriculture pest control. However, there is little information on their toxicity and mutagenicity in human cells and in whole animals. Therefore, UDS assay and SCE assay in human peripheral lymphocytes, and chromosome aberration analysis in bone marrow of rats have been used to assess the DNA-damaging activity of the above pesticides. Cyanazine proved non-genotoxic in all the test systems. Cyhexatin showed only weakly positive results for SCE induction in human lymphocytes, providing no concern for genotoxicological hazard. While dicamba did not show clastogenic effects in rodents, DNOC gave significant dose-related increases of structural chromosome aberrations in rat bone marrow cells. Female animals showed increased sensitivity to the toxic effects by DNOC at the highest dose. The results provide further information on the intrinsic genotoxic activity of the tested pesticides, which may contribute to the toxicological assessment of the risk associated with human exposure.

56. Lewis RG, Fortmann RC, Camann DE. 1994. Evaluation of methods for monitoring the potential exposure of small children to pesticides in the residential environment. Arch Environ Contam Toxicol 26(1):37-46. Abstract: A nine-home pilot study was conducted to evaluate monitoring methods in the field that may be used to assess the potential exposures of children aged 6 months to 5 years to pesticides found in the home environment. Several methods, some of which were newly developed in this study, were tested for measuring pesticide residues in indoor air, carpet dust, outdoor soil, and on the children's hands. Information was also collected on household characteristics, pesticides used and stored at the residence, and children's activities. Pesticides were detected at all nine study homes. With the exception of one home, at least one pesticide was detected in all matrices sampled at each house. Of the 30 target pesticides, 23 were detected during the study. The most frequently detected pesticides were chlordane, chlorpyrifos, dieldrin, heptachlor, and pentachlorophenol. The greatest number of pesticides and highest concentrations were found in carpet dust. The results of these investigations will be discussed in terms of performance of the methods and the distribution of pesticides across the various media sampled. -- pyrethrins, carbaryl, åDDT, chorothalonil, pendimethalin)Prowl), 2,4-dichloroghenoxyacetic acid (2,4-D), dicamba and glyphosate (Roundup) --

57. Cox C. 1994. Dicamba. Journal of Pesticide Reform 14 (1):30-35. Abstract: Each year in the Unites States, about 15 million acres of corn, 1.5 million acres of wheat, and 3 million lawns are treated with the herbicide dicamba. While its name is often not commonly recognized, this wide use, together with concens about its toxicology and its effects on out environment, make it important to scrutinize dicamba's hazards. The article discusses the use of dicamba, its mode of action, acute toxicology, neurotoxicology, chronic toxicology, reproductive effects, mutagenicity, carcinogenicity, human exposure, effects on wildlife, effects of non-target plants, persistence, and contaminants. Dicamba is a selective herbicide and is used to kill broad-leaved plants growing in corn, rights-of-way, and lawns. Several different forms of dicamba are used as herbicides, the dimethylamine salt and the sodium salt are the most common.

58. Potter WT, Garry VF, Kelly JT, Tarone R, Griffith J, Nelson RL. 1993 Mar. Radiometric assay of red cell and plasma cholinesterase in pesticide appliers from Minnesota. Toxicol Appl Pharmacol 119(1):150-5. Abstract: In this study we demonstrate the uses of radiometric assay to detect anticholinesterases in a human population (N = 80) exposed to a broad spectrum of pesticides. The assay is nondilutional. Therefore, anticholinesterase (AChE) agents with low binding affinity can be detected. Our initial results show statistically significant exposure-related decreases in either red cell (AChE) or plasma cholinesterase activity ((butyrl)cholinesterase; BuChE) occurred not only among pesticide appliers who use organophosphates, but also among appliers of the fumigant phosphine. These data extend earlier observations made in laboratory animals exposed to this fumigant. Significant exposure-related decreases in AChE activity were seen in herbicide appliers and appear to be associated with exposure to the herbicide 2-methoxy-3,6-dichlorobenzoic acid. There was no

evidence of exposure-related decreases in BuChE activity in herbicide appliers. Our in vivo data, coupled with preliminary in vitro studies of phosphine (50% AChE inhibition, 10 ppm) and 2-methoxy-3,6-chlorobenzoic acid (50% AChE and BuChE inhibition, 70 ppm), suggest that the radiometric assay may be used to detect a broader spectrum of biologically active anticholinesterase agents.

59. Kutz FW, Cook BT, Carter-Pokras OD, Brody D, Murphy RS. 1992 Oct. Selected pesticide residues and metabolites in urine from a survey of the U.S. general population. J Toxicol Environ Health 37(2):277-91. Abstract: Residues of toxic chemicals in human tissues and fluids can be important indicators of exposure. Urine collected from a subsample of the second National Health and Nutrition Examination Survey was analyzed for organochlorine, organophosphorus, and chlorophenoxy pesticides or their metabolites. Urine concentration was also measured. The most frequently occurring residue in urine was pentachlorophenol (PCP), found in quantifiable concentrations in 71.6% of the general population with an estimated geometric mean level of 6.3 ng/ml. Percent quantifiable levels of PCP were found to be highest among males. Quantifiable concentrations of 3,5,6-trichloro-2-pyridinol (5.8%), 2,4,5-trichlorophenol (3.4%), para-nitrophenol (2.4%), dicamba (1.4%), malathion dicarboxylic acid (0.5%), malathion alpha-monocarboxylic acid (1.1%), and 2,4-D (0.3%) were found, but at much lower frequencies. No quantifiable levels of 2,4,5-T or silvex were found. Preliminary analyses showed an apparent relationship between residue concentration and two measures of urine concentration (osmolality and creatinine). A large segment of the general population of the United States experienced exposure to certain pesticides, including some considered biodegradable, during the years 1976-1980.

60. Cantor KP, Blair A, Everett G, Gibson R, Burmeister LF, Brown LM, Schuman L, Dick FR. 1992. Pesticides and other agicultural risk factors for Non-Hodgkin's lymphoma among men in Iowa and Minnesota. Cancer Res 52:2447-2455. Abstract: Data from an in-person interview study of 622 white men with newly diagnosed non-Hodgkin's lymphoma and 1245 population-based controls in Iowa and Minnesota were used to measure the risk associated with farming occupation and specific agricultural exposures. Men who ever farmed were at slightly elevated risk of non-Hodgkin's lymphoma (odds ratio = 1.2, 95% confidence interval = 1.0-1.5) that was not linked to specific crops or particular animals. Elevated risks were found, with odds ratio generally 1.5-fold or greater, for personal handling, mixing, or application of several pesticide groups and for individual insecticides, including carbaryl, chlordane, dichlorodiphenyltrichloroethane, diazinon, dichlorvos, lindane, malathion, nicotine and toxaphene. Associations were generally stronger for first use prior to 1965 than more recently, and when protective clothing or equipment was not used. Small risks were associated with the use of the phenoxyacetic acid herbicide 2,4-dichlorophenoxyacetic acid, but the risks did not increase with latency of failure to use protective equipment. Exposure to numerous pesticides poses problems of interpreting risk associated with a particular chemical, and multiple comparisons increase the chances of false-positive findings. In contrast nondifferential exposure misclassification due to inaccurate recall can bias risk estimates toward the null and mask positive associations. In the face of these methodological and statistical issues, the consistency of several findings, both within this study and with observations of others, suggests an important role for several insecticides in the etiology on non-Hodgkin's lymphoma among farmers.

61. [Anonymous]. 1992. Huge RfD Exceedances Released by EPA with Warnings. Pesticide & Toxic Chemical News (April 8):28-31. Abstract: TMRC calculations assume pesticide is present on 100% of each crop for which it has a tolerance. Pesticides scheduled for tolerance revocation in 1992: EPN, dinoseb, terbuthylazine, perfuidone, endrin (all tolerances), captan (11 tolerances), nitrapyrin, (2 tolerances).

62. Moody DE, Narloch BA, Shull LR, Hammock BD. 1991 Dec. The effect of structurally divergent herbicides on mouse liver xenobiotic-metabolizing enzymes (P-450-dependent mono-oxygenases, epoxide hydrolases and glutathione S-transferases) and carnitine acetyltransferase. Toxicol Lett 59(1-3):175-85. Abstract: Male mice were treated with structurally diverse herbicides to study their effect on liver xenobiotic-metabolizing enzymes. Chlorfiurecol, trifluralin, alachlor, propham, MCPP and 2,4-DP caused increases in phase I (cytochrome P-450, ethoxycoumarin O-deethylase, and/or

aminopyrine N-demethylase) and phase II (microsomal epoxide hydrolase and cytosolic glutathione S-transferase) activities. MCPP and 2,4-DP also increased cytosolic epoxide hydrolase and carnitine acetyltransferase activities suggestive of peroxisome proliferation. Benthiocarb and molinate increased only some phase II enzyme activities. Dicamba, at the dose employed, caused mortality and decreases in some of the enzymes monitored. Most of the herbicides tested induced xenobiotic-metabolizing enzyme activities, the pattern of induction being dependent on herbicide structure.

63. Beasley VR, Arnold EK, Lovell RA, Parker AJ. 1991 Oct. 2,4-D toxicosis. I: A pilot study of 2,4-dichlorophenoxyacetic acid- and dicamba-induced myotonia in experimental dogs. Vet Hum Toxicol 33(5):435-40.Abstract: English Pointer dogs dosed po with encapsulated 2,4-dichlorophenoxyacetic acid (2,4-D) or 2-methoxy-3,6-dichlorobenzoic acid (dicamba) developed varying degrees of myotonia. Dogs given 175 or 220 mg of 2,4-D/kg body weight rapidly developed clinical and electromyographic (EMG) manifestations consistent with a diagnosis of myotonia or pseudomyotonia. Dogs given 2,4-D at 86.7, 43.7 or 8.8 mg/kg body weight developed subclinical manifestations of myotonia detectable only with an electromyograph. The administration of 2,4-D at 1.3 or 1.0 mg/kg body weight failed to produce detectable EMG changes. One dog given dicamba at 86.7 mg/kg body weight developed clinical and EMG manifestations of myotonia similar to those induced by the highest doses of 2,4-D.

64. Perocco P, Ancora G, Rani P, Valenti AM, Mazzullo M, Colacci A, Grilli S. 1990. Evaluation of genotoxic effects of the herbicide dicamba using in vivo and in vitro test systems. Environ Mol Mutagen 15(3):131-5.Abstract: The genotoxic effects of the herbicide dicamba have been studied by measuring 1) the unwinding rate of liver DNA from intraperitoneally (i.p.) treated rats (fluorimetric assay); 2) DNA repair as unscheduled DNA synthesis (UDS) induced in cultured human peripheral blood lymphocytes (HPBL); and 3) sister chromatid exchanges (SCE) in HPBL. Results show that dicamba is capable of inducing DNA damage since it significantly increases the unwinding rate of rat liver DNA in vivo and also induces UDS in HPBL in vitro in the presence of exogenous metabolic activation (S-9 mix). Furthermore, dicamba causes a very slight increase in SCE frequency in HPBL in vitro.

65. Arnold EK, Beasley VR. 1989 Apr. The pharmacokinetics of chlorinated phenoxy acid herbicides: a literature review. Vet Hum Toxicol 31(2):121-5.Abstract: The chlorinated phenoxy acid herbicides (CPAHs) appear to have similar pharmacokinetics. They are rapidly and almost completely absorbed from an oral dose. They distribute to other tissues and are highly protein-bound in the plasma. The CPAHs are rapidly eliminated unchanged in the urine by an active process in the kidneys. Increasing doses apparently influence absorption, metabolism, distribution and elimination of the CPAHs so that biological effects are increased. Combinations of CPAHs are likely to result in additive or potentiated biological effects. Data suggest that CPAH toxicosis may be alleviated by treatment with fluids and bicarbonate to increase urinary pH and volume, thereby increasing excretion.

66. US EPA. 1988. Health advisories for 50 pesticides.Abstract: These documents summarize the health effects of 50 pesticides including: acifluorfen, ametryn, ammonium sulfamate, atrazine, baygon, bentazon, bromacil, butylate, carbaryl, carboxin, chloramben, chlorothalonil, cyanazine, dalapon, dacthal, diazinon, dicamba, 1,3-dichloropropene, dieldrin, dimethrin, dinoseb, diphenamid, disulfoton, diuron, endothall, ethylene thiourea, fenamiphos, fluometuron, fonofos, glyphosate, hexazinone, maleic hydrazide, MCPA, methomyl, methyl parathion, metolachlor, metribuzin, paraquat, picloram, prometon, pronamid, propachlor, propazine, propham, simazine, 2,4,5,-T, tebuthiuron, terbacil, terbufos, and trifluralin. Topics discussed include: General Information and Properties, Pharmacokinetics, Health Effects in Humans and Animals, Quantification of Toxicological Effects, Other Criteria Guidance and Standards, Analytical Methods, and Treatment Technologies.

67. O'Brien MH. 1988. Dicamba. NCAP Fact Sheet (January 20).

68. Gaines TB, Linder RE. 1986 Aug. Acute toxicity of pesticides in adult and weanling rats. Fundam Appl Toxicol 7(2):299-308.Abstract: LD50 values were determined for 57 pesticides administered by the oral or dermal route to adult male and female Sherman rats. Thirty-six of the chemicals were also

tested by the oral route in one sex of weanlings. Nine pesticides tested by the oral route (bufencarb, cacodylic acid, dialifor, deltamethrin, dicamba, diquat, quintozene, phoxim, pyrazon) and four tested by the dermal route (bufencarb, chlordimeform, dichlofenthion, leptophos) were more toxic to females than to males whereas famphur and 2,4,5-T (oral route) were less toxic to females. Eighteen of the test chemicals were more toxic to the adult than to the weanling and four compounds (leptophos, methidathion, pyrazon, and sulfoxide) were more toxic to the weanling. In additional studies the variability of the LD50 value over a 1-year period was examined for two typical insecticides. Six consecutive bimonthly oral LD50 determinations for parathion and DDT in adults of both sexes indicated that the LD50 values were little affected by the time of year that the tests were done.

69. Makary MH, Street JC, Sharma RP. 1986. TOXICOKINETICS OF DICAMBA (3,6-DICHLORO-2-METHOXY-BENZOIC ACID) AND ITS 3,5-DICHLORO ISOMER FOLLOWING INTRAVENOUS ADMINISTRATION TO RATS. Pestic Biochem Physiol 25(1):98-104.

70. Makary MH, Street JC, Sharma RP. 1986. PHARMACOKINETICS OF DICAMBA ISOMERS APPLIED DERMALLY TO RATS. Pestic Biochem Physiol 25(2):258-263.

71. Grover R, Cessna AJ, Kerr LA. 1985 Feb. Procedure for the determination of 2,4-D and dicamba in inhalation, dermal, hand-wash, and urine samples from spray applicators. J Environ Sci Health B 20(1):113-28. Abstract: Analytical procedures for the simultaneous determination of residues of 2,4-D and dicamba from polyurethane foam plug air samplers, ethylene glycol impregnated glass-fiber filter paper dermal samplers, 1% sodium bicarbonate hand wash solution, and urine are presented. Residues were derivatized with diazomethane and quantitated using electron capture gas chromatography. Recoveries were greater than 80% at the limit of detection in all substrates. The limits of detection for both herbicides were 0.1 microgram/foam plug and 0.5 micrograms/filter paper, and in the urine, 1.7 micrograms/100 mL and 5.0 micrograms/100 mL for dicamba and 2,4-D, respectively.

72. Fraser AD, Isner AF, Perry RA. 1984 Oct. Toxicologic studies in a fatal overdose of 2,4-D, mecoprop, and dicamba. J Forensic Sci 29(4):1237-41. Abstract: A suicidal poisoning committed by a 61-year-old woman, who ingested an unknown quantity of Killex, containing in aqueous solution 100 g/L of (2,4-dichlorophenox)acetic acid (2,4-D), 50 g/L of mecoprop, and 9 g/L of dicamba as amine salts is described. Quantitation of chlorophenoxy acids was performed by extraction from an acidified mixture and concentration before high performance liquid chromatography analysis. All three herbicides were separated in a phosphate buffer/acetonitrile mixture at 280 nm on a RP-8 column. Concentrations of herbicides found were: in blood--520-mg/L 2,4-D, 530-mg/L mecoprop, and 170-mg/L dicamba; in urine--670-mg/L 2,4-D and 520-mg/L mecoprop; in bile--340-mg/L 2,4-D, 530-mg/L mecoprop, and 140-mg/L dicamba; and in liver--540-mg/Kg 2,4-D, 500-mg/Kg mecoprop, and less than 100-mg/Kg dicamba. Liquid chromatography was found to be a reliable method for herbicide quantitation in biological tissues and fluids. The technique offered definite advantages over ultraviolet spectrophotometry and avoids the derivatization requirement for gas chromatography.

73. Plewa MJ, Wagner ED, Gentile GJ, Gentile JM. 1984 Jun. An evaluation of the genotoxic properties of herbicides following plant and animal activation. Mutat Res 136(3):233-45. Abstract: Commercial and technical grades of 11 herbicides and 13 combinations of commercial grade herbicides were evaluated for their genotoxic properties with Salmonella typhimurium, Saccharomyces cerevisiae directly and following plant and animal activation, or with Zea mays. The herbicides were related by their use in commercial corn (maize) production. Commercial grade formulations of each herbicide and combination of herbicides were also evaluated in situ with the pollen waxy locus assay of Z. mays. Eradicane and bifenox were negative in all assays. Alachlor, propachlor, procyazine and SD50093 (a formulation of cyanazine plus atrazine) were positive in one assay. Cyanazine, dicamba and metolachlor were positive in 2 assays. Atrazine, simazine and butylate were tested only in situ. Atrazine and simazine were positive and butylate was negative. Of the combinations of herbicides evaluated with the 3 genetic assays, alachlor plus bifenox and procyazine plus metolachlor were

positive in 1 assay and metolachlor plus atrazine was positive in 2 assays. Of the combinations of herbicides evaluated only in situ, butylate plus atrazine, eradicane plus atrazine, eradicane plus cyanazine and metolachlor plus cyanazine were positive while butylate plus cyanazine was negative.

74. Yeary RA. 1984 Feb. Oral intubation of dogs with combinations of fertilizer, herbicide, and insecticide chemicals commonly used on lawns. Am J Vet Res 45(2):288-90.Abstract: Six Beagle dogs were orally intubated with mixtures of a urea-based fertilizer, 2,4-D, mecoprop (MCPP), dicamba, and either bensulide or chlorpyrifos. The mixtures were formulated as they are used in liquid application to lawns. The dogs were given volumes of 10 ml/kg of body weight, delivering the following quantities of each ingredient: urea--623 mg/kg, inorganic phosphorus (P2O5)--24 mg/kg, potassium (K2O)--66 mg/kg, 2,4-D--6.5 mg/kg, MCPP--3.26 mg/kg, dicamba--0.55 mg/kg, and either bensulide--60.93 mg/kg or chlorpyrifos--6.77 mg/kg. The dogs were given 3 consecutive daily doses of the mixture containing bensulide (round 1) or the mixture containing chlorpyrifos (round 2). The dogs did not exhibit any clinical signs of illness associated with the treatments. Effects on hematologic values or routine clinical chemical analyses did not occur with the round 2 mixture. Serum lactic dehydrogenase activity decreased by approximately 50% after a single dose of the round 1 mixture was given. Plasma cholinesterase decreased to approximately 50% of control values following either the round 1 or the round 2 mixture; this decrease was not accompanied by cholinergic signs of intoxication.

75. Murphy RS, Kutz FW, Strassman SC. 1983. Selected pesticide residues or metabolites in blood and urine specimens from a general population survey. Environ Health Perspect 48:81-86.Abstract: The preliminary unweighted data from NHANES II suggest rather widespread exposure of the general population aged 12-74 yr to certain pesticides. The data also suggest that most people are not occupationally exposed; they come incontact with these substances throught other sources. Due to selective sampling by poverty segments and age group, the final weighted results could change significantly from the results presented. Weighting will not significantly affect such results as those shown for DDT and its analogs (99% positive) and pentachlorophenol (79% positive).

76. Makary MH, Street JC, Draper WM. 1983. TOXICOKINETICS OF DICAMBA (3,6-DICHLORO-2-METHOXYBENZOIC ACID)ISOMERS IN THE RAT. Abstracts of Papers of the American Chemical Society 185(MAR):102-PEST.

77. Zhidkova LV. 1982 Oct. [Enzyme activity of the blood and tissues of individual organs in long-term exposure to dianate]. Gig Sanit (10):77-9.

78. Kagan NA, Aleksashina ZA, Buslovich SIu, Karaseva AE, Kolosovakaia VM. 1982 Aug. [Hygienic standard for the maximum permissible level of diamet-D residues in food products]. Gig Sanit (8):86-7.

79. Draper WM, Street JC. 1982. Applicator exposure to 2,4-D, dicamba, and a dicamba isomer. J Environ Sci Health B 17(4):321-39.Abstract: Potential respiratory and dermal exposure to applicators were estimated in a ground boom spray application of 2,4-D and dicamba. Time-weighted averages for airborne herbicide residues did not exceed 2.2 microgram/cu.m. in the cabs of application vehicles allowing only minor respiratory exposure. Dermal exposure was important as relatively large amounts of 2,4-D (1.2 - 18 mg) and dicamba (0.32-6.6 mg) were rinsed from applicators' hands. Urine analysis showed that the maximum elimination of herbicides occurred between 16 and 40 h after terminating exposure. A dicamba isomer (20% of the active material in the commercial formulation) was excreted in higher concentrations than dicamba in applicators' urine suggesting different toxicokinetic properties for the two compounds.

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81. Luciak M, Kita K, Kita I. 1980. [Morphological studies of chronic toxicity of Chwastox D]. Med Pr 31(3):177-84.Abstract: Chwastox D--herbicide for killing dicotyledonous weeds was evaluated

toxicologically, basing on studies on the mass and morphological picture of internal organs of rats receiving, over 13 weeks, 15, 60, 240 and 960 mg/kg of feeding stuff containing this herbicide. The animals exposed for 13 weeks to different doses of Chwastox D were found to develop inspecific pathomorphotic changes, like disturbed circulation, retrogressive, progressive and inflammatory changes. The pathomorpohologic changes were found to be increased with 240 and 960 mg of stuff. The observations indicated that the maximum allowable dose for rats is 60 mg/kg of the feeding stuff.

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83. Young JF, Haley TJ. 1977 Dec. Pharmacokinetic study of a patient intoxicated with 2,4-dichlorophenoxyacetic acid and 2-methoxy-3,6-dichlorobenzoic acid. Clin Toxicol 11(5):489-500.SEPAbstract: A simultaneous pharmacokinetic study of two chemicals has been conducted on a clinically stabilized human who had intentionally ingested a mixture of 2,4-D and Dicamba. The information developed can be useful to the clinical toxicologist in the management of similar cases.

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86. Mineau P, Morrison C, Whiteside M, Harding K. [2006?]. Developing risk-based rankings for pesticides in support of standard development at Environment Canada: Preliminary terrestrial rankings. Internal Document? 72 pp.SEPAbstract: [**Acute risk of mortality in birds at max application rate** > 0.90 for: naled, phorate, diazinon, phosmet, terbufos, chlorpyrifos, oxamyl, endosulfan, azinphos-methyl, carbofuran, triclorfon;...SEP**Acute mammalian mortality risk quotients** > 100 for Oxamyl, endosulfan, formetanatate, ethofumesate; >10 for 15 other pesticides,....SEP**Top combined acute risk pesticides (worst first)**: oxamyl, endosufan, diazinon, azinphos-methyl, carbofuran, chlorpyrifos, phosmet, naled, thiram, formetanate, methamidophos, trichlorfon, ziram, methomyl dimethoate, dichloran, acephate, endothall, diquat, captan, copper oxychloride, dichlobenil, linuron, MCPA, glyphosate (acid), 2,4-D (unspecified ester), MCPB (sodium salt, dicamba, chlorthal,...SEP**Top avian acute risk of granules and seed treatments** (<10 particles to HD5): diazinon, terbufos, imidacloprid, captan, carbathin, thiram, clothianidin, metalaxyl, chlorpyrifos, thiamethoxam, dazomet,...SEP**Top mammalian acute risk of granules and seed treatments** (<10 particles to HD5): terbufos, imidacloprid, thiram, diazinon,...SEP**Risk indices based on chronic threshold exceedance-days**SEP**Top pesticides with the highest reproductive risk to birds** (based on reproductive toxicity AND exposure: bensulide, diquat, thiram,, diazinon, dicofol, formetanate, metolachlor, permethrin, mancozeb, diuron,...SEP**Top pesticides with the highest reproductive risk tomammals** (based on reproductive toxicity AND exposure: diuron, formetanate, bensulide, metiram, mancozeb, thiram, linuron, paraquat, terbucil, MCPA...SEP**Top avian reproductive risk of granules and seed treatments** (<1 particle to avian chronic threshold): imidacloprid, diazinon, terbufos, thiram, captan, dazomet, mancozeb, carbathiin, diazinon, chlorpyrifos, thiamethozam, maneb, difenoconazole, imidacloprid, tebuconazole, thiram, tefluthrin,...SEP**Top mammalian reproductive risk of granules and seed treatments**SEP(<=0.01 particle to mammalian chronic threshold (cPAD): chlorpyrifos, diazinon, thiamethoxam, terbufos, carbathiin, thiram, dazomet, imidacloprid, thiamethoxam, captan, maneb, metalaxyl, difenoconazole, clothianidin, EPTC, ethalfluralin,...