Comparative Risks of Multiple Chemical Exposures

Final Report
for the
Legislative Commission on Minnesota Resources

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EXECUTIVE SUMMARY

This report, "Comparative Risks of Multiple Chemical Exposures," interprets what the results of a comparative risk analysis of the Minnesota Children's Pesticide Exposure Study (MCPES) data mean to human health. The Minnesota Department of Health (MDH) prepared this report for the Legislative Commission on Minnesota Resources (LCMR).

This report includes: (1) a summary of the methods used for exposure estimation, toxicity evaluation, and risk calculation; (2) the results of health risk assessment for individual chemicals and for multiple chemicals, using several approaches for combining exposures or risks; and (3) a discussion of the limitations of the analysis and what can be learned from the study.

The MCPES was conducted by the United States Environmental Protection Agency (US EPA) and national researchers to evaluate the feasibility of measuring concentrations of pesticides and polycyclic aromatic hydrocarbons (PAHs) in multiple environmental and personal media and in biological samples. The MDH received LCMR support to expand the study to include metals, volatile organic chemicals (VOCs), and herbicides. Samples of personal, indoor, and outdoor air; food; beverages; water; soil; house dust; blood; urine; and hair were collected and analyzed for environmental contaminants.

The objectives of the MCPES were to: (1) evaluate children's exposures to environmental contaminants, both individually and in combinations; (2) evaluate the relative significance of exposure pathways (i.e., ingestion, inhalation) for children; and (3) compare health risks posed by the chemicals studied. The goal of the MDH's comparative risk analysis was to provide decision-makers with information necessary to establish policy and set priorities for directing resources to reduce children's exposures to environmental contaminants. LCMR support expanded the number of chemicals that could be measured and compared, thereby allowing risks from pesticides to be put into perspective.

The MCPES was conducted during the summer of 1997. Researchers gathered personal data and pesticide use information and collected environmental, personal, and biological samples from 102 homes with children in Minneapolis, St. Paul, and Goodhue and Rice Counties. In an effort to ensure that some samples contained measurable quantities of pesticides, households that reported past pesticide use were disproportionately included in the study. Because participating households were not randomly selected, the results of this analysis cannot be extrapolated to the general population.

Generally, the children's exposures to noncarcinogens did not approach harmful levels. Whether chemical exposures were considered separately, or combined in a variety of ways, nearly all exposures were at levels that a child's body is expected to safely metabolize and eliminate. Children's total cancer risk from all exposures to carcinogens ranged from 2/100,000 to 7/10,000. Benzene was the single chemical that contributed a large share of each child's overall risk.

Hazards and risks described may either overestimate or underestimate participants' health risks from environmental exposures. Due to the many conservative assumptions incorporated in a risk

assessment, hazards and risks described may overestimate the health impact of exposures actually measured in the study. However, the MCPES describes only a portion of environmental health concerns; many potential contaminants were not measured. Therefore, hazards and risks described may underestimate overall risk to environmental contaminants. Finally, methods for considering the combined effects of environmental exposures are still under development. How to consider multiple risks was, in fact, the single most difficult task in interpreting the results of this study. Efforts led to a range of quantitative answers. However, any quantitative estimate must still be evaluated in terms of the public's tolerance for risk and perception of benefits. Currently, a comprehensive understanding of the public's willingness to accept risk in exchange for tradeoffs is lacking. In the meantime, policy should supplement science and professional judgment in making decisions concerning cumulative and comparative risk.

INTRODUCTION

This report interprets what the results of the MCPES mean to human health. The MDH prepared this report for the Legislative Commission on Minnesota Resources. Funding for this project was approved by the Minnesota Legislature, ML 1997, Chapter 216, Section 15, Subd. 10(a) Comparative Risks of Multiple Chemical Exposures, as recommended by the Legislative Commission on Minnesota Resources from the Minnesota Future Resources Fund.[1]

The MCPES, which was a sub-study for a much larger national pilot study, was specifically designed to test methods of measuring children's pesticide exposures. As initially proposed, the study included pesticides and polycyclic aromatic hydrocarbons. The Minnesota Legislature funded expansion of the study to include analysis of acid herbicides, metals, and volatile organic chemicals, common environmental contaminants. Using standard techniques for exposure estimation and risk assessment, the MDH evaluated data from the study to determine which, if any chemicals tested, either individually or in combination, posed risks to study participants. The intent of this evaluation was to conduct a comparative risk analysis to learn which chemical or chemicals of those measured pose the greatest risk to this subset of Minnesota children. This information is intended to aid decision-makers in establishing policy and setting priorities for directing resources to reduce children's exposures to environmental contaminants.

This report includes: (1) a summary of the methods used for exposure estimation, toxicity evaluation, and risk calculation; (2) the results of the health risk assessment for individual chemicals and for multiple chemicals, using several approaches for combining exposures or risks; and (3) a discussion of the limitations of the analysis and what can be learned from the study. An earlier interim report, "Comparative Risks of Multiple Chemical Exposures," prepared in June 1999, summarized the procedures for conducting the comparative risk analysis and the scientific support for that analysis in greater detail than is presented in this report. That report is available from the Health Risk Assessment Unit of the MDH Division of Environmental Health. Resources used in conducting the comparative risk analysis using MCPES data can be found following the text of this report.

METHODS

Sample Collection and Chemical Analysis

In the summer of 1997, researchers gathered information and collected environmental, personal, and biological samples from 102 homes with children in Minneapolis, St. Paul, and Goodhue and Rice Counties. By design, households that reported past pesticide use were disproportionately included in the study. Contractors for the United States Environmental Protection Agency analyzed the samples to measure concentrations of VOCs, PAHs, pesticides, and metals. The

[1] Language provided by the Legislative Commission on Minnesota Resources.

Centers for Disease Control and Prevention (CDC) performed chemical analysis of blood and urine samples. (For a list of the types of samples collected and chemicals measured, see Tables 1 and 2 in the Appendix.) The US EPA contractors performed data quality checking and analysis, and eliminated samples that did not satisfy quality standards.

Exposure Estimation

Exposure Algorithm

Using exposure algorithms developed by the US EPA, the MDH estimated each child's internal exposure to (or dose of) each chemical measured in ingestion media and to PAHs and pesticides measured in air. The general form of the algorithm is:

$$\text{Dose} = \frac{\text{Concentration x Intake Rate x Exposure Frequency x Exposure Duration}}{\text{Body Weight x Averaging Time}}$$

Inhalation toxicity values for VOCs can be directly compared to measured concentrations in air. Therefore, calculation of dose from the inhalation pathway was not necessary for VOCs.

The MDH incorporated concentrations and other information collected during the study into the algorithms and used exposure assumptions to complete the equations. Concentrations measured during the monitoring period (a four to six day period between May and September of a child's fourth through thirteenth years) were assumed to be representative of concentrations each participant would encounter on a daily basis throughout life. Calculations were based on the most complete data set available to the MDH as of May 1, 2000 and on individual participant reports provided by Research Triangle Institute (RTI), the primary US EPA contractor on the study.

Researchers sampled indoor, outdoor, and personal air. Each personal air sample was collected by an air monitor that a participating child carried in a backpack. Since the personal air samples were most representative of the children's actual exposures, chemical concentrations in personal samples, rather than concentrations in indoor or outdoor samples, were used in dose and risk calculations.

Noncarcinogens

Calculations for noncarcinogens used measured concentrations, children's body weights and, where available, intake rates measured in the study. Child appropriate exposure assumptions were used for other parameters. Assumptions were derived from the US EPA's Exposure Factors Handbook, scientifically developed models, and peer reported and reviewed scientific studies. (See Table 3 in the Appendix for a list of default assumptions applied in estimating exposure to noncarcinogens.)

Carcinogens

Calculations for carcinogens were based on an assumed lifetime of 70 years. Calculations for each participant applied the measured intake rate of food for the pre-adult years and used an assumed intake rate of food for the adult years. Body weight was varied to be representative of weight patterns throughout a lifetime. Again, exposure assumptions derived from the US EPA's Exposure Factors Handbook, models, and scientific studies were used for other parameters in the equations. (See Table 4 in the Appendix for a list of default assumptions applied in estimating exposure to carcinogens.)

Samples Below the Level of Detection

In many samples, contaminant concentrations could not be reliably measured; that is, if any amount of a contaminant was present, it was below the smallest amount that could be detected by the laboratory method used. In analyzing MCPES data, the MDH used several different methods of handling samples below detection. Unless otherwise stated, results reported below were arrived at by setting concentrations for samples below detection to one half the detection limit.

Toxicity Evaluation

Ingestion

The MDH evaluated toxicity information for each chemical to identify reference points for health effects. (See Table 5 in the Appendix for a list of the most sensitive health effect associated with each MCPES chemical.) For the ingestion pathway, values for most chemicals were reference doses (RfDs) or cancer potency slopes derived from the US EPA's Integrated Risk Information System (IRIS). The only exceptions were diazinon, for which IRIS lists no ingestion toxicity value, lead, and arsenic. A toxicity value for diazinon was adopted from the US EPA's Health Effects Assessment Summary Tables (HEAST). No ingestion toxicity value was identified for lead or for arsenic. Lead in dust was evaluated using a value derived from a regulatory cleanup level used by the MDH. Health risk from lead was evaluated by comparing available biological measurements, i.e., blood-lead levels, with the CDC's definition of elevated lead in blood (> 10 micrograms/deciliter [ug/dL]).

Inhalation

Inhalation toxicity values for VOCs were derived from several sources, including MDH draft Health Risk Values (HRVs), California Reference Exposure Levels (RELs), and ATSDR Minimal Risk Levels (MRLs). For p-dichlorobenzene, a chronic toxicity value was derived by adjusting a shorter-term HRV. The toxicity of chloroform is currently the subject of considerable discussion; for chloroform, an acute HRV was used. The following table lists sources of toxicity values for VOCs, in order of preference, and the VOCs for which each source was used.

Source	VOC
HRVs	Toluene, Styrene, Benzene, p-Dichlorobenzene, Chloroform
RELs	Xylenes, Trichloroethylene
MRLs	1,1,1-Trichloroethane, Tetrachloroethylene

With the exception of dichlorvos, for which a HRV has been established, no inhalation values were available for pesticides. The MDH used oral reference doses and cancer potency slopes from IRIS to develop inhalation toxicity values for pesticides.

No IRIS inhalation toxicity values were located for PAHs. Three noncarcinogenic PAHs, anthracene, fluoranthene, and pyrene, have oral reference doses. Based on physical and chemical characteristics of PAHs and the fact that they cause systemic toxicity, rather than affecting only the lungs, these oral values were used in the inhalation risk assessment. The California Office of Environmental Health Hazard Assessment (OEHHA) lists an inhalation unit risk for benzo(a)pyrene. For benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, chrysene, and indeno[1,2,3-c,d]pyrene, the OEHHA provides "potency equivalency factors" (PEFs); that is, numerical values that express toxicity of these less potent carcinogens as a fraction of the toxicity of benzo(a)pyrene, a closely related but more toxic chemical. Toxicity values for these PAHs were established using the OEHHA inhalation unit risk for benzo(a)pyrene and the PEFs. No toxicity information for acenaphthylene, benzo(ghi)perylene, or phenanthrene was found, and these three PAHs were not included in the risk assessment process.

Biological Samples

As stated above, health risk associated with lead exposure was evaluated by comparing available blood-lead levels with the CDC's definition of elevated lead in blood. Arsenic concentrations in hair were compared to an MDH benchmark of 0.5 micrograms/gram (µg/g).

Risk Assessment

Individual Chemicals

For each child in the study, the MDH compared estimated doses of each chemical in each ingestion or inhalation medium to chemical and pathway specific toxicity values. For a noncarcinogen, an exposure only reaches a "level of concern" when the dose is equal to or greater than the toxicity value; for a carcinogen, lifetime exposure at the toxicity value is associated with a small risk of cancer above the background rate. Measurements of contaminants in biological media (e.g., hair, urine, or blood) were compared to levels considered to be without health risk where such levels are known.

When a child was exposed to a chemical in more than one medium sampled (e.g., air and food) the MDH added each child's exposures (or incremental risks) across the media. Pesticides were

the only type of chemical for which extensive multi-media, multi-pathway concentrations were available to the MDH and were therefore the only type of chemical for which this analysis was performed. Only those exposures that result in the same health endpoint were added. Dichlorvos exposures from inhalation and ingestion were not added because the most sensitive endpoint for these exposures differs; the former has a neurological endpoint, while the latter has a cancer endpoint. (See Table 6 in the Appendix for a list of the medium or media in which each chemical was measured.)

Multiple Chemicals

In order to more closely approximate risk from the mixture of chemicals to which people are exposed every day, the MDH added incremental risks from all chemicals that result in the same health endpoint. The "same health endpoint" may be either a common disease or common target organ or organ system. For this analysis, all cancer is considered to be the same health endpoint. Although increasing concentrations of chemicals may evoke additional toxic responses, only the response occurring at the lowest concentration was considered. Chemicals included in the MCPES affect the following organs or organ systems at low doses: nervous system, liver, blood, and kidney. In addition, chemicals cause the following diseases or health outcomes: slowed growth, developmental effects, and cancer. Due to the absence of an applicable toxicity value, lead was not included in this analysis. Although the CDC has defined a blood-lead level of concern, there was no quantitative way to add this to other chemicals with developmental or neurological endpoints. Also, blood-lead results were below the CDC's level of concern. Table 5 in the Appendix shows the chemicals included in risk estimates for each health endpoint listed.

The MDH also looked at cumulative risk by adding risk only from those chemicals that cause the same effect by acting on the same molecular target or tissue through the same biochemical mechanism. MCPES chemicals that meet these criteria are the organophosphate pesticides: chlorpyrifos, diazinon, malathion, and dichlorvos (inhalation only). These pesticides act primarily by inhibiting the enzyme that stops transmission of nerve impulses.

Participant Reporting

In reporting results to participating families, the MDH used a different approach than the approaches described here. Participant reports provided each family with the concentrations measured in samples from that household and presented "reference values" to which measured concentrations could be compared. The reference values provided in participant reports were calculated for the "most sensitive" child in the study; that is, the child with the highest intake rate relative to body weight. In this report, risk was assessed for each child individually, using that child's own parameters for body weight and intake rates whenever available.

Comparative Risk

Finally, the MDH evaluated the data to determine whether, for MCPES chemicals, it could answer the question "Which is the worst?" Factors considered were calculated risk, the

prevalence of concentrations that lead to risk or non-negligible risk, and the prognosis and timing of the health endpoint.

(For a more complete description of risk assessment methods, see the Interim Report for the LCMR, Comparative Risks of Multiple Chemical Exposures, issued in June of 1999.)

RESULTS

Exposure

An essential question in a chemical risk analysis is whether there is a possibility for exposure. MCPES chemicals were found in a variety of the media sampled. The percentages of samples with detectable concentrations of chemicals are shown in the Appendix (Table 7). While these results show that there was a possibility for exposure, the mere presence of a chemical does not automatically imply a risk to health. Nor does the inability to measure a chemical necessarily mean that there is no risk to health. Additional information, including the level of internal exposure (i.e., dose), the toxicity of the chemical, and the sensitivity of laboratory methods (i.e., the detection limit, which is the lowest concentration that can be measured reliably), is necessary to know whether a chemical poses any risk to health. (For more information about health risks, see Risk section, below.)

Pesticides

Concentrations of pesticides in many environmental and personal samples were below levels that could be measured. No pesticides were detected in beverages, and only a few drinking water and soil samples had detectable levels of pesticides. Pesticides were found in air, food, and dust samples; however, the number of samples with measurable concentrations varied significantly depending on the chemical and medium.

The pesticide most often found in this study was chlorpyrifos, which was detected in 95% of the personal air samples, 67% of the food samples, and 62% of the surface dust samples. In personal air samples, the pesticide found next most frequently was cis-permethrin. The chlordanes, dieldrin, DDD, DDE, and DDT were fairly common in both air and food. (See the Discussion section for more information about these pesticides.) Two-thirds or more of the homes had measurable concentrations of the herbicides 2,4-D, MCPA, and/or MCPP in dust collected from floors or mats in entry ways. (For a list of scientific names for chemicals discussed in this paragraph, see the Glossary of Abbreviations at the end of this report.)

Urine samples were analyzed for the presence of a limited number of pesticides (or their breakdown products), including chlorpyrifos (3,5,6-trichloro-2-pyridinol), atrazine (atrazine mercapturate), malathion (malathion dicarboxylic acid), napthylene (1-naphthol and 2-naphthol), carbamates (1-naphthol), and 2,4-D. Detection of pesticides or their breakdown products in urine is a direct indication that exposure has occurred. Over 90% of the children in this study had

measurable levels in urine of 3,5,6-trichloro-2-pyridinol (TCPY), a metabolite of chlorpyrifos. In contrast, urine results showed that few children had measurable exposures to atrazine. Table 8 in the Appendix shows the metabolites measured, their parent compound(s), and the percent of samples in which the metabolites could be measured.

Volatile Organic Chemicals

Over 90% of personal air samples had detectable levels of all VOCs measured in the study except tetrachloroethylene. Over 80% of all personal air samples had detectable levels of tetrachloroethylene. VOC concentrations were higher in personal air than indoor air, and concentrations in indoor air were higher than concentrations in outdoor air.

Metals

MCPES metals were found in nearly all food and house dust samples. Arsenic was found in all food and dust samples, but in only 52% of hair samples. Mercury was found in over 80% of food samples and in all hair samples. Lead was found in over 80% of house dust samples. While some homes had high concentrations of lead (maximum 1900 nanograms per cubic centimeter, floor wipe), concentrations of lead in blood samples were not elevated (i.e., all blood samples were below the 10 µg/dl level of concern). Table 9 in the Appendix shows the percent of samples with measurable concentrations of metals in blood and hair.

Polycyclic Aromatic Hydrocarbons

Although PAHs were measured in food and dust as well as indoor, outdoor, and personal air, the data sets to which the MDH had access did not contain the food and dust measurements. All PAHs included in the study except indeno(1,2,3-c,d)pyrene were detected in over 50% of personal air samples. Anthracene, benzo(b)fluoranthene, benzo(ghi)perylene, chrysene, fluoranthene, phenanthrene, and pyrene were detected in over 90% of personal air samples; the last three were found in measurable quantities in all personal air samples tested. Measurements in personal air samples for most PAHs were higher than measurements in indoor or outdoor air.

Risk

Individual Chemicals

Noncarcinogens

Exposure to a noncarcinogen does not reach a level of concern unless the ratio of the exposure to the toxicity value (the “hazard quotient”) is equal to or greater than one. Below this level, the body is expected to effectively detoxify the substance in question, with no risk to health.

Generally, participants’ exposures to individual noncarcinogens at levels measured in any single medium did not reach levels of concern. That is, exposures were below toxicity values. There were a few exceptions, including lead in dust, dichlorvos in personal air samples, and arsenic in

hair. While calculations for participant reports, which were based on the child with the smallest body weight, indicated that one measured concentration of trichloroethylene reached a level of concern, when calculations were performed for each individual participant, no actual child's exposure reached a level of concern. For a summary of health results from individual noncarcinogens analyzed in the MCPES, see Table 10 in the Appendix.

Exposure estimates using concentrations of lead measured in house dust and standard exposure assumptions were above values derived from MDH cleanup levels. However, no child who supplied a blood sample had a blood-lead level that the MDH considered elevated. (The MDH adheres to CDC's reference value of 10 µg/dL.)

The measurement of dichlorvos in one child's personal air sample was more than 40 times higher than the next highest concentration. Long term exposure to this concentration in air could be a health concern.

Concentrations of arsenic in four hair samples reached or exceeded the MDH reference value. The MDH did not collect information on the source of the exposure. Concentrations of arsenic in food were measured, but the laboratory procedure did not distinguish between toxic forms of arsenic and nontoxic forms, which are generally more common. Children with high levels of arsenic in hair were not among those children with elevated concentrations of arsenic in food.

The US EPA recently reduced the acceptable exposure of chlorpyrifos by a factor of 10. Even with this additional safety factor, exposures estimated from concentrations in individual samples were not above a level of concern.

Carcinogens

Cancer "risk" is the probability of a life-long exposure causing cancer and is expressed as a statistical probability; for example, 1/1,000,000, 1/100,000, or 1/10,000. This can also be thought of as 1 cancer case in a population of 1,000,000, 100,000, or 10,000. When applied to assessment of risk from exposure to individual chemicals, this is an incremental risk; that is, it is the risk above the background rate of cancer. For many regulatory programs, including those run by the US EPA, risk management occurs between 1/1,000,000 and 1/10,000. The MDH's long-standing policy for acceptable incremental cancer risk is 1/100,000.

Most estimated exposures resulted in incremental cancer risks of less than 1/1,000,000. (All risks reported are a result of substituting one half the detection limit for the concentrations of samples that were below detection.) As described below, a few chemicals resulted in incremental cancer risk above MDH's acceptable risk level of 1/100,000, and one chemical resulted in incremental risk above 1/10,000. For a summary of incremental cancer risk from individual carcinogens in individual media analyzed in the Minnesota Children's Pesticide Exposure Study, see Table 11 in the Appendix.

Benzene was the single chemical that resulted in incremental risk higher than the lower US EPA regulatory level (1/1,000,000) for all children in the study. Maximum incremental risk was as high as 3/10,000. Mean incremental cancer risk from benzene was less than 5/100,000.

Except for DDD and DDE, risks from ingestion exposures to pesticides were higher than risks from inhalation exposures to pesticides for most children. At 5/100,000 and 6/100,000, respectively, maximum risks from inhalation exposure to DDD and DDE, exceeded the MDH's acceptable risk level. Risk at the 95th percentile of inhalation exposure was substantially lower for DDD (9/1,000,000) and somewhat lower for DDE (3/100,000).

Nearly all ingestion risk calculated was attributable to pesticides in food. No pesticides were detected in beverages and no individual pesticide was detected in more than two water samples. Even using high intake assumptions and assuming that concentrations in beverage samples were at the detection limit, risks from individual pesticides in beverages were below MDH's acceptable risk level. (For all pesticides except dieldrin, risks were less than 1/1,000,000.) For the few water samples above detection, risk using high intake assumptions was around or below 1/1,000,000. Except for dieldrin, detection limits were sufficiently sensitive to rule out unacceptable risk to children for whom no pesticides were detected in water.

Maximum incremental cancer risk from pesticides measured in food, except for dieldrin, was near or below 1/100,000. The maximum risk calculated from dieldrin was 6/10,000. However, fewer than fifteen percent of food samples had detectable levels of dieldrin, and the detection limit was not sufficiently sensitive to determine whether associated risk was below 1/10,000. (Issues related to dieldrin and associated pesticides are discussed below on pages 11 and 12.)

When incremental cancer risks from individual pesticides were added across media for each child, maximum cancer risk from pesticides other than dieldrin ranged from 2/100,000 to 6/100,000; mean risk ranged from 2/1,000,000 to 1/100,000. Maximum risk from dieldrin was 7/10,000; mean risk was 1/10,000. Risk ranges did not vary between calculations at central intake rates or high intake rates. For chlordane and dieldrin, ingestion media contributed more than 90% of the risk for 95% or more of the participants; for DDT, ingestion media contributed more than 80% of the risk for 90% or more of the participants. For DDE and DDD, inhalation was the risk driver for most children.

Inhalation exposures to carcinogenic PAHs were below or very close to MDH's acceptable risk level.

Multiple Chemicals

Noncarcinogens

One child's inhalation exposure to dichlorvos alone was above a level of concern. Consequently, all calculations of risks from multiple chemicals that include this chemical and this pathway were above a level of concern for this child. Since dichlorvos is an organophosphate and affects the

nervous system, risk assessments both for all organophosphates and for all chemicals that affect the nervous system were impacted.

Except for the child with the elevated inhalation exposure to dichlorvos, when exposures to individual pesticides from all media and pathways sampled were added for each child, no child's aggregate exposures to any single pesticide were at a level of concern. Relative to the ingestion pathway, the inhalation pathway contributed little toward risk for most children in the study. Even incorporating the EPA's recently recommended safety factor of 10 into the risk assessment for chlorpyrifos, chlorpyrifos exposures did not reach levels of concern for any individual child.

Children's overall exposures to organophosphates (chlorpyrifos, malathion, diazinon, and dichlorvos) did not reach a level of concern except for the child with the elevated inhalation exposure to dichlorvos.

Adding incremental risks from all chemicals that affect the same target organ or organ system, the child with the elevated exposure to dichlorvos was above a level of concern and one other child just reached a level of concern. For both these children, the nervous system was the target of concern. Tetrachloroethylene, a VOC, was the largest contributor to this risk for the child whose overall exposures to chemicals affecting the nervous system was just at a level of concern (i.e., the child's hazard index was 1). Exposures to chemicals affecting the nervous system did not reach a level of concern for any other child. Exposures to MCPES chemicals leading to other non-cancer endpoints, including slowed growth; developmental effects; and liver, blood, or kidney toxicity did not reach a level of concern for any child.

Carcinogens

When each participant's cancer risk from all chemicals in all media was added, incremental risk for the participant with the highest risk was 7/10,000, regardless of whether high or central intake assumptions were used for beverages and water. The driver for this participant and for other high risk participants was dieldrin. Benzene was a large contributor to each participant's overall risk. The smallest summed cancer risk for any of the participants was 2/100,000.

Comparative Risk

As applied to the MCPES, the question that the comparative risk analysis asked was "which chemical is worst?". Based on calculated risk, the prevalence of concentrations leading to incremental risk above regulatory levels, and the health outcome, cancer, the answer with regard to the MCPES chemicals is benzene. However, the MDH anticipates that there are Minnesotans who would find other illnesses or health conditions affecting children to be a greater concern than lifetime cancer risk. The combined exposures from the neurotoxins investigated in this study reached a level of potential health concern for one child. The MCPES measured only some of the possible neurotoxins present in the environment, so that actual risk from neurotoxins may be greater than that calculated in this study. (See Appendix Table 5 for a list of neurotoxins included in the MCPES.) If cancer is not considered, neurotoxins may be the group of chemicals that poses the greatest risk.

DISCUSSION

This risk analysis was performed for individual participants in the MCPES. Results pertain only to actual participants and cannot be extended to any greater population. One reason for this is that the study was designed to over-sample homes with higher pesticide use. Therefore, pesticide exposures estimated from this study may be higher than for a random sample of homes. MDH's collaborators are working on an analysis that weights the data according to a household's probability of selection. This analysis will allow generalization of results to a larger population.

Sources of Uncertainty

This report is the MDH's best effort to assess health risks to MCPES participants from chemical concentrations measured during the study. While the MCPES is the most complete set of data available about Minnesota children's exposures to environmental contaminants, results from the MDH's risk assessment effort must be viewed with caution. The sampling period in the study ranged from four to six days during participants' fourth through thirteenth years. There are inherent problems in extrapolating from 4 to 6 day exposures during childhood to the chronic or life-time exposures necessary to invoke the health effects in question. The timing of sample collection also raises questions as to the validity of this extrapolation. Samples were collected during the summer months when household pesticide use in Minnesota is likely to be more common. Therefore, this analysis may over-estimate long-term pesticide exposures and risks attributable to household pesticide use. This, in particular, casts doubt on the maximum risk calculated from measurements of dichlorvos in air.

In addition to the fundamental difficulty of extrapolating from short-term measurements to long-term exposures, this analysis is subject to the same uncertainties associated with every risk assessment; i.e., the assumptions incorporated in exposure estimation and data gaps in toxicity evaluation. Finally, in attempting to look at effects of multiple exposures, the MCPES is at the forefront of the science of risk assessment. Attempts to add risk must be viewed only as possible approximations to actual risk. Primary sources of uncertainty are described below.

Sample Collection and Analysis

The quality of any risk assessment is dependent upon the accuracy of the methods used to collect and analyze samples. Sometimes, despite all precautions, samples become contaminated during collection, shipping, or analysis, thereby invalidating the results. The MCPES suite of chemicals included a pesticide called heptachlor. A high percentage of samples of all media tested showed detectable levels of heptachlor. This was not expected, since heptachlor has not been in common use for many years. Levels of heptachlor reported for MCPES samples were much higher than levels reported for other studies. When a subset of samples reported to have high concentrations of heptachlor was subjected to reanalysis by another laboratory, no heptachlor was found. For these reasons, the original heptachlor results were considered invalid and are not included in this report. Because several other pesticides in the study belong to the same class of chemicals as

heptachlor, this circumstance casts some doubt on the reliability of the results for these other pesticides. These pesticides include: chlordane, dieldrin, DDD, DDE, and DDT.

Exposure Estimation

Exposure Assumptions

Most studies do not measure all parameters necessary to calculate internal exposure or dose; the MCPES is no exception. Consequently, assumptions were implemented in order to complete the exposure equations and arrive at estimates of risk. Scientific studies have provided ranges of values for standard exposure assumptions. Generally, for the purpose of health risk assessment, values that apply to 80 to 95% of the population are chosen in order to be protective. For example, in this analysis, two sets of calculations were performed for calculating risks associated with water intake; one set used an intake value representing median daily water consumption; the other used an intake value representative of the amount of water consumed by an individual at the 90th percentile of water consumption.

Biological Measurements

Exposure assumptions for the amount of dust a child ingests would have over-estimated lead exposure from measured concentrations of lead in house dust. No child in the study who supplied a blood sample had an elevated blood-lead level. Blood-lead levels, which are biological measurements of exposure, are inherently more reliable than exposure estimates modeled from environmental concentrations and exposure assumptions. Therefore, the blood-lead results obviated concern that would otherwise have arisen from MCPES risk estimates.

Samples Below Detection

Methods and instrumentation may not be sufficiently sensitive to accurately detect or measure the very small concentrations of chemicals that may be present environmental media. When the result of chemical analysis is below the limit of detection, it is impossible to say whether a chemical is present and, if so, where between zero and the detection level the concentration lies. The fewer samples that lie above the detection limit, the less the confidence that can be placed in the risk assessment. While relatively high percentages of some samples had detectable levels of certain chemicals, e.g., metals in dust and VOCs in air, many samples were below detection. For example, no beverage had detectable levels of any pesticide measured. (See Table 7 in the Appendix for a list of the percent of samples with detectable chemical concentrations.)

For the purpose of the MCPES analysis, the MDH set the concentration for samples below the detection limit to one half the detection limit. While this is an approach commonly used to estimate concentrations for such samples in order that they may be included in data analysis, there are a number of other approaches. One disadvantage of this approach is that it always assumes that some quantity of a chemical is present. Because the MDH used this approach, high detection limits for dieldrin and DDE resulted in calculated cancer risks above regulatory levels, even when there was no evidence of their presence.

Health risks from the levels of contaminants that may be present in the samples can be ruled out (or recognized as very small) if the detection level is sufficiently sensitive; that is, if there is no risk or only negligible risk associated with concentrations at the detection limit. Generally, detection limits in the MCPES were low enough to rule out risk from individual chemicals below detection. However, there were some notable exceptions; for example, dieldrin.

Toxicity Evaluation

In evaluating risk from any chemical, the health effect of interest is that which is the "most sensitive", i.e., the effect that can occur at the lowest exposure. Most contaminants will cause additional health effects at higher exposures. If a chemical causes cancer, the acceptable exposure (i.e., that exposure associated with an incremental cancer risk of 1/100,000) is typically lower than exposures that cause other health effects. Focusing on the most sensitive endpoint is adequate to address risk from exposure to individual chemicals. However, actual exposures involve a shifting array of multiple chemicals. This approach fails to account for smaller, secondary effects that contribute to cumulative risk from multiple exposures.

Risk Assessment

Concentrations of chemicals measured in the MCPES may not accurately represent the longer term and even lifetime (cancer) exposures that are assumed in chemical risk assessment. For the MCPES, sample collection occurred during a 4 to 6 day period between May and September of a participant's fourth through thirteenth years. Children's diets and activities may subject them to higher exposures than adults, so that extrapolation of exposures estimated from the sampling period to chronic or lifetime exposures may result in over-estimation. The sampling period occurred during summer months when pesticide use in Minnesota is likely to be highest; however, it may have missed higher concentrations of VOCs and PAHs that are likely to accumulate indoors during winter months.

Noncarcinogens

In risk assessment, chemicals that cause cancer (carcinogens) are treated differently than chemicals that do not cause cancer (noncarcinogens). For noncarcinogens, there is a level of exposure (called the threshold dose) below which a chemical shows no harmful effect. Doses below the threshold are taken into the body, metabolized, and passed out of the body without harm. Well-designed toxicity tests identify the threshold dose and the most sensitive health endpoint. The threshold dose is then reduced, typically by a factor of 100 to 300, to account for uncertainty in the data. Uncertainties may include gaps in data, lack of any human data, or lack of information about likely variability in the population. The reduced amount is considered the dose to which humans can be exposed every day–either one day or a lifetime--without harm.

Carcinogens

Under traditional risk assessment methods, any amount of a carcinogen, no matter how small, is considered to have the potential to cause cancer. For a carcinogen, the toxicity value is an upper-bound on the probability that an individual exposed to a certain quantity of a chemical will

develop cancer as a result of this exposure. It is important to know that cancer risk values are upper estimates of the cancer rate associated with a lifetime of exposure. The true risk is likely to be lower and may be zero.

Regulatory programs evaluate carcinogens in terms of both risks to individuals (the probability of cancer) and risks to populations (the number of cancer cases above a background rate that a chemical at a certain dose might cause in a population of a certain size). Generally, the incremental rate of cancer considered acceptable by the US EPA is a risk between 1/10,000 and 1/1,000,000 over a 70-year exposure period. For certain regulatory and policy actions, the MDH considers a 1/100,000 risk of cancer as acceptable (that is, a risk that should not require public health action). Whether or how well regulatory benchmarks reflect public values is unknown.

Challenges and Lessons Learned

Chemical Toxicity

No toxicity data was available for some exposures. The MDH was able to identify toxicity values for certain chemicals and pathways using techniques such as route to route extrapolation or toxic potency relative to another, better researched chemical. However, no toxicity values could be identified for a few chemicals, precluding their inclusion in the risk analysis. This problem is not uncommon. Of the thousands of chemicals known about, only a relatively small number have been subject to rigorous toxicity testing. The immense cost of thorough toxicity testing is an impediment to efforts to further knowledge about the health effects of any chemical in isolation, much less co-occurring chemicals.

Biological Measurements and Health

Biological measurements are a definitive indication as to whether exposure has occurred. However, exposure alone is not the whole story. Finding the metabolite of a chemical in a biological sample supplies no information as to the source of the exposure. Additionally, science may not yet be able to state either the level of the exposure or whether that exposure constitutes a health risk. For example, TCPY, a metabolite of the pesticide chlorpyrifos, was found in over 90% of urine samples tested. Since chlorpyrifos will break down into TCPY in the environment, this indicates that children were exposed either to chlorpyrifos or to TCPY already in the environment. Researchers are working to establish a quantitative relationship between TCPY in urine and measurements in the environment.

Multiple Exposures

Traditional risk assessment has focused on exposure to a single chemical through a single pathway at any given time. In reality, people are constantly exposed to a shifting array of chemicals through one or more pathways. Merely attempting to identify and quantify the components of this shifting milieu poses difficulties. Practical considerations prevent measurement of the myriad chemicals that may be present, so that a risk assessor must make an educated guess as to what

may be present in order to selectively measure chemicals. Finally, chemical analysis techniques may not be sufficiently sensitive to detect chemicals that are present. As discussed above, sometimes risk from chemicals below detection can be ruled out; sometimes it cannot.

Combining Risks

The reality of multiple exposures is significant to health risk for a variety of reasons. Exposures to particular chemicals may add across pathways. Exposures to different chemicals with the same endpoint or the same mechanism of toxicity may be additive. Interaction of different chemicals in the body may not simply be additive; the net effect may be greater than (synergism) or less than (antagonism) the sum of the effects that each chemical would have separately. Burdening one detoxification system may impair the functioning of another detoxification system. As the total body burden of toxic substances increases, less sensitive endpoints may come into play at lower doses than they would for a singular exposure. For most chemicals and systems, science does not have answers to these questions. Finally, policy makers have not thoroughly examined the issue of whether a different standard of acceptable risk should be applied to total risk than is applied to incremental risk or to all risks associated with a discrete event or hazardous site.

Problems with Methods for Adding Risk

To respond to the challenge of moving from the traditional approach toward a closer approximation of risk from real exposures, risk assessors have formulated a number of methods for adding risks from multiple exposures. Each model has inherent problems; at very least, no model accounts for risk from chemicals that were not measured. There is no consensus within the scientific community on appropriate methodology to achieve a true and complete picture of total risk.

One method of assessing risk from multiple exposures is to add risk from all chemicals that result in the same health endpoint, whether that endpoint is a common disease or common target organ or organ system. Inherent in this approach is the assumption that the chemicals share a common mechanism of toxic action; that is, they bring about the same result in the same way. While this assumption may be unfounded, the mechanism of toxic action is known for relatively few chemicals. Problems with this approach are especially evident with respect to cancer. Scientists and medical professionals know that cancers are not the same: they have different etiologies and progress differently. Yet, this approach treats all cancer as the same.

Recognizing that chemicals may act differently to achieve the same outcome, risk assessors may choose to cumulate risk only from those chemicals known to cause the same effect by acting on the same molecular target or tissue by the same biochemical mechanism of action. This method poses intensive information requirements. Current research efforts seek to determine which chemicals can be grouped for the purpose of this method. Even if it is determined that grouping is appropriate, a single group of chemicals provides only a small piece of the total risk picture.

Sensitive Subpopulations

In evaluating a chemical's toxicity, risk assessment generally incorporates an uncertainty factor to account for individual differences in sensitivity. Differences in sensitivity often reflect differences in absorption, distribution, metabolism, and excretion (pharmacokinetics). These differences may be a function of age, health or nutritional status, or genetic variation. Slower or less complete metabolism resulting from immature or less efficient systems may increase toxicity caused by the parent compound. Conversely, more rapid or more thorough metabolism may increase toxicity when toxicity is caused by a metabolic product. In addition to metabolic differences, physiological differences may lead to increased sensitivity. Children are particularly vulnerable to certain chemicals because of incomplete development of the blood-brain barrier, a system that limits entry of substances into the brain. Generally, there is little information as to whether the uncertainty factor provides an adequate margin of safety for sensitive individuals, either when the causes of sensitivity exist in isolation or when they occur together.

Lead, which was included in the MCPES, is an example of a chemical that is absorbed differently, depending on age. Whereas only approximately 10% of lead ingested by adults passes into the bloodstream, 40% of lead ingested by young children passes from the gastrointestinal tract into the bloodstream and remains in the body. Poor nutrition results in increased absorption, thereby compounding risk. Hazard is further increased by incomplete development of the blood-brain barrier.

In addition to differences in metabolism that may put them at greater risk, children may also be at greater risk if a chemical interferes with developmental processes. Of the MCPES chemicals, chloroform is known to be a developmental toxicant. In addition, mercury (in the form of methylmercury) and lead have neurotoxic effects during periods of fetal and infant development. Developmental effects of other chemicals may occur, but at levels that cause more serious health effects (such as fetotoxicity).

US EPA regulations recently put in force require more rigorous testing of pesticides for developmental effects. However, this more rigorous protocol applies only to pesticides, not to other chemicals that may be present in or released into the environment. Furthermore, possible increases in sensitivity due to age, impaired health, and genetic variation remain to be addressed. While there is great demand for better and more thorough toxicity information, given differences between animals and humans and ethical considerations surrounding chemical testing, certain toxicity information may not be attainable.

Acceptable Risk

Acceptable health risk exists because there are tradeoffs between the costs and benefits of decreasing the likelihood of an adverse health outcome. Factors in this equation include the magnitude, time of onset, and duration of the impairment associated with the health effect; the availability of compensatory mechanisms; competing health concerns; economics; and lifestyle expectations and choices. Finally, risk itself is not a certainty, but a probability. The balance

between what an individual is willing to "pay" to diminish risk and the level of risk that the individual will deem "acceptable" in light of the costs associated with further diminution of risk is a subjective judgment that will differ between individuals. Regulators must establish realistic standards that are responsive to all values represented in society.

Current methods for evaluating whether risk from chemicals in the environment is acceptable are based on incremental risk. While this is appropriate to a chemical by chemical, pathway by pathway risk assessment, it may be unrealistic as risks from multiple chemicals and pathways are concatenated. This is especially true in light of levels of some chemicals that are naturally present in the environment. A shift in risk assessment science from single exposures toward multiple exposures should be accompanied by a concomitant shift from acceptable incremental risk toward acceptable total risk.

Exposure to a noncarcinogen is considered to be "without risk" if it is below a certain level. An exposure above that level raises health concerns. Essentially, overexposure to a noncarcinogen is considered unacceptable. From the standpoint of health, it is desirable to apply this same standard to multiple exposures. However, this may not be realistic, nor even possible.

The regulatory standard for allowable or acceptable risk from a carcinogen is one additional case of cancer in a population of ten thousand to one million people. This is a very low rate compared to the underlying rate of cancer in the population. In the United States, the underlying rate of cancer from all causes is 25% at 70 years of age and 50% throughout a lifetime. This means that by the age of 70 years, one in four Americans has had some form of cancer, and by the time of death, half of the population will have had cancer of some kind at some time.

Scientists attribute most cancers to tobacco use and diet. Only about 2% of cancers are directly attributed to environmental pollutants. However, these estimates address only primary causes. A growing body of evidence indicates that multiple interacting factors play a role in the development of many cancers.

Comparative Risk

As applied to the MCPES, the question that the comparative risk analysis asked was "which chemical is worst?". A number of factors play a role when making this call, so that the answer may differ, depending on the weight accorded each factor. (For a more thorough discussion of factors that might be considered, see the Interim Report for the LCMR, Comparative Risks of Multiple Chemical Exposures, issued in June of 1999.) However, the answer for the MCPES is clear: benzene. This conclusion is based on calculated risk, the prevalence of concentrations leading to incremental risk above regulatory levels, and the health outcome, cancer.

While the answer for this study was clear, it is easy to envision a situation where the conclusion would be less clear. For example, had a chemical with a developmental outcome been measured at levels leading to risk for many children, the MDH would have had to balance cancer against a developmental endpoint. The result here is not clear and invokes both subjective judgments and

assumptions regarding such factors as the magnitude and acceptability of the disability and the time frame for development of cancer.

Voluntary Versus Involuntary Risks

Assumption of some risks is a matter within personal control. These risks are usually a function of how we choose to live, such as whether we smoke, what we eat, and what products we use. Other risks, often related to where we live, cannot be as easily avoided. National values of independence and personal freedom are exercisable rights that determine the former types of choices. However, because the individual cannot control the latter type of risks, it is up to the government to decide whether and how much to regulate in order to reduce risks.

CONCLUSIONS

Generally, children's exposures to noncarcinogens did not approach harmful levels. Whether chemical exposures were considered separately, or combined in a variety of ways, nearly all exposures were at levels that the child's body could safely metabolize and eliminate.

Children's total cancer risks from all exposures to carcinogens ranged from 2/100,000 to 7/10,000. While dieldrin was the greatest contributor for participants at the high end of the range, the accuracy of dieldrin measurements is questionable. Benzene was a large contributor to the overall risk for each child in the study. Cancer risks calculated in this study cannot be validated; even the upper end of these risk estimates, equivalent to 7 cancer cases in 10,000 children exposed over a lifetime to the highest measurements from this study, is too small to be detected in epidemiological studies.

This study describes only a portion of environmental health concerns to Minnesota children. This study provides the most complete picture to date of environmental exposures of a subset of Minnesota children. However, despite the variety of media sampled and the large number of chemicals analyzed, many potential contaminants were not measured. Due to the many assumptions necessarily incorporated into a risk assessment, hazards and risks described may overestimate or underestimate the health impact of the exposures measured in the study. Furthermore, lack of toxicological data prevented the MDH from interpreting some of the measurements that were made. Finally, science does not currently provide definitive methods for considering the combined effects of these exposures.

The single most difficult task in interpreting the results of this study was how to consider combining risks from multiple chemicals and/or exposures. This concern led to an evaluation of and experimentation with alternative methods that have been suggested in scientific papers. These methods produced a range of quantitative answers to questions about cumulative and comparative risk. However, other, perhaps more crucial questions may only be answered through research on the public's tolerance for risk and perception of benefits. In the meantime, policy should supplement science and professional judgment in making decisions concerning cumulative and comparative risk.

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[1] Language provided by the Legislative Commission on Minnesota Resources.

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GLOSSARY OF ABBREVIATIONS

2,4-D	2,4-dichlorophenoxyacetic acid
CDC	Centers for Disease Control and Prevention
DDD	p,p'-dichlorodiphenyl dichloroethane
DDE	p,p'-dichlorodiphenyldichloroethylene
DDT	p,p'-dichlorodiphenyltrichloroethane
EOHSI	Environmental and Occupational Health Sciences Institute
HEAST	Health Effects Assessment Summary Tables (US EPA)
HRV	Health Risk Values (Minnesota Department of Health)
IRIS	Integrated Risk Information System (US EPA)
LCMR	Legislative Commission on Minnesota Resources
MCPP	2-(2-methyl-4-chlorophenoxy)propionic acid
MCPA	2-methyl-4-chlorophenoxyacetic acid
MCPES	Minnesota Children's Pesticide Exposure Study
MDH	Minnesota Department of Health
MRL	Minimal Risk Level (Agency for Toxic Substances and Disease Registry)
OEHHA	California Office of Environmental Health Hazard Assessment
PAH	Polycyclic aromatic hydrocarbon
PEF	Potency equivalency factors
REL	California Reference Exposure Level
RfD	Reference Dose (US EPA)
RTI	Research Triangle Institute
TCPY	3,5,6-trichloro-2-pyridinol
ug/dL	Micrograms lead per deciliter of blood
µg/g	Micrograms per gram
US EPA	United States Environmental Protection Agency
VOC	Volatile organic chemical

APPENDIX

Table 1 – Types of Media Sampled and Analyzed for the Minnesota Children's Pesticide Exposure Study

Type of Media		
Environmental	**Personal**	**Biological**
Indoor Air	Personal Air	Urine
Outdoor Air	Food	Hair
Tap Water	Beverages	Blood
Dust – Living Area		
Vacuum Dust – Entry Way Floor		
Soil		

Table 2 – Chemicals Measured in the Minnesota Children's Pesticide Exposure Study

Metals	VOCs	PAHs	Pesticides	Pesticide Metabolites
Lead Arsenic Mercury	Benzene Chloroform Tetrachloroethylene Styrene Toluene p-Dichlorobenzene m,p-Xylene o-Xylene 1,1,1, Trichloroethane Trichloroethylene	Benzo(a)pyrene Benzo(a)anthracene Acenaphthylene Benzo(ghi)perylene Fluoranthene Phenanthrene Pyrene Indeno(123-c,d)pyrene Anthracene Chrysene Benzo(b)fluoranthene Benzo(e)pyrene Benzo(k)fluoranthene	Chlorpyrifos Diazinon Atrazine Malathion Chlordane Dieldrin Heptachlor Dichlorvos Simazine Alachlor Metolachlor Endosulfan I Permethrin 4,4'-DDE 4,4'-DDD DDT 2,4-D MCPP MCPA	3,5,6-Trichloro-2-pyridinol Atrazine Mercapturate Malathion Dicarboxylic Acid 1-Naphthol 2-Naphthol 2,4-D

Appendix
Table 3 – Exposure Assumptions: Ingestion Pathway / Non-Cancer Endpoints

Objective: To estimate average daily dose from exposure along the ingestion pathway. Average daily dose will be estimated from measurements made during the monitoring period of the Minnesota Children's Pesticide Exposure Study and, where necessary, from exposure assumptions.

Equation:

$$\text{Dose} = \frac{\text{Contaminant Concentration x Intake Rate}}{\text{Body Weight}}$$

Factor		Value	Source
Concentration in:	Food	Measured Concentration or ½ Detection	MCPES data
	Beverages	Measured Concentration or ½ Detection	MCPES data
	Water	Measured Concentration or ½ Detection	MCPES data
	Soil	Measured Concentration or ½ Detection	MCPES data
	Dust	Measured Concentration or ½ Detection	MCPES data
Intake rate:	Food	Measured Intake Rate	MCPES data
	Beverages	Measured Intake Rate	MCPES data
	Water	**Central Value:** Children < 11 0.75 L/day Children ≥11 1 L/day **Conservative Value:** Children < 11 1.3 L/day Children ≥11 1.7 L/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 3.
	Soil[1]	**Central Value:** Children < 6 100 mg/day Children ≥ 6 75 mg/day **Conservative Value:** Children < 6 200 mg/day Children ≥ 6 150 mg/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 4. ‣ Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) Guidance Manual, 1994. ‣ Walker and Griffin. 1998. Site-Specific Data Confirm Arsenic Exposure Predicted by U.S. Environmental Protection Agency. *Environmental Health Perspectives.* 106:133-139. ‣ Consultation with Minnesota Pollution Control Agency staff regarding draft document "Exposure Equations and Default Values." ‣ Professional judgment.
	Dust[1]	**Central Value:** Children < 6 100 mg/day Children ≥6 75 mg/day **Conservative Value:** Children < 6 200 mg/day Children ≥6 150 mg/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 4. ‣ Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) Guidance Manual, 1994. ‣ Walker and Griffin. 1998. Site-Specific Data Confirm Arsenic Exposure Predicted by U.S. Environmental Protection Agency. *Environmental Health Perspectives.* 106:133-139. ‣ Consultation with Minnesota Pollution Control Agency staff regarding a draft document "Exposure Equations and Default Values." ‣ Professional judgment.
Body Weight		reported weight for each child	MCPES data

[1] Relatively few studies have investigated children's intake rate of dust, as distinct from their intake rate of soil. Because the literature suggested that intake is approximately 55% dust and 45% soil, the conservative estimate of mean intake recommended by the US EPA was apportioned equally between soil and dust.

Appendix
Table 4 – Exposure Assumptions: Ingestion Pathway / Cancer Endpoints

Objective: To estimate lifetime average daily dose from exposure for the ingestion pathway. Lifetime average daily dose will be estimated from measurements made during the monitoring period of the Minnesota Children's Pesticide Exposure Study.

Equation:

$$\text{Dose} = \sum \frac{\text{Contaminant Concentration} \times \text{Intake Rate} \times \text{Exposure Frequency} \times \text{Exposure Duration}}{\text{Body Weight} \times \text{Averaging Time}}$$

Factor		Age Range	Value	Source
Concentration in:	**Food**	Lifetime[1]	Measured Concentration or ½ Detection	MCPES data
	Beverages	Lifetime[1]	Measured Concentration or ½ Detection	MCPES data
	Water	Lifetime[1]	Measured Concentration or ½ Detection	MCPES data
	Soil	Lifetime[1]	Measured Concentration or ½ Detection	MCPES data
	Dust	Lifetime[1]	Measured Concentration or ½ Detection	MCPES data
Intake rate:	**Food**	Lifetime[2]	Measured Intake Rate	MCPES data
	Beverages[3]	0 - 10 years[4]	**Central Value:** 0.75 L/day **Conservative Value:** 1.3 L/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 3. ‣ Professional judgment.
		11 - 19 years[4]	**Central Value:** 1 L/day **Conservative Value:** 1.7 L/day	
		> 19 years	**Central Value:** 1.4 L/day **Conservative Value:** 2.3 L/day	
	Water[5]	0 - 10 years	**Central Value:** 0.75 L/day **Conservative Value:** 1.3 L/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 3, esp. Tables 3-30, 3-33.
		11 - 19 years	**Central Value:** 1 L/day **Conservative Value:** 1.7 L/day	
		> 19 years	**Central Value:** 1.4 L/day **Conservative Value:** 2.3 L/day	

Appendix Table 4, continued

Intake rate, continued	**Soil**[6]	0 - 5 years	**Central Value:** 100 mg/day **Conservative Value:** 200 mg/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 4. ‣ Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) Guidance Manual, 1994. ‣ Walker and Griffin. 1998. Site-Specific Data Confirm Arsenic Exposure Predicted by U.S. Environmental Protection Agency. *Environmental Health Perspectives.* 106:133-139. ‣ Consultation with Minnesota Pollution Control Agency staff regarding a draft document "Exposure Equations and Default Values."
		6 - 12 years	**Central Value:** 75 mg/day **Conservative Value:** 150 mg/day	
		> 12 years	50 mg/day	
	Dust[6]	0 - 5 years	**Central Value:** 100 mg/day **Conservative Value:** 200 mg/day	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 4. ‣ Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) Guidance Manual, 1994. ‣ Walker and Griffin. 1998. Site-Specific Data Confirm Arsenic Exposure Predicted by U.S. Environmental Protection Agency. *Environmental Health Perspectives.* 106: 133-139. ‣ Consultation with Minnesota Pollution Control Agency staff regarding a draft document "Exposure Equations and Default Values."
		6 - 12 years	**Central Value:** 75 mg/day **Conservative Value:** 150 mg/day	
		> 12 years	50 mg/day	
Body Weight[7]		0 - 5 years	14.1 kg	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 7, esp. tables 7-3, 7-11. (Age ranges set according to ranges provided for other factors in algorithm. Weight listed is average weight for range, based on weights listed in table 7-3 of the Exposure Factors Handbook, assuming a life span of 75 years and using weights of 71.8 kg for persons 19-75and 5.98 kg for infants through 6 months.)
		0 - 10 years	20.7 kg	
		6 - 12 years	32.8 kg	
		11 - 19 years	56.4 kg	
		> 12 years	70.6 kg	
		> 19 years	71.8 kg	
Averaging Time			75 years	‣ US EPA. Exposure Factors Handbook, 1997, Chapter 8.

Appendix Table 4, continued

1. Contaminant concentrations measured in the various media surveyed by this study were assumed to be representative of "background"; that is, levels to which participants would be exposed during a lifetime. Measured contaminant levels were applied throughout the entire lifetime to calculate lifetime average daily dose. The assumption may not be valid for all households for pesticides, since households that indicated pesticide use were over-sampled.

2. The food intake rate measured for each study participant (expressed in mg/kg-day) was assumed to continue throughout life. It is likely that this assumption contributed to the conservatism of the exposure assessment in several ways. First, children have higher metabolisms than adults and consume more food per unit body weight, so that actual intake for adults may be over-estimated. Second, the mix of foods in an adult's diet is likely to differ from that in a child's diet. The diet of a child is, in fact, thought to contain a higher proportion of foods with high pesticide residues. Thus, estimates of doses of pesticide residues ingested during adult years may also be high. Although a more precise method of estimating doses received by adults dose would be preferable, adult-specific data were not collected in this study of children's exposures, the method of collection of food data did not allow estimation of intake rates of specific foods, and measurements of contaminant levels were not associated with particular foods.

3. The Exposure Factors Handbook offers no specific recommendations as to the intake rate for non-water beverages. Here, assumptions as to the intake rate of beverages mirror those recommended for the intake rate of water.

4. For ease of calculation of lifetime exposures, the intake rate of beverages during childhood was based on assumptions, rather than extrapolating each child's measured intake rate during the study period throughout childhood.

5. Assumptions selected for water intake are based on studies of tap water intake. Because some beverages, intake of which is tabulated separately, may have been tap water-based, total calculations of the amount of beverages and water consumed per study participant may be conservative.

6. Relatively few studies have investigated children's intake rate of dust, as distinct from their intake rate of soil. Because the literature suggests that intake is approximately 55% dust and 45% soil, the conservative estimate of mean intake recommended by the EPA was apportioned equally between soil and dust.

7. In calculating lifetime dose, doses are calculated for each age range required based on assumptions for various of the exposure factors. For example, age ranges for soil and dust ingestion were 0 - 5 years, 6 - 12 years, and over 12 years. Average body weights corresponding to age ranges established by other exposure factors were computed using figures provided in the US EPA's Exposure Factors Handbook.

Appendix

Table 5 – Most Sensitive Health Endpoints Associated with the Minnesota Children's Pesticide Exposure Study Chemicals

Health Endpoint	Chemical Type	Chemical
Nervous System	VOCs	1,1,1-Trichloroethane Styrene Tetrachloroethylene Toluene Trichloroethylene m,p-Xylene o-Xylene
	Pesticides	Diazinon Dichlorvos (inhalation only) Malathion Chlorpyrifos
	Metals	Lead Mercury
Liver	VOCs	p-Dichlorobenzene
	Pesticides	cis- and trans-Permethrin
	PAHs	Fluoranthene
Developmental	VOCs	Chloroform
Cancer	VOCs	Benzene
	Pesticides	cis- and trans-Chlordane DDD DDE DDT Dieldrin Dichlorvos (ingestion only)
	PAHs	Benzo(a)pyrene Benzo(a)anthracene Chrysene Benzo(k)fluoranthene Indeno[1,2,3-cd]pyrene Benzo(b)fluoranthene
Blood	Pesticides	Simazine Alachlor
	PAHs	Fluoranthene
Slowed Growth	Pesticides	Simazine Atrazine Metolachlor Endosulfan I
Kidneys	PAHs	Pyrene Fluoranthene

[1] This chemical was not included in an evaluation of combined risks, due to the absence of an appropriate toxicity value.

Appendix

Table 6 – Chemical Analyses Performed for the Minnesota Children's Pesticide Exposure Study

Medium	Pesticides	PAHs	VOCs	Metals
Indoor Air	Pesticide Suite 1[1]	All PAHs	All VOCs	
Outdoor Air	Pesticide Suite 1[1]	All PAHs	All VOCs	
Personal Air	Pesticide Suite 1[1]	All PAHs	All VOCs	
Food	Pesticide Suite 1[1]	All PAHs[2]		Arsenic, Mercury
Tap Water	Pesticide Suite 1[1]			
Beverages	Pesticide Suite 2[3]			
Dust -- Living Area	Pesticide Suite 3[4]	All PAHs[2]		Arsenic, Lead
Vacuum Dust – Entry Way	Pesticide Suite 4[5]			
Soil	Pesticide Suite 3[4]			
Hair				Arsenic, Mercury
Urine	Pesticide Suite 5[6]			
Blood				Lead

[1] Pesticide Suite 1: Atrazine, Chlorpyrifos, Diazinon, Malathion, DDD, DDE, DDT, Dieldrin, Heptachlor, cis- and trans-Chlordane, Alachlor, Dichlorvos, Endosulfan I, Metolachlor, Simazine, cis- and trans-Permethrin

[2] Although PAHs were measured in food and dust, data were not made available to the MDH.

[3] Pesticide Suite 2: Atrazine, Chlorpyrifos, Diazinon, Malathion, DDD, DDE, DDT, Dieldrin, Heptachlor, cis- and trans-Chlordane

[4] Pesticide Suite 3: Atrazine, Chlorpyrifos, Diazinon, Malathion

[5] Pesticide Suite 4: MCPP, MCPA, and 2,4-D

[6] Pesticide Suite 5 includes the following pesticides and their metabolites (in parentheses): Chlorpyrifos (3,5,6-trichloro-2-pyridinol), atrazine (atrazine mercapturate), malathion (malathion dicarboxylic acid), carbamates (1-naphthol), napthylene (1-naphthol and 2-naphthol), and 2,4-D

Appendix

Table 7 – Percent of Measurable Samples: Environmental and Personal Media

		Percent of Measurable Samples									
		90-100	80-89	70-79	60-69	50-59	40-49	30-39	20-29	10-19	0-9
Personal Air Samples	PAHs	Anthracene Benzo(b)fluoranthene Benzo(ghi)perylene Chrysene Fluoranthene* Phenanthrene* Pyrene*	Acenaphthylene	Benzo(a)anthracene	Benzo(e)pyrene	Benzo(a)pyrene Benzo(k)fluoranthene	Indeno(123-c,d)pyrene				
	VOCs	Benzene* Chloroform* p-Dichlorobenzene 1,1,1-Trichlorethane Styrene Toluene* Trichloroethylene m,p-Xylene* o-Xylene*	Tetrachloroethylene								
	Pesticides	Chlorpyrifos	cis-Permethrin	DDT	DDE Diazinon cis-Chlordane trans-Permethrin	Malathion Metolachlor trans-Chlordane	Alachlor Dieldrin	Endosulfan I		DDD Atrazine Dichlorvos	Simazine
Food	Pesticides				Chlorpyrifos trans-Chlordane	Malathion	DDE DDT cis-Chlordane		DDD Alachlor Simazine cis-Permethrin	Atrazine Dieldrin trans-Permethrin	Diazinon Dichlorvos Endosulfan I Metolachlor
Beverages	Pesticides										DDD DDE DDT Atrazine Chlorpyrifos Diazinon Dieldrin Malathion cis-Chlordane trans-Chlordane

Appendix Table 7, continued

		90-100	80-89	70-79	60-69	50-59	40-49	30-39	20-29	10-19	0-9
Water	**Pesticides**										DDD DDE DDT Alachlor Atrazine Chlorpyrifos Diazinon Dichlorvos Dieldrin Endosulfan I Malathion Metolachlor Simazine cis-Chlordane cis-Permethrin trans-Chlordane trans-Permethrin
Soil	**Pesticides**										Atrazine Chlorpyrifos Diazinon Malathion
Surface Dust	**Pesticides**				Chlorpyrifos						Atrazine Diazinon Malathion
Floor Dust	**Pesticides**		MCPA MCPP		2,4-D						
Food	**Metals**	Arsenic*	Mercury								
Dust	**Metals**	Arsenic*	Lead								

Percentages rounded to nearest whole number.

* Detected in 100% of samples.

Appendix
Percent of Measurable Samples: Biological Media

Table 8 – Percent of Measurable Samples: Urine

Metabolite	Parent Compound(s)	% of Samples with Measurable Levels
3,5,6-Trichloro-2-pyridinol	Chlorpyrifos	92
Atrazine Mercapturate	Atrazine	2
Malathion Dicarboxylic Acid	Malathion	36
1-Naphthol	Carbamates, Naphthylene	45
2-Naphthol	Naphthylene	39
2,4-D	2,4-D	54

Table 9 – Percent of Measurable Samples: Blood and Hair

Biological Medium	Substance	% of Samples with Measurable Levels
Blood	Lead	91
Hair	Arsenic	52
	Mercury	100

Appendix
Table 10 – Health Risk Summary for Noncarcinogens

Volatile Organic Chemicals (VOCs) in Personal, Indoor, And Outdoor Air			
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent Potentially at Risk**
1,1,1-Trichloroethane	affects nervous system	100%	0%
p-Dichlorobenzene	affects liver	100%	0%
Benzene	cancer	(See Cancer Risk Table)	
Chloroform	developmental	100%	0%
Styrene	affects nervous system	100%	0%
Tetrachloroethylene	affects nervous system	99.6%	0.4%
Toluene	affects nervous system	100%	0%
Trichloroethylene	affects nervous system	100%	0%
m,p-Xylene	affects nervous system	100%	0%
o-Xylene	affects nervous system	100%	0%

Pesticides in Personal, Indoor, And Outdoor Air			
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent Potentially at Risk**
Dichlorvos	affects nervous system	99%	1%
Simazine	affects blood; slowed growth	100%	0%
Atrazine	slowed growth	100%	0%
Diazinon	interferes with nerve transmissions	100%	0%
Alachlor	affects iron storage by red blood cells	100%	0%
Malathion	interferes with nerve transmissions	100%	0%
Chlorpyrifos	interferes with nerve transmissions	100%	0%
Metolachlor	slowed growth	100%	0%
Endosulfan I	slowed growth	100%	0%
trans-Chlordane	cancer	(See Cancer Risk Table)	
cis-Chlordane	cancer	(See Cancer Risk Table)	
4,4'-DDE	cancer	(See Cancer Risk Table)	
Dieldrin	cancer	(See Cancer Risk Table)	
4,4'-DDD	cancer	(See Cancer Risk Table)	

Appendix, Table 10, continued

4,4'-DDT	cancer	(See Cancer Risk Table)	
cis-Permethrin	affects liver	100%	0%
trans-Permethrin	affects liver	100%	0%

Polycyclic Aromatic Hydrocarbons (PAHs) in Personal, Indoor, And Outdoor Air			
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent Potentially at Risk**
Benzo(a)pyrene	cancer	(See Cancer Risk Table)	
Benzo(a)anthracene	cancer	(See Cancer Risk Table)	
Acenaphthylene	----	NA[2]	
Anthracene	no observed effects	100%	0%
Chrysene	cancer	(See Cancer Risk Table)	
Benzo(e)pyrene	----	NA[1]	
Benzo(ghi)perylene	----	NA[1]	
Benzo(k)fluoranthene	cancer	(See Cancer Risk Table)	
Fluoranthene	affects liver, kidneys, blood	100%	0%
Phenanthrene	----	NA[1]	
Pyrene	affects kidney	100%	0%
Indeno[1,2,3-cd]pyrene	cancer	(See Cancer Risk Table)	
Benzo(b)fluoranthene	cancer	(See Cancer Risk Table)	

Pesticides in Drinking Water			
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent Potentially at Risk**
Dichlorvos	cancer	(See Cancer Risk Table)	
Simazine	affects blood; slowed growth	100%	0%
Atrazine	slowed growth	100%	0%
Diazinon	interferes with nerve transmissions	100%	0%
Alachlor	affects iron storage by red blood cells	100%	0%
Malathion	interferes with nerve transmissions	100%	0%

[2] NA = Not available. No reference value is available.

Appendix, Table 10, continued

Chlorpyrifos	interferes with nerve transmissions	100%	0%
Metolachlor	slowed growth	100%	0%
Endosulfan I	slowed growth	100%	0%
trans-Chlordane	cancer	(See Cancer Risk Table)	
cis-Chlordane	cancer	(See Cancer Risk Table)	
4,4'-DDE	cancer	(See Cancer Risk Table)	
Dieldrin	cancer	(See Cancer Risk Table)	
4,4'-DDD	cancer	(See Cancer Risk Table)	
4,4'-DDT	cancer	(See Cancer Risk Table)	
cis-Permethrin	affects liver	100%	0%
trans-Permethrin	affects liver	100%	0%

Pesticides in Food				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Dichlorvos	cancer	(See Cancer Risk Table)		
Simazine	affects blood; slowed growth	100%	0%	0%
Atrazine	slowed growth	100%	0%	0%
Diazinon	interferes with nerve transmissions	100%	0%	0%
Alachlor	affects iron storage by red blood cells	100%	0%	0%
Malathion	interferes with nerve transmissions	100%	0%	0%
Chlorpyrifos	interferes with nerve transmissions	100%	0%	0%
Metolachlor	slowed growth	100%	0%	0%
Endosulfan I	slowed growth	100%	0%	0%
trans-Chlordane	cancer	(See Cancer Risk Table)		
cis-Chlordane	cancer	(See Cancer Risk Table)		
4,4'-DDE	cancer	(See Cancer Risk Table)		
Dieldrin	cancer	(See Cancer Risk Table)		
4,4'-DDD	cancer	(See Cancer Risk Table)		
4,4'-DDT	cancer	(See Cancer Risk Table)		
cis-Permethrin	affects liver	100%	0%	0%
trans-Permethrin	affects liver	100%	0%	0%

Appendix, Table 10, continued

Metals in Food				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Arsenic	----	NA		
Mercury	affects nervous system	100%	0%	0%

Pesticides in Beverages			
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent Potentially at Risk**
Atrazine	slowed growth	100%	0%
Diazinon	interferes with nerve transmissions	100%	0%
Malathion	interferes with nerve transmissions	100%	0%
Chlorpyrifos	interferes with nerve transmissions	100%	0%
trans-Chlordane	cancer	(See Cancer Risk Table)	
cis-Chlordane	cancer	(See Cancer Risk Table)	
4,4'-DDE	cancer	(See Cancer Risk Table)	
Dieldrin	cancer	(See Cancer Risk Table)	
4,4'-DDD	cancer	(See Cancer Risk Table)	
4,4'-DDT	cancer	(See Cancer Risk Table)	

Pesticides in Surface Dust (Loading)[3]				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Atrazine	slowed growth	100%	0%	0%
Diazinon	interferes with nerve transmission	100%	0%	0%
Malathion	interferes with nerve transmission	100%	0%	0%
Chlorpyrifos	interferes with nerve transmission	100%	0%	0%

[3] Reference value is based on ingestion of contaminated soil or dust from hand-to-mouth transfers.

Appendix, Table 10, continued

Metals in Surface Dust (Loading)[4]				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Arsenic	----	NA		
Lead	affects nervous system	NA		

Herbicides in Vacuum Dust (Concentration)[3]				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
2,4-D	affects blood, liver, kidney	100%	0%	0%
MCPP	affects kidney	100%	0%	0%
MCPA	affects kidney, liver	100%	0%	0%

Pesticides in Soil[3]				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Atrazine	slowed growth	100%	0%	0%
Diazinon	interferes with nerve transmission	100%	0%	0%
Malathion	interferes with nerve transmission	100%	0%	0%
Chlorpyrifos	interferes with nerve transmission	100%	0%	0%

Metals in Hair				
Substance Measured	**Most Sensitive Health Effect**	**Percent of Samples Below a Level of Concern**	**Percent for which Results can not be Interpreted**	**Percent Potentially at Risk**
Arsenic	----	94%	1%	5%
Mercury	affects nervous system	100%	0%	0%

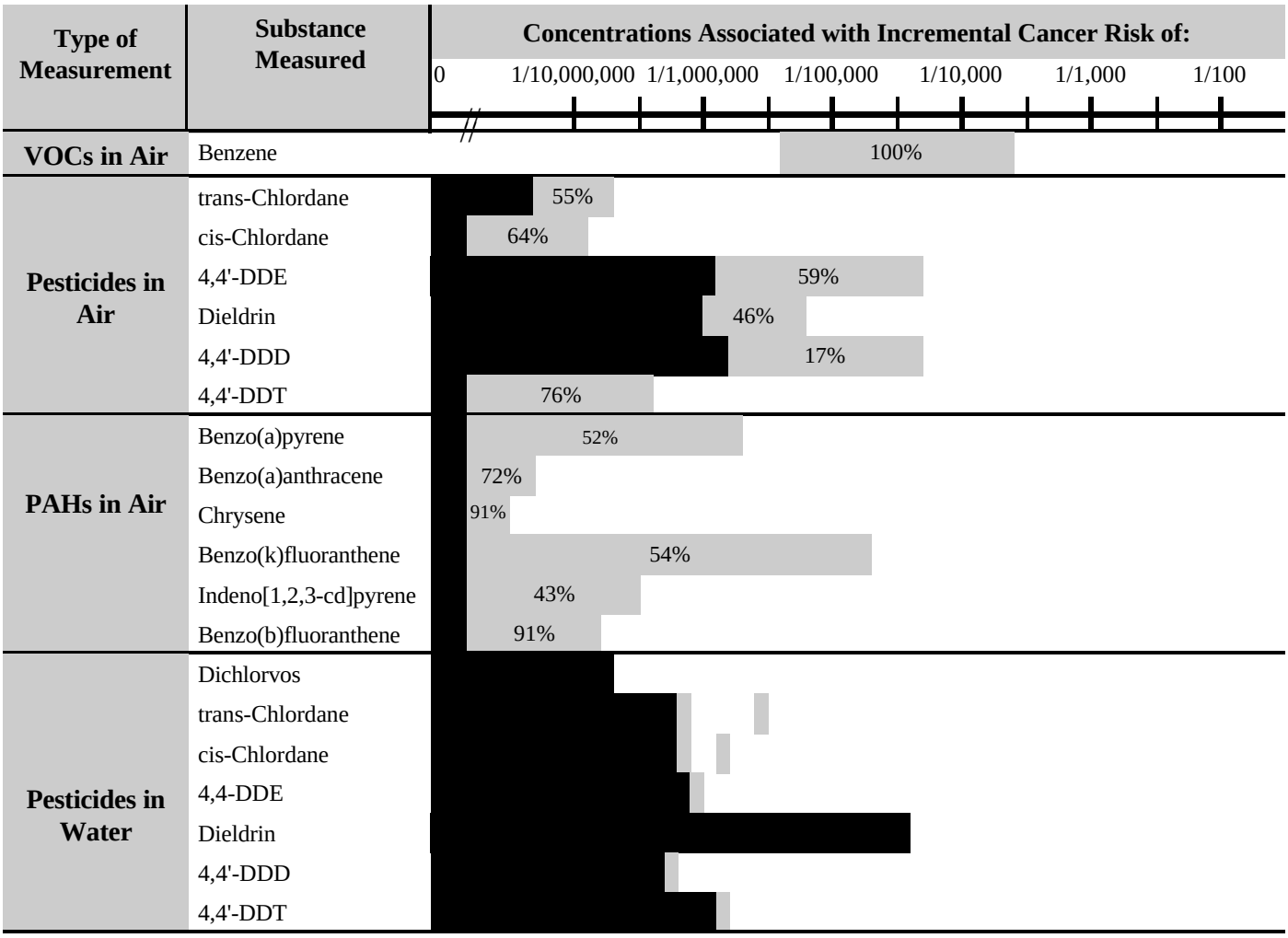
[4] Reference value is based on ingestion of contaminated soil or dust from hand-to-mouth transfers.

Appendix

Table 11 – Incremental Cancer Risk from Carcinogens Analyzed in the Minnesota Children's Pesticide Exposure Study

"Incremental cancer risk" is an upper estimate of the lifetime cancer rate associated with an exposure. The true risk is likely to be lower and may be zero. Incremental cancer risk shown in this table was calculated using data measured in the Minnesota Children's Pesticide Exposure Study and conservative assumptions for lifetime parameters. The values shown here should not be used for any purpose other than interpreting the results for participants in the study.

Incremental cancer risk for samples that could be measured lie within the shaded area. The percent of measurable samples is indicated. Risk from "ND" samples is indicated by solid black. Since the actual value of an "ND" sample may be zero, risk from "ND" samples is shown to extend down to zero.



Appendix Table 11, continued

Type of Measurement	Substance Measured	Concentrations Associated with Incremental Cancer Risk of:
		0 / 1/10,000,000 / 1/1,000,000 / 1/100,000 / 1/10,000 / 1/1,000 / 1/100
Pesticides in Food	Dichlorvos	5%
	trans-Chlordane	67%
	cis-Chlordane	48%
	4,4-DDE	43%
	Dieldrin	14%
	4,4'-DDD	27%
	4,4'-DDT	49%
PAHs in Food	Data available to the Minnesota Department of Health do not allow calculation of incremental cancer risk to participants from exposures to PAHs in food.	
PAHs in Dust	Data available to the Minnesota Department of Health do not allow calculation of incremental cancer risk to participants from exposures to PAHs in dust.	