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Potential Risks from Exposure to Organic Compounds in Indoor Air

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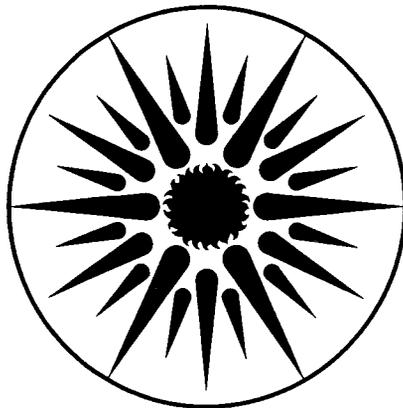
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**POTENTIAL RISKS FROM EXPOSURE TO ORGANIC
COMPOUNDS IN INDOOR AIR**

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ABSTRACT

This report is a preliminary assessment of the potential risks of cancer, reproductive effects, and miscellaneous toxic effects from exposures to individual organic compounds which have been detected in indoor air. Published data on indoor concentrations of organic compounds were compiled. The principal basis for estimates of cancer risk were data from animal studies. Potency factors used in the risk calculations were as estimated by EPA and by Gold, *et al.* (1984, 1986). EPA potency factors were estimated by "unit risk," the lifetime risk to humans from daily inhalation of a unit concentrations (e.g., $1 \mu\text{g}/\text{m}^3$). Gold *et al.*, estimated a TD50 which is the daily dose rate which would induce tumor in half the test animals that would have remained tumor-free at zero dose. The TD50s were converted to "human equivalent inhalation" TD50s to estimate cancer risks for median and maximum concentrations. Maximum likelihood (MLE) risks and 95% upper confidence limit risks were also calculated. For reproductive effects, the "lowest effective dose" (LED) in animals was converted to a "human equivalent inhalation" dose and compared to the maximum and the mean or median indoor concentrations reported for that compound.

The overall possible cancer risk from lifetime exposure to mean concentrations of indoor organic compounds, estimated as the sum of the risks for the 24 compounds which had significant risks, was between 28×10^{-5} and 980×10^{-5} . The higher limit is comparable to that for indoor radon. The greatest proportion of the total risk was due to formaldehyde. Benzene, dichloromethane, chlordane, lindane, and perchloroethylene and vinylidene chloride also accounted for substantial fractions of the total risk.

The fraction of exposed population at relatively high risk ($>10^{-3}$ risk) was estimated for several chemicals based on the distribution of concentrations measured in a small example of 15 homes. This analysis was used to illustrate the importance of the standard deviation in estimating high-risk populations.

Chemicals reported to cause serious (birth defects) reproductive effects at doses less than 1000 times doses expected from inhalation of the maximum recorded indoor concentrations included benzene, ethylbenzene, di(2-ethylhexylphthalate), pentachlorophenol, vinylidene chloride, and p-xylene. Chemicals reported to cause less serious effects, such as oestrous disorders or growth retardation of the fetus at doses within a factor of 100 of doses expected from indoor air exposure, were benzene, chlordane, diazinon, formaldehyde, and nicotine.

Based on the limited data available, it is concluded that risks of adverse health effects do not appear to be large in the great majority of homes. In some fraction of homes, however, a significant health risk may exist.

Recommendations for further study include:

- (1) measurements of indoor air concentrations for selected (targeted) compounds;
- (2) source characterization of those chemicals that pose the greatest risk;
- (3) extension of the toxicological data base to include compounds found in indoor air for which toxicological data are unavailable; and
- (4) assessment of aggregate effects of chemicals and of complex mixtures.

LIST OF ABBREVIATIONS

CV	Coefficient of variation
LD50	Lethal dose for 50% of the exposed population
LED	Lowest effective dose; lowest dose which produced an effect considered positive by the author(s) of the study
LED _h	Human inhalation equivalent of lowest effective dose
LOAEL	Lowest observed adverse effect level
MLE	Maximum likelihood estimate of risk
MOS	Margin of safety; ratio of NOEL to exposure level
NOAEL	No observed adverse effect level
TD50	Chronic dose rate in mg/kg/day which would induce tumors in half of the test animals at the end of a standard life span for the species, if there are no tumors in the test animals.

I. INTRODUCTION

Increasing experience with so-called "complaint, "sick", or "tight" buildings suggests the occurrence of adverse effects on humans from exposure to organic chemicals in indoor air. However, but for a few exceptions such as formaldehyde, chlordane, and pentachlorophenol, the complaints cannot be attributed with any certainty to individual chemicals. Furthermore, while the experience to date constitutes an important indicator of a potential problem, complaints are generally limited to acute or irritant effects, such as unpleasant odors, upper respiratory or eye irritation, or headaches. Thus, such complaints may not serve as effective indicators of more life-threatening end points, such as cancer or reproductive damage, if only because these toxic effects do not require acute exposure and occur after a time lag.

Despite indications from complaint buildings that organic compounds occur in sufficient quantities to cause acute effects, so far there has been neither: 1) an assessment of the overall importance of organic chemicals indoors as a cause of any class of toxic effects; nor 2) identification of the most important contributors to such effects. Nonetheless, substantial data are available, primarily from studies of animal and human toxicology, on the toxic effects of many of the chemicals that occur indoors. Effective utilization of such information can help to narrow the focus of future studies by targeting high-risk chemicals and by identifying toxic effects to examine in epidemiological studies. Considering the many chemicals present in indoor air, at widely varying concentrations, and the limitations in sensitivity of epidemiological studies, identification of hazardous substances can best be done by targeting groups of people highly exposed to chemicals of particular concern. The full range of toxicological data should be brought to bear as a basis for indicating which chemicals (or chemical classes) are worthy of attention, as well as for indicating beforehand the potential importance of various classes of effects (e.g., cancer or reproductive damage).

A serious problem in this endeavor is our lack of knowledge of the degree to which interactions between chemicals, in the air or in humans, are critical factors in producing toxic

effects. Toxicological studies generally provide information on the effects of individual chemicals. Obviously, interactions can, in principle, either increase or decrease the size and number of effects of a mixture as compared to the mere addition of individual effects. Nonetheless, until we can refine our theoretical and experimental knowledge of pertinent interaction mechanisms, we should utilize information on individual compounds to the fullest possible extent, while bearing in mind its limitations.

In this study we have examined the current literature reporting concentrations of organic chemicals in indoor environments to construct a nominal list of 144 chemicals that occur indoors. We have then surveyed the known toxicological properties of these chemicals individually, relying primarily on results from animal studies. We have also limited our analysis to toxic effects resulting from chronic or sub-chronic exposures. We have made rough estimates of the concentrations that might be expected to cause toxic effects in humans and have compared these to measured concentrations in indoor air as an approximate index of the significance of indoor exposures. In the case of carcinogens, we have estimated risks.

It should be noted that some of the individual compounds found in indoor air are effective indicators of the presence of complex mixtures, e.g., nicotine, indicates the presence of tobacco smoke. In this study, we have not attempted to assess the risks of exposure to such complex mixtures, but have rather focused on the many individual volatile organic compounds which have been measured in indoor air.

Evaluating the risks at indoor concentrations is complicated, not only by the potential importance of interactions, but also by fundamental limitations in toxic effects data. Present information is incomplete, uncertain, and -- in some fraction of the cases -- even in error. A major difficulty is an incomplete framework within which to estimate the frequency or type of effects at low concentrations relative to the high doses at which toxicity has been observed in animals or humans. Moreover, conversion factors often have to be applied to the animal data

to yield risk factors for humans, and the potential importance of route of administration may have to be considered. As a practical matter, the data will never be sufficiently complete to permit unambiguous application to human environmental exposures. It is therefore necessary to utilize incomplete data as fully and carefully as possible. The present work is aimed at assessing the overall potential for indoor pollutants to produce toxic effects (primarily cancer or reproductive effects), and to indicate what compounds might contribute substantially to human risk. This work should be viewed as part of a continuing effort, which ought to include further toxicological experiments, as well as epidemiological studies of heavily exposed parts of the population.

II. METHODS

A. Compilation of a Nominal List of Organic Compounds and Indoor Air Concentrations.

The primary sources for the list (Table 1) were the published literature and presentations made at the Third International Conference on Indoor Air Quality and Climate in Sweden in 1984. We have not attempted to survey the literature exhaustively, but rather to assemble a reasonably comprehensive and representative collection of information on which we could base a preliminary analysis.

Many sampling and analytical techniques are represented in the studies from which concentration data were taken. We recognize that not all methods are equally good in terms of sensitivity, accuracy, precision, and specificity. Since a rigorous assessment of validity was beyond the scope of this preliminary study, data of poor quality may have been included. However, it should be recognized that uncertainties in some of the other steps in risk assessment are sufficiently large, that order of magnitude estimates of concentration may be satisfactory at this stage of methodological development.

Table 1 lists 144 chemicals for which we found concentration data. From each report we have, when possible, recorded the maximum and the median (or mean if the median was unobtainable) values measured. With only 1 or 2 exceptions (see Table 1 footnotes), all concentration data are direct field measurements in homes and public buildings (primarily office buildings). Our main focus was to assemble concentration measurements that reflected everyday exposure in normal (non-complaint) homes and offices. For example, we have not included concentrations of formaldehyde in UFFI homes. Also not included are concentrations measured in industrial occupational settings or unusual exposure situations such as high concentrations of ethylene oxide recorded in a hospital (Sterling and Sterling, 1984) and high concentrations of benzo(a)pyrene from bituminous coal used in cooking stoves in small dwellings in India (Dave, 1984).

While there are reasons to suspect that frequency distributions of organic concentrations would vary according to the types of buildings (e.g., office buildings versus homes) due to differences in building materials, construction practices, ventilation systems, cleaning products and consumer products, data are insufficient to characterize these differences. A broad spectrum of organic compounds (e.g., alkanes, oxygenated hydrocarbons, halogenated hydrocarbons, and aromatic hydrocarbons) has been observed in both types of buildings. A large number of compounds (generally from fifty to several hundred), have been observed in both types of buildings, and the concentrations are typically low relative to standards for air concentrations in industrial settings. Therefore, we did not distinguish between concentrations in offices and homes in our analysis, though they are indicated in Table 1.

B. Scaling Factors.

Conversion from a non-inhalation route of exposure in rodents to its approximate inhalation equivalent was as follows (Anderson, 1983): We assumed 100% absorption via all routes of administration. To obtain an "inhalation-equivalent" 24-hour airborne concentration (in $\mu\text{g}/\text{m}^3$), the average daily dose (in $\mu\text{g}/\text{kg}/\text{day}$) was divided by the breathing rate of the test animal (rat: $0.64 \text{ m}^3/\text{kg}/\text{day}$; mouse: $1.3 \text{ m}^3/\text{kg}/\text{day}$). In the three cases where carcinogens were administered via the inhalation route (1,2-dibromoethane, formaldehyde, and vinylidene chloride), we used the same scaling factors as Gold, *et al.* (1984) to estimate the 24-hour airborne exposure in $\mu\text{g}/\text{m}^3$.

We assumed that duration of dosing had no effect in the animal experiments or in human exposures, and have estimated effects assuming continuous exposure for 24 hours each day. For example, the concentration in an inhalation experiment in which rodents were exposed 6 hours each day was adjusted by multiplying by 6/24. The error introduced by making this

simplifying assumption will depend upon the pharmacokinetic profile of each particular chemical. We have not included single-dose studies in this analysis, but have pointed out pertinent single-dose studies when they represent the only information on potential toxicity of a particular substance.

C. Calculation of Carcinogenic Risk.

We present several estimates of lifetime risks. (1) Using the multi-stage model as described by Crump (1982), maximum likelihood (MLE) and 95% upper confidence interval (UCL) risks were estimated for each indoor air concentration assuming additivity [see Crump (1982) for explanation]. (2) Risks were also calculated from the most potent TD50 (Sawyer, *et al.*, 1984; Peto, *et al.*, 1984) estimated by Gold, *et al.* (1984,1986,1987). The TD50 has been defined as the chronic dose rate in mg/kg/day which would induce tumors in half of the test animals at the end of a standard lifespan for the species, if there are no tumors in the control animals. We have assumed this value is a point on a linear dose response curve, and have approximated the risk per unit dose by dividing 0.5 by the TD50 (estimated as the equivalent dose in $\mu\text{g}/\text{m}^3$). When Gold, *et al.* (1984,1986,1987) reported that curves were non-linear we have indicated this by modifying the risk estimate with a "less-than" (<) or "greater-than" (>) sign. (3) The EPA estimates were calculated from the unit-risk values for exposure to a lifetime airborne concentration of $1 \mu\text{g}/\text{m}^3$ (Anderson, 1983; EPA, 1985a-f, 1986), assuming linearity.

D. Margin of Safety (MOS).

In general, most toxic effects other than cancer may be considered to act via mechanisms which would lead one to expect a threshold dose, below which no effect would occur. This threshold will vary among chemicals, depending upon their mechanism of action, and will also vary among species. Thus, unless there is specific knowledge of mechanisms, it is not possible to use a particular model to extrapolate risk below administered doses.

A commonly used approach for risk assessment is to estimate a "no observed effect level" (NOEL), which is then compared to the exposure level. The ratio of these two is called the "margin of safety" (MOS). The determination of a NOEL requires toxicological data of sufficient completeness to distinguish between a dose that produced no effect because it was far below the threshold, and one that produced no effect because it was just below the threshold. Such dose-response data exist for only some of the compounds on our list.

Instead of attempting to estimate a NOEL, we have recorded the lowest dose which produced an effect considered positive by the author of the study, and we have termed this the "lowest effective dose" (LED). In the ideal case, the LED would be very close to the NOEL. However, just as a NOEL will be under-estimated from a study administering a small number of doses, so will an LED be over-estimated. We have estimated LEDs for each chemical for three types of toxic effects: reproductive (including fetotoxicity); systemic (including mutagenesis); and irritation to the eyes and nose. Margins of safety (MOS) for each chemical were calculated by dividing the LED by concentrations in indoor air. Although we have attempted to exclude dubious results, since LEDs were calculated from single studies our estimates should not be considered definitive.

E. Calculation of the Fraction of Population at High Risk.

Concentration distributions were characterized as approximately lognormal, and geometric means (GM) and standard deviations (GSD) were calculated, based on the usual formulations of these parameters:

$$\ln GM = (1/N) \sum_i \ln y_i, \quad (1)$$

and,

$$(\ln GSD)^2 = (1/[N - 1]) \sum_i [\ln y_i - \ln GM]^2, \quad (2)$$

where y_i is the i th measurement. The lowest concentration (C) corresponding to a designated "high risk" level was then calculated, using methods described above. This was then combined with the GM and GSD estimates, to calculate the corresponding value of "z" in the Normal Probability Error Function tables:

$$(\ln C - \ln GM) / \ln GSD = z \quad (3)$$

The fraction of population at a higher risk than that corresponding to C was then determined by subtracting "z" from the appropriate value (usually 0.5).

III. DISTRIBUTIONS OF INDOOR CONCENTRATIONS

The available data on concentrations of chemicals in the indoor environment are relatively meager. For few chemicals do we have sufficient direct information to state what the frequency distribution of concentrations across homes in the U.S. is, nor are we able to cite average exposures with much accuracy. * Table 1 indicates that for most compounds only a few measurements have been performed, sometimes in circumstances where concentrations are expected to be higher than average.

Because of the scarcity of data for a specific compound, data in Table 1 have been grouped without taking into account sampling times or within-building locations. For benzene, for example, DeBortoli, et al. (1985) sampled four homes for 4 to 7 days; the remaining 11 for unspecified time periods; Lebret, et al. (1984) sampled for five to seven days; and Wallace, et al. (1984) and Pellizzari, et al. (1984) sampled for 12-hour periods. At present, too little is known about temporal variations (and spatial distributions) of organic concentrations to assess what effect this would have on estimates of concentrations. Thus, even in the best examples, there is great uncertainty in the estimates.

The principal exception to these generalizations about organics is formaldehyde, of which many measurements have been performed in a variety of indoor environments. Thus, we can say with some assurance, at least in certain classes of buildings, what average concentrations are. Moreover, the distribution of formaldehyde concentrations has been found to have a long tail to high concentrations, which is consistent with a log normal distribution (e.g., Figure 1, from Nero & Grimsrud, 1983). Distributions for other organics, though data are less extensive (e.g., Lebret, 1985; Hawthorne, *et al.*, 1984), appear to take a similar form (e.g., Figure 2). These may be compared with the frequency distribution of radon in homes

*Only preliminary results of the TEAM study were available when this work was in progress.

(Nero, *et al.*, 1986), shown in Figure 3. Note in particular the general shape of the lognormal function calculated from the radon data and the fact that it conforms to the actual data extremely well.

It is unfortunate that distributional data for organic compounds are so limited, because such information can be extremely useful in assessing exposures and their population risks. For example, for pollutants that are thought to produce adverse health effects via a mechanism involving a threshold, it would be useful to estimate the fraction of exposures that are likely to be near or above the predicted threshold. In most cases the threshold exposure will be much larger than mean exposures and will occur less frequently (i.e., they will be in the tail of the distribution). Thus, some knowledge of the distributional form is required to estimate the risk. Even for effects such as cancer, not generally believed to act through a threshold mechanism, significant individual risk will, in most cases, also apply only to those in the tail of the distribution of exposure.

In later sections of this report (IV.B.1.c.; IV.B.2.b.), as an illustrative example, we examine the distribution of carcinogenic risk for several carcinogens using house-by-house concentrations from one study (DeBortoli, *et al.*, 1985). These concentration data were obtained for only 15 buildings (14 homes and one office building), but, as apparent in Figure 4, the rough distributional forms are not inconsistent with a lognormal distribution. As a general characteristic, the concentrations span a large range, an order of magnitude or more, even for this very small sample. Further, as a general characteristic, the bulk of the measurements are grouped at relatively low concentrations, with some fraction at substantially higher levels. It is not useful, given these limited data, to attempt to determine how well various distributional forms fit the data. On the other hand, it is clear that the overall distribution is sufficiently similar to the general form of a lognormal distribution that lognormal parameters can be used to characterize the data approximately.

Because the data were collected in Italian homes, which could differ with respect to organic concentrations in U.S. homes, the DeBortoli data were compared with what is probably the most extensive set of data collected in U.S. homes, the TEAM data-set consisting of measurements in 350 homes in Bayonne and Elizabeth, New Jersey and representing a target population of 128,000 people (Pellizzari, et al., 1987). The median concentrations for the ten compounds in the DeBortoli study which were also measured in the TEAM study were compared to the estimated frequency distributions from the TEAM study for the overnight personal samples (which are believed to best characterize the indoor residential concentrations). The ten compounds were: benzene, chloroform, 1,1,1-trichloroethane, tetrachloroethylene, trichloroethylene, carbon tetrachloride, dichlorobenzene, ethylbenzene, 3-, and 4-xylene, and 2-xylene. The DeBortoli data were, on average, at the 71th (± 30) percentile as compared to the TEAM results. Thus, the DeBortoli concentrations are somewhat higher than those found in the TEAM study, but are not inconsistent with them.

Possible reasons for the higher concentrations are related to the different locales and study designs. Sampling times were not the same, as noted previously -- the use of night-time samples in the TEAM study versus samples most likely taken during the day in the DeBortoli study. There also may have been differences in construction practices and materials, and possible differences in consumer products in the homes.

In any case, the differences in concentrations are not large. We chose to use the DeBortoli data because of this, because they represent a relatively large set of volatile organic compounds (35 versus 15 compounds for the TEAM study) and because the data were available on a house-by-house basis, allowing us to examine risk to groups of chemicals on this basis.

The width, or spread, of a lognormal distribution is characterized by the geometric standard deviation (GSD). A variety of research on indoor pollution has indicated that many

characteristics directly associated with indoor air quality are lognormally distributed, often with GSDs in the vicinity of 2 to 3. It thus may not be unreasonable to assume that a similar GSD would be found for most organics. However, though this simple assumption might hold in most cases, it will cause us to overlook important sources of risk by not identifying exceptional cases. It is the compounds that are very broadly distributed (i.e., chemicals that have GSDs larger than 2-3) that will pose the greatest individual risks to the greatest number of people. For most of the chemicals listed in Table 1, not enough information is available even to *estimate* the GSD, and hence the fraction of the total population exposed to relatively high concentrations.

For the compounds reported by DeBortoli *et al.*, we have calculated the GSD for those compounds where 75% or more of the measurements gave values above detection limits, assigning a value of one half the detection limit to those falling below the limit. For the total of 20 chemicals satisfying this criterion, GSDs ranged from 1.7 (formaldehyde) to 6.6 (n-Undecane). Fifteen of the 20 fell below 4.0, and of the five exceeding 4.0, four were highly correlated across the houses (discussed further below). These four were n-nonane, n-decane, n-undecane, and n-dodecane. (The fifth was ethylbenzene, with a GSD of 4.3.). Thus, even in this small sample of 20 chemicals, 25% had GSDs that greatly exceeded the 2-3 range.

An additional use of the distributional form is to aid in the determination of overall exposure (or risk) to mixtures of compounds. If compounds in the mixture are independently distributed, an average value for overall exposure is simply the sum of the mean concentrations of each. This, however, does not address the question of the co-distribution of compounds (i.e., whether or not the concentrations of individual chemicals are correlated due to common factors such as the ventilation rate or emission sources.) This is a key issue, since the greatest exposure, and hence the greatest risk, will occur when groups of high risk chemicals tend to occur together. For such chemicals, it should be possible to use a simple additive model to sum the individual distributions, taking into account co-distribution by use

of appropriate weighting factors.

It may be possible to deduce such information from a detailed knowledge of emission profiles of consumer products, building materials, etc., in combination with information on use patterns. This would be a complex, though possibly rewarding approach.

Another approach to determine appropriate weighting factors is to use house-by-house concentration data to empirically identify co-distributed compounds. We have done this using the data from the 15-home study of 34 compounds by DeBortoli, et al. (1985). Statistically significant ($p < 0.05$) correlation coefficients and associated P-values are listed in Table 2. There are a number of highly significant correlations in the Table. Most obvious are correlations between: (1) n-nonane, n-decane, n-undecane, n-dodecane and n-butanal; (2) benzene, toluene, ethylbenzene, the xylenes, and the trimethylbenzenes, along with n-heptane and n-octane; (3) the trimethylbenzenes are, in addition, correlated with the aliphatic series beginning with n-nonane, and with naphthalene. These chemicals are, for the most part, common solvents, some of which are frequently found in mixtures.

This kind of information can be useful in deciding how to include groups of compounds in models aimed at estimating overall exposure and risk. For example, in Table 2, two groups of carcinogens are significantly correlated: dichloromethane and chloroform, and 1,1,1-trichloroethane, tetrachloroethane, and trichloroethylene. Thus, in this small sample of homes, we can predict that people living in homes with a high concentration of, say, dichloromethane, will also be exposed to a high concentration of chloroform.

IV. TOXICITY AND RISK

In what follows we examine several aspects of the toxic potential of the chemicals in Table 1. Results are reported in four sections: (1) Acute toxicity, as measured by the LD50 (lethal dose for 50% of the exposed population); (2) carcinogenicity; (3) reproductive effects (including fetal toxicity); and (4) other systemic effects and irritation.

The general approach is to utilize available toxicity data (mostly from tests in animals) to estimate the lowest airborne concentrations of each chemical which would be required to produce an equivalent toxic response in humans. We then calculate a margin of safety (MOS) by comparing these concentrations to concentrations in indoor air. Discussion of chemicals is limited to those which produce adverse health effects in test animals or humans at doses equivalent to airborne concentrations within a factor of 1000 of those actually encountered in indoor air. For carcinogens, we also calculate individual lifetime risks. For several chemicals which are carcinogens or have produced adverse reproductive effects in animals, we also used house-by-house concentration data from one study (DeBortoli, *et al.*, 1985), to calculate the fraction of the population that is exposed to relatively high concentrations, and hence potentially at relatively high risk of cancer or reproductive effects. Using these approaches we have attempted to determine which among the 144 chemicals listed in Table 1 pose the greatest risk. The chemicals and toxic effects discussed are listed in Table 3.

Since we are exposed to chemicals in indoor air as a complex mixture, of greatest interest is overall risk from these combined exposures. Though one can apply additive models in certain situations where there is evidence that chemicals in mixtures are acting through common mechanisms, we have addressed this issue here only to a limited degree and only for carcinogens (see section IV.B.2.).

A. Use of the LD50 as an Indicator of Toxic Potential.

A general measure of the toxic potential of chemicals is the LD50 (Lethal Dose 50). This is the single dose which causes the death of 50% of a test group of animals (usually rats or mice) in a standard time frame. The LD50 is a useful number for several reasons. First, its determination is relatively unambiguous. The protocol is quite simple and standardized, and the endpoint, death, is clear-cut. This makes comparisons across chemicals more straightforward and less subject to uncertainty than comparisons using results of tests for other toxic endpoints. Second, it is the most commonly conducted toxicity test, thus permitting a broad spectrum comparison of the toxicity of the large group of organic chemicals in indoor air, many of which have not been tested for other toxic effects. Finally, the LD50 ranking can also provide a general indication of the relative potential potency of chemicals to induce certain other toxic endpoints. In particular, it has recently been shown (Zeise, *et al.*, 1984) that, for carcinogens, the LD50 and carcinogenic potency are correlated.

In Figure 5 we have plotted the oral LD50s in rats for the chemicals in Table 1 for which such data are available. More relevant to indoor air exposures would be inhalation LD50s. However, many fewer chemicals have been tested by the inhalation route as compared to the oral route. Since we wished to illustrate an index of toxicity over the greatest possible number of chemicals, we have illustrated the oral LD50 results. As apparent from the Figure, the LD50s of most chemicals span two orders of magnitude, from about 400 to 30,000 mg/kg. A group of 14 chemicals forms a considerably more potent cluster, extending the range two more orders of magnitude. Most of the chemicals in this higher potency group are used primarily as pesticides. Exceptions are ethylene dibromide (mainly used as a gasoline additive, though being phased out); ethylene oxide (a sterilant); allyl alcohol (used in the manufacture of herbicides); acrolein (also in diesel exhaust and cigarette smoke); and dimethylnitrosamine (in cigarette smoke). Finally, one very potent toxin, hydrogen cyanide (HCN), and one very weak toxin, freon (CFM), extend the range of LD50s to more than 5 orders of magnitude.

Though the ranking of LD50 in Figure 5 gives some idea of the comparative toxic potentials of these chemicals, the degree of hazard in humans depends also on the exposure. It is tempting to use the inverse of the LD50 as a potency scale, and multiply by concentrations in indoor air to obtain a rough ranking. We have in fact done this, but wish to point out that this is not a ranking of risk, because by calculating this ratio we assume a linear dose response and the absence of thresholds, which in most cases will not be true. It is thus simply an ordering of the chemicals based on how far actual indoor air exposures are from the LD50. In Table 4 are the 20 highest fractions obtained by dividing the "equivalent" airborne LD50, estimated from the oral rat values in Figure 5 by the maximum concentrations in indoor air (from Table 1). This "equivalent" value is calculated only so the numerator and denominator can be in the same units. It is probably an underestimate since the LD50 is a single dose, and the converted values are estimated as a concentration which will result in the same dose, on a mg/kg-body weight basis, when inhaled over a 24 hour period, assuming 100% absorption.

Almost half of the highest ranked exposures in Table 4 are unusually high exposure situations, such as heavily smoke-filled rooms and complaint buildings. A significant number are also "special use" types of chemicals, such as pentachlorophenol, and pesticides. If a similar calculation is made using mean concentrations from Table 1, the ratio for 8 chemicals is less than 100,000. These are: nicotine: 8,100; dichloromethane: 17,000; formaldehyde: 27,000; allyl alcohol: 29,000; ethanol: 85,000; phenol: 65,000; n-butanol: 71,000; delta-3-carene: 71,000).

In addition to being a convenient way of ordering the compounds, these values may provide some insight that is more obviously relevant to risk. We have compared all of the LEDs calculated in this study for chronic or acute toxic effects (including carcinogenesis) to the corresponding LD50s. Almost all are within a factor of 1,000 of the LD50 (data not

shown). Thus, a comparison of indoor exposures to the LD50 may be useful in two ways:

(1) It may provide an indication of the extent to which toxic effects from indoor exposures are being produced at detectable levels. Since the LD50 is a measure of the lowest effective dose (in animals), we might expect that toxic effects (even though they may be occurring) from exposure to compounds present at concentrations much more than a factor of 1000 below the LD50 would not be detectable. Examined from this perspective, the most obvious result is that, in most cases, the ratios of LD50s to actual exposures are very large. In cases where the "inhalation-equivalent LD50s" are underestimated, as discussed above, the ratios are even larger than they appear on the Table. Since, the ratios for only 7 chemicals are within a factor of 1000 and all ratios based on mean concentrations are *much* greater than 1000, this suggests that toxic effects produced at a rate observable experimentally are likely to be very few indeed. It also suggests that, if such effects occur it will most likely be in relatively high-exposure situations -- i.e., as previously stated, at the high end of the exposure distributions.

(2) This scale may also be useful in developing testing priorities. A number of compounds for which LD50s have been determined have not been tested for other toxic effects. It might be important, therefore, to be sure that any chemicals present in indoor air at concentrations within, say, a factor of 5,000 of the LD50, have been tested for a variety of toxic endpoints of interest. There are 12 such chemicals on Table 4. Some of these have been rather extensively tested, but a number have not.

B. Carcinogenic Risk

1. Risk from Exposure to Individual Compounds.

a. The Ratio of TD50 to Indoor Exposure.

The difference between doses that produce cancer in test animals and human exposures in

indoor air is of interest as an indication of: (1) Whether any carcinogens are present at sufficiently high concentrations to produce effects that may be experimentally observable; and (2) the ranges over which uncertain extrapolation models must be applied to estimate risk. These are approximated by tabulating the ratio of the adjusted TD50 to indoor air concentrations (Table 5).

Several points are apparent from examining these ratios. Most striking is the similarity of the "inhalation-equivalent" TD50 ($1247 \mu\text{g}/\text{m}^3$) to concentrations of formaldehyde to which some humans may be chronically exposed. Some measurements in non-UFFI homes have actually exceeded this value (see Table 1). However, since considerable irritation would be expected at such concentrations a more realistic upper limit estimate of a concentration to which long term exposures might conceivably occur may be the HUD standard for mobile homes ($500 \mu\text{g}/\text{m}^3$). We have used this to obtain the "Maximum" ratio reported in Table 5.

The choice of a reasonable upper limit for chronic exposure is complex. Because of the decay rate of formaldehyde (half life = 4 years) the HUD standard may be too high as a reasonable upper limit estimate of lifetime exposure. Most new homes would presumably meet the standard, and then show a decrease in concentration over time. On the other hand the HUD standard is only a design standard. Individual mobile homes are not tested for compliance and measurements higher than $500 \mu\text{g}/\text{m}^3$ have been reported, as shown in Table 1. Thus, $500 \mu\text{g}/\text{m}^3$ may not be an unreasonable upper limit estimate.

The HUD standard is only 2-3 times less than the "inhalation-equivalent" TD50. This is certainly within the range over which dose response effects have been demonstrated in animal cancer tests. There is a great deal of continuing discussion as to whether a threshold (practical or theoretical) exists for formaldehyde carcinogenesis. Such considerations do not have great impact on the key observation that at least some individuals may be exposed chronically to concentrations of formaldehyde that are within an order of magnitude of the actual doses that

have produced cancer in animals. Thus, they may be within the range of observable dose response.

In Table 5, the ratios for most other carcinogens are much greater than for formaldehyde. Ratios for only 4 chemicals are <100. These are: chlordane (28); vinylidene chloride (43); heptachlor (56); and tetrachloroethylene (81). The concentrations for chlordane and heptachlor were made relatively soon after termiticide treatment, but they may not be unreasonable upper limit estimates of some long term exposure situations, since these compounds are known to remain active for long periods (30 years and perhaps longer) (U.S. Air Force, 1982). However, the number of people exposed to such concentrations is probably not large since the great majority of airborne measurements have been far below the maximum values listed. We do not have a mean or median estimate available.

The evidence for carcinogenicity of vinylidene chloride is limited (IARC, 1986). It appears to be a weak carcinogen in rodents, and the effect is marginal (IARC, 1986; Gold, *et al.*, 1984). Though the chemical is found indoors, it appears to be primarily an outdoor pollutant (IARC, 1986). It has not frequently been detected in homes, though in a very small number of cases relatively high concentrations have been reported. We do not know if these would be expected to occur chronically. If such chronic exposures do occur, provided the limited animal data are correct, risk in these homes could be substantial.

Tetrachloroethylene appears to have both indoor and outdoor sources. A major indoor use is as a cleaning solvent, and the widely varying concentrations measured suggest intermittent use, as might be expected. Thus, the maximum concentration in Table 5 is most likely not representative of a chronic exposure situation. The mean concentrations reported for both vinylidene chloride and tetrachloroethylene are much lower than the maximum values, and yield ratios of 420 and 13,000 respectively.

If carcinogenic potential is examined only from this perspective -- that is, only from a consideration of whether we are exposed to any carcinogens at concentrations that might be within an observable dose-response range - then the conclusion must be that the carcinogen of greatest concern is formaldehyde. For several other carcinogens the data are suggestive, but more detailed information on chronic exposures are needed to make a definitive assessment.

b. Estimates of Individual Risk.

In Table 6 are four estimates of lifetime cancer risk from continuous exposure to the maximum or mean concentrations of the 24 carcinogens. Except as indicated in the Table footnote, the estimates derived from the multi-stage model [labeled maximum likelihood (MLE) and 95% upper confidence limit (UCL)], and from the TD50 were all calculated from the dose-response data used by Gold, et al. (1984,1986,1987) to estimate the TD50 that was the most potent among the experiments analyzed. The MLE and UCL estimates are not strictly comparable to the TD50 estimate however, because Gold, et al used lifetable data, and we used summary data in the multi-stage model. The column labeled "EPA" was calculated directly from published EPA unit-risk (risk from exposure to 1 ug/m³) values (Anderson, 1983; EPA, 1985a-f, 1986) assuming linearity.

In most cases, the multi-stage MLE is either the lowest estimate, or similar to the lowest estimate. Also, the MLE, and the TD50-derived estimates are quite similar, which agrees with the observation that most of these curves are consistent with linearity (Gold, et al., 1984,1986,1987). For only 3 chemicals (1,1-dichloroethane, formaldehyde, and heptachlor) do these two estimates differ by more than a factor of 10. In these 3 cases, the MLE is much lower than the TD50-derived estimate. For formaldehyde and heptachlor this is probably due primarily to the non-linearity of the dose-response curves. For 1,1-dichloroethane the reason is less clear, for as Gold, et al (1984) report, the dose response is consistent with a linear

model when lifetable data are used. It is even linear using only the summary data (L. Gold, personal communication). We have not examined the reason for differences between our UCL(95%) estimates and those of EPA. None differ by more than an order of magnitude. These differences almost certainly reflect relatively minor differences in the analyses, such as dose response data or species scaling factors.

The MLE lifetime risk estimates for seven carcinogens (benzene, chlordane, dichloromethane, formaldehyde, lindane, tetrachloroethylene, and vinylidene chloride) are $>10^{-3}$ at the maximum recorded indoor air concentrations. Chlordane was discussed in the previous section. Lindane has led to contamination problems in homes treated with wood preservatives (Van der Kolk, 1984; Gebefugi & Korte, 1984), and has been found in the air of homes even months after treatment at concentrations as high as $40 \mu\text{g}/\text{m}^3$ (Van der Kolk, 1984). Though undergoing regulatory review (EPA, 1983), it is still a widely used pesticide. EPA assessed risk from a variety of exposures, including those resulting from a number of household uses (EPA, 1979b). Several of these resulted in quite high lifetime risks. For example, estimated lifetime risk from waxing household floors every 3 weeks with wax containing lindane was 2.16×10^{-3} , and from use of treated shelf paper was 1.19×10^{-4} . The estimates we quote in Table 6, ranging from $2.5\text{-}4.1 \times 10^{-3}$, were calculated based on maximum levels found some months after treatment with a wood preservative, making the assumption these levels might be considered an upper limit for chronic exposure. Since lindane is less persistent than most other chlorinated hydrocarbon insecticides this is most certainly an oversimplification. The risk calculated from mean exposures is considerably less ($0.83\text{-}1.4 \times 10^{-5}$).

Estimates for dichloromethane are among the highest in Table 6, both at maximum and mean or median concentrations. It is unclear whether concentrations in the range of the maximum listed in Table 1 ($5000 \mu\text{g}/\text{m}^3$) would occur chronically. Unfortunately, we have measurements on dichloromethane from only one study (DeBortoli, *et al.*, 1985) involving 15 homes. The range of dichloromethane concentrations among these homes was very large, more

than a factor of a thousand, and levels higher than 1000 were found in only 2 of the 15 homes studied. Common sources of dichloromethane are paint, paint strippers, and spray cans. The high concentrations observed by DeBortoli could reflect the coincidence of occasional usage close to the time measurements were made. These levels are far higher than the highest measurements made in outdoor air [e.g., EPA reports about $50 \mu\text{g}/\text{m}^3$ as a maximum annual average to which people may be exposed who live near dichloromethane production facilities (EPA, 1985f)].

The high concentrations measured by DeBortoli are much lower than those resulting from use of such common sources of dichloromethane as paint strippers and aerosol spray paints (Girman and Hodgson, 1986). For example, average concentrations in the breathing zone during paint stripping are about $3.5 \times 10^6 \mu\text{g}/\text{m}^3$, and use of aerosol spray paints results in concentrations averaging about $1.4 \times 10^6 \mu\text{g}/\text{m}^3$. These concentrations are hundreds of times the highest levels recorded by DeBortoli. Though these activities are usually engaged in for relatively short periods of time, regular usage would impact significantly on chronic exposure patterns, and could substantially increase risk.

It is difficult to exclude the possibility that some chronic indoor exposures to benzene, tetrachloroethylene, and vinylidene chloride might approach the maximum levels listed in Table 1. For benzene, even the maximum concentrations measured in indoor air are well below human odor and irritation thresholds. These are, respectively, $2 \times 10^4 \mu\text{g}/\text{m}^3$ (Verschueren, 1983) and $8 \times 10^4 \mu\text{g}/\text{m}^3$ (Fishbeck, *et al.*, 1978). Based on doses toxic in animal studies, this is probably also true for tetrachloroethylene and vinylidene chloride. Mean or median exposures are much less than the maximum values (the average ratio is 88), though for all three of these chemicals, the risk, even at mean concentrations, is $>10^{-5}$. This risk, though not totally insignificant, is very small relative to risk at the maximum concentrations. Thus, the most important question to answer is what fraction of the population is exposed to relatively high concentrations for long periods of time. We have addressed this

question in a preliminary way in the next section.

Based on the TD50, the mean lifetime risk for formaldehyde is 950×10^{-5} , by far the largest cancer risk estimated from mean exposures. The risk estimated at the upper 95% confidence limit using the multi-stage model also places formaldehyde well ahead of the other carcinogens on Table 6. Risks from dichloromethane, benzene, and vinylidene chloride exposure rank second on this scale -- 6-9 times less than formaldehyde. The MLE estimate for formaldehyde risk -- 0.37×10^{-5} -- is a factor of 180 times less than the estimate at the 95%UCL, and one of the smallest mean risks. This dramatic difference is most likely due to the extreme non-linearity of the carcinogenesis dose-response in the rat tests, which is fully taken into account by the MLE estimate, but not by the linear extrapolation from the TD50.

c. The Fraction of the Population at High Risk.

For benzene, formaldehyde, carbon tetrachloride, tetrachloroethylene, and trichloroethylene we have estimated what fraction of the population may be at relatively high risk. For this exploratory exercise, we have utilized the house-by-house concentration data from a 15-home study (DeBortoli *et al.*, 1985), and have calculated the percent of the exposed population in these homes that would be expected to be at greater than 1 in a thousand lifetime risk of cancer. Results of these calculations are in Table 7.

We have made 3 estimates of the concentration of each compound required for a risk of 10^{-3} : the maximum likelihood (MLE); the corresponding 95% lower confidence interval estimate (LCL); and an estimate calculated from the TD50, assuming linearity. All 3 estimates suggest that 1% or more of the population are at $>10^{-3}$ risk from exposure to benzene. The estimates for formaldehyde vary from an extremely small fraction up to more than 99% of the population.

If the geometric standard deviations of indoor concentrations of various carcinogens are similar, the results of this type of analysis, in terms of the relative hazard attributable to the different chemicals, will not be in disagreement with the analysis based only on mean risks (Table 6; Wallace, 1986). However, as seen by comparing Tables 6 and 7, ranking the chemicals based on the fraction of people at high risk can be strongly dependent on the breadth of the concentration distributions of different chemicals. For example, using the MLE estimates in Table 6, the ratio of risks from exposure to trichloroethylene and carbon tetrachloride are: 1.9 using the maximum concentrations; and 0.44 using the mean or median concentrations. Thus, based on the maximum or the mean values, the risks from exposure to trichloroethylene and carbon tetrachloride do not differ greatly, varying over a range of only about 4. However, a very different picture of the ratio of risks is seen when calculated from the values presented in Table 7. Thus, the MLE risk from exposure to trichloroethylene is 0.014%; and the z-value of 5.67, for risk from exposure to carbon tetrachloride, corresponds to a risk of about 7.1×10^{-7} (K. Revzan, personal commun.). The ratio of these is almost 20,000, leading to a very different picture of the relative risks from exposure to these two chemicals. This is because the geometric standard deviation for trichloroethylene (3.47) is much greater than that for carbon tetrachloride (1.87).

Similarly, depending on the degree to which the standard deviations differ, the relative risks of other chemicals will also be affected. Another example is benzene and formaldehyde. Based on the 95% confidence limit estimates of risk from exposure to mean concentrations in Table 6, the risk from formaldehyde exposure is about 10 times that from benzene exposure. However, using the 95% confidence interval values in Table 7, benzene poses a high risk to 3 times more people than formaldehyde. This difference is due to the relatively narrow distribution of formaldehyde among the DeBortoli homes as compared to benzene. We will consider the relative merits of the two methods of estimating risk illustrated in Tables 6 and 7 further in the Discussion.

2. Overall Carcinogenic Risk

The material presented in Tables 5-7 refers to risk from exposure to individual chemicals, whereas in the indoor environment, exposures are to mixtures of chemicals. This raises the immediate question of the basis for estimating the total risk. Though synergistic or inhibitory effects between carcinogens have been observed in a few instances, there is insufficient knowledge of such interactions to adopt any model for combined effects. Furthermore, even for classes of chemicals for which an additive model might be appropriate (e.g., chemicals with similar mutagenic mechanisms), the biological basis for additivity is insufficient to justify use of such a model without building in substantial uncertainty. Nevertheless, additivity is the first order expectation, and in what follows, we have assumed that the total risk is equal simply to the sum of the individual risks.

Below we have looked at overall carcinogenic risk in two ways. First, we have estimated total mean risk, and secondly we have examined the distribution of risk among exposed populations.

a. Total Mean Risk.

We used the simple additivity model to sum mean risks estimated for each individual carcinogen, where such information was available [mean indoor concentration data were not available for almost all the pesticides in Table 1, nor for dimethylnitrosamine, N-nitrosopyrrolidene, and PCBs]. This was done for the risks presented in Table 6, yielding totals for mean lifetime risk of $28-980 \times 10^{-5}$. This approximately 40-fold range is primarily caused by the large discrepancies in the estimates for formaldehyde risk, as already discussed. Using the high estimate, the risk is dominated by formaldehyde (950×10^{-5}) and is about 1 in 100. If the smallest estimate is used the overall risk drops precipitously, to roughly 1 in 5000,

and formaldehyde is one of the smaller risks (0.37×10^{-5}), approximately 15 times less than dichloromethane or benzene.

b. The Distribution of Risk.

The concentrations of 7 carcinogens measured by DeBortoli *et al.* were used to examine total risk on a house-by-house basis. These results are in Table 8. As evident from the coefficients of variation (CV = standard deviation/mean), the distribution of risk across homes for most of the carcinogens is broader than the distribution of total risk from all chemicals combined, shown at the bottom. The CV for the individual chemicals ranges from 51-210%, but for all chemicals combined the CV is 52%. There are two factors which produce this effect. First, if the chemicals present were strongly correlated, the CVs for individual and total risks would be similar. The fact that they are not suggests that many of the chemicals are independently distributed, leading to differences in the individual CVs and to a smaller variance in the total risk. Second, the most broadly distributed chemicals do not contribute very much to the overall risk, which tends to be dominated by formaldehyde and benzene. Thus, it is primarily the fact that these 2 chemicals are not strongly correlated which leads to the smaller overall CV. [We note that dichloromethane and chloroform are significantly correlated; (see Table. 2).

C. Reproductive Effects

For the chemicals listed in Table 1, we searched the published literature for studies reporting adverse effects on reproduction after sub-chronic or chronic administration. Most compounds have been tested only sparingly or not at all; a few have been tested in a number of studies. We have taken a broad view of reproductive effects, and, in addition to obvious birth defects, attempted to identify studies in which the lowest chronic doses elicited fetal toxicity (regardless of whether this was accompanied by maternal toxicity) and relatively minor, possibly reversible effects.

The adequacy of studies varies greatly. Although we have not developed systematic criteria to screen studies for adequacy, we have in all cases attempted to insure that the studies we selected were screened for adequacy by expert groups, in particular the IARC and the EPA, or were selected for inclusion in the evaluated reference collections of Shepard (1983) or Barlow and Sullivan (1982). Systematic screening criteria have been developed by Rowen-West, *et al.* (1987), and we have also indicated when a study was considered by that group to satisfy their criteria (D.R. Bishop, personal communication).

In Table 9 are listed those chemicals which were reported to cause reproductive effects at doses equivalent to inhalation daily (over a 24-hour period) of airborne concentrations less than 1000 times the maximum concentration recorded in Table 1 (i.e., at doses indicating less than a 1000-fold margin of safety). In all but one case (formaldehyde) results are from tests in rodents. (The formaldehyde study was a human study.) Obviously, there may be large errors introduced by the simplifying assumptions of this procedure, as we have discussed elsewhere in this report.

The severities of the effects recorded in Table 9 vary. Some reproductive LEDs have been determined from studies demonstrating fetal death or abnormalities, whereas others are from studies demonstrating reversible, less life-threatening effects, such as reduced birth weight. We have, to a limited degree, attempted to take these differences into account by dividing reproductive effects into three categories: Birth defects; less serious effects; and reproductive toxicity. Since the chemicals in Table 9 have not been thoroughly tested for the full range of harmful reproductive effects, one cannot conclude that the absence of a compound from a particular category means the absence of an effect.

Six compounds (benzene, ethyl benzene, di(2-ethylhexyl)phthalate, pentachlorophenol,

vinylidene chloride, and p-xylene) have been shown to cause obvious birth defects at doses lower than the estimated margin of safety of 1000. Benzene has also been observed to cause an alteration in the oestrus cycles in rodents at doses estimated to be only a factor of 13 higher than some indoor air concentrations.

Four other compounds have produced effects comparatively less serious than obvious birth defects: chlordane and diazinon (postnatal endocrine dysfunction); formaldehyde (menstrual disorders in women); and nicotine (reduced birth weight). Effects of formaldehyde on human menstrual cycles, which were observed at concentrations considerably less than some indoor concentrations of formaldehyde, and less than a factor of 10 above average indoor levels may be of significance. Although the single study reporting this effect cannot be considered definitive (e.g., see Anon, 1984; OSHA, 1985), the potential importance of the finding strongly suggests the need to examine the question further. Effects in rodents due to chlordane were also quite close (within a factor of only 3) to concentrations recorded in treated homes. In addition to the results in Table 9 for nicotine, several other studies have observed changes in fetal breathing movements in women smoking only a single cigarette. A spectrum of cardiac effects have also been observed in fetuses in the rhesus monkey and in mice after exposure to single, relatively low doses of nicotine. Diazinon produced effects at doses within a factor of about 70 of the indoor concentration recorded in Table 1.

Finally, six additional compounds were observed to cause lethality or embryotoxicity at various times during development after administration of daily doses within the MOS of 1000. These were: chloroform, dimethylacetamide, dimethylnitrosamine, heptachlor, lindane, and trichloroethylene. Among these lindane and heptachlor produced effects at doses within a factor of only ten of the maximum indoor concentrations; the other three compounds were active at doses a factor of 100 or more the maximum indoor levels.

If the LEDs in Table 9 are taken as rough indicators of potency, and each of the three

"severity" categories are examined separately, several observations are evident: (1) Among the 6 compounds listed in the 'birth defects' category, all but pentachlorophenol have roughly the same estimated airborne LEDs, on the order of $1 \times 10^5 \mu\text{g}/\text{m}^3$; (2) Among the 5 chemicals for which "less serious" effects are recorded, chlordane, diazinon, and formaldehyde have similar LEDs, and benzene and nicotine are roughly 50 times weaker; (3) Among the 6 compounds for which LEDs for lethality or general toxic effects are recorded in Table 9, results are not as clustered, and range over four orders of magnitude. Dimethylnitrosamine stands out as the most potent toxin, followed by heptachlor and lindane, which are about 50 times weaker than dimethylnitrosamine. The weakest of the six is dimethylacetamide, some 30,000 times less potent than dimethylnitrosamine.

It is possible that some of these chemicals may act additively or synergistically. However, in the absence of any evidence for this, the additive model applied to aggregate effects across chemicals (as was done for carcinogens), does not appear justified.

An examination of the Table indicates that margins of safety of all six compounds in the "birth defects" category are much higher (on the average, 100 times higher) than those in the "less serious" category. This raises the important point that compounds, at doses far below those that might cause obvious birth defects, may produce more subtle, yet not clearly harmless effects (such as menstrual disorders or lowered birth weights). The amount of toxicological testing that is aimed at detecting such effects is very limited. This is unfortunate, since it is these effects that appear to be more likely occurrences at relatively low-dose exposures in the indoor environment. Certainly, without knowledge of the sensitivity of humans compared to rodents, or of the shape of the dose-response curve, it is not possible to exclude the possibility that birth defects can occur. However, obvious birth defects seem a much less likely possibility, as the very large differences in the margins of safety for these two kinds of effects in Table 9 suggest.

In general, for the compounds we have examined, the daily doses required to induce observable reproductive effects are less than those required to produce carcinogenic effects. This can be seen by comparing the lowest effective doses (LEDs) for compounds that are both reproductive toxins and carcinogens. In Table 10 we compare the TD50s (Table 5), the lowest average daily lifetime doses (adjusted to their "inhalation-equivalent" values) which produced cancer at a higher incidence than in controls (Gold, *et al.*, 1984, 1986), and the "inhalation-equivalent" reproductive effects LEDs for the 10 reproductive toxins that are also carcinogens. With only two exceptions (birth defects produced by benzene and vinylidene chloride), the doses required to elicit adverse reproductive effects are considerably less than the carcinogenesis LEDs.

For reproductive effects in general there is not the theoretical justification for extrapolation over large dose-ranges that exists for carcinogenesis. Therefore, it is hard to know if there is any risk of adverse reproductive effects when margins of safety are high (as most are in Table 9), since exposures may be below some biological threshold. Consequently, it is even more important for reproductive effects than for carcinogenesis that we have a sense of what fraction of the population is exposed to doses that are not far below the LED. To examine this, we have used geometric means and standard deviations calculated from the data of DeBortoli, *et al.* (as was done for carcinogenic risk) to estimate what fraction of the DeBortoli population would be exposed at levels high enough to result in an MOS of <100 (Table 11). As shown, for the 5 chemicals in Table 9 examined by DeBortoli *et al.*, by far the largest numbers of people at high risk are those exposed to formaldehyde and benzene.

D. Miscellaneous Toxic Effects

The main purpose of this analysis was to determine if there were any compounds in Table 1 not already discussed in previous sections with evidence of potential to cause toxic effects

other than cancer or reproductive effects at doses less than 1000 times indoor air concentrations. Miscellaneous toxic effects of carcinogens and reproductive toxins are indicated in the text of those sections, or in the Appendix.

As in the previous sections, the discussion here is limited to toxic effects which are the result of chronic or sub-chronic exposures. Odor thresholds are indicated in the Appendix, but have not been included here as a toxic effect.

This section differs from previous sections in that it represents a much less extensive survey of the published literature. We have relied primarily on RTECS (1984), TLV Doc., (1985), and the IARC Monograph series (1973-1986).

The results of this limited survey are in Table 12. Except for ethylamine (results were from a study in rabbits) effects of all other compounds were observed in humans. With one exception (Wayne and Orcutt, 1960), all studies were in occupational settings. They thus carry with them all the uncertainties of such studies (e.g., simultaneous exposure of workers to relatively high concentrations of a variety of compounds). Three chemicals in Table 12 (cyclohexane, hexane, and methanol) were toxic at these relatively low concentrations only after UV irradiation in atmospheric mixture with NO_2 in a study designed to study possible causes of the effects of smog (Wayne and Orcutt, 1960). Even these low concentrations are quite far above the maximums measured in indoor air.

Acrolein, dichlorvos, and dibutylphthalate are the only chemicals for which an MOS of ten or less was calculated. Acrolein is a powerful lacrymogen. The anti-cholinesterase activity of dichlorvos has been well documented in both animals and humans. Effects reported at $100 \mu\text{g}/\text{m}^3$ were only observed in pregnant females, children, or in people who were ill. The study cited for dibutylphthalate is quite old, and to our knowledge has not been repeated. Other investigators have reported hematologic effects, but only at a much higher dose.

V. DISCUSSION

A. Summary and Discussion of the Major Sections of the Report.

We have examined the question of whether exposure to airborne organic compounds in non-industrial, indoor environments constitutes a significant health problem. This is an exceedingly complex issue that we have neither the information nor methodology to examine in a wholly satisfying manner. Many organics in indoor environments have not even been identified; concentrations of many that have been identified are incompletely determined. Even when extensive monitoring data are available, we do not know how best to represent its complexities (e.g., varying concentrations over time and from house to house) in the context of assessing risk: should we attempt to determine an overall mean or median; are the data best represented as a distribution; if so, what is the most accurate distributional form? Many chemicals have not been tested for toxicity at all, and few if any have been tested thoroughly in ways that are relevant to the indoor exposure situation. Most toxicology tests are performed using laboratory animals, and we have a very limited understanding of how to relate these results to humans. Given such a situation, the best that one can do is to design a relatively simple framework in which to structure the problem, incorporating many assumptions. Within that framework, one can then try to ask meaningful questions, keeping in mind that the answers will be limited by the framework. The framework that forms the basis for the major portion of this study is based on the concept of 'margin of safety' (MOS), which is simply the ratio of exposure estimated to be required to produce an observable effect in laboratory animals to actual human exposure. To estimate this, human exposure was represented by the maximum or mean concentrations (CONC) measured in buildings (Table 1), and toxic doses were represented by the "lowest effective dose" (LED) observed to produce a toxic effect in laboratory animals (or humans). After adjusting this LED using appropriate scaling factors to its estimated "inhalation-equivalent" in humans if exposure was continuous daily in indoor air (LED_h), the ratio $LED_h/CONC$ was calculated. This we used as an approximate measure of margin of safety. Applying this procedure to the 144 chemicals for which indoor concentration

measurements were available, we chose for more in depth analysis: (a) all carcinogens; and (b) all other toxins with an estimated MOS < 1000. This procedure resulted in the identification of 44 chemicals (Table 3).

We then structured an analysis of these compounds to address two major questions: (1) Which organic compounds, among those occurring in indoor air, have the greatest potential for contributing to adverse health effects; and (2) overall, does risk from exposure to organic compounds in indoor air constitute a significant health problem? Below is a brief summary of the major conclusions of each section of the report.

1. Concentration Distributions and Risk Estimation.

The data presently available on concentrations of chemicals in the indoor environment are meager. For few chemicals do we have sufficient direct information to characterize the frequency distribution of concentrations, nor are we generally able to cite average exposures with much accuracy. The limitations of information available from monitoring is evident from the data given in Table 1, where, in most cases few measurements have been performed, sometimes in circumstances where concentrations are expected to be far higher than average. Even in the best examples, the averages cited can be used for assessment purposes only with great uncertainty.

The principal exception to these generalizations about organic compounds is formaldehyde, of which many measurements have been performed in a variety of indoor environments (see Anon, 1984 for a summary). The distribution of formaldehyde concentrations is skewed toward high concentrations, and is approximately a log normal distribution. This has also been observed for radon (Nero, *et al.*, 1986), and frequency distributions for other chemicals involving smaller numbers of homes are not inconsistent with this picture (e.g., Lebret, 1985; Hawthorne, *et al.*, 1984).

Knowledge of the distribution is extremely important in cancer risk assessment, because it permits one to estimate what fraction of the population is at relatively high risk. Risk estimates obtained by extrapolating over many orders of magnitude may well stretch the limits of extrapolation models beyond what is biologically reasonable. Of greater scientific credibility are estimates for populations that are exposed to doses of carcinogens that are not too far from the doses that have been observed to induce tumors in laboratory animals. If adequate exposure distributions are available, such populations can readily be determined (e.g., Table 7). Since the exposure distributions of various compounds differ from each other, risks can be dramatically different when estimated based on mean or maximum exposures alone versus estimated using standard deviations (compare Tables 6 & 7). Even if data are inadequate to describe the distribution, if it is possible to say that the overall distributional forms are sufficiently similar to the general form of a lognormal distribution, then the data may be characterized approximately using lognormal parameters.

2. Use of the LD50 as an Indicator of Toxic Potential

We have employed a scale (the ratio of an estimated inhalation LD50 to measured concentrations of compounds in indoor air) to indicate the extent to which toxic effects from indoor exposures may be produced at experimentally detectable levels. Many chemicals for which a rodent LD50 is known have not been tested extensively for other toxic effects. For chemicals that have been thoroughly tested, LEDs for toxic effects are almost all within a factor of 1000 of the LD50. Therefore, by looking at which chemicals are present in indoor air at concentrations within a factor of about 1000 of the LD50, we may be able to get some idea of which compounds have the potential to produce observable toxic effects. This type of scale may also be useful in developing testing priorities.

Overall, we conclude (Table 4): (a) In all but a few cases, the concentrations of individual chemicals that people are exposed to in indoor air are so much less than the LD50s

of those chemicals (many thousands of times less), that it is unlikely that these chemicals would cause any toxic effects at experimentally detectable rates; (b) For the few compounds where the ratios are relatively low, exposures are in relatively unusual situations which are not likely to result in chronic exposures. The seven chemicals that have been measured in indoor environments at concentrations within a factor of 1000 of the estimated LD50 are: acrolein; hydrogen cyanide; pentachlorophenol; nicotine; formaldehyde; dichloromethane; and ethylamine. Of these, only acrolein and formaldehyde are known to produce toxic (irritant) effects in humans from exposure to these doses. It would not be surprising, however, if as yet undetected toxic effects were also produced by the other chemicals.

3. Carcinogenic Risk

We have taken a broad overview of possible carcinogenic risks from exposure to organic compounds in indoor air and have used several approaches to compare risks from exposure to different chemicals. We have also briefly addressed the question of overall risk. Several points are of particular interest.

a. Overall Risk from Organic Chemicals as Compared to Other Cancer Risks.

We used the simple additivity model to sum mean risks estimated for each of the 24 carcinogens examined (Table 6). The total ranged between $28-980 \times 10^{-5}$, roughly 1 in 100 to 1 in 4,000, depending upon which of the 4 risk estimates are summed. The 40-fold difference between these estimates is caused primarily by the large discrepancies in estimates for formaldehyde risk (discussed further below). It is difficult to know how much meaning to attach to these estimates, considering uncertainties associated with the individual risk estimates and with the simple addition of risks. Nonetheless, it is of interest to compare these figures with the total risk of actually getting cancer, or with the risk of getting a particular kind of cancer. The total lifetime risk of getting cancer is about 1 in 4. Lung cancer, one of the most common types of cancer, and the one of most obvious concern for exposure from inhalation,

has an age-adjusted rate, in white males, of about 1 in 1000 per year (Pitot, 1986). Over a 70 year lifespan this is about 1 in 13. The total lifetime cancer risk summed for the 24 carcinogens in Table 3 is 0.35-13% of this value.

For further comparison, the average lifetime incidence of lung cancer due to indoor radon is estimated to be about 1 in 300 (Nero, *et al.*, 1986), which is comparable to the higher estimates for the organic chemicals, and about an order of magnitude greater than the low estimate. It is important to note that the uncertainty in the risks from organic compounds is substantially larger than uncertainty in the radon estimate. This is because of fragmentary information on exposures and because of the need, in most cases, to make large extrapolations from animal data (factors of 60 to 10,000 as shown in Table 5). In contrast, the radon exposures require extrapolation over only a factor of 5 from exposures where effects have been observed. Another important difference is that the observed effects from radon daughters are lung cancers among human populations (i.e., various miner groups) rather than in laboratory rodents. Though interpretation of these human studies requires consideration of potential confounding factors such as smoking or other substances in mine air, the preponderance of evidence yields a risk factor that is thought to be uncertain by only a factor of two or three (NCRP, 1984).

b. Formaldehyde.

There is a 2600-fold difference among the four mean risk estimates presented in Table 6. The maximum likelihood (MLE) estimate is the smallest, 0.37×10^{-5} , and the linear extrapolation from the TD50 is the largest, 950×10^{-5} . This discrepancy is most likely primarily due to the nonlinearity of the carcinogenesis dose-response curve in rats, which is so pronounced as to produce this discrepancy even over the relatively small extrapolation range (a factor of 23: see Table 5). This nonlinearity is also reflected in the quite large difference between the MLE estimate and its upper 95% confidence limit of 67×10^{-5} . For several

reasons it is important that we do not dismiss these higher estimates on the grounds that they do not fully take into account the nonlinearity of the rat dose-response. First, because of the high order of non-linearity, the MLE estimate is extremely non-robust, which is to say that it would be very different if only a few more or less tumors had been observed. Since there are only 4 points (including the control) on the dose-response curve, its exact shape is very poorly defined, and consequently the MLE estimate is highly uncertain. Second, much of the non-linearity is apparently due to the muco-ciliary clearance system (Swenberg, *et al.*, 1985), and there is no reason to believe the shape of the dose response will be similar in humans and rats.

Finally, it is useful to consider how the risk estimates in Table 6 compare with the lifetime rate of nasal cancer in the U.S. population and with results of epidemiological studies on populations exposed to higher than average levels of formaldehyde. (It is not certain that human cancers due to formaldehyde would necessarily be nasal cancers, though given the high chemical reactivity of formaldehyde it would not be surprising if this were true.) The lifetime incidence of nasal cancer in the U.S. has been reported to be $23-45 \times 10^{-5}$ (CPSC, 1982). If most nasal cancers are due to formaldehyde exposure, this is comparable to the upper confidence interval estimates of risk (67×10^{-5}) from lifetime exposure to the mean concentrations of formaldehyde in Table 6. In contrast, the MLE estimate yields a rate that is 62-120 times less than the observed U.S. rate.

Several recent epidemiological studies have found higher than expected incidences of nasal cancer in different populations exposed chronically to formaldehyde (Blair, *et al.*, 1986; Hayes, *et al.*, 1984; Olsen and Jensen, 1984). In all of these studies, though a higher than expected incidence of nasal cancer was observed, the association was not significant. The interpretation of the results is also complex for other reasons. For example, in two of the studies the observations were confounded by concurrent exposure to wood dust (known to cause nasal cancer), though an increase in nasal cancer remained elevated when the analysis was controlled

for wood dust (Hayes, *et al.*, 1984; Olsen and Jensen, 1984). In the Blair, *et al.* (1986) study, there was a deficit for cancer of the buccal cavity and pharynx combined, but the data (see Table 5 in Blair, *et al.*) indicate a more than 3-fold increase over expected rates in the exposed population when the nasopharynx is examined separately. Though these results are only suggestive, the fact that all three studies have independently found some association between nasal cancer and formaldehyde exposure is of interest. Without more knowledge of the age structure of the study populations it is not possible to compare the results of these studies with that predicted from the risk estimates in Table 6. However, we may make a rough comparison by considering only the high exposure category. For example, in the Blair, *et al.* study about 1,000 workers were considered at risk from chronic exposures higher than 2,000 $\mu\text{g}/\text{m}^3$. If we assume these are 6 hour exposures and adjust them to the equivalent 24-hour values (500 $\mu\text{g}/\text{m}^3$), the UCL estimate of 9.3×10^{-3} from Table 3 would suggest that, if these workers were exposed for a lifetime, $(9.3 \times 10^{-3})(1,000) = 9$ cancers would occur. Since the Blair, *et al.* study only considered causes of mortality, and the risk estimate is of expected incidence, we might assume approximately a 50% cure-rate, adjusting the estimate downward to 4-5 expected cases. Since workers were not observed for their lifetimes, this number is still too high. Blair, *et al.* did not observe any nasal cancers among this high exposure group. This may not be inconsistent with the prediction from the UCL estimate, and it seems worthwhile to examine this point more carefully using the lifetable data.

In sum, the formaldehyde case is complex, as many others have discussed (e.g., Anon, 1984; Swenberg, *et al.*, 1985). Formaldehyde is an ubiquitous indoor pollutant, and it appears likely that it is present in some homes at concentrations that are not very far from doses that have produced cancer in rodents. It is important to refine the risk estimates to determine if formaldehyde is responsible for most of the cancer risk (as suggested by the highest estimates), or a relatively small per cent of the risk (as suggested by the lowest estimates), or a significant, though not dominant fraction (as suggested by the UCL estimates). Based on the considerations discussed here, the UCL estimates appear, at least currently, to be the least

problematic as they neither ignore nor overinterpret the poorly defined non-linear dose-response in rats, and they do not incorporate the assumption that the dose-response in humans will be as non-linear as in rats.

4. Reproductive Effects

We have divided reproductive effects into three general categories: birth defects; so-called "less serious" effects; and fetal toxicity. Only chronic exposures and LEDs less than 1000 times measured concentrations in indoor air were considered. A total of 16 chemicals were thus identified (Table 9).

As for carcinogens, distributional exposure data is needed to assess potential risks more precisely. Thus, it would be helpful to know what fraction of the exposed population is at more than some level of risk we might consider to be minimal. We have looked at this in an illustrative way in Table 10.

In general, the doses causing birth defects appear to be considerably higher than those causing "less serious" effects, such as oestrus disorders in dams, or growth retardation of the fetus. Among the 9 reproductive toxins present in indoor air at concentrations within a factor of 100 of the estimated LED, all but pentachlorophenol produce toxic effects in the 'less serious' categories. Thus, at the relatively low concentrations encountered in indoor air, these types of relatively subtle effects appear much more likely than more obvious birth defects. Since it may be quite difficult to detect these effects, this raises an important point relevant to possible epidemiological strategies aimed at identifying risks. This is discussed further below.

5. Miscellaneous Toxic Effects

The twelve compounds listed in Table 12 have not been examined in the other sections of the report, and have produced systemic toxic effects or irritation in humans at concentrations

within a factor of 1000 measured concentrations in indoor air.

In Table 13 we have listed, for each of the four general toxic effects categories examined, the chemicals that appear to dominate the overall risk in each class. The criteria for selecting them were as follows: (1) Carcinogens were selected if any of the lifetime risk estimates in Table 6 were more than 10^{-3} at the maximum indoor concentration listed. (2) Reproductive toxins were selected if the estimated margin of safety at the maximum concentrations listed was <100 . (3) Systemic toxins and irritants were selected from Table 12 if the estimated MOS was ten or less. (4) Compounds which do not otherwise appear in Table 13, which have an LD50 (adjusted to an "airborne- equivalent-concentration") within a factor of 5,000 of the maximum indoor air concentrations reported. Each of these compounds is discussed in detail in the Appendix. This list is only a first approximation based on relatively limited information, but it may provide some focus for further investigation.

B. Recommendations

Overall, though risk in the majority of homes does not appear to be large, in some fraction of homes a significant health risk does appear to exist. The analysis we have presented in this study is preliminary, designed to focus attention on those individual chemicals likely to pose the greatest risks and to stimulate further study. Below we briefly discuss some recommendations for further study.

(1) An attempt should be made to obtain indoor air concentration data on targeted chemicals (such as those in Table 13). This need not be a massive survey, but the sample of homes should be sufficiently large to estimate parameters of exposure distributions. We have illustrated elsewhere in the report how comparisons based on mean risk can be dramatically affected by taking into account the form and standard deviation of exposure distributions. In this regard we have suggested that a valuable measure of risk is the "fraction of people at

high risk" (see Tables 7,11 and discussion in text, pp. 36-39). Provided a selection of sample homes representative of the housing stock is made, a number on the order of about 100 should be sufficient.

(2) There should be a thorough source characterization of chemicals that may pose the greatest risk. This is important for two reasons. First, it may suggest possible means of mitigation; and second, it can be an aid in identifying high risk situations produced when groups of chemicals are emitted from the same sources (such as is shown in Table 2).

(3) The toxicological data supporting the designation of a number of chemicals as relatively high risk (Table 3: references in Appendix and relevant Tables) is inadequate. Further laboratory studies to confirm isolated reports and to clarify questionable data are needed. In addition, many chemicals present in indoor air at relatively high concentrations (e.g., the alkyl benzenes and alkanes) have either not been tested or tested only in an extremely limited fashion. A candidate list of chemicals for testing in a battery of toxicological tests should be formulated, drawing on some of the information collected in this report, and taking into account other factors, such as structure/activity considerations and short-term test results. Tests designed to test effects of chronic exposures are most relevant to the usual indoor air exposure situation.

(4) Except in a very limited way (Section IV.2.) we have not considered possible aggregate effects of chemicals or of complex mixtures. There is a need to develop scientifically based criteria that may guide such analyses. It may be fruitful to identify groups of chemicals, or toxic endpoints, on which an aggregate analysis would be justified. Examples of such groups might be the environmental tobacco smoke, acetylcholinesterase inhibitors, or aliphatic compounds, many of which produce narcotic effects.

C. Potential Use of Epidemiological Studies

A major question is the potential utility of epidemiological studies in helping to pinpoint problems. In principle, epidemiological studies would provide the strongest evidence of an indoor air pollution health problem from chronic exposures to organics. However, because of the difficulties in conducting such studies, the primary consideration must be whether, even if some adverse health effects are occurring, a study can be designed capable of detecting it. There are two basic problems. First, selection of the toxic effects to be studied; and second, design of a study that will detect the effects. These are actually inter-related, since what we choose to look for can influence the likelihood of detection. Some insight into this is provided by the following consideration of difficulties involved in detecting carcinogenic and reproductive effects in exposed populations.

As discussed above, we cannot rule out the possibility that some fraction of the exposed population is at a relatively high lifetime risk of cancer ($>10^{-3}$) from exposures to organics in indoor air. To prove this, it would be necessary to show that the risk was greater among people exposed over long periods to indoor environments containing higher concentrations of carcinogens than other environments. Because of the high background rate of cancer (a lifetime incidence rate of about 25%) it would be exceedingly difficult (unless some very rare form of cancer was being produced), to detect what would be rather small differences between "high" and "low" risk groups. Even if the increase in cancer rate were great enough to be detected, it is not clear that we know enough to identify and select "high" and "low" risk study populations from risk estimates. For example, one might wish to design a study to target only certain carcinogens. However, the number of carcinogens in indoor air is sufficiently large, so that additivity effects between carcinogens, or simply errors in the very rough risk estimates might cause the real apportionment of risk to be quite different.

For some of the same reasons, detection of an increased risk of reproductive effects such

as malformations may also be extremely difficult, and most likely impossible, using an epidemiological approach. There is no indication among the data we examined that we should expect that obvious birth defects are occurring from the relatively low level exposures in indoor air. Even if rare cases do occur, it is unlikely they would be detected in an epidemiologic study. Other less serious reproductive effects may be more easily studied. Examples of such effects are low birth weight, menstrual disorders, and disfunction of enzymes in newborns. It is important that we do not dismiss such effects out of hand, as we cannot know the extent to which they may adversely affect the organism over the long term. On examination, we may wish to designate some of these effects as trivial, and hence not of concern. This may not be true of others, however, and it would be worthwhile to explore means whereby a consensus among scientists and policymakers might be reached as to which among these more subtle effects we may wish to designate "adverse". Methods of reliably recording and tests for detecting such insults would be useful for future epidemiologic studies.

The assessment of the role of epidemiology in clarifying potential problems must be tempered by a recognition of its intrinsic limitations in detecting modest increases in disease rates for endpoints that have large total rates. This is the usual situation for airborne pollutant exposures, and our understanding the risk from organic exposures will ultimately depend primarily on fuller understanding of the biochemical basis for disease initiation and development. With current progress being made on various classes of diseases, as well as on the basic biochemical behavior of genetic material, it can be anticipated that, in the foreseeable future, the basis for estimating low level risks will be much more complete. For the present, such estimation must depend on incomplete biochemical, toxicological and epidemiological information.

D. Conclusion

For the near future, several general conclusions may be drawn from the present

investigation. The first, and most straightforward, is the need for improved information as suggested above: on sources and exposures, on health effects from animal and human studies, on the treatment of aggregate effects. Further development of a comprehensive and consistent framework to assess adverse health effects of indoor organics is needed, which includes determination of the importance of individual chemicals or classes.

The problem of airborne organic exposures should be evaluated by including data on organics present in the indoor environment, as well as in ambient air. The total indoor exposure, while apparently not as important as some other risks that people routinely accept (such as that from automobile accidents, or even from radon), appears large compared with the risks of individual chemical exposures that have been the subject of regulatory action. Such evaluation should examine alternate risk assessment approaches, and identify fruitful lines of research to reduce areas of uncertainty. The implications can be rather broad, including significant alteration of the focus of research and regulatory attention and the development of a more complete perspective on risk assessment and management.

The current focus on individual chemicals in isolation appears extremely shortsighted and inadequate. Looking at one tree at a time contributes little to an appreciation of the total forest of air pollution exposure. This is not to say that investigation of the effects of isolated chemicals has no value. But it is equally important to investigate the full exposure picture, not only because of potential interactions, but because the total effect of such exposures should be a crucial element in evaluating both the importance of specific exposures and the opportunity for risk reduction. Does it make any sense to regulate an individual chemical in a specific setting without consideration of other exposures to that chemical or without an appreciation of the total exposure to all toxic chemicals?

Thus, the work to date leads to recognition of the size and estimated effect of the total exposure to organic chemicals in the indoor environment. It remains to be seen whether

further work on indoor airborne chemicals, of the kind suggested above, will alter or support these general observations.

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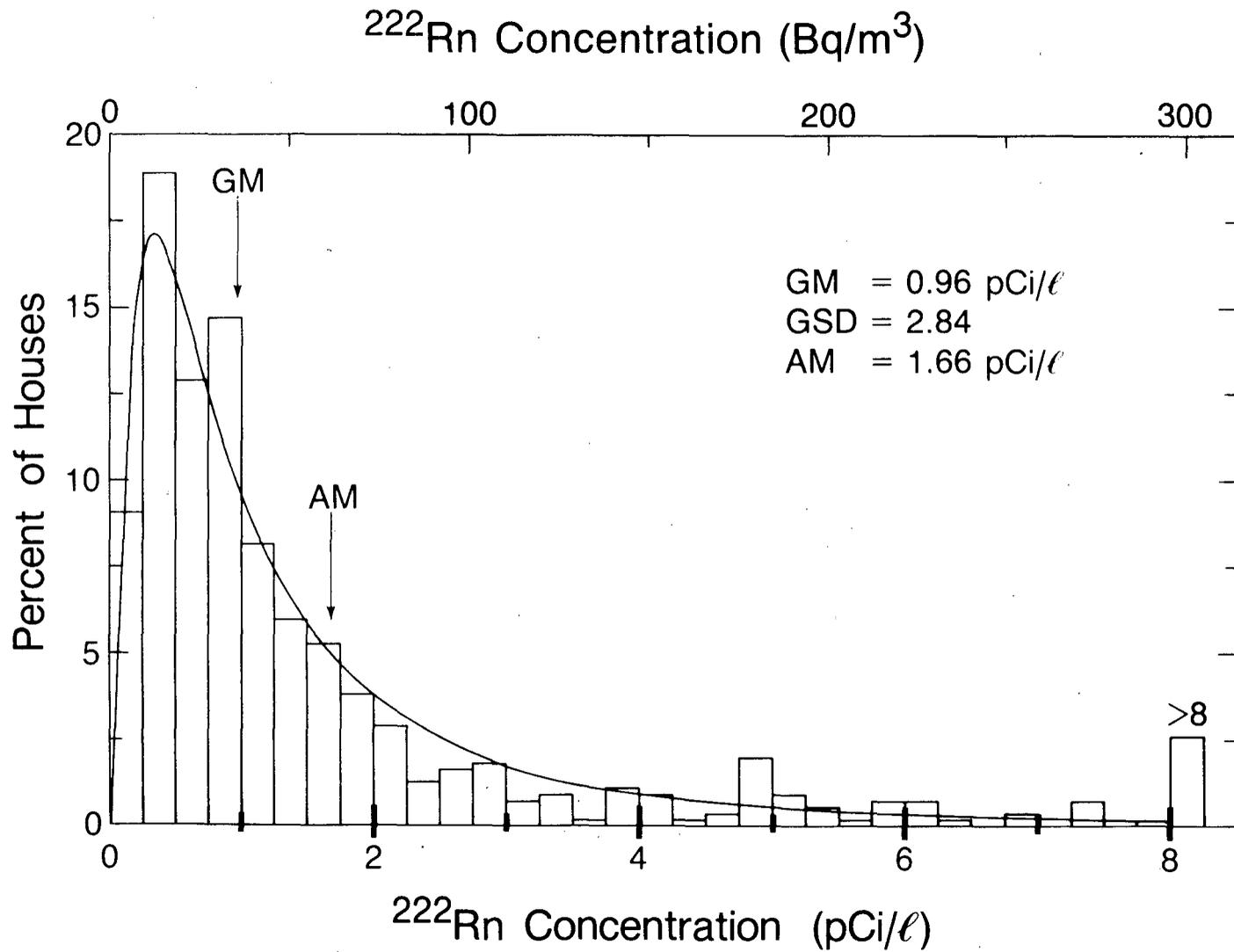
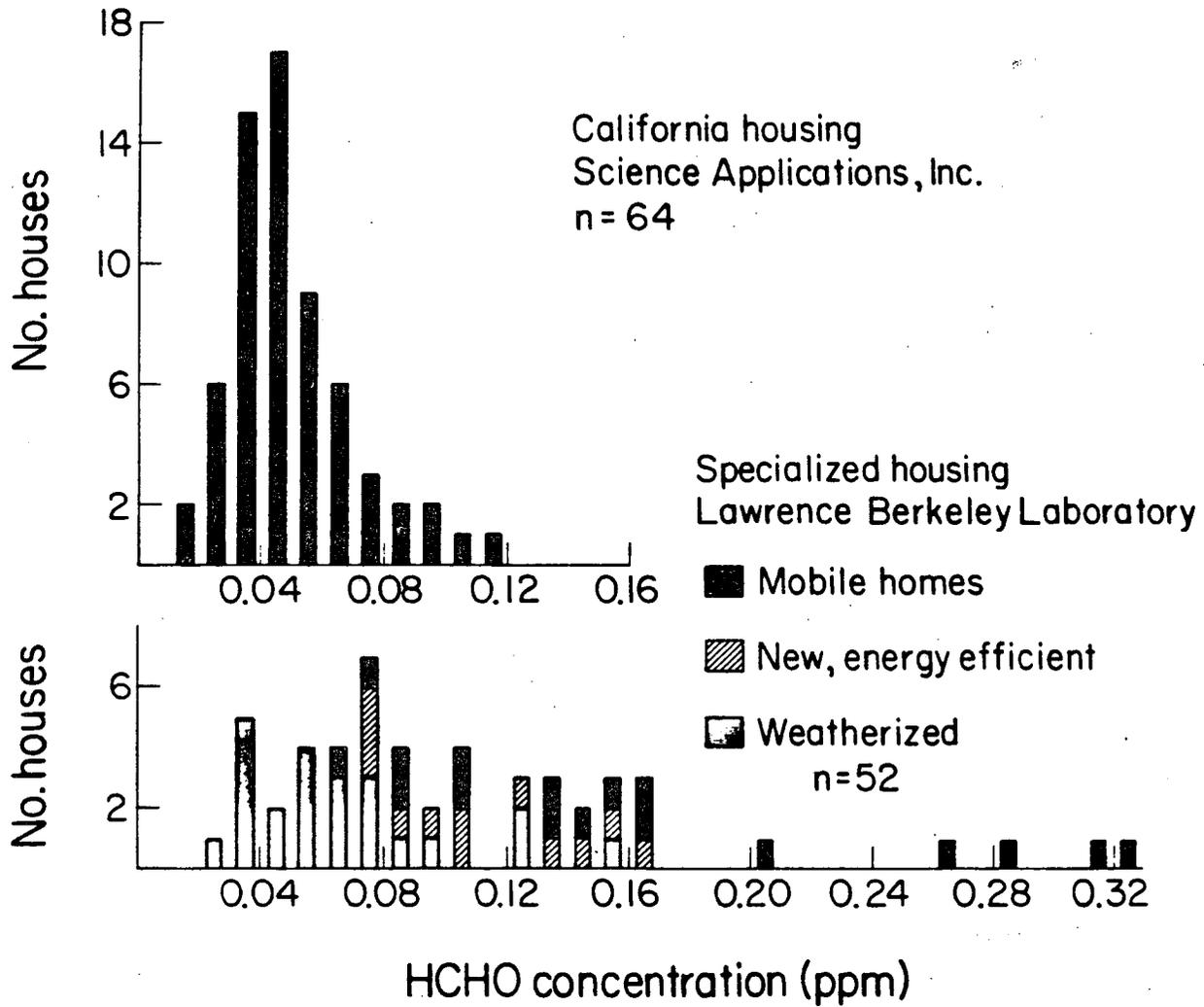


Figure 1.

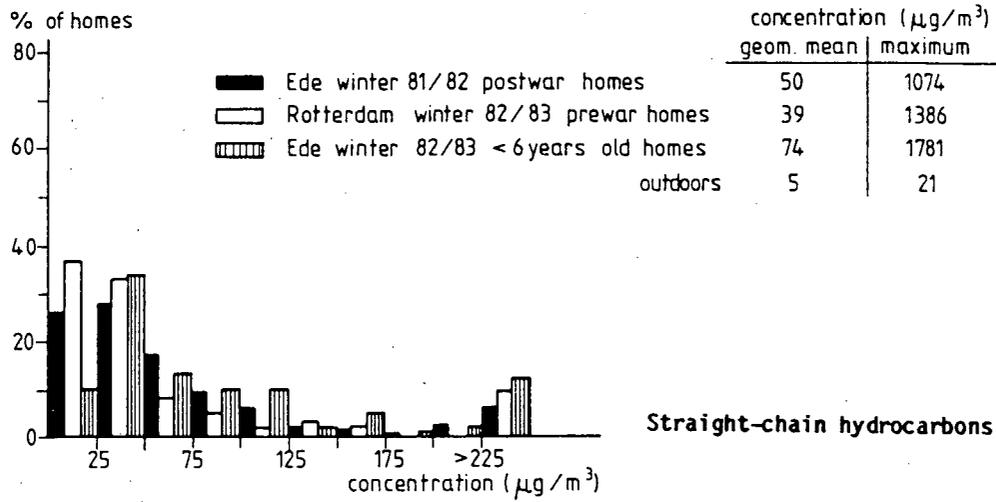
Histogram of ^{222}Rn radon concentrations in residences, aggregated from 552 individual data points in 19 data-sets. The smooth curves are the lognormal and Gaussian functions corresponding to the indicated parameters and a Weibull function with parameters determined by fit to the data. The Gaussian and Weibull functions can be made to fit reasonably well to portions of the data, e.g., to the peak or to the tail, but not to the entire distribution. (Reproduced from Nero, et al., 1986).

RESIDENTIAL INDOOR AIR HCHO CONCENTRATION

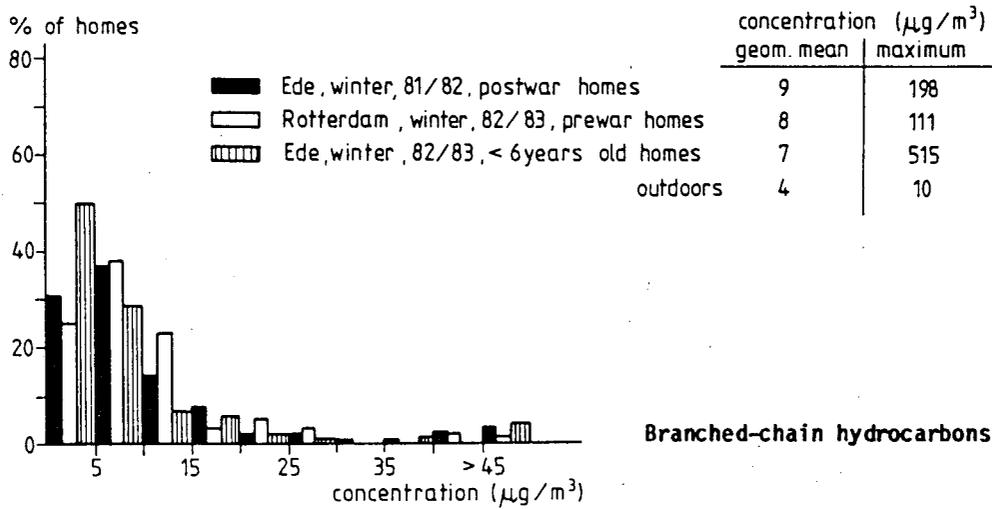


XBL 834-1572

Figure 2. Histogram of formaldehyde concentrations in residences. (Reproduced from Nero & Grimsrud, 1983).



Straight-chain hydrocarbons



Branched-chain hydrocarbons

XBL 864-1577

Figure 3. Frequency distribution, geometric mean, and maximum concentrations ($\mu\text{g}/\text{m}^3$) of five groups of volatile organic compounds in three age-groups of homes. (Reproduced from Lebret, 1985).

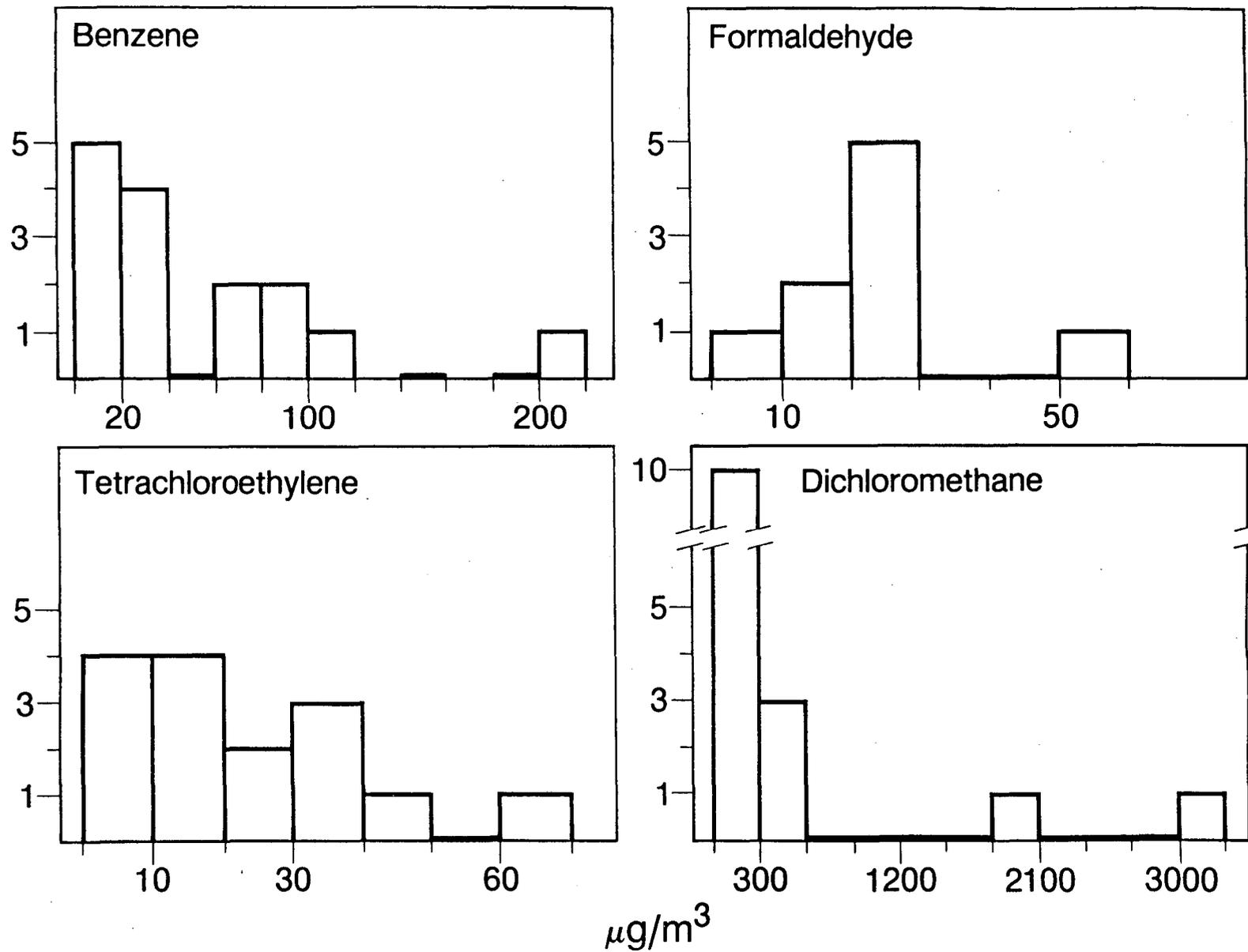
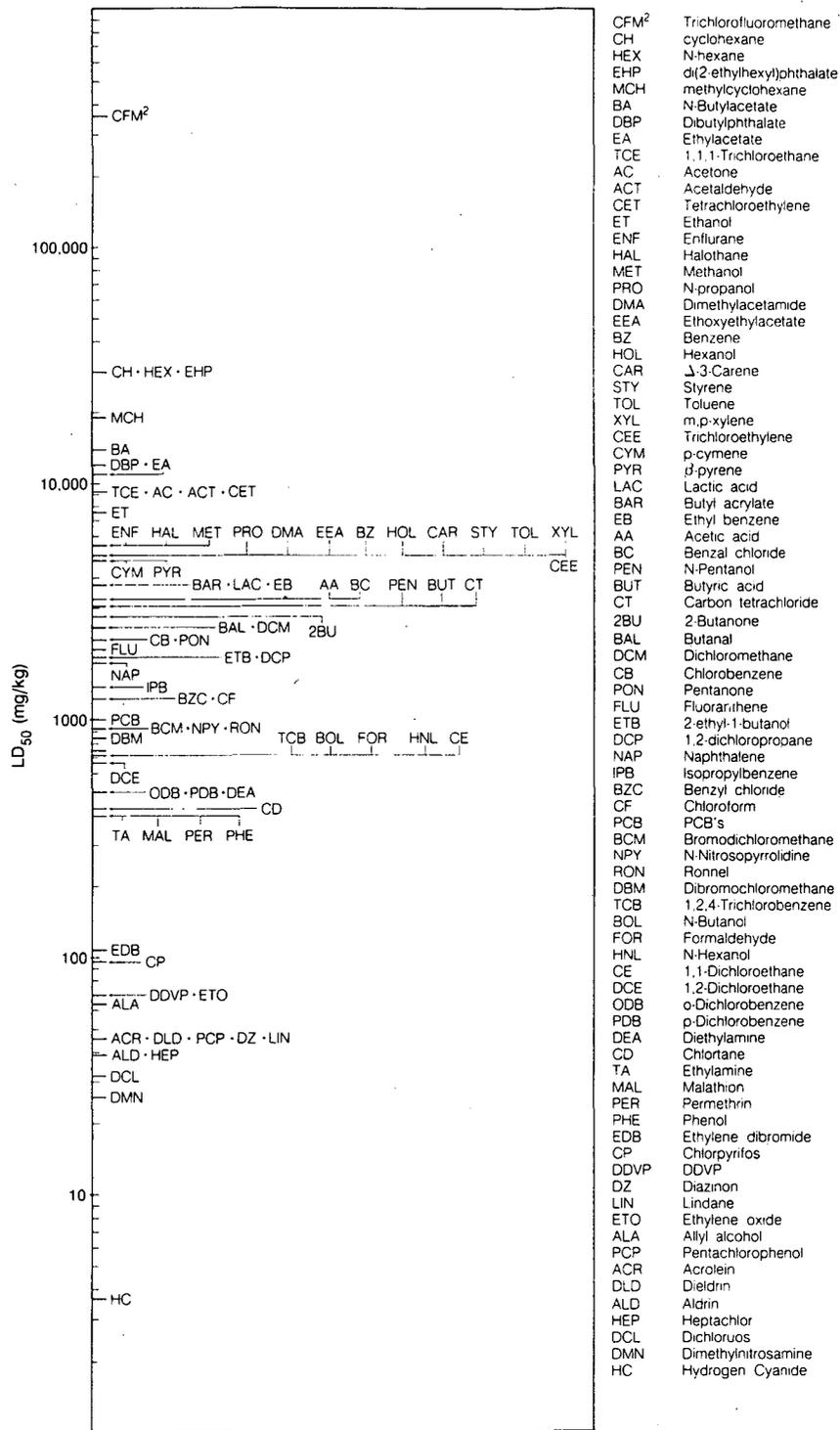


Figure 4. Frequency distribution of concentrations of four compounds from one 15-home study. Data are from DeBortoli, *et al.*, 1985. The number of homes is plotted on the ordinate; $\mu\text{g}/\text{m}^3$ is plotted on the abscissa.



XBL 864-1581

Figure 5. Oral rat LD50s, plotted on a log scale.

Table 1. Indoor Concentrations of Organic Compounds in Residences and Office Buildings

CHEMICAL	RTECS# ¹	TYPE ²	N ³	CONCENTRATION (ug/m ³) ⁴		REFERENCE
				Maximum	Median or Mean	
Acetaldehyde	AB1925	H	15	48.0	10.0	DeBortoli, et al., 1985
		P	1	7.7	5.7	Wang, 1975
		P	1	-	0.18	"
		C	1	-	29.0	DeBortoli, et al., 1985
Acetic acid	AF1225	P	1	25.0	23.0	Wang, 1975
		P	1	-	4.7	"
		C	1	500.0	-	Yocum, et al., 1984
Acetone	AL315	H	15	157.0	23.0	DeBortoli, et al., 1985
		P	1	21.0	-	Johansson, 1978
		P	1	69.0	53.0	Wang, 1975
		P	1	-	0.49	"
		C	1	-	9.0	DeBortoli, et al., 1985
Acrolein	AS105	E	1	1900.0	-	Hugod, 1984
		E		863.0	-	Jermini, et al., 1976
Aldrin	I021	H	6	0.550	-	Reinert, 1984
Allyl alcohol	BA5075	P	1	9.4	6.8	Wang, 1975
		P	1	-	0.24	"
Benzal chloride	CZ5075	E ⁵	1	13.0	10.0	Rittfeldt, et al., 1984
Benzaldehyde	-	H	40	124.0	19.0	Hawthorne, et al., 1984
Benzene	CY14	H	15	204.0	35.0	DeBortoli, et al., 1985
		H	134	150.0	9.9	Lebret, et al., 1984
		H ⁶	355	54.0	16.0	Wallace, et al., 1984
		H	NS	50.0	-	Seifert, 1982
		H ⁶	85	120.0	13.0	Hartwell, et al., 1984a
		P	2	36.0	12.0	Pellizzari, et al., 1984

Table 1 (continued)

		P	2	27.0	6.1	"
		C	1	27.0	18.0	Turiel, et al., 1981
		PM	17	387.0	4.6	Wallace, 1982
Benzfluoranthene	CU14	H	6	0.007	0.0014	Sexton, 1984
Benzo[ghi]perylene	DI62005	H	NS	0.15	-	Seifert, 1982
		H	6	0.0031	0.00065	Sexton, 1984
Benzo[a]pyrene	DJ3675	H	6	0.0034	0.0007	Sexton, 1984
		H	NS	0.0607	0.0135	Deshpande, et al., 1984
		H	NS	0.030	-	Seifert, 1982
Benzo[e]pyrene	DJ42	H	6	0.0019	0.00055	Sexton, 1984
Benzyl chloride	XS8925	E ⁵	1	5.0	3.0	Rittfeldt, et al., 1984
Bromodichloromethane	PA531	H ⁶	20	9.0	0.055	Hartwell, et al., 1984b
		PM	17	4.4	0.56	Wallace, 1982
Butanal (butyraldehyde)	ES2275	H	15	34.0	<1.0	DeBortoli, et al., 1985
		C	1	-	<1.0	"
n-Butanol	E014	P	1	160.0	17.0	Berglund, et al., 1982
		M	44(20)	80.0	16.0	Monteith et al., 1984
2-Butanone	EL6475	H	15	38.0	4.0	DeBortoli, et al., 1985
		C	1	-	<2.0	"
n-Butylacetate	AF735	H	8	4.0	-	Wanner & Kuhn, 1984
		P	11	2.9	-	"
Butylacrylate	UD315	C	1	48.0	-	Yocum, et al., 1984
n-Butylbenzene	CY907	H	134	40.0	2.3	Lebret, et al., 1984

Table 1 (continued)

Butyric acid	ES5425	P	1	55.0	49.0	Wang, 1975
		P	1	-	6.2	"
Camphene	EX1055	M	44(19)	278.0	24.9	Monteith, et al., 1984
Carbon tetrachloride	FG49	H	15	12.0	7.0	DeBortoli, et al., 1985
		H	134	0.40	<0.4	Lebret, et al., 1984
		H ⁶	355	5.7	1.5	Wallace, 1984
		H ⁶	20	13.0	0.17	Hartwell, et al., 1984a
		H ⁶	27	17.0	0.075	"
		H ⁶	11	3.8	1.3	"
		H ⁶	85	14.0	1.4	Hartwell, et al., 1984b
		P	6	0.64	0.41	Pellizzari, et al., 1984
		P	6	3.0	0.86	"
	C	1	-	<1.0	DeBortoli, et al., 1985	
delta-3-Carene	FH84	H	46	220.0	105.0	Molhave, 1979
Chlordane	PB98	H	NS	10.0	-	Beall & Ulsamer, 1981
		H	4800	40.0	-	Reinert, 1984
		H	9	3.2	-	Jurinski, 1984
Chlorobenzene	CZ0175	H	134	0.40	<0.40	Lebret, et al., 1984
		H ⁶	20	0.70	0.026	Hartwell, et al., 1984a
		H ⁶	11	0.75	0.035	"
		PM	17	2.1	0.35	Wallace, 1982
Chlorodifluoromethane (Freon)	PA639	H	NS	-	0.18	Beall & Ulsamer, 1981
Chloroform	FS91	H	15	15.0	<1.0	DeBortoli, et al., 1985
		H ⁶	355	17.0	3.4	Wallace, 1984
		H	NS	200 ⁷	-	Seifert, 1982
		H ⁶	20	26.0	3.7	Hartwell, et al., 1984a
		H ⁶	27	6.4	0.008	"
		H ⁶	11	47.0	7.6	"

Table 1 (continued)

		H ⁶	85	215.0	2.9	Hartwell, et al., 1984a
		P	6	3.1	1.7	Pellizzari, et al., 1984
		P	6	2.6	1.1	"
		C	1	-	<1.0	DeBortoli, et al., 1985
		PM	17	17.5	4.0	Wallace, et al., 1982
Chlorpyrifos (dursban)	TF63	H	NS	2.0	-	Beall & Ulsamer, 1981
		H	NS	2.0	-	Reinert, 1984
Chrysene	GC07	H	6	0.0014	0.0005	Sexton, et al., 1984
Coronene	GM54	H	6	0.0011	0.00025	Sexton, et al., 1984
Cumene	-	H	40	13.0	1.8	Hawthorne, et al., 1984
Cyclohexane	GU63	H	134	22.0	2.0	Lebret, et al., 1984
p-Cymene	G2595	H	134	32.0	1.6	Lebret, et al., 1984
DDVP	FC315	H	NS	10.0	-	Reinert, 1984
n-Decane	HD655	H	15	1100.0	10.0	DeBortoli, et al., 1985
		H	46	2770.0	42.0	Molhave, et al., 1979
		H	134	430.0	31.0	Lebret, et al., 1984
		H	40	81.0	11.0	Hawthorne, et al., 1984
1-Decene	-	H	NS	-	0.26	Beall & Ulsamer, 1981
Diazinon	TF3325	H	NS	2.0	-	Beall & Ulsamer, 1981
		H	NS	2.0	-	Reinert, 1984
Dibenz[a,h]anthracene	HN2625	H	6	0.0005	0.0001	Sexton, et al., 1984
Dibromochloromethane	PA636	PM	17	0.12	-	Wallace, et al., 1982
1,2-Dibromoethane	KH9275	PM	17	<0.14 ⁸	-	Wallace, et al., 1982

Table 1 (continued)

Dibutylphthalate	TI0875	C	NS	16.0	9.2	Virgin, 1984
Dichlorobenzene ⁹	CZ45	H ⁶	20	60.0	0.09	Hartwell, et al., 1984b
		H ⁶	27	120.0	2.1	"
		H ⁶	11	21.0	5.5	"
		H ⁶	85	915.0	2.8	Hartwell, et al., 1984a
		P	6	8.9	4.1	Pellizzari, et al., 1984
		P	6	1.7	1.2	"
		M	44(36)	9.2	1.8	Monteith, et al., 1984
		PM	17	73.0	3.8	Wallace, et al., 1982
m-Dichlorobenzene	CZ4499	H	134	9.1	<0.60	Lebret, et al., 1984
		H ⁶	355	82.0	3.8 ¹⁰	
o-Dichlorobenzene	CA45	M	44(2)	1.4	0.72	Monteith, et al., 1984
		PM	17	2.4	0.14	Wallace, et al., 1982
p-Dichlorobenzene	CZ455	H	134	140.0	7.2	Lebret, et al., 1984
		C	1	-	<5.0	DeBortoli, et al., 1985
		M	44(27)	63.0	8.5	Monteith, et al., 1984
1,1-Dichloroethane	KI0175	PM	17	1.8	0.06	Wallace, et al., 1982
1,2-Dichloroethane	KI0525	H ⁶	20	15.0	0.025	Hartwell, et al., 1984b
		H ⁶	27	69.0	3.6	"
		H ⁶	11	4.7	0.04	"
		PM	17	12.8	0.58	Wallace, et al., 1982
Dichlorofluoromethane	PA84	H	NS	2500.0	-	Seifert, 1982
Dichloromethane (methylene chloride)	PA805	H	15	5000.0	225.0	DeBortoli, et al., 1985
		C	1	-	<10.0	DeBortoli, et al., 1985
1,2-Dichloropropane	TX9625	H ⁶	27	2.1	0.01	Hartwell, et al., 1984b
		H ⁶	20	45.0	0.025	"

Table 1 (continued)

		PM	17	0.10	-	Wallace, et al., 1982
Dichlorvos	TC035	H	NS	10.0	-	Beall & Ulsamer, 1981
Dieldrin	I0175	H	12	0.47	-	Reinert, 1984
Diethylamine	HZ875	C	1	76.0	-	Yocum, et al., 1984
1,3-Diethylbenzene	CZ562	H	NS	-	0.25	Beall & Ulsamer, 1981
Di(2-ethylhexyl)phthalate	T1035	P	NS	230.0	<60.0	Vedel & Nielsen, 1984
Dimethylacetamide	AB77	C	1	4713.0	-	Yocum, et al., 1984
Dimethylcyclohexane	-	C	1	13.0	8.5	Turiel, et al., 1981
Dimethylcyclopentane ⁹	-	H	134	7.8	0.3	Lebret, et al., 1984
Dimethylnitrosamine	I00525	H	NS	0.8 ¹¹	-	Seifert, 1982
		H		-	<0.005 ¹²	IARC, 1978
		P		0.24 ¹³	-	"
		P	NS	0.061 ¹³	-	Matsushita & Mori, 1984
		P	NS	0.066	-	"
2,4-Dimethylpentane	-	C	1	10.0	7.5	Turiel, et al., 1981
n-Dodecane	JR2125	H	15	220.0	3.0	DeBortoli, et al., 1985
		H	134	120.0	4.5	Lebret, et al., 1984
		H	40	675.0	9.0	Hawthorne, et al., 1984
		C	1	-	4.0	DeBortoli, et al., 1985
Enflurane	KN68	P ¹⁴	16	3000.0	1400.0	Sterling and Sterling, 1984
Ethanol	KQ63	H	46	550.0	385.0	Molhave, et al., 1979
		H	NS	-	50.0	Seifert, 1982
		P	1	.66.0	-	Johansson, 1978

Table 1 (continued)

		P	1	85.0	71.0	Wang, 1975
		P	1	-	4.2	"
Ethoxyethylacetate	KK8225	E	-	-	5.9	Molhave, 1982
Ethyl acetate	AH5425	H	NS	-	0.11	Beall & Ulsamer, 1981
		P	1	32.0	14.0	Wang, 1975
		P	1	-	1.8	"
Ethylamine (ethanamine)	KH21	C	1	750.0	0.49	Yocum, 1984
Ethylbenzene	DA07	H	15	109.0	14.0	DeBortoli, et al., 1985
		H	134	45.0	5.0	Lebret, et al., 1984
		H	355	22.0	6.5	Wallace, et al., 1984
		H	40	161.0	7.5	Hawthorne, et al., 1984
		H ⁶	85	320.0	6.1	Hartwell, et al., 1984a
		P	2	196.0	25.0	Pellizzari, et al., 1984
		P ¹⁴	16	-	8000.0	Sterling and Sterling, 1984
		C	1	-	2.0	DeBortoli, et al., 1985
2-Ethyl-1-butanol	EL385	C	1	23.0	15.0	Turiel, et al., 1981
Ethylene oxide	KX245	P ¹⁴	16	770,000.0	150,000.0	Sterling and Sterling, 1984
Fluoranthene	LL4025	H	NS	0.12	-	Seifert, 1982
Formaldehyde ¹⁵	LP8925	H	15	52.0	26.0	DeBortoli, et al., 1985
		H	41	124.0	37.0	Anon, 1984
		H	378	124.0	43.0	"
		H	40	-	74.0	"
		H	64	136.0	62.0	"
		H		255.0	77.0	Hawthorne, et al., 1984
		P		>372.0	58.0	"
		P	6	112.0	87.0	Berglund, et al., 1982
		C	1	-	35.0	DeBortoli, et al., 1985
		M	431	3720.0	471.0	Anon, 1984

Table 1 (continued)

		M	50	372.0	124.0	"
Halothane	KH655	p ¹⁴	16	34000.0	5200.0	Sterling and Sterling, 1984
Heptachlor	PC07	H	NS	1.8	-	Reinert, 1984
		H	9	15.0	-	Jurinski, 1984
n-Heptane	M177	H	15	76.0	8.0	DeBortoli, et al., 1985
		H	134	68.0	5.3	Lebret, et al., 1984
		C	1	7.0	6.0	Turiel, et al., 1981
		C	1	-	1.0	DeBortoli, et al., 1985
1-Heptene	MJ885 ¹⁶	H	NS	-	1.9	Beall & Ulsamer, 1981
n-Hexadecane	-	H	134	2.9	<0.3	Lebret, et al., 1984
		H	40	21.0	3.8	Hawthorne, et al., 1984
Hexanal	MN7175	H	15	58.0	5.0	DeBortoli, et al., 1985
		C	1	-	6.0	"
n-Hexane	MN9275	H	15	590.0	14.0	DeBortoli, et al., 1985
		H	134	107.0	7.3	Lebret, et al., 1984
		C	1	-	3.0	DeBortoli, et al., 1985
n-Hexanol	MQ4025	H	NS	-	1.5	Beall & Ulsamer, 1981
Hydrogen cyanide	MW6825	E	1	85.0	-	Hugod, 1984
		E	1	56.0	-	Hoffman, et al., 1984
Indeno[c,d]pyrene	NK93	H	6	0.0037	0.00065	Sexton, et al., 1984
Isooctane	SA332	H	NS	-	0.11	Beall & Ulsamer, 1981
Isopropylbenzene	GR8575	H	134	11.0	0.70	Lebret, et al., 1984
Lactic acid	OD28	C	1	1.9	-	Yocum, et al., 1984

Table 1 (continued)

Lead	OF7525	H	6	0.12	0.041	Sexton, et al., 1984
Limonene	OS81	H		167.0	16.0	Hawthorne, et al., 1984
		H	15	480.0	57.0	DeBortoli, et al., 1985
		H	134	216.0	38.0	Lebret, et al., 1984
		H	46	120.0	70.0	Molhave, et al 1979
		C	1	-	170.0	DeBortoli, et al., 1985
		M	44(35)	164.0	12.5	Monteith, et al., 1984
Lindane	GV49	H	NS	50.0	-	Van der Kolk, 1984
Malathion	WM84	H	NS	2.0	-	Beall & Ulsamer, 1981
		H	NS	2.0	-	Reinert, 1984
Methanol	PC14	H	NS	-	100.0	Seifert, 1982
		P	1	73.0	52.0	Wang, 1975
		P	1	-	1.3	"
3-Methyl-2-butanone	EL91	H	NS	-	0.04	Beall & Ulsamer, 1981
Methylcyclohexane	GV6125	H	134	50.0	2.9	Lebret, et al., 1984
		C	1	8.0	5.8	Turiel, et al., 1981
1,2-Methylethylbenzene (o-ethyltoluene)	XT25	H	134	72.0	4.4	Lebret, et al., 1984
1,3-methylethylbenzene (m-ethyltoluene)	-	H	134	165.0	8.1	Lebret, et al., 1984
1,4-Methylethylbenzene (p-ethyltoluene)	XT255	H	134	77.0	4.0	Lebret, et al., 1984
3-Methylheptane	-	H	NS	-	3.7	Beall & Ulsamer, 1981
2-Methylhexane	-	H	134	54.0	4.3	Lebret, et al., 1984

Table 1 (continued)

		C	1	9.0	-	Turiel, et al., 1981
3-Methylhexane	-	H	134	44.0	3.4	Lebret, et al., 1984
		C	1	12.0	10.0	Turiel, et al., 1981
1-Methylnaththalene	QJ963	H	134	2.2	<0.3	Lebret, et al., 1984
2-Methylnaphthalene	-	H	40	17.0	2.6	Hawthorne, et al., 1984
2-Methylnonane	-	C	1	73.0	41.0	Turiel, et al., 1981
3-Methylpentane	-	H	134	100.0	4.9	Lebret, et al., 1984
Naphthalene	QJ0525	H	15	70.0	7.0	DeBortoli, et al., 1985
		H	134	14.0	1.0	Lebret, et al., 1984
		H	40	675.0	13.0	Hawthorne, et al., 1984
		C	1	-	3.0	DeBortoli, et al., 1985
		M	44(12)	64.0	9.6	Monteith, et al., 1984
Nicotine	QS525	P	NS	33.0	-	Matsushita & Mori, 1984
		P	2	55.0	10.0	Malaspina, et al., 1984
		P	NS	127.0	-	Matsushita & Mori, 1984
		C	1	13.0	-	Yocum, et al., 1984
		E	1	130.0	-	Hugod, 1984
		E	1	280.0	-	Hoffmann, et al., 1984
N-Nitrosopyrrolidine	UY1575	P	NS	0.036	-	Matsushita & Mori, 1984
		P	NS	0.027	-	"
Nonanal	-	H	15	82.0	6.0	DeBortoli, et al., 1985
		C	1	-	<2.0	"
		M	44(41)	43.8	13.6	Monteith, et al., 1984
n-Nonane	RA6115	H	15	165.0	12.0	DeBortoli, et al., 1985
		H	134	270.0	18.0	Lebret, et al., 1984
		H	46	630.0	180.0	Molhave, et al., 1979

Table 1 (continued)

		H	40	98.0	8.5	Hawthorne, et al., 1984
		P	1	2.1	-	Johansson, 1978
		C	1	63.0	36.0	Turiel, et al., 1981
n-Octane	RG84	H	15	65.0	12.0	DeBortoli, et al., 1985
		H	134	60.0	5.2	Lebret, et al., 1984
		C	1	-	4.0	DeBortoli, et al., 1985
PCBs (all isomers)	TQ135-1376	H	NS	0.5	-	Seifert, 1982
Pentachlorophenol	SM63	H	2	0.70	0.60	Gebefugi & Korte, 1984
		C ¹⁷	NS	200.0	-	Van der Kolk, 1984
		C		50.0	10.4	Levin & Hahn, 1984
n-Pentadecane	RZ18	H	40	12.0	2.4	Hawthorne, et al., 1984
		H	134	3.6	1.5	Lebret, et al., 1984
n-Pentanol	SB98	H	NS	-	0.25	Beall & Ulsamer, 1981
		P	1	28.0	21.0	Wang, 1975
		P	1	-	0.37	"
3-Pentanone (diethylketone)	SA805	P	1	20.0	7.9	Wang, 1975
		P	1	-	2.9	"
Permethrin	GZ1255	H	NS	1.0	-	Van der Kolk, 1984
Perylene	SE3794	H	NS	0.02	-	Seifert, 1982
Phenol	SJ3325	P	1	18.0	17.0	Wang, 1975
		P	1	-	3.9	"
alpha-Pinene	DT7	H	15	605.0	34.0	DeBortoli, et al., 1985
		H	46	830.0	315.0	Molhave, et al., 1979
		C	1	-	<1.0	DeBortoli, et al., 1985
		M	44(31)	79.0	12.5	Monteith, et al., 1984

Table 1 (continued)

beta-Pinene	DT5077	H	15	104.0	9.0	DeBortoli, et al., 1985
		C	1	-	<1.0	"
n-Propanol	UH8225	H	NS	-	0.15	Beall & Ulsamer, 1981
n-Propylbenzene	DA875	H	134	27.0	1.8	Lebret, et al., 1984
Pyruvic acid	-	C	1	5.9	-	Yocum, et al., 1984
Ronnell	TG0525	H	NS	2.0	-	Beall & Ulsamer, 1981
		H	NS	2.0	-	Reinert, 1984
Styrene	WL3675	H	355	4.6	1.8	Wallace, et al., 1984
		H ⁶	85	54.0	1.8	Hartwell, et al., 1984a
		M	44(30)	36.0	3.0	Monteith, et al., 1984
		PM	1	13.0	8.5	Pellizzari, et al., 1984
		PM	1	3.2	1.4	"
Terpene (C ₁₀ H ₁₆)	-	P	1	198.0	105.0	Berglund, et al., 1982
		P	1	5.9	-	Johansson, 1978
Tetrachloroethylene	KX385	H	15	64.0	13.0	DeBortoli, et al., 1985
		H	134	205.0	4.1	Lebret, et al., 1984
		H ⁶	355	26.0	6.4	Wallace, et al., 1984
		H ⁶	20	28.0	1.6	Hartwell, et al., 1984b
		H ⁶	27	69.0	0.4	"
		H ⁶	11	34.0	2.5	"
		H ⁶	85	250.0	5.6	Hartwell, et al., 1984a
		P	2	7.3	2.1	Pellizzari, et al., 1984
		P	2	98.0	3.3	"
		C	1	-	3.0	DeBortoli, et al., 1985
		M	44(27)	103.0	6.3	Monteith, et al., 1984
		PM	17	718.0	5.9	Wallace, et al., 1982
n-Tetradecane	X88	H	134	8.0	2.1	Lebret, et al., 1984

Table 1 (continued)

		H	40	74.0	5.4	Hawthorne, et al., 1984
		M	44(37)	57.0	5.5	Monteith, et al., 1984
Toluene	XS525	H	15	378.0	93.0	DeBortoli, et al., 1985
		H	NS	200.0	-	Seifert, 1982
		H	8	6.5	-	Wanner & Kuhn, 1984
		H	134	700.0	55.0	Lebret, et al., 1984
		H	46	350.0	95.0	Molhave, et al., 1979
		H	40	655.0	44.0	Hawthorne, et al., 1984
		P ¹⁴	16	-	4500.0	Sterling and Sterling, 1984
		P	1	161.0	48.0	Berglund, et al., 1982
		P	16	20.0	-	Wanner & Kuhn, 1984
		P	1	24.0	-	Johansson, 1978
		P	1	31.0	6.9	Wang, 1975
		P	1	-	1.2	"
		C	1	28.0	20.0	Turiel, et al., 1981
		C	1	-	17.0	DeBortoli, et al., 1985
		M	44(16)	40.0	9.2	Monteith, et al., 1984
1,2,3-Trichlorobenzene	DC2095	H	134	2.7	<0.8	Lebret, et al., 1984
1,2,4-Trichlorobenzene	DC21	H	134	15.0	<0.8	Lebret, et al., 1984
1,3,5-Trichlorobenzene	DC21001	H	134	8.3	<0.08	Lebret, et al., 1984
1,1,1-Trichloroethane	KJ2975	H	15	125.0	20.0	DeBortoli, et al., 1985
		H	NS	50.0	-	Seifert, 1982
		H ⁶	355	78.0	17.0	Wallace, et al., 1984b
		H ⁶	20	155.0	6.2	Hartwell, et al., 1984b
		H ⁶	27	243.0	1.5	"
		H ⁶	11	31.0	20.0	"
		H ⁶	85	880.0	16.0	Hartwell, et al., 1984a
		P	2	122.0	21.0	Pellizzari, et al., 1984
		P	2	883.0	150.0	"
		C	1	-	7.0	DeBortoli, et al., 1985
		PM	17	1069.0	61.0	Wallace, et al., 1982

Table 1 (continued)

Trichloroethylene	KX455	H	15	112.0	12.0	DeBortoli, et al., 1985
		H	NS	50.0	-	Seifert, 1982
		H	134	106.0	<1.5	Lebret, et al., 1984
		H ⁶	355	12.0	2.3	Wallace, et al., 1984
		H ⁶	20	2.0	0.096	Hartwell, et al., 1984b
		H ⁶	27	6.4	0.075	"
		H ⁶	11	1.3	0.86	"
		H ⁶	85	47.0	2.0	Hartwell, et al., 1984a
		P	2	1.9	0.67	Pellizzari, et al., 1984
		P	2	70.0	4.9	"
C	1	10.0	8.5	Turiel, et al., 1981		
C	1	-	3.0	DeBortoli, et al., 1984		
PM	17	182.0	5.4	Wallace, et al., 1982		
Trichlorofluoromethane	PB6125	H	15	230.0	21.0	DeBortoli, et al., 1985
		H	NS	70.0	-	Seifert, 1982
		C	1	-	1.0	DeBortoli, et al., 1985
n-Tridecane	YD3025	H	134	19.0	1.9	Lebret, et al., 1984
		H	40	113.0	9.4	Hawthorne, et al., 1984
		C	1	-	2.0	DeBortoli, et al., 1985
1,2,3-Trimethylbenzene	DC33	H	134	40.0	2.3	Lebret, et al., 1984
1,2,4-Trimethylbenzene	DC3325	H	134	280.0	14.0	Lebret, et al., 1984
		H	46	1140.0	170.0	Molhave, et al., 1979
		H	15	150.0	32.0	DeBortoli, et al., 1985
		C	1	-	<1.0	"
1,3,5-Trimethylbenzene (mesitylene)	OX6825	H	15	59.0	8.0	DeBortoli, et al., 1985
		H	134	99.0	3.6	Lebret, et al., 1984
		H	40	39.0	4.1	Hawthorne, et al., 1984
		C	1	-	3.0	DeBortoli, et al., 1985
1,1,3-Trimethylcyclohexane ¹⁸	GV765	C	1	19.0	-	Turiel, et al., 1981

Table 1 (continued)

n-Undecane	YQ1525	H	15	950.0	91.0	DeBortoli, et al., 1985
		H	134	190.0	13.0	Lebret, et al., 1984
		H	46	2360.0	670.0	Molhave, et al., 1979
		H	40	115.0	10.0	Hawthorne, et al., 1984
		P	1	2.7	-	Johansson, 1978
		M	41	41.0	4.4	Monteith, et al., 1984
Vinylidene chloride	KV9275	H ⁶	27	12.0	0.015	Hartwell, et al., 1984b
		PM	17	416.0	5.3	Wallace, et al., 1982
2-Xylene	ZE245	H	15	132.0	17.0	DeBortoli, et al., 1985
		H	8	14.0	-	Wanner & Kuhn, 1984
		H ⁶	355	15.0	5.0	Wallace, et al., 1984b
		H ⁶	85	46.0	5.0	Hartwell, et al., 1984a
		P	2	129.0	27.0	Pellizzari, et al., 1984
		P	11	11.0	-	Wanner & Kuhn, 1984
		C	1	-	8.0	DeBortoli, et al., 1985
		M	44(33)	110.0	8.8	Monteith, et al., 1984
3-Xylene	ZE2275	H ¹⁰	15	390.0	46.0	DeBortoli, et al., 1985
		H ^{6,10}	355	47.0	14.0	Wallace, et al., 1984
		H	46	910.0	145.0	Molhave, et al., 1979
		H ^{6,10}	85	120.0	16.0	Hartwell, et al., 1984a
		H ¹⁰	40	697.0	30.0	Hawthorne, et al., 1984
		P ¹⁶	1	11.9	-	Johansson, 1978
		P ^{14,16}	16	1x10 ⁵	5.8x10 ⁴	Sterling and Sterling, 1984
		C ¹⁶	1	44.0	-	Turiel, et al., 1981
		C ¹⁰	1	2075.0	-	Yocum, et al., 1984
		C ¹⁰	1	-	6.0	DeBortoli, et al., 1985
		M ¹⁰	44(37)	345.0	37.0	Monteith, et al., 1984
4-Xylene	ZE2625	P	2	17.0	9.5	Pellizzari, et al., 1984
		P	2	294.0	50.0	"

¹ Registry of Toxic Effects of Chemicals (RTECS) (1982,1984).

Table 1 (continued)

² H = home; P = public building; C = complaint building; E = experimental chamber or modeling study; M = manufactured home; PM = personal monitor.

³ N indicates the number of buildings in which measurements were made. When measurements were below the detectable limit, we have indicated the number of buildings in which measurements were above the detectable limit in parenthesis. NS = not specified.

⁴ The number of measurements made in each building varied considerably among the different reports. The specific details are indicated below for each citation. Anon, 1984: Maxima and means are from data in Table 3. Beall & Ulsamer, 1981: Maxima on pesticides are from the text; values in Table 1 were assumed to be $\mu\text{g}/\text{m}^3$; we reported values in Table 1 only if they did not also appear in Molhave, et al., 1979. Berglund, et al., 1982: The large and small room data in Figures 2 and 3 were combined. There were 2 rooms sampled at 3 different times over which the mean was determined. DeBortoli, et al., 1985: Medians and maxima were calculated from Table 1; the medians were determined from 4-7 day averages over 15 homes. In the case of N=1, only the 4-7 day average for one complaint building is given. Deshpande, et al., 1984: Maximum and mean are from Table 7; authors report the mean for 60 samples, but the number of buildings is not specified. Gebefugi and Korte, 1984: Data are from Tables 1 and 2, and were assumed to be mean values. A median was determined for 3 rooms (2 rooms in one house and one in another); Hartwell, et al., 1984b: Since multiple sites were examined, all 3 medians and maxima in Table 2 were recorded. Hartwell, et al., 1984a: Medians and maxima are from Table 2. Hoffman, et al., 1984: Values reported are from Table 2; since room was very smoke-filled, data were recorded as maxima. Hugod, 1984: Data are from Figures 4,5,7; a chamber study examining effects of smoking; only maxima were recorded; there were 3 experiments conducted at 2 different times over which we determined the mean. Johansson, 1978: Maxima were estimated from Figure 2; data are from one room when occupied and unoccupied. Jurinski, 1984: Data are from Table 2; data in the 'pre-treat' category were considered maxima. Lebret, et al., 1984: Means and maxima in Table 1a were recorded. Levin and Hahn, 1984. Malaspina, et al., 1984: Median and maximum were calculated from Table 1 and 2; there were 3 rooms in one office tower and 5 in another over which we determined a median; air intake data were not included. Matsushita and Mori, 1984: Only office data in Table 3 were used; the number of buildings was not specified. Molhave, et al., 1979: The mean of the medians in Table 2 for 7 new and 39 older buildings were calculated. Monteith, et al., 1984: Means and maxima are from Table 1; manufactured homes were assumed to be mobile homes; there were 3 rooms in one office tower and 5 in another over which we determined a median. Pellizzari, et al., 1984: Data are from Tables 2,3, and 4; medians and maxima were calculated from indoor measurements only; the medians were calculated from several measurements in 2 different buildings. Reinert, 1984: Data are from Tables 3 and 4: measurements made immediately after application were not taken. Rittfeldt, et al., 1984: Modeled results from building material emissions; maxima and medians are from Table 3; median is determined from concentrations at 3 different ventilation rates. Seifert, 1982: Maxima are from Table 8 and the text; number of buildings not specified. Sexton, et al., 1984: Data are from Tables 2 and 3; medians were

Table 1 (continued)

calculated from indoor measurements of 6 buildings measured at 2 different times. Turiel, et al., 1981: Data are from 1 office building reported in Tables 4 and 5; data on benzene were not used; a.m./p.m. measurements in Table 4 were taken as replicates; the values we report are the means of the a.m./p.m. measurements in Table 4 and the values reported in Table 5. Van der Kolk, 1984: Data from an unspecified number of buildings are from Table 1. Vedel & Nielson, 1984: Maximum and mean for 3 rooms given in text but number of buildings not specified. Virgin, 1984: Median was calculated from data in Table 1; measurements were in newly painted homes with symptoms of 'white leaf' disease. Wallace, et al., 1982: Data are from Tables 13 and 14; the number we report is the average of the two medians reported (one median was from a group of 6 people, the other from a group of 11), and the high number of the range. Wallace, et al., 1984: Data are from Table 2; the 90th percentile values were taken as maxima; there were 705 personal samples taken from 355 people. Wang, 1975: Medians were calculated from data in Table 2; we recorded them as maxima because measurements were in new buildings prior to occupancy. Wanner and Kuhn, 1984: Data are means from Table 2; we recorded them as maxima because measurements were in new buildings prior to occupancy. Yocum, et al., 1984: Data are from Table 1; 0.49 is the mean of the low and high values recorded after ventilation adjustments for ethylamine.

5 Concentrations were calculated by authors from emission rate measurements.

6 Overnight personal monitor.

7 Air above an indoor swimming pool.

8 1,2-Dibromoethane was not detected in any samples. The value presented is the limit of detection.

9 Isomers not specified.

10 Includes the para isomer.

11 In the interior of new motor vehicles.

12 Average of reports from urban and suburban non-smoker residences.

13 Maximum of 8 values reported from measurements in smoke-filled public buildings (e.g., bar, discotheque).

14 Hospital

15 We have not included the many measurements made in complaint buildings and UFFI buildings.

16 Mixed isomers

17 Probably a complaint building, though this was not specified in Van der Kolk (1984).

18 The isomer was not specified in Turiel, et al (1981). We have specified the 1,1,3-isomer because it is the only isomer for which toxicology data were found.

TABLE 2. Correlations Among Chemicals Measured by De Bortoli, et al. (1984) in 15 Homes.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34			
1) Formaldehyde																																					
2) Acetaldehyde						0.63																															
3) Butanal			0.55																0.81	0.97	0.97	0.97	0.74														
																			**	**	**	**	*														
4) Hexanal										0.60									0.59	0.59	0.58	0.58	0.58														
5) Nonanal																																					
6) Acetone					0.74																				0.62	0.72	0.76	0.70	0.71	0.64			0.70				
					*																					*	**	*									
7) 2-Butanone																																					
8) Trichlorofluoromethane							0.88	0.84																													
							**	*																													
9) Dichloromethane								0.75																													
								*																													
10) Chloroform																																					
11) 1,1,1-Trichloroethane											0.79	0.65																									
											**	*																									
12) Carbon Tetrachloride												0.55							0.60					0.53	0.55	0.67	0.64	0.63	0.56						0.72		
																									*	*											
13) Trichloroethylene													0.74																								
													*																								
14) Tetrachloroethylene																																					
15) 1,4-Dichlorobenzene																																					
16) N-Hexane																																					
17) N-Heptane																				0.76						0.91	0.85	0.74	0.66	0.84	0.93	0.95			0.90		
																				**						**	**	**	*	**	**	**			**	**	

P-Values are indicated as follows: No star: p<.05; *:p<.01; **:p<.001

TABLE 2. House by House Correlations Among Chemicals. (Continued)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	
18) N-Octane																								0.71	0.70	0.64	0.58	0.73	0.79	0.83					0.90
																								*	*	*		*	*	*					**
19) N-Nonane																				0.89	0.89	0.89	0.87			0.52	0.55		0.89	0.82	0.68	0.80			
																				**	**	**	**						**	*			*		
20) N-Decane																					1.0	0.99	0.81						0.86	0.80	0.68	0.78			
																					**	**	**					*	*	*		*			
21) N-Undecane																						1.0	0.85						0.92	0.95					0.98
																						**	**					**	**					**	
22) N-Dodecane																							0.85						0.88	0.92					0.98
																							**					*	**					**	
23) N-Tridecane																								0.53					0.83	0.89					0.95
																												*	*					**	
24) Benzene																									0.92	0.80	0.70	0.85	0.85	0.89					0.81
																									**	**	*	**	*	*				*	
25) Toluene																										0.95	0.89	0.94	0.90	0.89					0.68
																										**	**	**	**	*					
26) Ethylbenzene																											0.98	0.96	0.90	0.85	0.65	0.75			
																											**	**	**	*					
27) 1,3+1,4-Xylene																												0.94	0.86	0.80	0.75	0.83			
																												**	**	*	*				
28) 1,2-Xylene																													0.97	0.94			0.63	0.74	
																												**	**						
29) 1,3,5-Trimethylbenzene																														0.98				0.85	
																													**				*		
30) 1,2,4-Trimethylbenzene																																		0.89	
																																		**	
31) -Pinene																																	0.97		
																																	**		
32) -Pinene																																			
33) Limonene																																			
34) Naphthalene																																			

P-Values are indicated as follows: No star: p<.05; *:p<.01; **:p<.001

Table 3. All carcinogens, and other chemicals causing toxic effects detected in animal experiments at chronic or sub-chronic doses less than 1000 times maximum indoor air concentrations¹

<u>Compound</u>	<u>Carcinogenesis²</u>	<u>Reproductive Effects</u>	<u>Misc. Systemic Toxic Effects or Irritation</u>
Acetaldehyde	[+]		+
Acetone			+
Acrolein			+
Aldrin	+		
Benzene	+	+	+
Benzo[a]pyrene	(+)		
n-Butanol			+
Carbon tetrachloride	(+)		
Chlordane	+	+	
Chloroform	+	+	
Chlorpyrifos			+
Cyclohexane			+
Diazinon		+	
Dibenz[a,h]anthracene	(+)		
1,2-Dibromoethane	(+)		
Dibutylphthalate			+
1,1-Dichloroethane	(+)		
1,2-Dichloroethane	+		
Dichloromethane	+		+
Dichlorvos	[+]		+
Dieldrin	(+)		
Di(2-ethylhexyl)phthalate	+	+	
Dimethylacetamide		+	+
Dimethylnitrosamine	+	+	
Ethanol	(+)		
Ethylamine			+
Ethylbenzene		+	+
Formaldehyde	+	+	+
Heptachlor	+		+
n-Hexane			+
Hydrogen cyanide			+
Lindane	+	+	
Malathion	[(+)]		
Methanol			+
Nicotine		+	
N-Nitrosopyrrolidine	(+)		
PCBs (Arochlor 1260)	(+)		
Pentachlorophenol		+	

Table 3. (Continued)

<u>Compound</u>	<u>Carcinogenesis²</u>	<u>Reproductive Effects</u>	<u>Misc. Systemic Toxic Effects or Irritation</u>
Styrene	(+)		
Tetrachloroethylene	+		+
Trichloroethylene	(+)	+	+
1,2,4- and 1,3,5-Trimethylbenzene			+
Vinylidene chloride	+	+	+
p-Xylene		+	

¹ Parenthesis () indicate that the lowest effective dose administered in the carcinogenesis test used to estimate risk, after adjusting to an "equivalent" airborne concentration (see Methods), was >1000 times the maximum indoor concentration recorded in Table 1. Brackets [] indicate data exist suggesting the compound may have carcinogenic potential, but the evidence was either equivocal, or the route of administration was either skin painting or subcutaneous, which we chose not to use in estimating risk.

Table 4. Top 20 compounds ranked according to the ratio of LD50 to the maximum indoor air concentration

<u>Chemical</u>	<u>LD50/CONC.</u>	<u>Conc. (μ g/m³)</u>
Acrolein	38	1,900*
Hydrogen cyanide	33	85*
Nicotine	290	280*
Formaldehyde	340	3,720*
Pentachlorophenol	380	200*
Dichloromethane	770	5,000
Ethylamine	830	750*
Dimethylacetamide	1700	4,700*
Lindane	2400	50
m-Xylene	3700	2,100*
Heptachlor	4200	15
Dichlorvos	5000	10
p-Dichlorobenzene	5600	140
n-Butanol	7700	160
Allyl alcohol	11000	9.4
Toluene	11000	700
Diethylamine	11000	76*
DDVP	11000	10
1,2-Dichloroethane	14000	69
1,1,1-Trichloroethane	17000	880

* Smoke-filled room, complaint building, or mobile home

Table 5. Ratio of the most potent TD50 to concentrations measured in indoor air.

Carcinogen	Estimated "Human-Equivalent" TD50 ($\mu\text{g}/\text{m}^3$) ¹	TD50/Concentration ²	
		Maximum	Mean or Median
Aldrin	570	1000	-
Benzene	1.2×10^5	310	8600
Benzo[a]pyrene	8500	1.3×10^5	1.2×10^6
Carbon tetrachloride	8.8×10^4	5200	$<6.3 \times 10^4$
Chlordane	1100	28	-
Chloroform	3.7×10^4	790	$<1.4 \times 10^4$
Dibenz[a,h]anthracene	4500	9.0×10^6	4.5×10^7
1,2-Dibromoethane	1700	$>1.2 \times 10^4$	-
[1,1-Dichloroethane ³	8.4×10^5	4.7×10^5	1.4×10^7]
1,2-Dichloroethane	8600	124	7800
Dichloromethane ⁴	1.8×10^6	355	$<1.5 \times 10^4$
Dieldrin	420	890	-
Di(2-ethylhexyl)-phthalate	3.6×10^6	1.6×10^4	6.0×10^4
Dimethylnitrosamine	180	225	-
Ethanol	1.3×10^7	3.3×10^4	9.9×10^4
Formaldehyde ⁵	1247	2.5^6	23
Heptachlor	840	56	-
Lindane	1.2×10^4	240	-
N-Nitrosopyrrolidine	3300	9.2×10^4	-
PCB's (Aroclor 1260)	1600	3200	-
[Styrene ³	2.8×10^5	5200	8.5×10^4]
Tetrachloroethylene	5.8×10^4	81	1.3×10^4
Trichloroethylene	3.2×10^5	1800	$>9.4 \times 10^4$
Vinylidene chloride	1.8×10^4	43	420

¹ Except as indicated, values were calculated from the most potent TD50s reported by Gold, *et al.* (1984,1986) as described in Methods. For 1,2-dibromoethane, formaldehyde, and vinylidene chloride, which were tested via the inhalation route, we estimated the "human-equivalent" TD50 by converting the value reported by Gold, *et al.* to $\mu\text{g}/\text{m}^3$ using their species scaling factors. Dichlorvos and malathion were not included, as the experiments from which the TD50s were calculated were considered to be negative by the NCI (Gold, *et al.*, 1984). The NCI/NTP-sponsored bioassay for lindane was also considered negative. The TD50 used was from another study that was positive. 1,1-Dichloroethane and styrene are in brackets because results of the animal bioassays were judged suggestive by the NCI (Gold, *et al.*, 1984).

² Except as indicated, maxima are from Table 1. The mean is the average of all means or medians reported in Table 1.

³ The experiment from which the TD50 was calculated was judged suggestive by the NCI (Gold, *et al.*, 1984).

⁴ The TD50 has not been calculated by Gold, *et al.* (personal communications). We have estimated a value as the lowest administered dose resulting in a significant incidence of cancer (NTP, 1986) and adjusted for 24-hour exposure as indicated in Methods.

⁵ The most potent TD50 was 0.798 mg/kg/day in male rats. (L.S. Gold, personal communications).

⁶ We have used $500 \mu\text{g}/\text{m}^3$ as the highest plausible concentration for chronic exposure (see text).

Table 6. Estimates of carcinogenic risk from lifetime exposure to 24 carcinogens in indoor air.

Carcinogen	Risk estimated from maximum concentrations (x10 ⁻⁵) ¹				Risk estimated from mean or median concentrations (x10 ⁻⁵) ¹			
	MLE	UCL(95%)	EPA	TD50	MLE	UCL(95%)	EPA	TD50
Aldrin	18.0	57.0	NA	48.0	-	-	-	-
Benzene	128.0	207.0	270.0	>160.0	4.6	7.4	9.8	5.7
Benzo[a]pyrene ²	0.45	0.73	20.0 ³	0.4	0.048	0.077	2.3	0.042
Carbon tetrachloride	8.1	12.0	25.5 ⁴	9.7	0.66	0.95	2.1	<0.8
Chlordane	1300.0	1600.0	NA	1800.0	-	-	-	-
Chloroform ⁵	40.0	50.0	108.0 ⁶	66.0	2.2	2.7	6.1	<3.6
Dibenz[a,h]anthracene	0.0025	0.0039	NA	0.0055	0.0005	0.00078	NA	0.0011
1,2-Dibromoethane	1.4	1.8	0.84	<4.1	-	-	-	-
[1,1-Dichloroethane ⁶	1.1x10 ⁻⁷	0.040	NA	0.11	1.1x10 ⁻¹⁰	0.0013	NA	0.0035]
1,2-Dichloroethane	62.0	80.0	179.0 ⁷	<390.0	0.99	1.3	2.8	<6.3
Dichloromethane ⁸	180.0	253.0	2100.0	NA	8.1	11.0	120.0	NA
Dieldrin	53.0	110.0	NA	56.0	-	-	-	-
Di(2-ethylhexyl)-phthalate	2.8	4.9	NA	3.2	0.72	1.3	NA	0.84
Dimethylnitrosamine	38.0	67.0	400.0	222.0	-	-	-	-
Ethanol	2.7	4.2	NA	1.4	0.95	1.5	NA	0.46
Formaldehyde ⁹	312.0	928.0	650.0	9000.0	0.37	67.0	69.0	950.0
Heptachlor	18.0	410.0	NA	<900.0	-	-	-	-
Lindane	250.0	410.0	NA	>270.0	0.83	1.4	-	>0.97
N-Nitrosopyrrolidine	1.0	1.7	NA	0.54	-	-	-	-
PCB's (Aroclor 1260)	18.0	21.0	NA	15.0	-	-	-	-
[Styrene ¹⁰	8.4	12.0	NA	9.7	0.51	0.76	NA	0.59]
Tetrachloroethylene ¹¹	130.0	160.0	35.0	620.0	0.79	1.0	0.22	3.9
Trichloroethylene ¹²	15.0	20.0	23.0	29.0	0.29	0.39	0.44	<0.54
Vinylidene chloride ¹³	1080.0	1600.0	2100.0	1300.0	7.3	11.0	14.0	8.1

1 MLE and UCL(95%) estimates were calculated as described in Methods using the dose response data given by Gold, et al (1984,1986) corresponding to the experiment yielding the most potent result as measured by the TD50, except as follows: benzene was estimated from exp. number 331; and dimethylnitrosamine from exp. number 2043. The estimates labeled 'EPA' were obtained by multiplying the EPA unit risk values, as cited, by the appropriate indoor air concentrations from Table 1. The estimate labeled 'TD50' was obtained from the most potent TD50 assigned by Gold, et al (1984, 1986) assuming linearity. Mean indoor air concentrations were determined as indicated in the footnote to Table 2. 1,1-Dichloroethane and styrene are in brackets because results of the animal cancer tests were judged suggestive by NCI (Gold., et al., 1984).

2 In this study, benzo[a]pyrene was administered orally, in the drinking water. Benzo[a]pyrene appears to be at least as potent when administered to hamsters via inhalation (Thyssen, et al., 1981). The lowest effective dose in the inhalation study correspond to 24 hour inhalation of about 2500 ug/m³, which produced about a 25% increase in incidence above controls. This would produce risk estimate not dissimilar from that estimated here.

3 Calculated from a unit risk estimate of 3.3 x 10⁻³ (EPA, 1984a).

4 Calculated from a unit risk estimate of 1.5 x 10⁻⁵ (EPA, 1984e).

5 Concentrations in air over an indoor swimming pool and the high value measured by Hartwell, et al (1984a) were not included.

Table 6. (continued)

- 6 The experiment used by Gold, et al (1984) to estimate the TD50 was classified equivocal by NTP (RTECS, 1984). 1,1-dichloroethane was only detected in 2 of 17 measurements (Wallace, et al., 1982). The concentration used is one-half the limit of detection in the study.
- 7 Calculated from a unit risk estimate of 2.6×10^{-5} (EPA, 1985f).
- 8 MLE and UCL (95%) were estimated as described in Methods from overall rates of alveolar/bronchiolar neoplasms in male mice as reported by NTP, p149 (1986). The EPA value was calculated from their unit risk estimate of 4.1×10^{-6} (EPA, 1985d).
- 9 MLE and UCL (95%) were estimated from experimental results used by Gold, et al to calculate the most potent TD50 (L. Gold, personal commun.). These were nasal squamous cell carcinomas in male rats that survived at least 24 months or died naturally before 24 months. The EPA estimate was based on a unit risk value of 1.3×10^{-5} (EPA, 1986).
- 10 The experiment from which estimates were made was considered not conclusive by NTP (Gold, et al., 1984).
- 11 Calculated from a unit risk estimate of 4.8×10^{-7} (EPA, 1985e).
- 12 Calculated from a unit risk estimate of 1.3×10^{-6} (EPA, 1985c).
- 13 Calculated from a unit risk estimate of 5×10^{-5} (EPA, 1985b).

Table 7. Percent of exposed population at greater than 10^{-3} risk

	Concentration Distribution of Chemical ($\mu\text{g}/\text{m}^3$) ¹		Concentration for 10^{-3} Risk ² ($\mu\text{g}/\text{m}^3$)			Percent of population at > 10^{-3} Risk ²		
	GM	GSD	MLE	LCL	TD50	MLE	LCL	TD50
Benzene	37	2.48	305	190	240	1.0	3.6	2.0
Formaldehyde	22.9	1.73	342	79	5.5	z=4.93	1.2	>99.0
Carbon tetrachloride	6.03	1.87	210	146	180	z=5.67	z=5.09	z=5.42
Tetrachloroethylene	16.2	2.28	580	446	120	z=4.34	z=4.02	0.75
Trichloroethylene	12.7	3.47	1170	880	630	0.014	0.03	0.08

¹ Geometric mean (GM) and geometric standard deviation (GSD) were calculated from the data of DeBortoli, et al. (1985).

² The maximum likelihood estimate (MLE) and 95% lower confidence limit on dose (LCL) were estimated using GLOBAL82 (Crump, 1982); values in the TD 50 column were calculated from the TD50, assuming linearity. The unit risk factors derived by EPA were not used in this table because we did not wish to assume linearity would necessarily be a valid assumption up to the 10^{-3} risk level.

³ To determine this fraction we used Normal Probability Error Function tables. For example, for benzene MLE estimate: $(\ln 305 - \ln 37)/\ln 2.48 = 2.32 = z$. This, in the error function table, corresponds to 0.4898. Thus, the fraction of the which population distribution above $305 \mu\text{g}/\text{m}^3$ is $0.5 - 0.4898$, or about 1%. The value of z has been listed instead of percent for all $z > 3.9$ (percent < 0.01).

Table 8. House-by-house cancer risk based upon one study (DeBortoli, et al., 1985)

	Houses (Risk x 10 ⁻⁵) ¹															CV(%) ²	Range (max/min)
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>10</u>	<u>11</u>	<u>12</u>	<u>13</u>	<u>14</u>	<u>15</u>		
Benzene (7.4/14)	4.8	5.8	8.5	9.0	35	33	12	10	48	56	19	43	21	16	110	97	23
Carbon tetrachloride (.95/1.4)	2.7	2.0	1.4	2.7	7.5	6.8	4.8	4.1	6.1	3.4	5.4	8.1	8.1	1.4	7.5	51	6.0
Chloroform (2.7/2.6)	<1.0	<1.0	<1.0	<1.0	1.0	16	<1.0	2.1	1.0	8.3	2.1	<1.0	<1.0	<1.0	<1.0	>160	>8.3
Dichloromethane (2.7/225)	4.7	<0.12	<0.12	<0.12	<0.12	60	4.3	3.5	2.9	<.06	36	<.06	<.06	2.7	7.1	>210	>1000
Formaldehyde (51/53)	50	19	8.7	26	48	30	39	25	14	16	24	28	25	7.7	15	51	6.5
Tetrachloro- ethylene (1.0/4.5)	7.3	1.8	2.7	2.0	0.67	4.4	2.2	2.9	7.6	1.8	6.9	5.6	14	2.2	10	78	21
Trichloro- ethylene (0.39/3.4)	1.6	.11	.92	.46	.34	1.4	.80	2.3	1.1	.80	9.9	4.8	13	2.4	3.0	130	120
Total Risk:	72	30	23	41	93	152	64	50	81	86	103	91	82	33	154	52	6.7

¹The 95% upper confidence level risk estimated for mean indoor air concentrations, as shown in Table 3, was divided by the mean concentration to approximate a 'unit-risk' factor. This was then multiplied by the concentrations measured in each house.

²CV = coefficient of variation = (standard deviation of risk)/(mean risk).

³The numerator is the 95% upper confidence level (UCL) risk (x10⁻⁵) estimated from mean indoor concentrations (see Table 3). The denominator is the mean concentration in all homes for which we have data.

Table 9. Estimates of Margins of Safety for Exposure to Chemicals with Potential for Producing Reproductive Effects¹

<u>CHEMICAL</u>	<u>LED</u> ₃ (ug/m ³)	<u>EFFECT</u> ⁷	<u>CONCENTRATION</u> MAX/MEAN OR MEDIAN ₃ (ug/m ³)	<u>MOS</u> (LED/CONC.)	<u>REFERENCE</u>
<u>BIRTH DEFECTS</u>					
Benzene	1.6x10 ⁵	Low incidence of brain and skeletal defects	390/14	410/1.1x10 ⁴	Kuna and Kapp, 1981
Ethylbenzene	1.2x10 ⁵	Developmental abnormalities	320/9.8 ⁶	375/1.2x10 ⁴	Batelle, 1981
Di(2-ethylhexyl) phthalate	1.6x10 ⁵	Small increase in birth defects	230/60	695/2,670	Shiota, et al, 1980
Vinylidene chloride	9.4x10 ⁴	significant delay in ossification of skull and other defects	416/2.7	226/3.5x10 ⁴	Murray, et al, 1979
p-Xylene	1.5x10 ⁵	Some evidence of skeletal retardation	294/30	510/5000	Ungvary, et al, 1980
<u>LESS SERIOUS EFFECTS</u>					
Benzene	5,000	Alteration in oestrous cycles	390/14	13/360	Alilova and Ulanova, 1975
Chlordane	120	Postnatal endocrine disfunction	40/-	3.0/-	Cranmer, et al, 1978
Diazinon	138	Hepatic and adrenal disfunction	2.0/-	69/-	Cranmer, et al, 1978
Formaldehyde	430	Menstrual disorders in women	3700/53 ⁴	0.12/8.0	Shumilina, 1975

Table 9 (continued)

<u>CHEMICAL</u>	<u>LED</u> ($\mu\text{g}/\text{m}^3$)	<u>EFFECT</u> ⁷	<u>CONCENTRATION</u> MAX/MEAN OR MEDIAN	<u>MOS</u> (LED/CONC.)	<u>REFERENCE</u>
Acetaldehyde		Growth retardation; cardiovascular and CNS anomalies			O'Shea and Kaufman, 1979
<u>REPRODUCTIVE TOXICITY</u>					
Dimethylacetamide	4.4×10^5	Embryo lethality (maternally toxic)	4700/-	93/-	Merkle and Zeller, 1980
Chloroform	4.3×10^4	Embryotoxicity (some maternal toxicity)	$47^9 / < 2.6$	$915 / > 1.7 \times 10^4$	Schwetz, et al, 1974
Lindane	780	Disturbances in oestrous cycles; Lowered viability of embryos and delayed development	50/-	16/-	Naishtein & Leivobich, 1971
Dimethylnitrosamine	15	Increase in perinatal death	0.06/-	253/-	Anderson, et al, 1978
Pentachlorophenol	2,300	Embryolethality	200/5.5	12/418	Schwetz, et al (1974)
Trichloroethylene	9.1×10^4	Reduction in fetal weight and resorptions	182/3.4	$500 / 2.7 \times 10^4$	Cited in Barlow and Sullivan, 19__.

Table 10. A comparison of the lowest effective doses (LEDs) required to produce observable carcinogenic and reproductive effects

	<u>Carcinogenesis¹</u>		<u>Reproductive Effects²</u>
	<u>LED</u>	<u>TD50</u>	<u>LED</u>
			<u>Birth Defects</u>
Benzene	1.8x10 ⁴	1.2x10 ⁵	1.6x10 ⁵
Di(2-ethylhexylphthalate)	9.2x10 ⁵	3.6x10 ⁶	1.6x10 ⁵
Vinylidene chloride	7600	1.8x10 ⁴	9.4x10 ⁴
			<u>Less Serious Effects</u>
Benzene	1.8x10 ⁴	1.2x10 ⁵	5000
Chlordane	461	1100	120
Formaldehyde	1760	1247	430
			<u>Reproductive Toxicity</u>
Chloroform	2.3x10 ⁵	3.7x10 ⁴	4.3x10 ⁴
Dimethylnitrosamine	63	180	15
Heptachlor	770	840	60
Lindane	3.7x10 ⁴	1.2x10 ⁴	780
Trichloroethylene	5.6x10 ⁵	3.2x10 ⁵	9.1x10 ⁴

¹ LED and TD50 were the "inhalation equivalent" values calculated from the values reported by Gold, et al. (1984, 1986, 1987) in experiments which produced the "most potent" TD50. The LED was considered to be the lowest average daily dose which produced an incidence of cancer higher than the controls. Note that the LEDs for the cancer tests and reproductive tests are not strictly comparable since the LED listed by Gold, et al. is the average daily dose and the doses in the reproductive tests were actually administered doses.

² The reproductive LEDs are as listed in Table 9.

Table 11. Percent of Exposed Population at a Margin of Safety Less Than 100 for Reproductive Effects.

<u>Chemical</u>	<u>Exposure</u>		<u>MOS = 100</u>	
	<u>GM</u>	<u>GSD</u>	$\mu\text{g}/\text{m}^3$	$\frac{\%}{1}$
Benzene	37	2.48	50	37
Ethylbenzene	13.9	4.27	1200	0.11
Formaldehyde	22.9	1.73	4.3	100
Trichloroethylene	12.7	3.47	910	0.03
p-Xylene ²	57.7	2.90	1500	0.11

¹ See footnote to Table 7 for method of calculation.

² Values from DeBortoli et al. (1985) were for the mixture of 1,3- and 1,4-xylene.

Table 12. Miscellaneous Toxic Effects and Irritation to the Eyes with MOS <1000¹

<u>CHEMICAL</u>	<u>LED</u> ($\mu\text{g}/\text{m}^3$)	<u>EFFECT</u>	<u>CONCENTRATION</u> Max/(Mean or median) ($\mu\text{g}/\text{m}^3$)	<u>MOS</u> (LED/Conc.)	<u>REFERENCE</u>
Acetone	2.5x10 ⁴	Physiological, involving central nervous system in humans	157/21	159/1190	Sedov, et al., 1977
Acrolein	583	Moderate irritation to eyes	1900/2.0 ²	0.31/290	TLV Doc., 1985
n-Butanol	7.7x10 ⁴	Mildly irritating to humans	160/17	480/4500	TLV Doc., 1985
Chlorpyrifos	345	Plasma cholinesterase depression	2.0/-	170/-	Griffin, et al., 1976
Cyclohexane ³	1.8x10 ⁴	Irritation to eyes and nose	22/2.0	818/9000	Wayne and Orcutt, 1960
Dibutylphthalate	120	Abnormal electroencephalogram responses in humans	16/9.2	.7.5/13	Cited in Vedel and Nielson, 1984
Dichlorvos	100	Cholinesterase depression in humans	10/-	10/-	Cited in IARC, 1979
Ethylamine	1.6x10 ⁴	Severe irritation to eyes of rabbits	21/3.3x10 ⁴	125/1.9x10 ⁵	TLV Doc., 1985
n-Hexane ³	7.2x10 ⁴	Irritation to eyes and nose	590x11 ⁴	122/6500	Wayne and Orcutt, 1960
Hydrogen Cyanide	5000-13,000	Headaches, weakness, throat irritation, vomiting	10/-	500/-	El Ghawabi, et al., 1975
Methanol ³	6700	Irritation to eyes and nose	73/51	92/131	Wayne and Orcutt, 1960
1,2,4 + 1,3,5 - Trimethylbenzene	5.4x10 ⁴	Fatigue and headaches in humans	1240/60 ⁵	44/900	Battig, et al., 1956

¹ Included in this table are only those chemicals which are not already listed in Tables 6 or 9. Miscellaneous toxic effects or irritant properties of carcinogens and reproductive toxins are discussed in the text of those sections and in the Appendix.

² This is not a mean, but is more representative than the "maximum" of concentrations that might be encountered in indoor environments where heavy smoking occurs, such as in bars or restaurants (see Appendix).

³ Irritation at this concentration occurred after UV irradiation in a mixture with NO₂, which generates ozone and other photochemical pollutants. Concentrations in complaint buildings were not used in calculating the mean.

⁴ Concentrations in complaint buildings were not used in calculating the mean.

⁵ The maximum and average concentrations for the two isomers were summed.

Table 13. Chemicals of Special Interest¹

Carcinogens

Benzene
Chlordane
Chloroform
1,2-Dichloroethane
Dichloromethane
Dieldrin
Dimethylnitrosamine
Formaldehyde
Heptachlor
Lindane
Tetrachloroethylene
Vinylidene chloride

Reproductive Toxins

Benzene
Chlordane
Diazinon
Dimethylacetamide
Formaldehyde
Heptachlor
Lindane
Nicotine
Pentachlorophenol

Miscellaneous Toxic Effects

Acrolein
Dibutylphthalate
Dichlorvos

LD50

Ethylamine
Hydrogen cyanide
m-Xylene

¹ Carcinogens: lifetime risk > 10⁻³ at maximum concentrations.
Reproductive toxins: MOS < 100 at maximum concentrations.
Miscellaneous toxins: MOS < 10 at maximum concentrations.
Chemicals with a measured LD50 (not otherwise appearing in the table): MOS < 5000.

APPENDIX

The material in the tables must be taken together with the discussions of individual chemicals. The tables are intended only as a means of focussing attention on chemicals likely to pose the greatest risk, and cannot, without discussion, stand alone. Thus, both the toxicology and exposure profiles for each chemical are unique. Also, some chemicals are used in specialized circumstances for limited periods of time; others are ubiquitous indoor pollutants. Some have been thoroughly tested and the experiments used to estimate the MOS have been verified by replication. For other chemicals, testing is very limited and results are less certain. It is important to take all of these factors into account in evaluating overall potential hazard. In this Appendix, we have brought together both the concentration and toxicology information for each chemical, as a baseline perspective from which an overall, more thorough evaluation of each might proceed. Toxicological tests in animals have been the primary source for the Appendix, though some material, particularly irritation effects, are from observations in humans. Results of in vitro tests or single dose tests have not been included.

ACETALDEHYDE

Acetaldehyde is one of several bioeffluents discussed. It is also emitted from certain paints (Huber and Jackson, 1966) and is the primary metabolite of ethanol. The concentrations found indoors range between very low levels - 0.18 ug/m^3 - to about 50 ug/m^3 (Wang, 1975; DeBortoli, et al., 1985). Most acetaldehyde indoors is probably due to expired air from humans. Wang (1975) found the concentration of acetaldehyde in a lecture room filled with people to be about 40 times the concentration in the same empty room. Not surprisingly, acetaldehyde is a common indoor air component. It was one of only three chemicals (of 34 examined) found in every home in a recent study (De Bortoli, et. al., 1985).

Acetaldehyde is a relatively non-toxic chemical, and is not considered an obvious irritant to humans at doses below $360,000 \text{ ug/m}^3$ (Sittig, 1985), though the odor threshold is only about 22 ug/m^3 (geometric mean) (Vershueren, 1983).

There are several reports that high doses of acetaldehyde produced tumors in rodents after inhalation of as low as $1.4 \times 10^6 \text{ ug/m}^3$ 6 hours per day. However, the evidence has been considered equivocal (IARC, 1985). A more recent carcinogenicity test in rats was also positive (Woutersen, et al., 1984). Acetaldehyde can cause sister chromatid exchanges in human lymphocytes in vitro after exposure to about $37,000 \text{ ug/m}^3$ for 48 hours (Obe, et al., 1979). It has also been shown to have adverse reproductive effects 40 mg/kg (O'Shea & Kauffman, 1979,1981) and to cause DNA cross-linking at very low doses - only 13 ug/kg (Obe, et al., 1979). Both of these studies

however used only a single injection and are difficult to extrapolate to chronic indoor exposures.

ACETONE

Acetone is a bioeffluent, and a common constituent of indoor air, where it is found at concentrations considerably higher than in outdoor air (DeBortoli, et. al., 1985). It is a normal constituent in human breath, at concentrations of approximately 1200 ug/m^3 (Jansson & Larsson, 1969). It is also a common solvent in, for example, paints and varnishes, and the principal ingredient in fingernail polich remover. The concentration of acetone indoors may be quite dependent on how many people are present (Wang, 1975; Johansson, 1978).

Physiological effects of acetone involving central nervous system changes have been recorded in humans breathing acetone at $100,000 \text{ ug/m}^3$ for 6 hours (Sedov, et al., 1977) Even if we assume no dose-rate effect, and adjust this exposure over a 24 hour period [$6/24(100,000) = 25,000 \text{ ug/m}^3$], this is more than 150 times the highest indoor concentration reported in the studies we have reviewed (Table 1), and several thousand times higher than the mean concentration. The 100% odor-recognition concentration is $725,000 \text{ ug/m}^3$, and the odor threshold is $2.0 \times 10^4 \text{ ug/m}^3$ (geom. mean) (Verschueren, 1983), over 100 times the highest indoor concentrations in Table 1. Acetone, therefore, does not appear likely to present any significant hazard at these concentrations.

ACROLEIN

Acrolein is a component of cigarette smoke, smoke from wood combustion, and diesel and rotary engine exhaust. It is also used as a slimicide in the manufacture of paper and paperboard. We have very limited concentration data on acrolein. In one study very high concentrations of side-stream cigarette smoke (about 20 ppm) were maintained in an experimental chamber (Hugod, 1984). In this study concentrations as high as 1900 ug/m³ of acrolein were measured in the gas phase. The mean concentration measured was about 1,000 ug/m³ (N=6). These values do not appear representative of common exposures. Other studies have reported only 2-50 ug/m³ in bars and restaurants where there was heavy smoking (Jermini, et al., 1976; Harke, et al., 1972).

Acrolein is a powerful lacrymogen (formerly it was used as tear gas), and greatly irritates the conjunctiva and the mucous membranes of the respiratory organs. Exposure in air at a level of 2,300 ug/m³ is intolerable, causing lacrymation and marked eye, nose and throat irritation within a period of 5 minutes (Fassett, 1963; Sim & Pattle, 1957: cited in IARC, 1979a; RTECS, 1984). The lowest dose at which irritation effects have been reported is 583 ug/m³, which is moderately irritating in humans (TLV Doc., 1985). The 100% odor recognition concentration for acrolein is about 47,000 ug/m³, far above highly irritating concentrations [odor threshold = 512 ug/m³ (geom. mean)] (Verschueren, 1983). In the U.S., the TLV is 250 ug/m³. In rats, inhalation exposure for 41 hours at concentrations of 4,800 ug/m³ or for 20 hours at a concentration of 9,400 ug/m³

caused elevated hepatic alkaline phosphatase activity (Murphy, et al., 1964: cited in IARC, 1979a). It is unlikely humans would be exposed to such doses, which are twice the intolerable exposure level (2,300 ug/m³). The powerful irritant properties of acrolein, which are manifested at doses below which other systemic toxic effects may occur, would seem to be the major potential effect of acrolein in indoor air.

BENZENE

Benzene is a ubiquitous outdoor and indoor air pollutant. It is a common solvent in, for example, paints, waxes, glues, and cleaning agents. It is also a component of cigarette smoke, and concentrations in indoor air have been correlated with cigarette smoking (Lebret, et al., 1984). We have reviewed studies which measured concentrations in private homes (DeBortoli, et al., 1985; Lebret, et al., 1984; Wallace, 1984; Hartwell, et al., 1984a), a complaint building (Turiet, et al., 1981), public buildings (Pellizzari, et al., 1984; Johansson, 1978); and a personal monitor study (Wallace, et al., 1982). The average concentrations reported by these authors are quite similar (see Table 1). The mean across studies is 14 ug/m^3 , and the coefficient of variation is 66%, relatively small compared to many other chemicals. (Great variability, however, has been observed in some studies. Notably, Wallace, et al., (1982) found values an order of magnitude or more different at two localities.) The highest value reported was 387 ug/m^3 , in a personal exposure study (Wallace, et al., 1982) which included both indoor and outdoor exposures. Relatively high values have also been reported in some homes (DeBortoli, et al., 1985).

Though benzene has indoor sources, in most of the studies we reviewed, the indoor to outdoor concentrations did not differ greatly (Hartwell, et al., 1984a: I/O=2; Pellizzari, et al., 1984: I/O=2; Lebret, et al., 1984: I/O=1; Wallace, 1984: I/O=2.2 Johansson, 1978: I/O=1). This is no doubt due to the fact that there are many outside sources of benzene. In fact, indoor levels of benzene have

been correlated with outdoor concentrations (Hartwell, et al., 1984a). In only one study (DeBortoli, et al., 1985) was a relatively high I/O ratio reported. The average ratio in this study was 4, and the maximum value was 18. Since this was a study of Italian homes, this may indicate something unique to that area.

The toxicological properties of benzene have been reviewed extensively (e.g., IARC, 1982a; EPA, 1984b (and previous documents)). Hematopoietic effects have been observed in humans exposed in the workplace -- for example, in workers exposed over several years to as low as 8×10^4 ug/m³ of benzene (Fishbeck, et al., 1978 - cited in IARC, 1982). This concentration is somewhat higher than the odor threshold for benzene (2.4×10^4 ug/m³ - Verschueren, 1983), and some 200 times higher than the maximum value measured in the studies we reviewed, and almost 6,000 times higher than the average concentration of benzene in indoor air.

Other effects of somewhat uncertain implications as to adverse health consequences, have been observed at much lower doses. Avilova & Ulanova (1975) (cited in IARC, 1982a) reported an alteration of oestrous cycles in rats exposed to atmospheres of only 5,000 ug/m³ for a 4 month period, and chromosome aberrations in human lymphocytes of individuals exposed to as little as 3.2×10^4 ug/m³ for periods of one month to 26 years (Picciano, 1979 -- cited in IARC, 1982a). A low incidence of brain and skeletal defects in newborn rats have been reported after exposure to 1.6×10^5 ug/m³ 7 hours each day during pregnancy (equivalent to about 4.7×10^4 for 24 hours) (Kuna & Kapp, 1981 -- cited in IARC, 1982a).

The lowest toxic dose we have found is from a recent study (Erexson, et al., 1986), which reported a significant dose related increase in micronuclei in bone marrow erythrocytes from male rats after a 6 hour exposure to as low as 1 ppm benzene. This dose is approximately equivalent to 812 ug/m^3 for a 24 hour exposure. The same study reported significant increases in SCEs in peripheral blood lymphocytes at somewhat higher doses (3 ppm). 812 ug/m^3 is only about twice the highest concentration of benzene reported in the studies we reviewed, certainly an inadequate margin of safety. It is of obvious importance to confirm the results of this possibly important study.

Leukemogenic effects of benzene in humans exposed in industrial settings has been much debated, though there is now general agreement that benzene is a human leukemogen (IARC, 1982a). The Carcinogen Assessment Group at EPA has estimated a unit risk factor for benzene of 0.7×10^5 (Anderson, 1983), and we have calculated a similar figure based on the TD50 of Gold, et al. (1984), which they estimated from results of a gavage study in rats conducted by the NCI/NTP. In this study, the lowest daily dose producing an effect was equivalent to about $18,000 \text{ ug/m}^3$, using our rough method of route conversion. The concentrations to which humans were exposed in the epidemiological studies used by EPA to estimate the unit risk factor are difficult to ascertain. Lifetime average exposure levels used by EPA are about $10,000 \text{ ug/m}^3$ (EPA, 1979a); not too dissimilar from the estimated equivalent concentrations used in the animal study. These concentrations are far above usual levels in indoor air -- some 700

times the average concentrations in homes. However, they are only about 25 - 50 times greater than the highest concentrations reported in the studies we reviewed. This is not a large margin of safety, especially since human exposure to benzene is often supplemented by occupational exposures, and since closely related alkyl benzenes are common constituents of the air in homes, present at quite high concentrations. None of these chemicals have been as thoroughly tested for carcinogenic potential as has benzene, and some may have carcinogenic potential.

BENZO(A) PYRENE (BaP)

Benzo (a) pyrene along with many other polycyclic aromatic hydrocarbons (PAH), is produced by combustion processes, and thus is a component of auto exhaust, residential wood and oil smoke, cigarette smoke, and cooking emissions (Sexton, 1984; IARC, 1983a), all complex mixtures. Despite the large number of indoor sources of BaP, the indoor/outdoor ratios of BaP concentrations, except in specific cases, do not appear to be elevated (Sexton, 1984; Deshpande, et al., 1984). Exceptions occur in homes using kerosene space heaters or near busy highways (Deshpande, et al., 1984), and in heavy tobacco-smoking areas (IARC, 1983a). In homes using wood-burning heat however, indoor/outdoor ratios were close to unity (Sexton, 1984). However, outdoor concentrations of BaP tend to be elevated in areas in which woodburning is prevalent (Cooper, 1980). Maximum values in areas of dense tobacco-smoking appear to be in the range of about 0.02 ug/m^3 in the air of restaurants or at public gatherings (IARC, 1983a) to 0.06 ug/m^3 , in homes using kerosene space heaters (Deshpande, et al., 1984). Since BaP is virtually always found together with a number of other PAH, and since a number of PAH have similar toxic properties, it is pertinent to examine the total measured PAH concentration. In one study available to us, Sexton (1984) monitored concentrations of eight PAH in six homes of non-smokers using wood-burning heat. The total average concentration of these eight PAH was 0.0064 ug/m^3 , and the maximum total concentration, found in one of the homes, was 0.021 ug/m^3 . These concentrations are consistent with more recent measurements of 8 PAH

in burning homes in Wisconsin (Daisey et al., 1987). These totals are on order of magnitude estimates only since there are typically more than 100 individual PAH present in this fraction, many at low concentrations.

In evaluating overall risk from exposure to BaP, or to PAH, it is important to consider that significant exposure also occurs from certain foods. For example, smoked foods or foods exposed to a direct flame in cooking, such as charcoal-broiled meat are important sources. 200 g of a well-done charcoal broiled steak contains about 1.6 ug BaP (Lijinsky & Shubik, 1964 - cited in IARC, 1983a). Assuming this is ingested by a 70 kg person, this would roughly correspond to inhalation of an atmospheric concentration of 0.079 ug/m³ for 24 hours, which is in approximately the same range as the highest values reported in the indoor air studies reviewed above.

Benzo (a) pyrene is a potent animal carcinogen. Like other PAH it appears to be most effective when administered via skin painting or sub-cutaneous injection (IARC, 1973), though it is also quite active administered orally (reviewed by Gold, et al., 1984) or via inhalation (Thyssen, et al., 1981). In a lifetime inhalation study, Thyssen, et al. (1981) exposed Syrian hamsters to 2.2, 9.5, or 46.5 mg/m³ for 3-4.5 hours daily. The two higher doses caused an increased incidence of tumors, especially in the nasal cavity, larynx and trachea. The dose of 9.5 mg/m³ corresponds roughly to inhalation of 2,500 ug/m³ over a 24 hour period each day. This is similar to the equivalent lowest effective dose (3.3 mg/kg) in the oral administration study examined by Gold, et al. (1984). 2500 ug/m³ is

more than 40,000 times greater than even the quite high indoor concentration reported by Desphande, et al. (1984).

Benzo (a) Pyrene also appears to have some potential to cause adverse reproductive effects in test animals (e.g., See IARC, 1983a), and can cross the placenta, at least in mice and rats. Unfortunately we were unable to locate a study in which the administered dose was sufficiently well defined to estimate a lowest effective dose.

n-BUTANOL

n-Butanol is primarily an indoor pollutant, where it is found at concentrations several times higher than outdoors. It is a common solvent, and some exposure may occur in connection with hobby-related activities. It has also been detected in emissions from plywood and carpeting (Monteith, et al., 1984). In one study measuring n-butanol levels over time, the concentrations decayed rapidly over the first year of life of the building in which measurements were made.

n-Butanol is mildly irritating to humans at 77,000 $\mu\text{g}/\text{m}^3$ (TLV Doc., 1985), and its odor threshold has been variously reported as from 10,000 $\mu\text{g}/\text{m}^3$ to 329,000 $\mu\text{g}/\text{m}^3$ (TLV Doc., 1985, Molhave, 1982, Verschueren, 1983). Even the highest concentrations recorded in the two studies we examined (160 $\mu\text{g}/\text{m}^3$) are about 60-fold lower than the lowest odor threshold reported for this chemical, and almost 500 times below the concentration at which mild irritation occurs. Thus, any effects from indoor air exposure to n-butanol at these concentrations is unlikely.

CARBON TETRACHLORIDE (CCl₄)

We reviewed five studies which measured CCl₄ in indoor air (DeBortoli, et al., 1985; Lebret, et al., 1984; Wallace, 1984; Hartwell, et al., 1984a,b; Pellizzari, et al., 1984). In general, concentrations appear to be very low. In all but one of these five studies, the mean (or median) levels reported were at or below 1.5 ug/m³. Only the DeBortoli, et al. (1985) study measured consistently higher concentrations, reporting a mean of 7.0 ug/m³. Since this study was done in Italy, this could reflect some difference in Italian homes. The coefficient of variation across homes in the DeBortoli study was relatively small, only 50%. However, over time, as measured by Lebret, et al. (1984), the coefficient of variation in individual homes was quite high (over 300%). CCl₄ also frequently appears either to not be present, or to be present below detectable limits. Lebret, et al. (1984) detected it in less than 1% of 134 homes, and Hartwell, et al. (1984b) depending on the locale of the study, found CCl₄ in 50 to 100% of samples. The quite high between-home variability found by Lebret, et al. might suggest highly variable indoor sources, however, there are also major outdoor sources of CCl₄. If outdoor sources are a major factor in determining indoor levels, this would explain why indoor-outdoor ratios all are quite close to 1 (1.3, 1.9, 2.3, 1.5), and also why, in the Hartwell, et al. study (1984b), there was a significant correlation between indoor and outdoor concentrations. Finally, average indoor concentrations are quite close to estimates of average ambient

concentrations of CCl_4 , which are about 1.0 ug/m^3 (reviewed in IARC, 1979b).

In the toxicology studies we have reviewed, exposure to 22 ppm for 7 hours per day over 200 days, roughly corresponding to exposure to $4.2 \times 10^4 \text{ ug/m}^3$ 24 hours each day, led to only very slight toxic effects in the liver (Rechnagel & Ghoshal, 1966; Adams, et al., 1952 - discussed in IARC, 1979). A similar situation is seen for reproductive effects. Reproductive toxicity in the form of retarded development was seen in fetuses of rats exposed on days 6-15 of gestation to concentrations of 1890 and 6300 mg/m^3 , roughly corresponding to $5.5 \times 10^5 \text{ ug/m}^3$ over 24 hours (Schwetz, et al., 1974b).

There is no adequate inhalation carcinogenesis experiment of which we are aware. Recent gavage experiments in mice and rats have shown CCl_4 can produce liver tumors. The lowest effective dose in these studies was 824 mg/kg/day , administered over the lifetime of the animals, and this resulted in tumors in all test animals (Gold, et al., 1984). The TD50 estimated from this experiment is 114 mg/kg/day , roughly equivalent to daily exposure to $8.8 \times 10^4 \text{ ug/m}^3$, assuming no difference in sensitivity due to the inhalation route. This concentration is more than 5,000 times the highest indoor air concentration reported in the 5 studies reviewed.

CHLORDANE

Chlordane, an organochlorine pesticide, was formerly widely used as an insecticide, but since 1983 has only been used as a termiticide. It is normally applied in mixture with heptachlor, and is restricted to subterranean application. However, even this restricted use of chlordane should be carefully scrutinized as potentially causing some risk since residential application is common, and relatively high airborne concentrations of chlordane have been detected in treated homes, especially in basements (Reinert, 1984; Jurinski, 1984).

Both chlordane and heptachlor are carcinogenic in laboratory animals. The highest airborne concentrations we have found reported are about 40 ug/m^3 (Reinert, 1984), though the great majority of airborne measurements have been far lower. The estimated airborne concentration which, if breathed for a lifetime, would be equivalent to the lowest dose producing tumors in laboratory mice (Gold, et al., 1984) after oral administration (0.6 mg/kg/day), is 460 ug/m^3 , a factor of only about 12 higher than the high concentration reported by Reinert. Since chlordane is very stable, post-treatment exposure could occur for relatively long periods of time. More extensive exposure assessments over time are needed to more accurately assess cancer risk.

Reproductive effects have been noted in mice after daily oral administration throughout gestation of doses as low as 160 ug/kg/day , estimated to be roughly equivalent to 120 ug/m^3 , only a factor of 3 higher than concentrations in some homes. Though the reproductive

effects noted were rather subtle, involving postnatal endocrine disfunction (Crammer, et al., 1978: cited by Rowen-West, et al., 1987), they do suggest some risk may exist. This is especially true since long term exposure is not required for the effect, and possible differences in sensitivity between mice and humans or differences due to different routes of exposure in the laboratory and human exposure situations are certainly possible.

The National Academy of Sciences has suggested an airborne exposure limit of 5 ug/m³ to chlordane. Clearly, some of the airborne levels reported following termiticide treatment far exceed this limit (cited in Jurinski, 1984).

CHLOROFORM

A number of studies have measured chloroform levels in homes (DeBortoli, et al., 1985; Wallace, 1984; Seifert, 1982; Hartwell, et al., 1984a,b; Pellizzari, et al., 1984). In almost all cases chloroform is present at quite low levels, detectable in only about 50% of samples (e.g., DeBortoli, et al., 1985; Hartwell, et al., 1984b). The indoor/outdoor ratio in most studies is between 3-10 (Wallace, 1984; Hartwell, et al., 1984a,b), but in one group studied by Hartwell, et al. (1984a) the ratio was only 0.69.

Chloroform is also a common organic chemical found in drinking water and can be released into indoor air. In the study of Wallace (1982), about 150 ng/ml were found. Assuming humans drink about 1 liter of tap water each day, this would correspond to a daily intake of about 2.1 ug/kg, which in turn would be equivalent to an airborne concentration of about 7.4 ug/m³. This is quite similar to the concentrations reported in indoor air (Table 1).

At very high doses (Schwetz, et al., 1974a) chloroform is an anesthetic. It also has quite a high odor threshold - 1.2×10^6 ug/m³ (geometric mean) (Verscheuren, 1983).

Chloroform is a carcinogen in mice and rats (Gold, et al., 1984), producing tumors in 70% of animals administered 144 mg/kg/day by gavage. This roughly corresponds to inhalation each day of airborne chloroform at 1.1×10^5 ug/m³, which is a factor of over 2,000 greater than the highest concentration measured in the studies we reviewed.

At a slightly higher concentration (1.5×10^5 ug/m³) administered over a 7 hour period (roughly equivalent to 4.4×10^4 ug/m³ over 24 hours) daily during days 6-15 of gestation, embryotoxicity in rats has been reported (Schwetz, et al., 1974a). Though some maternal toxicity was observed in the Schwetz, et al. study, chloroform showed much greater embryotoxicity.

CHLORPYRIFOS (DURSBAN)

Chlorpyrifos is an organophosphate pesticide commonly found in the indoor air of homes (Reinert, 1984). It is an active inhibitor of plasma cholinesterase, and causes plasma cholinesterase depression in humans at doses as low as 0.1 mg/kg/day (Griffin, et al., 1976: cited in TLV Doc., 1985). This is roughly equivalent to inhalation of 345 ug/m³ over a 24 hour period. A 1980 EPA study (cited in Reinert, 1984) found airborne concentrations of chlorpyrifos of 0.2-2 ug/m³ in homes up to 30 days after treatment with the insecticide. The highest of these concentrations is 173 times lower than the dose found to produce cholinesterase depression. Since this may well be below the threshold for this effect, it does not necessarily suggest any serious hazard exists from exposure to these levels. However, since chlorpyrifos is only one of a number of organophosphate pesticides commonly present in residential indoor air [others are Ronnel, dichlorvos, malathion, and diazanon (Beall and Ulsamer, 1981)], it would seem appropriate to consider combined exposure to the cholinesterase inhibitors in estimating possible risks. Concentration data indicating the concurrence of various organophosphate pesticides in homes is needed in order to make such an estimate.

CYCLOHEXANE

Cyclohexane is found in paint and varnish removers, and is a common solvent (TLV Doc., 1985). It is a common organic chemical constituent of indoor air in homes, but is present at quite low concentrations [$<22 \text{ ug/m}^3$ in one large study (Lebret, et al., 1984)]. In this study the concentrations indoors were about 4 times higher than outdoors.

There is a limited amount of toxicological information available on cyclohexane, but it appears to be a relatively non-toxic chemical. At $1.1 \times 10^6 \text{ ug/m}^3$ it is detectable by odor and is somewhat irritating to the eyes and mucous membranes of humans (Treon, et al., 1943: cited in TLV Doc., 1985). No toxic effects were noted in rabbits, even after exposure to 434 ppm 6 hours per day. This is roughly equivalent to $3.8 \times 10^5 \text{ ug/m}^3$ 24 hours each day (TLV Doc., 1985). In the presence of NO_2 , however, and ultraviolet radiation, cyclohexane can produce moderate eye irritation at much lower concentrations ($1.8 \times 10^4 \text{ ug/m}^3$) after less than 90 seconds exposure, probably due to generated ozone and other photochemical products. (Wayne and Orcutt, 1960). Thus, there is no indication that any adverse health effects should be expected from typical indoor air concentrations of cyclohexane.

DIAZINON

Diazinon is an organophosphate pesticide that is commonly found in the indoor air of homes (Beall and Ulsamer, 1981; Reinert, 1984). Oral doses of 0.05 mg/kg/day for 28 days (roughly corresponding to inhalation of 167 ug/m³ over a 24 hour period) have been reported to cause reduction, by more than a third, of plasma cholinesterase activity in humans (Geigy, 1967: cited in TLV Doc., 1985). This dose is at least 400 times higher than the concentrations that have been measured in homes, which are less than or equal to 2 ug/m³. In a study in mice, Crammer and Avery (1978) detected hepatic and adrenal disfunction in offspring of dams treated during pregnancy with only 0.18 mg/kg/day, roughly equivalent to exposure of humans to 138 ug/m³. This is about 70 times the highest concentrations reported in homes. Potential effects of diazanon during the critical period of pregnancy should be considered in light of possible additive effects with other organophosphate pesticides which also occur frequently in homes (e.g., chlorpyrifos, chlordane, Ronnel, dichlorvos, malathion).

1,2 - DIBROMOETHANE (EDB).

EDB, as shown in Figure 5, is a relatively toxic chemical compared to most chemicals found in indoor air. The oral LD50 for rodents has been reported to be between 55 and 420 mg/kg. Fortunately, there are only very small amounts of EDB present in air, either outdoors or indoors. In over 500 ambient air samples from various locations in the state of California, collected over a 2-year period (ARB, 1985), EDB was detected above the 0.04 ug/m³ reporting limit in only 30% of samples. Average concentrations (assuming 1/2 the reporting limit for samples with no reported value) were only about 0.05 ug/m³ (ARB, 1985). In the only indoor air study monitoring for EDB that we have located (Wallace, et al., 1982), EDB could not be detected in any of some 17 samples analyzed. The limit of detection in this study was 0.28-0.38 ug/m³, some 7 times higher than ambient concentrations in the ARB study. Thus, indoor air concentrations could have been substantially higher than outdoors and still gone undetected in this study.

At sub-toxic doses as low as 1.25 mg/kg, administered intraperitoneally daily to male rats prior to mating, EDB has been reported to cause behavioral problems in offspring (Fanini, et al., 1984). This is roughly equivalent to human exposure to 2,000 ug/m³, which is some 5,000 times the upper end of the limit of detection range reported by Wallace, et al., (1982). Doses which have produced cancer in rodents are much higher. In rats, 7.8 x 10⁴ ug/m³, administered over a lifetime 6 hours daily, produced cancer in the majority of test animals (summarized in OSHA, 1983). Even, adjusting

this for 24 hour exposure in humans ($=1.9 \times 10^4 \text{ ug/m}^3$), the dose is still some 50,000 times higher than the upper end of the limit of detection range reported by Wallace, et al. Of some interest may be the synergistic effect of exposure to EDB in the carcinogenesis of a pesticide, disulfiram (discussed in OSHA, 1983). Until recently, the major source of EDB in ambient air was emissions from pesticide applications. However, nearly all pesticidal uses of EDB are now prohibited. The other major source of EDB is from its use in leaded gasoline as a lead scavenger. This use has also been decreasing, and will decrease even more if EPAs proposed lead standard is implemented. Thus, though there may be traces of EDB in indoor air, and ambient air, the human exposure levels are very small compared to many other organics, and compared to the doses of EDB that have been shown to produce cancer or any other toxic effects.

DIBUTYLPHTHALATE

Dibutylphthalate is a commonly used plasticizer, a component of many indoor paints (Virgin, 1984), and is also used in many building materials (Vedel and Nielson, 1984). It has a very low vapor pressure (TLV Doc., 1985), but can occur as an aerosol and adsorb on dust particles in air. In a newly painted room, Virgin (1984) found concentrations as high as 16 ug/m^3 , including true vapor concentration (expected to be very low) and material on dust particles. Virgin reported a median concentration of 9.2 ug/m^3 in the seven homes he examined. Dibutylphthalate, at these concentrations, causes chlorophyll depletion in certain plants, and there was evidence of this in all homes examined by Virgin.

Dibutylphthalate is considered a relatively non-toxic chemical (TLV Doc., 1985). The chemical, at oral doses greater than 70 mg/kg given throughout gestation, does however, have adverse reproductive effects in mice (Shiota, et al., 1980: cited in Shepard, 1983). This dose is roughly equivalent to human exposure to a concentration of $54,000 \text{ ug/m}^3$. This is a factor of more than 3000 times the highest indoor air concentration reported by Virgin. The TLV is $5,000 \text{ ug/m}^3$. Blood changes in humans have been reported after exposure to lower concentrations (about $4,000 \text{ ug/m}^3$). These are some 250 times greater than the highest concentration reported by Virgin (cited in TLV Doc., 1985). Vedel and Nielson (1984) cite an old study (Menshikova, 1971) in which atmospheric concentrations as low as 120 ug/m^3 resulted in abnormal electroencephalogram responses in humans. The same investigator reported some biochemical changes in rats

exposed over a 3 month period continuously to doses of about 100 ug/m³. It would be of interest to confirm these findings.

1,1-DICHLOROETHANE

In only one study reviewed were concentrations of this chemical monitored (Wallace, et al., 1982), and this was a personal exposure study which combined indoor-outdoor exposures. For only 2 of 17 individuals participating in the study was 1,1-dichloroethane detected, though these 2 concentrations (1.8 and 0.93 ug/m³) appeared to be relatively high compared to the limit of detection in the study (0.12 ug/m³). In this study the chemical was not found in breath samples, or in tap water. We are unaware of sources of this chemical.

1,1-Dichloroethane is a relatively non-toxic chemical. The TLV is 810,000 ug/m³ (TLV Doc., 1985). In a 90 week gavage study in rats, there was some evidence of carcinogenicity (Gold, et al., 1984), though results were largely negative in mice in a concurrent study, and the NCI/NTP evaluated this evidence as only suggestive (RTECS, 1984; Gold, et al., 1984). The lowest average effective dose in this study was about 477 mg/kg/day, roughly corresponding to a 24-hour inhalation exposure of 7.5×10^5 ug/m³. This is a factor of almost half a million greater than the highest airborne concentrations reported by Wallace, et al., (1982).

1,2-DICHLOROETHANE

The most likely primary sources of 1,2-dichloroethane in air are from use as a lead scavenging agent in gasoline (though this use is being phased out by EPA), as a degreaser, a fumigant on upholstery and carpets, and as a solvent in paint removers (Merck Index, 1983). Except in areas close to high emission sources, ambient levels are usually quite low -- less than 2 ug/m³ (EPA, 1985e). We have reviewed one study which measured indoor air concentrations of 1,2-dichloroethane (Hartwell, et al., 1984b), and one in which 24-hour personal monitoring devices were used (Wallace, et al., 1982). In the Hartwell, et al. study, concentrations in indoor air of residences in three locations (North Carolina, Louisiana, and Texas) were above detectable limits in only about 50% of measurements. The maximum concentration reported was 69 ug/m³, and between both studies, the average concentrations reported varied from 0.025 - 0.58 ug/m³. Also, in all cases indoor/outdoor ratios were close to 1, suggesting the typical source of 1,2-dichloroethane is outdoor air.

The EPA has recently reviewed the toxicology of 1,2-dichloroethane (EPA, 1985e), and most of what follows has been drawn from that source. 1,2-dichloroethane has produced carcinogenic effects in rodents when administered by gavage, but in what appear to be quite adequate studies, negative results were obtained when the chemical was administered via inhalation. The reason for this difference is not clear, especially since a comparison of other toxic effects appears to indicate that effective doses administered by the oral and inhalation routes are similar. Differences in sensitivity

between the two rodent strains used in these studies is a possible explanation (Hooper, et al., 1980).

If we assume, for the purposes of this discussion, that the effective dose in the gavage experiment can be converted to the inhalation route, the lowest effective dose (24 mg/kg/day) in the rat (Gold, et al., 1984), would correspond roughly to 3.8×10^4 ug/m³. This is approximately equal to the estimated LOAEL (lowest observed adverse effect level) for toxic effects from chronic, intermittent exposure of humans, which EPA estimated at 10-37 ppm (about 4.1×10^4 ug/m³ to 1.5×10^5 ug/m³). Rodents appear to be less sensitive than humans, as the NOAEL for chronic exposure quoted by EPA (4.1×10^5 ug/m³) is about an order of magnitude higher than the LOAEL for humans. Though there were some early, unconfirmed reports of reproductive effects occurring in rodents from exposures to concentrations in air as low as 5000 ug/m³ for 4 hours/day for 1-9 months (Vozovaya and Malyarova, 1971: cited in Rao, et al., 1980), this work has not been confirmed, and later work has reported essentially no effects from exposure of rats to atmospheres up to 4.1×10^5 ug/m³ for 7 hours/day during pregnancy (Rao, et al., 1980).

Carcinogenic risk from exposure to airborne 1,2-dichloroethane is uncertain because of the conflicting results obtained from exposing rodents by the oral and inhalation routes. Even if we assume the LED used in the gavage experiment can predict effects from inhalation exposure, the ratio of this dose to the highest concentration reported in indoor air is over 500; and the ratio to the highest mean or median dose reported (3.6 ug/m³) is over 10,000.

DICHLOROMETHANE

Short term exposure to very high concentrations of dichloromethane can occur from use of paint strippers. In chamber studies, Girman and Hodgson (1986) measured concentrations of $3.5\text{-}12.3 \times 10^6 \text{ ug/m}^3$. These are extremely high, but of course, occur for only short periods of time. Relatively high doses can also occur from other sources. Dichloromethane is used as propellant and carrier in spray cans, is a common solvent, and is also used as a fumigant (TLV Doc., 1985). In a sample of 15 homes in Italy, DeBortoli, et al. (1985) measured widely varying concentrations of dichloromethane. The maximum concentration was $5,000 \text{ ug/m}^3$, and the median only 225 ug/m^3 (DeBortoli, et al., 1985).

Only very recently were adequate inhalation carcinogenesis tests completed for dichloromethane (NTP, 1986). In the NTP study rats and mice of both sexes were treated for 6 hours a day, 5 days/week, over a 2 year period, with 1000, 2000, and 4000 ppm. A high percentage of animals developed liver, lung and mammary tumors. Subtle reproductive effects of dichloromethane have also been observed, though it is not a highly active compound (see discussion in Barlow & Sullivan, 1982). In one study (Hardin & Manson, 1980), after exposure of rats to 4500 ppm for 6 hours per day, 7 days a week before and during gestation, fetal body weight was reduced by 10%. This dose is roughly equivalent to $4 \times 10^6 \text{ ug/m}^3$ 24 hours per day.

Dichloromethane is not a particularly potent toxin as compared to many other chemicals found in indoor air. Carcinogenic and

reproductive effects are, as indicated above, observed in laboratory animals only at quite high doses. However, some risk from exposure to dichloromethane in indoor air may exist, because in some cases concentrations can be quite high. Some indoor exposures, especially in specialized circumstances such as applying paint strippers, can be very high. Concentrations of $3.5\text{--}12.3 \times 10^6 \text{ ug/m}^3$, such as workers and consumers may be exposed to, are more than 10 times the TLV for dichloromethane ($3.6 \times 10^5 \text{ ug/m}^3$) (TLV Doc., 1985). This is also well above the odor threshold, of about $3.9 \times 10^5 \text{ ug/m}^3$ (geom. mean) (Verschuieren, 1983). It clearly presents an unsafe situation, certainly for acute effects. Since exposure to these concentrations is for such a short period of time, it is difficult to draw any conclusion regarding possible cancer risk. Perhaps of greater concern are possible reproductive hazards to pregnant women, since hazardous exposure does not need to be of long duration if it occurs during the critical stages of pregnancy.

A cancer risk cannot be excluded in homes that have relatively high concentrations of dichloromethane present for long periods of time. The lowest dose producing cancer in mice, in the NTP study, was only 700 times the highest concentration found in the DeBortoli study. If we take into account the fact that the dose in the mouse study was only administered for a 6 hour period each day whereas many people spend almost all their time indoors, the adjusted carcinogenic dose would be $3.5 \times 10^6 \text{ ug/m}^3 \times 6/24 = 8.8 \times 10^5 \text{ ug/m}^3$. This is only 175 times the highest concentration in the DeBortoli study. It is thus important to gain a better understanding of what fraction of

homes might have such high dichloromethane concentrations over long periods of time.

DICHLORVOS

Dichlorvos is an organophosphate insecticide. It has some household uses, commonly in flea collars and no-pest strips. In homes using commercial pest strips, concentrations as high as 240 $\mu\text{g}/\text{m}^3$ have been measured (cited in IARC, 1979b). This high concentration does not appear common, as a 1980 EPA survey of homes reported concentrations of only 0.5-10 $\mu\text{g}/\text{m}^3$ (Beall & Ulsamer, 1981). In 1978, FAO/WHO (cited in IARC, 1979b) established a maximum ADI (acceptable daily intake) of 0.004 mg/kg (roughly corresponding to inhalation over a 24 hour period of 14 $\mu\text{g}/\text{m}^3$), which is similar to the high end of the concentration range found by EPA. The TLV is much higher than this (at least as of 1979) -- 1000 $\mu\text{g}/\text{m}^3$.

Dichlorvos is an alkylating agent, and thus, not unexpectedly is a mutagen, albeit a weak one (reviewed in IARC, 1979b). Tests for carcinogenicity have been negative or equivocal in most experiments. Gold, et al. (1984) report one positive result in female rats exposed in a lifetime study to inhalation of about $0.4 - 4.4 \times 10^4 \mu\text{g}/\text{m}^3$ dichlorvos. However, this most likely does not indicate carcinogenic potential, as the significant increase was only for rat pituitary tumors, which occur at high spontaneous rates (L.S. Gold, personal commun.). The study was considered negative by authors, as indicated by Gold, et al. (1984). At roughly similar doses (4,000 $\mu\text{g}/\text{m}^3$) administered during gestation, fetal weight was slightly depressed in offspring of rabbits, though this study was reported as an abstract and is difficult to evaluate (Thorpe, et al., 1972: cited in IARC, 1979b). The primary effect of dichlorvos at relatively low doses

appears to be anticholinesterase activity, which has been well documented in animals and humans. For example, when 11 male and 7 female factory workers were exposed for 8 months to an average concentration of 700 ug/m^3 , plasma cholinesterase activity was inhibited by approximately 60%. However, one month after exposure ceased, levels returned to normal (reviewed in IARC, 1979b). In some cases effects have been noted after exposure to airborne concentrations as low as about 100 ug/m^3 , a concentration about 10 times higher than the highest levels found in homes. It may be of some interest that effects at these low concentrations were only observed in pregnant females or children, or in people who were ill (cited in IARC 1979b).

DIELDRIN

Dieldrin is now banned in the United States, though it is still produced and exported. We have limited indoor air concentration data on dieldrin -- one report indicates measurements in homes treated with termiticides are as high as 0.47 ug/m^3 (Reinert, 1984). The carcinogenicity of dieldrin in mice is well established, though the significance of this finding for human risk is controversial because the primary tumors produced are liver tumors which also occur spontaneously in the mouse (for discussion, see IARC, 1974).

The lowest dose producing a significant increase in the incidence of liver tumors in mice was about 0.1 mg/kg/day (Gold, et al., 1984), roughly equivalent to breathing airborne dieldrin at a concentration of 77 ug/m^3 . This concentration is lower than the TLV for dieldrin, which is 250 ug/m^3 (TLV Doc., 1985), and less than 200 times higher than the indoor air concentration reported by Reinert. Other toxic effects of dieldrin appear to be produced at concentrations much higher than those found to produce cancer. The only study we have found in which significant reproductive effects were reported was that of Ottolenghi, et al. (1974: cited in Shepard, 1983), in which single oral doses were administered to hamsters and mice. This however, is contradicted by Dix, et al. (1977: also cited in Shepard, 1983), who found no teratogenic effects in mice orally dosed with up to 4 mg/kg/day .

Dieldrin is very stable in the environment, can accumulate in human body fat. As a carcinogen active at relatively low doses it

could pose substantial risk to humans in countries where exposure is still occurring over long periods of time.

DI(2-ETHYLHEXYL) PHTHALATE (DEHP)

DEHP and dibutylphthalate are the two most commonly used phthalates, and are present in many building materials (Vedel and Nielsen, 1984). Though indoor concentrations of DEHP as high as $1,200 \text{ ug/m}^3$ (cited in Vedel and Nielsen, 1984) have been reported, most home and office building concentrations appear to be much lower. Vedel and Nielsen report levels from $110\text{--}230 \text{ ug/m}^3$ in one office, and levels below their detectable limit of 60 ug/m^3 in two others. Concentrations 10-100 times lower have been reported in homes (cited in Vedel and Nielsen). Even the highest concentrations reported by Vedel and Nielsen are below the odor threshold, and are about 5 times lower than the TLV of $5,000 \text{ ug/m}^3$ (TLV Doc., 1985).

DEHP has produced tumors in rats and mice (Gold, et al., 1986). The lowest effective dose in mice was 1410 mg/kg/day , administered orally over a period of two years. This approximately corresponds to $1.1 \times 10^6 \text{ ug/m}^3$ airborne concentration, which is about 1000 times the highest concentrations reported by Vedel and Nielsen (1200 ug/m^3). DEHP, when fed to mice at 0.2% in the diet throughout gestation, has also caused an increase in birth defects, of borderline significance, which become more frequent at higher doses (Shiota, et al. 1980: cited in Shepard, 1983; Rowen-West, et al., 1987). This dose, using conversion factors for food consumption per day and inhalation rate (Anderson, 1983), approximately corresponds to an airborne concentration of $2.0 \times 10^5 \text{ ug/m}^3$. This is about 900 times the highest dose measured by Vedel and Nielson (230 ug/m^3).

DIMETHYLACETAMIDE

Limited indoor air concentration data are available for dimethylacetamide. One study (Yocum, et al., 1984) reported concentrations as high as 4713 ug/m^3 in an energy-efficient office building in which occupants complained of odors and eye and throat irritation. After adjustments to the ventilation the concentration was drastically reduced -- more than 100 fold. It is unlikely that dimethylacetamide accounted for the complaints of workers in the buildings. Its 100% odor recognition concentration is $167,400 \text{ ug/m}^3$ [odor threshold = $9.1 \times 10^4 \text{ ug/m}^3$ (geom. mean)] and its TLV is about $36,000 \text{ ug/m}^3$ (TLV Doc., 1985).

There has not been extensive toxicology testing of dimethylacetamide, but of those studies available the lowest daily dose which produced a toxic effect caused embryoletality, at maternally toxic doses in rabbits. The chemical was administered via the stomach tube from the 6th to the 18th day after implantation (Merkle & Zeller, 1980). This dose (300 ul/kg/day) is roughly equivalent to breathing $4.4 \times 10^5 \text{ ug/m}^3$ over a 24 hour period, a dose which is almost 100 times greater than the highest concentrations measured in the office building studied by Yocum.

DIMETHYLNITROSAMINE (DMN).

In air, the primary sources of DMN appear to be tobacco smoke and emissions from industrial processes (see IARC, 1978 for review). In buildings polluted with tobacco smoke, measurements up to 0.24 $\mu\text{g}/\text{m}^3$ have been reported (cited in IARC, 1978). In one report, even higher levels were measured in the interior of new motor vehicles (Seifert, 1982). Most measurements appear to be substantially lower (Matushita and Mori, 1984; IARC, 1978) (see Table 1). In outdoor air, except in certain isolated cases near industrial pollution sources, levels are quite low. Seifert (1982) reported measurements ranging between 0.002-0.1 $\mu\text{g}/\text{m}^3$, and frequently concentrations are below detection limits (IARC, 1978). Dimethylnitrosamine also is found in some water sources, occurs naturally in foods, and is even endogenously produced in the digestive tract. Chlorination of drinking-water can result in DMN levels of 0.02-0.82 $\mu\text{g}/\text{l}$ (Cohen & Bachman, 1978: cited in IARC, 1978). Assuming humans drank a liter of this water daily, this would correspond to breathing air containing 0.04 $\mu\text{g}/\text{m}^3$ of DMN, which is similar to intake in a smoke-filled room. Similar levels of exposure can come from many foods, including cheeses, meat and fish, and alcoholic beverages. Quite high levels (up to 80 $\mu\text{g}/\text{kg}$) have been found in some meats, notably frankfurters (Wasserman, et al., 1972: cited in IARC, 1978). If one assumes consumption of 200 g of such meat per day, this is roughly equivalent to breathing an atmosphere at 0.8 $\mu\text{g}/\text{m}^3$. Obviously, the total intake of DMN will vary enormously for different

individuals, depending on the time spent in smoke-filled rooms, consumption of certain foods, etc.

Dimethylnitrosamine is a well documented carcinogen in rodents. The data used for the risk estimated in Table 6 were estimated from a study in rats, in which DMN was administered daily as an oral dose over the lifetime of the animals. The lowest dose producing cancer in this study was 50 ug/kg (cited in Gold, et al., 1984). Again, using the rough route conversion method, this corresponds to breathing 78 ug/m³ 24 hours each day. This value is similar to the dose producing cancer in an inhalation experiment in rats and mice (200 ug/m³) (Moiseev & Benemansky, 1975: cited in IARC, 1978). An important consideration in evaluating the carcinogenic risk from DMN is the observation that, unlike many other carcinogens, DMN is capable of inducing cancer after only a single dose. DMN is also mutagenic in most mutagenesis test systems (reviewed in IARC, 1978), though doses required to induce mutagenesis are very high compared to the daily doses used in the cancer studies. Single doses ranging from 4.4 mg/kg to 5,000 mg/kg, in various tests involving in vivo administration (including transformation in vitro of cells taken from treated animals, the dominant lethal assay, chromosome aberration, and host mediated assays) were required to induce an effect. These are single dose studies, and we have not yet located data from chronic mutagenesis studies, which would be more relevant to compare to doses that produce cancer.

Finally, we have located one reproductive study, in mice, where DMN administered for 10 weeks before and during pregnancy in the

drinking water at only 0.1 ppm (roughly equivalent to inhalation of 13 ug/m^3) caused a significant increase in perinatal death (Anderson, et al, 1978). The same author also reported a carcinogenic effect in strain A mice in offspring of dams treated during pregnancy with only about 0.90 ug/kg/day in the drinking water (Anderson, et al, 1979). The effective dose is difficult to evaluate in this study because exposure continued after birth. However, calculated only on the basis of maternal exposures the dose was extremely small, corresponding to inhalation of less than 1 ug/m^3 in air. The effective dose may have been much higher, however.

Because of the multiple sources of possible exposure to DMN, and lack of the information necessary to combine these in an overall estimate of exposure, an estimate of overall risk is not really possible. Considering only indoor air exposures, which, especially for people consuming certain foods, may be a small proportion of their total daily intake, the lowest estimated daily dose producing cancer (78 ug/m^3) is only about 100 times higher than the very high indoor concentrations reported by Seifert (1982), but over 1,000 times the value more commonly reported in smoke-filled rooms. The lowest effective dose in the reproductive study is only about 16 times the concentration reported by Seifert.

ETHANOL

Ethanol is a ubiquitous constituent of indoor air. It is a common solvent found in many consumer products such as perfumes, deodorant sprays, etc., and is also a constituent of human breath resulting from both normal metabolism and alcohol consumption. In the several studies we have reviewed (Seifert, 1982; Molhave, 1979; Johansson, 1978; Wang, 1975) indoor air concentrations vary from a few $\mu\text{g}/\text{m}^3$ up to several hundred (Molhave, 1979). Concentrations of ethanol are highly correlated with the presence of humans, which reflects the important contributions to the total concentration from human breath and personal consumer products (Johansson, 1978). Other sources are also implied, however, suggested by the observation of Molhave (1979), that ethanol concentrations in new homes are substantially higher than in older homes.

Ethanol has an odor threshold of $1.9 \times 10^6 \mu\text{g}/\text{m}^3$ (TLV Doc., 1985), [Verschueren, 1983, says $9.8 \times 10^4 \mu\text{g}/\text{m}^3$ (geom. mean)] [100% odor recognition concentration = $1.2 \times 10^7 \mu\text{g}/\text{m}^3$] and does not cause irritation of the eyes or respiratory tract until very high concentrations are reached (almost $1 \times 10^7 \mu\text{g}/\text{m}^3$). After UV irradiation, in a mixture with NO_2 , ethanol at $3.8 \times 10^4 \mu\text{g}/\text{m}^3$ produces mild eye irritation after short term exposure (Wayne and Orcutt, 1960), due to generation of photochemical products such as ozone.

Ethanol appears to be a weak carcinogen. Lifetime doses of 2.5 g/kg/day administered in the drinking water to rats produced a significant increase in tumors in the liver, pancreas, pituitary, and

adrenal glands (Gold, et al., 1986). These doses are more than 10,000 times higher than the highest indoor air concentrations recorded in Table 1. There has been a great deal of discussion and controversy surrounding the possibility that ethanol, at moderate doses, may cause adverse reproductive effects in humans (e.g., see Shepard, 1983). The available evidence suggests that abnormalities may occur when mothers drink more than 2 alcoholic beverages per day while pregnant. If we assume 2 drinks per day correspond approximately to 2 ounces of alcohol per day, this would roughly indicate that equivalent intake from airborne sources would require a concentration in air of a minimum of 2.7×10^6 ug/m³ (assuming 100% absorption). This is almost 5,000 times the highest value measured in homes.

ETHYLAMINE

Ethylamine was one of the major organic chemicals found in an energy-efficient office building in which employees complained of odors and eye irritation, headaches, and lassitude (Yocum, et al., 1984). The highest concentration measured was 750 ug/m^3 . After adjustments to the ventilation were made, the concentration of ethylamine was dramatically reduced to only about 1 ug/m^3 . Other amine derivatives were also found, and were also reduced after adjustment of the ventilation, so it is uncertain how much ethylamine contributed to the adverse health effects. It may have contributed to the odor problem, since its odor threshold is only about 290 ug/m^3 (geom. mean) and the 100% odor recognition level is $1,500 \text{ ug/m}^3$ (Verscheren, 1983). Toxicology data on ethylamine is limited (RTECS, 1984). The lowest dose producing a toxic effect that we have found is 100 ppm, roughly equivalent to $5.5 \times 10^4 \text{ ug/m}^3$, which, in rabbits, caused irritation of the cornea, and produced lung, liver, and kidney damage after exposure for a six week period (Brieger & Hodes, 1951: cited in TLV Doc., 1985). This dose is about 75 times higher than the highest concentration recorded in the complaint office building.

ETHYLBENZENE

Ethylbenzene is a common constituent of indoor air (DeBortoli, et al., 1985; Lebert, et al., 1984; Wallace, et al., 1984; Pellizzari, et al., 1984; Hartwell, et al., 1984 Sterling, 1984). The highest concentration reported in homes in the studies we have reviewed was 320 ug/m^3 (Hartwell, et al., 1984a), and the median concentrations in the 4 studies that examined indoor air in homes were 14 ug/m^3 (DeBortoli, et al., 1985), 5 ug/m^3 (a mean concentration) (Lebert, et al., 1984), 6.5 ug/m^3 (Wallace, et al., 1984), and 6.1 ug/m^3 (Hartwell, et al., 1984), which are all quite similar. Similar levels were reported in an energy-efficient office building (Pellizzari, et al., 1984a), though there appeared to be considerable variation between concentration levels measured in different offices. Finally, a comparatively high level was reported in a hospital - $8,000 \text{ ug/m}^3$ (Sterling and Sterling 1984). This measurement may not be typical of all hospital environments. It was made in a laboratory using organic solvents in Harlem Hospital in New York (Sterling, personal commun.). Ethylbenzene is also a common constituent of outdoor air, but occurs in higher concentrations in indoor air. The mean indoor/outdoor ratios in the studies we reviewed ranged between about two to six. The indoor and outdoor concentrations were not significantly correlated in one study (Hartwell, et al., 1984a), suggesting indoor sources. Ethylbenzene is only one of a number of alkyl benzenes that are important indoor contaminants. Petroleum distillate fractions have been suggested as a possible source of many of these (DeBortoli, et al., 1985).

Ethylbenzene has a TLV of $4.4 \times 10^5 \text{ ug/m}^3$, over 1000 times the highest concentration reported in homes. At concentrations higher than this, there have been reports of fatigue, headaches, and irritation of the respiratory tract (Bardodej and Bardodejova, 1970). There is one report (Battelle, 1981) indicating ethylbenzene may cause developmental abnormalities in offspring of rats after inhalation by dams of $4.2 \times 10^5 \text{ ug/m}^3$ for 7 hours a day during pregnancy. The estimated equivalent exposure over a 24 hour period would then be 1.2×10^5 , which is about 400 times greater than the highest concentration in homes measured in the four studies. The dose producing reproductive abnormalities in rats is only about 15 times higher than the concentration reported in Harlem Hospital. Thus, some risk may exist from exposure of pregnant women to such very high doses in hospitals. The odor threshold is only 400 ug/m^3 (Molhave, 1979), and it would thus most likely be quite noticeable at these high concentrations.

FORMALDEHYDE

A great deal has been written about formaldehyde contamination in indoor air, primarily from particle board and urea-formaldehyde foam insulation (UFFI) (reviewed in Anon, 1984; EPA, 1984d). Our purpose here is not to review the formaldehyde case exhaustively, but to provide a context for evaluating potential risks of other organics, the analysis of which is the major focus of this report.

In specialized residences such as mobile homes and UFFI-homes, measured levels of formaldehyde have been recorded at concentrations higher than several thousand ug/m^3 , but mean values in multi-home studies tend to be much lower (reviewed in Anon, 1984). For example, in 6 studies of some 2000 or more mobile homes or homes with UFFI, both complaint and non-complaint homes, mean concentrations were, in ug/m^3 : 150, 67, 475, 1124, and 116. By way of comparison, formaldehyde concentrations in non-UFFI, non-specialized homes tend to be lower. Among such studies (also reviewed in Anon, 1984) covering over 500 homes, mean values were, in ug/m^3 , 37, 43, 62, and 58, with the highest values recorded being more than 375 ug/m^3 . Thus, on the average, formaldehyde in the specialized residences was about 8 times higher than in standard, non-complaint residences. Formaldehyde also tends to be somewhat higher in new buildings (e.g., see Anon, 1984; Berglund, et al., 1982), on the order of 100 ug/m^3 .

Formaldehyde is a carcinogen in rats, at concentrations as low as about 7,000 ug/m^3 (Kerns, et al., 1983). This is similar to the highest concentrations recorded in UFFI or complaint homes. Since exposure of humans to these concentrations occurs only rarely, and

for short duration, and since irritation at this concentration would be acute, of greater interest is the fact that the dose producing cancer in rats is only a little more than an order of magnitude higher than the average concentration of formaldehyde in specialized residences, and less than 200 times the mean value in standard residences. These are not large ranges over which to extrapolate effects of carcinogens, and a potential cancer risk from long term exposure to formaldehyde in homes and buildings should be considered. This is especially of concern because in the rat studies animals were exposed for only 6 hours each day. The concentration corresponding to an equivalent intake over 24 hours, such as would occur in many homes, would be only about 1750 ug/m^3 , which is only a factor of about 30 greater than the average concentrations found in homes.

There is some evidence that formaldehyde can cause reproductive effects, though it is not definitive (IARC, 1982a; Anon, 1984; Shepard, 1983; Barlow & Sullivan, 1982). One inhalation study in rats reported that 1000 ug/m^3 continuous exposure during pregnancy caused a prolongation of pregnancy accompanied by histological changes (Gofmekler, 1968: cited in Barlow and Sullivan, 1982). However, the results of this study have been considered questionable because of the incomplete nature of the report (Barlow & Sullivan, 1982). It was considered supportive evidence by another group (Rowen-West, et al., 1987: D. Bishop, personal commun.), though other studies cited considered adequate by this group used much higher doses [e.g., Marks, et al., (1980)]. An additional suggestion that

formaldehyde may pose some reproductive risk from exposure to relatively low doses comes from a study of women exposed to concentrations of formaldehyde in an occupational situation that were estimated to be 430 ug/m^3 (Olson & Dossing, 1982: cited in Anon, 1984 and IARC, 1982a). This study reported that these women had a history of menstrual irregularities. 430 ug/m^3 is quite a low concentration, several times lower than the TLV of 1500 ug/m^3 , and in the range that can be tolerated by most people. It is important that more extensive animal and human studies be undertaken to define more adequately any potential for reproductive effects that formaldehyde might have. Several such studies were reported as either planned or underway (Anon, 1984).

The most immediate, obvious, and well established effect of formaldehyde is its effect as an acute irritant. At doses of 125 ug/m^3 and higher most people experience irritation of the eyes, nose and throat (Anon, 1984). This can occur without detection of odor. The 100% odor threshold is 1300 ug/m^3 (Verschueren, 1983), but some individuals can detect concentrations as low as 60 ug/m^3 (NAS, 1981). Thus, there appears to be great variation in sensitivity among individuals. The TLV is 1500 ug/m^3 (TLV Doc., 1985). In animal experiments, the lowest concentration producing what might be termed a systemic toxic effect appears to be 390 ug/m^3 , which caused increased airway resistance in the guinea pig (Amdur, 1960: cited in TLV Doc., 1985).

HEPTACHLOR

The only remaining use of heptachlor is for subterranean treatment of wood destroying insects. It is usually applied in a mixture with chlordane, in which chlordane is the major component. However, because of a significant difference in vapor pressure, heptachlor is usually present in air at higher concentrations than chlordane (Jurinski, 1984). In the two reports we reviewed, heptachlor concentrations as high as 15 ug/m^3 were found in the basement of a treated home 3 months after application (Jurinski, 1984). In the same home, chlordane concentrations were only 0.4 ug/m^3 . The average value reported in this study, which measured airborne levels in 7 buildings, was however only 3.2 ug/m^3 .

Heptachlor is a carcinogen in mice (IARC, 1979b; Gold, et al., 1984), and possibly also in rats (Gold, et al., 1984). In the mouse study the chemical was administered orally, and the lowest dose which produced a significant carcinogenic effect was 1.3 mg/kg/day administered over the lifetime of the animals. An upper limit of risk can be estimated by assuming that lifetime exposures might never exceed a cumulative dose equivalent to exposure to the maximum concentration of heptachlor measured in indoor air (15 ug/m^3) for 1 year. The daily dose would then be equivalent to breathing 1/70th of this concentration over a 70 year lifetime (0.21 ug/m^3). The National Academy of Sciences has suggested an exposure limit of 2 ug/m^3 , almost 10-times higher than this value (cited in Jurinski, 1984). Using the exposure estimate of 0.21 ug/m^3 , and assuming the TD50 lies on a linear dose response curve, the number of expected

cancers per 10^5 people exposed over a lifetime would then be about 13.

Of possible interest is a report (Cerey, et al., 1973: cited in IARC, 1979b) that long term exposure of rats to only about 40 ug/kg/day resulted in a significant number of resorbed fetuses in the second and third generation, and cytogenetic effects in the bone marrow of the treated animals. This is more than 30 times lower than the dose which produced cancer in the test cited above, and much closer to the concentrations reported in treated homes. 40 ug/kg/day is roughly equivalent to the dose expected from exposure to about 60 ug/m³, which is only about 4 times the maximum concentration cited above. The Cerey, et al. study, however, only appeared as an abstract, and though not criticized by IARC (1979b), should not be considered definitive without the full report.

N-HEXANE

n-Hexane is a ubiquitous organic chemical in indoor air (Lebret, et al., 1984; DeBortoli, et al., 1985). Its presence has been correlated with the concentration of respirable suspended particulate matter (RSP), suggesting that tobacco smoking is a source. It is also a common solvent. Concentrations are highly variable among different homes. 590 ug/m³ was found in one home, but the median value among 15 homes was only 14 ug/m³ (DeBortoli, et al., 1985).

Information on the toxicology of n-hexane is scant, but the chemical does not appear to be highly toxic. It has produced essentially negative results in reproductive studies in animals. For example, administration of 1000 ppm for 6 hours each day (roughly equivalent to 9×10^5 ug/m³ for 24 hours each day) during different periods of pregnancy caused only transient postnatal delay in growth of offspring in a rat study (Bus and Tyl, 1979). This was a minimal effect at a concentration 10 times the TLV. Also, the report is contradicted by another study using the same dose levels (cited in Shepard, 1983). Much lower concentrations of n-hexane (20 ppm) in the presence of small amounts of NO₂ and UV-irradiation, produce eye irritation in humans after only 90 seconds exposure (Wayne and Orcutt, 1960), due presumably to the generation of ozone and other photochemical products.

Even the highest concentration measured in the homes surveyed in the two studies we have reviewed (590 ug/m³) is over 100 times lower than the lowest concentration observed to produce any effect (Wayne and Orcutt, 1960). Since the reproductive study in rats recorded

only a minimal effect, at an over 1000 times higher concentration ($2.9 \times 10^5 \text{ ug/m}^3$); it seems unlikely that n-hexane poses any risk at concentrations found in homes.

However, alkanes, as a group, can be present at rather high concentrations in indoor air. For example, DeBortoli, et al. (1985) report the total concentration of alkanes ($\text{C}_6\text{-C}_{12}$) in the homes they surveyed to be as high as $13,000 \text{ ug/m}^3$. Since these chemicals are quite similar in chemical structure, the mechanisms of action of some may overlap. It may therefore be important to consider the combined effects of alkanes in evaluating overall risk.

HYDROGEN CYANIDE (HCN)

The primary source of HCN in indoor air is cigarette smoking. In two studies measuring levels in smoke-filled rooms, concentrations as high as 85 ug/m^3 were recorded with a mean value of 48 ug/m^3 (Hugod, 1984).

Hydrogen Cyanide is lethal at high doses, though there is not consensus in the literature as to a chronic LED for lethality. Though one estimate suggests that exposure to as little as $12,000 \text{ ug/m}^3$ for 30 minutes would be lethal to about 1% of people exposed (McNamara, 1976), much higher concentrations are usually cited. For example, a review by Einhorn (1975) indicates exposure to as much as $40,000 \text{ ug/m}^3$ for several hours causes only slight symptoms (headache).

The TLV for HCN cyanide is about $10,000 \text{ ug/m}^3$ (Verschuieren, 1983). The only chronic study we have found is that of El Ghawabi, et al. (1975: cited in TLV Doc., 1985), in which workers exposed for periods of about 7 years to concentrations between 4,500 and 12,500 ug/m^3 exhibited a variety of symptoms such as headaches, weakness, changes in taste and smell, irritation of throat, and vomiting. The threshold odor-recognition concentration has been reported as low as about 200 ug/m^3 (Verschuieren, 1983), a factor of about two compared to the highest levels reported in heavily smoke-filled rooms.

LINDANE

Lindane, an insecticide, has led to contamination problems in homes treated with wood preservatives (Van der Kolk, 1984; Gebefugi & Korte, 1984). It has been found in the air of homes, even long periods after treatment, at concentrations as high as 40 ug/m³ (Van der Kolk, 1984). In 1977 EPA issued a rebuttable presumption against lindane based on its oncogenicity, fetotoxicity, and reproductive effects. As a result, though EPA intends to curtail some uses of lindane (EPA, 1983), it is still a widely used pesticide.

Lindane is a carcinogen in mice after lifetime oral administration (IARC, 1979b). Gold, et al. (1984) have estimated a TD50 as low as 12 mg/kg/day. This roughly corresponds to the dose inhaled from continuous 24-hour exposure to airborne concentrations of 9200 ug/m³, which is about 230 times greater than the highest concentrations reported by Van der Kolk in the air of homes treated with wood-preserving paints several months after application. It is 51,000 times the indoor air concentrations reported in the only other study we reviewed (Gebefugi and Korte, 1984). Since exposure to lindane in contaminated homes comes not only from the air, but from dust particles, and by dermal exposure from contaminated clothing and furniture (Gebefugi and Korte, 1984), overall risk would be best determined by including all of these sources.

Lindane has also been observed to have adverse reproductive effects in animals (Naishtein & Leibovich, 1971: cited in IARC, 1979b). An oral dose of 0.5 mg/kg/day for 4 months to female rats inhibited fertility, lowered the viability of embryos, and delayed

their physical development. This dose roughly corresponds to daily exposure to 780 ug/m^3 , which is only about 20 times the highest concentrations reported by Van der Kolk long periods after treatment with wood preservatives. We have not found irritation data or odor thresholds for lindane, so it is not clear at what concentrations residents might become aware of the presence of the chemical. In view of the many sources of exposure, and the fact that exposure for very long periods is not required to produce reproductive effects, lindane residues in homes treated with wood preservative paints could pose some reproductive risk.

MALATHION

Malathion, an organophosphate pesticide, is a widely used broad spectrum insecticide. Measurements in homes of airborne concentrations up to 2 ug/m^3 have been reported (Beall and Ulsamer, 1981; Reinert, 1984). Most of the organophosphate insecticide residues on food are malathion (reviewed in IARC, 1983b). In the U.S., studies have estimated average levels of 0.00013 mg/kg of food (though elsewhere in the world --i.e., India -- levels in food have been measured as much as 20,000 times higher). Estimates of daily intake from food, in studies in Canada, range between less than $0.0001\text{--}0.042 \text{ ug/kg}$ body weight. The upper limit of this is roughly equivalent to breathing airborne concentrations of 0.15 ug/m^3 over a 24-hour period. Hence, concentrations such as those cited by Beall and Ulsamer (1981) and Reinert (1984) represent a much greater source of exposure than pesticide residues on food.

Malathion is a relatively non-toxic chemical. The TLV for malathion is $15,000 \text{ ug/m}^3$. It is a weak inhibitor of acetylcholinesterase. In a human experiment, Moeller and Rider (1962: cited in IARC, 1983b) administered a daily oral dose for 14 days roughly equivalent to inhalation of 1200 ug/m^3 every 24 hours. This is much higher than the maximum concentrations reported in indoor air (2 ug/m^3). There is little evidence for carcinogenic potential of malathion. Thorough bioassays in rats and mice have been judged negative by the NCI/NTP (RTECS, 1984). IARC (1983b) has also concluded there is no evidence that malathion is a carcinogen.

METHANOL

Methanol is one of the most common bioeffluents found in indoor air, and its presence is correlated with the presence of people (Wang, 1975). (The other three most common bioeffluents are CO₂, ethanol, and acetone.) Other sources are certain foods and liquors (Wang, 1975). In several classrooms filled with students, Wang found the average concentration of methanol of about 52 ug/m³. Other studies report on the order of 100 ug/m³ (Seifert, 1982).

At very high concentrations methanol can produce neurological effects (RTECS, 1984; Seifert, 1982). The TLV is 260,000 ug/m³, many times higher than indoor concentrations. The odor threshold is roughly 7.3×10^4 (geom. mean) (Verschueren, 1983). The lowest dose that we have found which caused any toxic response was several times higher than this: 270,000 ug/m³. In a study of workers, exposure to this concentration caused severe headaches (Kingsley & Hirsch, 1955: cited in TLV Doc., 1985). This is almost 3000 times higher than the highest concentrations reported in indoor air by the three studies we reviewed (Wang, 1975; Seifert, 1982). At much lower concentrations (6700 ug/m³) however, in combination with small amounts of NO₂ and ultraviolet radiation, methanol can cause moderate eye irritation (Wayne and Orcutt, 1960). Even this concentration is almost 70 times the highest levels reported in homes.

NICOTINE

The source of nicotine in indoor air is, of course, tobacco smoking. We reviewed three studies which measured indoor air concentrations of nicotine. In two of these (Hugod, 1984; Hoffmann, et al., 1984) levels were measured in small rooms, continuously polluted with side-stream smoke from cigarettes. Quite high levels were reported, up to 130 and 280 $\mu\text{g}/\text{m}^3$ respectively. Three studies reported measurements in the field, from various locations in public buildings in what appeared to be relatively congested smoking areas such as a coffee shop, bar, etc. (Matsushita and Mori, 1984; Malaspina, et al., 1984) and in a complaint office building (Yocum, et al., 1984). In these studies the nicotine concentrations were lower, ranging from 10-55 $\mu\text{g}/\text{m}^3$. Almost all detectable nicotine was removed by adjusting the ventilation in the complaint office building.

While there is some evidence that nicotine has co-carcinogenic properties (Bock, 1980), the results are complex (some doses appear to enhance carcinogenesis and others to inhibit it). Of possibly greater interest are studies examining effects of nicotine on the fetus during pregnancy. An older study in the rhesus monkey reported that single intravenously administered doses of nicotine produced tachycardia in the fetus (Suzuki, et al., 1971). This is supported by more recent work. Fazel and Goeringer (1983) found a spectrum of cardiac defects in newborn mice after exposure of dams on day 10 of gestation to smoke from 2 cigarettes (approximately 1.9 mg nicotine). Also, Erikson, et al. (1983) reported changes in fetal breathing movements in healthy women in late gestation after smoking

a single cigarette. These effects were correlated with maternal nicotine levels, though other components of smoke cannot be excluded as possible causes. Since all of these studies used single doses, or doses administered over very short time periods, it is not clear that these can be extrapolated to estimate an equivalent chronic exposure. But it would be important to determine what such equivalent doses would be, since the doses used in these studies are quite close to some indoor air exposures.

Significantly higher doses, in the rat (0.05 mg/ml administered in the drinking water for 23 days during gestation: roughly corresponding to 4500 ug/m³) reduced the size of newborns (Moser & Armstrong, 1964: cited in Shepard, 1983).

It is of interest that the oral lethal dose of nicotine for humans has been reported as only 1 mg/kg (quoted in Suzuki, et al., 1971), which is considerably lower than the rodent, or rhesus monkey LD50s, suggesting that humans may be more sensitive to toxic effects of nicotine than these laboratory animals. If this greater sensitivity extends to effects on the fetus during pregnancy, exposure of pregnant women to nicotine in smoking environments could be of some concern.

PENTACHLOROPHENOL (PCP)

Pentachlorophenol has commonly been used as a pesticide, and indoors as a wood preservative. A decision has been made in the Netherlands that no indoor application should take place, and in the U.S., the EPA issued a rebuttable presumption against PCP in 1978 (EPA, 1978). In the three studies we reviewed, PCP was reported at concentrations as high as 200 ug/m³ in homes 1-3 months after application (Van der Kolk, 1984). Values reported in the other two studies were much lower. In an energy-efficient office building in which complaints were registered, Levin and Hahn (1984) reported maximum values of 50 ug/m³, and an average value of 27 ug/m³. Gebefugi and Korte (1984), reported a concentration of 0.6 ug/m³ in a complaint home more than 9 years after treatment. The average exposure of workers in a number of factories using PCP as a wood preservative was 13 ug/m³ (Arsenault, 1976: cited in IARC, 1979b). Exposure to PCP may also occur from other sources (e.g., pesticide residues on food), and many people have sufficient exposure such that PCP was detected in a large majority of homes in a random sample (cited in Levin and Hahn, 1984).

In rats, the oral LD50 of PCP is roughly equivalent to 2.2×10^5 ug/m³ (IARC, 1979b); the TLV for PCP is 500 ug/m³; and at 1,000 ug/m³ it causes painful irritation to the eyes and upper respiratory tract (Verschueren, 1983). The lowest dose we have found which produced a toxic effect was in a 90 day study in rats in which PCP was administered daily by the oral route. As low as 3 mg/kg/day (roughly equivalent to 4,100 ug/m³), produced haemolytic changes, increased

liver and kidney weights and hepatic alterations (Johnson, et al., 1973: cited in IARC, 1979b).

Pentachlorophenol has been negative in carcinogenesis tests in rats and mice (IARC, 1979b; Gold, et al., 1984). It has shown some potential to produce adverse reproductive effects. In one rat study, orally administered doses of 5, 15, 30 and 50 mg/kg were given to rats during gestation on days 6-15. The dose of 5 mg/kg/day produced delayed ossification of skull bones in the fetus (Schwetz, et al., 1974c: cited in Shepard, 1983; Rowen-West, et al., 1987; and EPA, 1984c). This is roughly equivalent to daily exposure to 7,700 ug/m³, which is about 40 times higher than the highest doses of PCP reported in complaint homes.

In evaluating the potential risk from exposure to PCP, it is important to keep in mind that commercially produced PCP contains significant amounts of chlorinated dibenzo-para-dioxins and polychlorinated dibenzofurans (IARC, 1979b). This should be taken into account in overall evaluations of risk.

TETRACHLOROETHYLENE

Tetrachloroethylene (perchloroethylene) was frequently monitored in the studies have reviewed (DeBortoli, et al., 1985; Lebret, et al., 1984; Wallace, et al., 1982; 1984; Monteith, et al., 1984; Hartwell, et al., 1984a,b; Pellizzari, et al., 1984). The mean indoor concentration, among results reported by these groups, was 4.5 ug/m³, and the maximum was 250 ug/m³ (Hartwell, et al., 1984a). [Wallace, et al., (1982), in a personal exposure study, reported a maximum concentration of 718 ug/m³.] Though tetrachloroethylene is a commonly monitored chemical, it is not always detected. Thus, Lebret, et al. (1984) and Monteith, et al., (1984) detected it in only about 50% of samples. Others (Hartwell, et al., 1984a,b) report detection in nearly 90% of samples. This could reflect differences in the sampling method and protocol resulting in samples below the limit of analytical detection or differences in the study population. In general, when mean values are compared, levels of tetrachloroethylene, though somewhat higher indoors than outdoors (mean ratios were between 1-2), appear to be very different only in isolated cases. Thus, Lebret, et al. (1984) monitored indoor air of four homes over a six-month period, and found coefficients of variation of 32, 61, 98, and in one home, 286%. In Monteith, et al.'s study, concentrations in manufactured housing varied over more than 1500 fold, as compared to only a 40 fold outdoors. And, in the study of Pellizzari, et al., (1984), the mean indoor/outdoor ratio was only slightly more than 1, although a few individual measurements were very high (98 ug/m³). These findings are consistent with a

substance which has both indoor and outdoor sources, with indoor sources only occasionally present. This might be expected for tetrachloroethylene whose major use indoors appears to be as a cleaning solvent. A number of halogenated hydrocarbons are common constituents of drinking water, and it is therefore useful to know the relative proportion of human intake that is accounted for by air as compared to water. Wallace, et al., (1982) examined this at two sites, one in North Carolina and the other in Louisiana. They found very low levels of tetrachloroethylene in drinking water, and reported that almost all intake was from air.

The adverse health effects of tetrachloroethylene have recently been reviewed by EPA (EPA, 1985a). Though there is some epidemiological evidence in dry-cleaning workers that tetrachloroethylene can cause human cancer, these studies are considered equivocal by EPA. The major evidence for carcinogenic potential of this compound is from results of a cancer bioassay in mice. Animals were dosed by gavage over a lifetime, and the lowest dose producing an effect was roughly equivalent to 1.8×10^5 ug/m³ (Gold, et al, 1984). This concentration is very near the lower limit of observed toxic effects in humans. Dizziness, eye and mucous tissue irritation, headache and sleepiness have been reported after relatively short-term exposure to about 6.8×10^5 ug/m³ (Stewart, et al., 1977 - cited in EPA, 1985a).

The "inhalation-equivalent" dose cited above which produced cancer in rats is equivalent to lifetime inhalation of concentrations some 720 times greater than the highest concentration reported in the

studies reviewed [excluding the very high value reported by Wallace, et al., (1982) in a personal exposure study]. It is some 40,000 times higher than the mean concentration reported. The other toxic effects discussed above occurred at roughly the same concentrations (about 10^5 - 10^6 ug/m³).

In laboratory animals, several studies have reported biochemical changes in animals treated with doses as low as 1×10^5 , though there appears to be some uncertainty as to the validity of these studies (discussed in EPA, 1985a). Reproductive effects (reduction in fetal body weight) have been reported after exposure of mice via inhalation 7 hours per day for 10 days during pregnancy to concentrations of 2.0×10^6 ug/m³ (Schwetz, et al., 1975--cited in EPA, 1985a).

TRICHLOROETHYLENE

Trichloroethylene is a common component of both outdoor and indoor air, and has frequently been measured in studies monitoring concentrations of organics in indoor air (Hartwell, et al., 1984a,b; Wallace, et al., 1982; Turiel, et al., 1981; Pellizzari, et al., 1984; Wallace, et al., 1984; Lebret, et al., 1984; DeBortoli, et al., 1985). In general, trichloroethylene is present at quite low concentrations, usually only a few ppb or less, and in most studies, about half the time it is not detected. In general, it also does not appear to be present indoors at concentrations that are a great deal higher than concentrations in outdoor air (e.g., Hartwell, et al., 1984a,b; Turiel, et al., 1981). An exception is the measurement reported in a new, energy-efficient office building (Pellizzari, et al., 1984), which was more than 100 times the outdoor concentration. It thus appears, that this common solvent has both outdoor and indoor sources, but that in most homes the levels indoors are not greatly increased over those outdoors.

Toxic effects of trichloroethylene were recently reviewed (Kimbrough and Mitchell, 1985). Trichloroethylene is a carcinogen in mice when administered orally over the lifetime of the animal (Gold, et al., 1984). The lowest average daily dose causing an incidence of tumors higher than in the controls (724 mg/kg/day) is roughly equivalent to 557,000 ug/m³ in air breathed in over a lifetime. In all of the studies we have surveyed, the highest concentration of trichloroethylene recorded was 183 ug/m³ (Wallace, et al., 1982),

which is more than 3,000 times lower than the lowest dose producing cancer in mice.

There are several older studies that indicate irritant effects of trichloroethylene at rather low doses ($2.7 \times 10^4 \text{ ug/m}^3$) can occur (RTECS, 1984). However, these must be evaluated with suspicion, as trichloroethylene, in the past, contained several percent of hepatotoxic ethane derivatives (TLV Doc., 1985). At high concentrations, trichloroethylene does have toxic effects on the central nervous system, and in fact, was used as an anesthetic. One report indicated headaches, dizziness, and sleepiness were caused in humans after exposure to concentrations of $5.7 \times 10^4 \text{ ug/m}^3$ (TLV Doc., 1985). This is near the odor threshold of $2.4 \times 10^5 \text{ ug/m}^3$ (geom. mean) (Verschueren, 1983), and several hundred times higher than even the highest indoor air trichloroethylene concentrations of which we are aware. Also, of some interest is the observation that simultaneous exposure to caffeine or alcohol may markedly augment the toxic effects of trichloroethylene (Stewart, et al., 1977: cited in TLV Doc., 1985).

Of some interest is one report that trichloroethylene, at 100 ppm for 4 hours/day, 7 days/week from day 6-20 of pregnancy, produced a significant reduction in fetal weight and an increase in resorptions (Healy & Wilcox, 1978: cited in Barlow & Sullivan, 1982). This dose is roughly equivalent to daily exposure of humans to $9.1 \times 10^4 \text{ ug/m}^3$. This study, however, only appeared in abstract form, and other more completely reported studies were largely negative at much higher doses. It is difficult to draw a definitive conclusion,

though, because in the negative studies the chemical was administered earlier in pregnancy. Even if the positive study were valid, the concentration was 500 times the highest trichloroethylene concentration reported in Table 1, again suggesting no significant risk.

1,2,4-TRIMETHYLBENZENE AND 1,3,5-TRIMETHYLBENZENE (MESITYLENE)

These are common air pollutants, occurring in over 90% of homes examined in the air monitoring studies we reviewed (Lebret, et al., 1984; DeBortoli, et al., 1985; Molhave, 1979; Hawthorne, et al., 1984). 1,2,4-trimethylbenzene, in the two studies which measured both isomers, was present at considerably higher concentrations than mesitylene. The mean concentration reported among the various studies for the 1,2,4 isomer was 54 ug/m^3 , and for the 1,3,5 isomer, was 4.7 ug/m^3 . Whereas the amounts of the 1,3,5 isomer measured were quite consistent among the studies, the amounts of the 1,2,4 isomer varied greatly (see Table 1). Both isomers are present indoors at concentrations much higher than outdoors (as much as 23 times higher for 1,2,4-trimethylbenzene).

Workers in a painting shop complained of fatigue and headaches after inhalation of as little as $5.4 \times 10^4 \text{ ug/m}^3$ (Battig, et al, 1956). The odor threshold for the 1,2,4-isomer is about one - tenth that of the 1,3,5-isomer ($450 \text{ vs } 4500 \text{ ug/m}^3$) (Molhave, 1979). Both trimethylbenzene isomers in an unconfirmed study, were reported to produce lethal effects in rats after several hours inhalation of only $2 \times 10^4 \text{ ug/m}^3$ (Dyshinevich, 1979). This author recommended that the release of these compounds from materials be limited to no more than 1 ug/m^3 . This study is in conflict with another inhalation study (Rossi & Grandjean, 1957: cited in TLV Doc., 1985) in which no toxic effects were noted in rats exposed to $8.5 \times 10^6 \text{ ug/m}^3$ for periods of 10 to 21 days. Without more information, it is not possible to resolve these conflicting reports. The few other available studies

have used other routes of administration and other species, and thus are not strictly comparable. They report lethal effects at much higher equivalent doses than that reported by Dyshinevich (RTECS, 1984).

In some homes these chemicals, especially the 1,2,4 isomer, can occur at quite high concentrations relative to most other organics. For example, Molhave (1979) reported a maximum concentration of 1140 $\mu\text{g}/\text{m}^3$, which, when compared to the dose reported to produce toxic effects in humans, is a factor of about 50 times lower, assuming inhalation over a 24 hour period.

VINYLLIDENE CHLORIDE

We have reviewed two studies which measured airborne concentrations of vinylidene chloride (1,1-dichloroethylene). Wallace, et al., (1982) used personal monitors to collect 24-hour measurements, and thus reports values of combined indoor and outdoor exposures. Vinylidene chloride was found in almost all samples in this study. The maximum concentration reported was 416 ug/m^3 , and the median was 5.3 ug/m^3 . The concentration in drinking water was also measured, and was far less than the concentration found in air. Hartwell, et al. (1984b) employed overnight personal monitors for sampling, thus permitting an estimate to be made of indoor concentrations. 58 homes were surveyed in this study, and vinylidene chloride was found in a relatively low percentage of the homes. It appeared to be mainly an outdoor pollutant (the indoor/outdoor ratio was only 0.08), though a few high measurements were made indoors. The maximum indoor measurement was 12 ug/m^3 and the median was only 0.015 ug/m^3 .

Vinylidene chloride may be a weak carcinogen in rodents, though evidence for this is limited (IARC, 1982b). The lowest dose that appeared to produce a positive effect was 9.88 mg/kg/day (cited in Gold, et al., 1984). This dose was administered via inhalation to male mice over a 2 year period, and corresponds to 24 hour per day exposure to a concentration in air of about $6,900 \text{ ug/m}^3$ (estimated using Gold, et al.'s scaling factors). This is only about 17 times the maximum concentration reported in the two concentration monitoring studies discussed above (416 ug/m^3). However, it is over

1000 times higher than the median concentration reported in that study.

Vinylidene chloride also caused birth defects in the rat. Administration of 80 and 160 ppm by inhalation for 7 hours a day on days 6-15 during pregnancy caused a significant delay in ossification of the skull and other skeletal defects (Murray et al, 1979: cited in Shepard, 1983; Barlow and Sullivan, 1983; Rowen-West, et al., 1987). This occurred at maternally toxic doses, and Barlow & Sullivan (1983) suggest that much of the fetotoxicity and teratogenicity may have been secondary to this. Correction of 80 ppm for 7 hours each day to an equivalent exposure over 24 hours per day results in an estimate of 94,000 ug/m³, over 10 times higher than the daily dose reported to cause cancer.

P-XYLENE

We have located only one study (Pellizzari, et al., 1984) in which concentrations of p-xylene were reported separately, as compared to in combination with meta and ortho isomers. In this study indoor concentrations in a well ventilated home for the elderly and in a new, energy-efficient office building, were reported. Levels in the home for the elderly were much lower than in the office building, with a maximum concentration of 17 ug/m³ and a median of 9.5 ug/m³ as compared to 294 ug/m³ and 50 ug/m³ respectively in the office building. In the home for the elderly, the indoor/outdoor ratios were relatively small (about 2) as compared to the office building, where ratios were as high as 600. The xylenes are common solvents, used in paints, resins and rubber cements, and also in petroleum solvents, which no doubt were contributory sources in the new office building.

There is limited toxicological data available on p-xylene. It does not, however, appear to be highly toxic. The lowest dose producing a toxic effect in a laboratory experiment that we have located is 150,000 ug/m³, in an experiment in which mice were exposed to p-xylene or its isomers at this and higher concentrations 24 hours each day for 8 days during pregnancy. (Ungvary, et al., 1980: cited in Barrow and Sullivan, 1983; Rowan-West, et al., 1987). p-Xylene was the most potent of the three isomers, and produced some evidence of skeletal retardation at the low dose, though most effects were seen at higher doses. The low dose is over 500 times greater than the highest dose reported in the new poorly ventilated office

building, and almost 10,000 times greater than the high concentration reported in the well-ventilated home for the elderly. If we assume as an upper limit estimate, that the xylene isomers all have similar toxic potential, and further, assume their combined concentration is not likely to exceed about 1500 ug/m³ (see Table 1), then the lowest dose producing some fetal abnormality in this study would still be 100 times greater than this "upper limit" indoor concentration.

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