Acute Toxicology of Components of Vegetation Smoke*

Frank N. Dost**

Contents

*This review and analysis was supported in part by the U.S. Department of Interior, Bureau of Land Management.

**Department of Agricultural Chemistry, Oregon State University, Weniger 339, Corvallis, OR.

Reviews of Environmental Contamination and Toxicology, Vol. 119.

I. Introduction

In spite of generations of experience, the basis for respiratory and eye irritation caused by vegetation smoke is not adequately understood. Increasing concern about the long- and short-term health consequences of residential, agricultural, and forestry burning is stimulating greater interest in examining the knowledge that does exist and in designing research that will answer some of the more important questions. This review is a study of existing literature that relates to acute effects of smoke arising from combustion of vegetation.

Combustion of vegetation is one of the most common of all chemical reactions and may be the least well understood. The multitudes of products of wood and foliage combustion are still not fully identified, and the relation between products and conditions of combustion is only partly clarified. It is obvious from laboratory study that emissions vary remarkably with fuel type and combustion conditions. Behavior of combustion products in the atmosphere is also still largely unknown. With the chemical nature of smoke still somewhat mysterious, it is not surprising that the chemical basis for acute smoke toxicity is also not adequately known. Our ignorance does not surprise firefighters, who know well that there are differences in irritancy among vegetation types and burn conditions.

The nature and risk of acute and chronic human health impacts of combustion products are just as far from resolution, at a time when more and more attention is being paid to the health of forest fire fighters and the effects of smoke exposure. However, even with research gaps and the uncertainties of product identity, effects of combustion conditions on the formation of specific products, exposure, and the nature of biological effects, it is still possible to make some progress in identifying the mechanisms of smoke toxicity with the available information.

The problem of concern to this review has three segments. The first is to examine the list of known chemical and physical components of vegetation smoke, and to identify the components that cause various acute effects associated with smoke exposure. The second is obviously the estimation of exposure, and the third is the prediction of human responses under fire line and the other environmental conditions.

A fourth segment, not in the purview of this paper, is in the arena of fire technology. With sufficient understanding of the amounts of products and their effects, modification of burning practices or fire-fighting procedures

might be sought to alter the impact of emissions on certain populations, if needed.

In surveying the spectrum of vegetation combustion products to produce the kinds of acute responses associated with smoke exposure, a relatively small group stand out. The aldehydes as a group seem most important; formaldehyde and acrolein are both produced in substantial quantities and seem most likely to produce adverse effects. Formic acid may be produced directly and may be at equilibrium with formaldehyde in the atmosphere, at least in condensed moisture. There is evidence that free radical precursors may survive long enough to deliver reactive species to the lung. Particulates are most obvious, but their role as an independent entity is unknown. Ozone is produced photochemically in the upper reaches of smoke plumes and may persist long enough to be a factor as the plume comes to ground. It is not likely to be present in the immediate fire zone.

Investigation of wood and cellulose smoke has shown an apparent presence of precursors that continue to give rise to free radicals for periods long enough to have significance in smoke toxicology. There is a great variety of free radical-producing reactions in cells, involving both basic metabolic activity of cells as well as enzymatic reactions of foreign chemicals. In many cases, the pathology resulting from interaction of such species has been studied. Various studies suggest that free radical activity in the lung results from cigarette smoking and that the cell damage attributable to free radicals from an exogenous source is similar to that associated with those arising within the cell.

The role of particulates, as physical entities, in smoke irritation is completely unknown. It is reasonable to assume that airborne particulates, which are largely condensed volatile organics, must have irritant properties or carry irritant molecules. However, there is not information enough to judge their potency independently of other smoke components.

This review does not discuss carbon monoxide or acetaldehyde. Carbon monoxide is of course a product of vegetation smoke, but it is a hazard in forest burning only in rare instances. This opinion is supported by a consensus of industrial hygienists and health professionals at a recent workshop on health effects of forest fire smoke on fire fighters (Ward et al. 1989). Acetaldehyde is produced in fires but levels at all locations relative to a fire are much lower than concentrations known to produce adverse effects. Numerous studies support this conclusion. Exposures ranging from 4 wk to 28 mon to concentrations of 400 to 750 ppm produced little evidence of irritation or any other response (Appelman et al. 1986; Woutersen et al. 1986).

Chronic or irreversible disease is also not discussed here, although obviously, any acute response of sufficient magnitude could cause long-lasting effects.

The approach in this review will be first to examine the data on emissions from vegetation combustion and their fate in the atmosphere that may lead to estimates of exposure of humans at the fire site or at more distant points. The available toxicology of the materials as it relates to irritant, allergic, and other toxic properties will then be reviewed, to lead to some estimate of health consequences of exposures. Some suggested research directions are offered at the end.

There are substantial data on the toxicology of some of the substances listed, particularly the aldehydes. They already constitute well established industrial or household hazards, and as such are described in a wealth of literature. The literature on ozone seems generally to discuss much higher concentrations than might be encountered in the context of fire, but there is enough information on lower exposures to suggest possible impacts from down-plume formation. Particulate matter as such, separate from the mix of accompanying materials, has not been investigated. Studies of free radicals are still developing, and at present it seems impossible even to estimate dose-response information, which makes inferences about health impact also highly speculative.

II. Formaldehyde and Formic Acid

A. Formation and Environmental Behavior

Data on emissions of formaldehyde in open combustion of vegetation are almost nonexistent. Most of the attention to formaldehyde has been related to its generation and release in industry, emissions from structural materials in homes, and exposures of direct users such as pathologists and embalmers.

With respect to combustion products, the bulk of attention has focused on the contribution of aldehydes to the total genotoxic activity of urban emissions and residential heating emissions. The irritant and allergic responses are considered as inconveniences when compared to the prospect of serious irreversible disease. Nonetheless, to the extent that a purposeful activity such as prescribed burning is economically important, even if inconvenience is the only concern it should be mitigated if possible. It is a fact that vegetation smoke has caused exacerbation of pre-existing respiratory disease, with much greater consequence than simple inconvenience. The contribution of formaldehyde, with its irritant and possible respiratory allergic character, must be examined.

Apparently formaldehyde is ubiquitous in the atmosphere; whether it is biological in origin or arising from human activities is immaterial. Schulam et al. (1985) compared levels in Schenectady and on Whiteface Mountain in New York in the month of August. In the particular week when both sites were sampled, the urban average was 6.7 ppb, with peaks reflecting commuter travel. At a more remote site, the average was 1.3 ppb, in a range of 0.6 to

2.36 ppb. In the latter case, the measurements were made over a 2-d period. Formaldehyde levels were higher in the second night, corresponding to, or perhaps leading to an increased ozone concentration. The implication is that formaldehyde is carried in weather systems from remote areas, and therefore may survive for extended periods. According to Schulam et al. (1985), it is interesting that every sample from both sites contained detectable levels of formaldehyde.

Singh et al. (1982) have measured low molecular weight chlorinated hydrocarbons plus formaldehyde in various remote sites, and in a Pacific coastal facility where the prevailing wind is from the sea. Other than shipping there would be little industrialization for some distance upwind. They determined that the background for formaldehyde is about 400 ppt (0.4 ppb). Levels in urban areas fall between 10 and 20 ppb (Platt et al. 1979; Schulam et al. 1985; Singh et al. 1982). Depending on the turnover rate for formaldehyde in the atmosphere, urban sources may influence atmospheres for some distance downwind.

There is little in the way of formaldehyde measurements in plumes from forest or agricultural burning. It is necessary to depend largely on data obtained from study of residential heating devices, which almost certainly does not properly represent the combustion of foliage and fine fuels consumed in most prescribed or wild fires, adding to our uncertainties.

The remarkable variability of findings on formaldehyde production from woodburning does not improve matters. Ramdahl et al. (1982) reported emissions of 40 to 60 mg formaldehyde/kg wood, in the presence of adequate oxygen. DeAngelis et al. (1980) measured an output of 300 mg/kg green pine fuel, and Lipfert (1982) reported a factor of 1600 mg/kg from residential stoves. Lipari et al. (1984) found emissions from fireplaces to range from 600 to 2300 mg total aldehydes/kg wood, 20 to 40% of which was formaldehyde. Burn rate influenced output; aldehyde emission diminished with higher rates of combustion. The range for formaldehyde appears to extend from 40 to as much as 700 mg/kg fuel, and it is obvious that the amounts are quite dependent on differences in conditions or methods. For the sake of simplification we can suggest that residential wood combustion produces up to 1.0 g formaldehyde/kg fuel wood on the basis of direct measurement.

The only field studies are those of Ward and Hardy (1984) and Reinhardt (1989). Ward and Hardy measured only acetaldehyde. However, formaldehyde should be expected in larger quantities than acetaldehyde, if the findings of Lipari et al. (1984) in studies of fireplace emissions are indicative of light fuel emissions. The outputs were 3.11 g/kg in the flaming phase and 2.62 g/kg in the smoldering phase of one fire, and 5 g/kg and 0.45 g/kg in another. These would suggest formaldehyde production possibly as high as 7 g/kg fuel. It is not clear how to reconcile such a high figure with the suggestion by Lipari et al. (1984) that increased burn rate lowers aldehyde production. Reinhardt

(1989) reported on a series of personal monitoring observations of firefighters in the Pacific Northwest. Exposures to formaldehyde and acrolein were so widely variable that general conclusions about exposure would be uncertain, but some individuals were exposed to at least momentary concentrations of both products that were in excess of short-term exposure limits.

It would be useful to determine whether there is a better relation between formaldehyde emission and some other index that would lead to more reliable estimates. Examples of such an indicator might be particulates or even polynuclear aromatic hydrocarbons (PAH), which have been studied more extensively in combustion emissions than formaldehyde. One study suggests that this may be possible. Kamens et al. (1984) in an examination of photochemical changes in dilute smoke, determined that the system contained 9 mg particulate/ppm formaldehyde/cubic meter or about 0.15 mg formaldehyde/mg particulate matter.

Use of an emission factor of 1.0 g formaldehyde/kg fuel consumed leads to a somewhat similar ratio. Dost (1986) in estimating exposures to polynuclear aromatic hydrocarbons in smoke, used an emission factor for particulates of 8.5 g/kg fuel consumed. One gram formaldehyde emitted per kg fuel would therefore be accompanied by 8.5 g of particulate; 1 mg particulate would be accompanied by 0.12 mg formaldehyde, compared to the 0.15 mg/kg of the Kamens work.

Even though these estimates are quite close for the purpose of the risk assessment later in this paper, a conservative conversion of 7 g formaldehyde/kg fuel estimated from the data of Ward and Hardy (1984) will be used. This arbitrary convention does little violence to the indirect estimate of 1 g/kg fuel made earlier, or the ratio of 1.25 g/kg that would arise from Kamens et al. With the kind of information available, even a ten-fold adjustment for conservatism is appropriate. In this connection, Lipari et al. (1984) have made the observation that national estimates of formaldehyde output from residential burning, which were about two decades old at the time, are unreliable. They are also inconsistent by ten-fold with extrapolations from current research coupled with estimates of fuel wood use. Because of these kinds of uncertainties as well as those mentioned earlier, there should be no illusions about the quality of the estimates used for this paper, except that it is likely that they will be found to be too high. Nevertheless, their use at this time allows general estimates of impact, and installs a scheme into which better data may be inserted.

The next question is the behavior of formaldehyde once it has been formed in combustion or other processes. There are measurements and kinetic models of the behavior of formaldehyde at higher altitudes and in cloud chemistry, but it is difficult to know just how they might apply to the low altitude and relatively dry atmosphere associated with most broad area burns.

Singh et al. (1982) reported that formaldehyde has a high rate of loss through photolysis, with a total loss rate per day of 88%. The dominant removal mechanism is through interaction with hydroxyl radical. In the context of vegetative burning it seems uncertain how applicable those rates might be, since most of the photolytic activity seems to have been studied at higher altitudes. Penetration of sunlight into a smoke plume is limited, as illustrated by studies of ozone formation in the plume, discussed later. It is clear that such activity continues for miles downplume, and it would be expected that formaldehyde removal would be a slow and continuous process as smoke thins.

The relation between formaldehyde and formic acid, either at altitude or at ground level is very important to both disappearance of formaldehyde and the formation of formic acid. Formic acid is a well-known product of formaldehyde oxidation in a moist environment, and it is appropriate to consider both in this section. Formic acid may also emerge directly from the flame if sufficient oxygen is present, but no direct measurements have been made.

The mechanism of atmospheric formation of formic acid from formaldehyde in cloud water has been described quite well by Chameides and Davis (1983). The mechanism apparently requires hydration of HCHO to $CH_2(OH)_2$ in the aerosol, which occurs after diffusion of gaseous HCHO into a droplet. The presence of gaseous OH and HO_2 redicals formed photochemically are also essential to the scheme. These radicals are ubiquitous in daytime atmosphere. The oxidation of $CH_2(OH)_2$ is not driven photochemically, and the OH radical reaction is necessary to produce the $CH(OH)_2$ radical which reacts with the high cloudwater O_2 to form formic acid. The process can result in theoretical concentrations of 35 to 65 ppt (v/v) gaseous formic acid, which is stated by the authors to be about an order of magnitude lower than actually found.

The equilibrium in a moist atmosphere has been modeled by Adewuyi et al. (1984) who calculate that the aqueous phase concentration of formic acid may reach as much as 1.2 μM, and in the gas phase up to 170 ppt. These levels are consistent with the findings of Chameides and Davis (1983). Such concentrations by themselves are trivial in a toxicological sense, but the difference between theory and empirical findings may suggest that other mechanisms than those mediated in an aqueous environment might exist.

Morrison and Heicklen (1979) have reported reactions producing formic acid from formaldehyde in a controlled gaseous environment at conditions more nearly approaching those that might exist near a fire. With oxygen at roughly 20% of the reaction atmosphere and a starting formaldehyde concentration of about 2600 ppm, the formic acid yield was about 2 M/M formaldehyde. A similar quantum yield appeared in an experiment with

oxygen at about 5% and formaldehyde at about 526 ppm. Irradiation time was 6 hr in the first case and 24 hr in the second. However, when 8 ppm nitric oxide was added to the system containing 2600 ppm formaldehyde the yield of formic acid was about 40 M/M; higher NO concentrations tended to quench the reaction. The behavior of the system at the low formaldehyde concentrations likely in a fire environment has apparently not been observed.

In spite of the observed effect of nitric oxide, it seems unlikely that NOx plays a significant part in any loss of formaldehyde in smoke from forest burning. Kleindienst et al. (1986) found that the formaldehyde levels in a large smoke chamber decreased only slightly in the presence of the approximately 100 ppb NOx levels generated by combustion. Added NOx to bring the level up to 500 ppb pushed formaldehyde losses up by as much as 67%. These differences would be important only if they reflect a formation of many moles of formic acid through a chain reaction such as Morrison and Heicklen described. In a relatively NOx-free atmosphere, it appears that the rate of formic acid formation from formaldehyde is not significant to the toxicology of smoke. Su et al. (1979) found that at 12.2 ppm formaldehyde, the rate of formic acid formation in a flash photolysis reactor was only 0.0017 ppm/min in the absence of NOx. This appears to be somewhat lower than the 6 hr yield of the Morrison and Heicklen study, but may not be inconsistent given differences in experimental systems. Veyret et al. (1982) also conducted flash photolysis experiments, usually at much lower oxygen pressures and much higher concentrations of NO (about 130 ppm). While these shed light on the fate of formaldehyde, as the authors point out, the observed mechanism does not account for the removal of formaldehyde from the atmosphere. Nor does it allow prediction of formic acid levels near a fire.

It is difficult to relate these studies to conditions within and surrounding a fire. However, the micro-environments in which fire chemistry takes place may be quite different within centimeters. It is possible that formaldehyde concentrations may be very high at certain points, and it is almost certain that oxygen concentrations will be quite low at certain points. We are also accustomed to ignore nitrogen oxides as trivial products in processes of wood and foliage combustion, but at certain points in the actual combustion zone, there may be significant amounts of nitric oxide. The role of water in the vapor state has apparently not been explored, and the water of combustion at certain points in the immediate burning zone may be a significant fraction of the atmosphere.

Another source of information that eventually may become useful in estimating the amount of formaldehyde produced in combustion arises from the extensive research on production of liquid fuels from wood. Studies on the wet oxidation of wood are generally carried out at oxygen tensions of up to 30 atmospheres and temperatures above 100°C, in the presence of substantial amounts of water. Obviously these conditions will not be met

in a fire. McGinnis et al. (1984) have found that such oxidation of cellulose produces substantial amounts of formic acid. At a water/cellulose ratio of 1/10, conversion to formic acid began at about 205°C and reached about 0.3 mol formate/mol cellulose glucose. In other words, about 3 carbons in 60 or 5% of cellulose carbon was converted to formic acid.

B. Toxicology of Formaldehyde

The toxicology of formaldehyde has been studied in detail befitting its status as a virtually ubiquitous atmospheric contaminant from an array of building materials, textiles, preservatives, and medical activities. The available data are extremely useful, but there has been virtually no attention to potential biological effects arising from formaldehyde as it is formed in combustion. The amounts formed in fire events have been poorly quantified, the interactions with other fire products are not known nor are the effects of fire conditions on formaldehyde concentrations understood. The associated question of the relation between formaldehyde and formic acid in a fire environment is a complete mystery.

In 1984 the proceedings of a Consensus Workshop on Formaldehyde were published (Hart et al. 1984), that provide an excellent review of the toxicology of formaldehyde. The workshop was organized at the request of the White House Office on Science and Technology Policy. The Workshop review is used as a basis for the following brief overview of the aspects of formaldehyde effects that might be of interest in the context of combustion product inhalation. Another very useful review was published by the National Research Council (1981). Certain additional specific research is also discussed.

Because the concern of this paper is with the acute and irritant effects of smoke components, the issue of carcinogenicity is not discussed. As we proceed, however, estimates of formaldehyde exposure that arise in the course of this evaluation can be inserted into the numerous risk calculations that have been made for formaldehyde in the occupational and residential context. As a generalization, however, it appears that exposures to aldehydes as smoke components do not constitute a carcinogenic risk, largely because of the infrequency and short duration of exposures.

The effort of the Workshop that is of most interest in the context of this report was done by the panel on immunology/sensitization/irritation. Five questions were posed:

a. Is formaldehyde a primary sensitizing agent or does it elicit a response only in presensitized populations?
b. If irritation, primary or secondary sensitization occurs, who are the susceptible populations?
c. What are the possible mechanisms for formaldehyde induced irritation/sensitization?

d. Do threshold levels exist for irritation/sensitization? If so, what are the levels and the concentration ranges? Do thresholds differ for different sensitized populations?
e. Is there evidence for effects of formaldehyde on the immune system?

Formaldehyde certainly causes direct irritation of both the skin and respiratory tract, but the evidence for true allergic responses in the respiratory tract is equivocal. It is a definite skin sensitizing agent that causes allergic contact dermatitis, usually appearing at about 24 hr and disappearing slowly after a maximum response at 48 to 96 hr. This effect is a classical delayed hypersensitivity in which formaldehyde conjugates with tissue protein and the product is seen as a foreign protein by the immune system, followed by the defense response of antibody deployment. It appears with somewhat less certainty to cause an immediate contact urticaria (wheal formation) that is immunologic in origin.

The irritation caused by formaldehyde may be mediated by effects on sensory receptors of the nose, eyes, and throat. This component appears accompanied by some tolerance, perhaps best exemplified by loss of olfactory sensation during sustained exposure to moderate levels of formaldehyde. Actual cellular damage may occur over several hours of exposure at sufficient levels, one characteristic of which is loss of ciliary activity of the cells lining the respiratory tract.

It is also possible to evaluate irritant potential by measuring respiratory reflex responses in intact animals. Barrow et al. (1986) have reviewed the reflex pathways involved. When an irritant is encountered, the respiratory rate and depth of inspiration decrease as a protective device. They found formaldehyde to be second only to acrolein in decreasing respiratory ventilation in the mouse. The dose-response data suggest that effects may occur at concentrations as low as 0.1 ppm, over 5 daily exposures of 6 hr each. Kane and Alarie (1977) demonstrated this system quite dramatically, by showing that mice exposed to 3.8 ppm formaldehyde for 10 min reflexly decreased respiratory rate from about 300 cycles/min to about 100. The decrement was 28% at 1 ppm and 18% at 0.5 ppm. Successive daily exposures for 3 hr produced progressively increasing responses. It is unclear how to resolve the meaning of the increasing sensitivity just discussed with the apparent 'inurement' to stimulus mentioned earlier.

It would seem that regardless of the source of irritation, the strength of the reflex decrease in respiratory activity in humans is not clear. If the reflex is not easily overridden, it could interfere with respiratory exchange in firefighters at times when energy is most needed.

For formaldehyde, the exposure thresholds of these effects are relatively low compared to levels that might be found in a structure incorporating large amounts of particle board, such as a mobile home. Eye, nose, and

throat irritation will be caused in most people at concentrations of 0.1 to 3 ppm, and the odor threshold is at about 0.05 ppm. Severe responses appear after exposure to 10 to 20 ppm.

Several summaries of the ranges of sensitivity of humans to formaldehyde have been prepared. A summary table by Bernstein et al. (1984) indicates an odor threshold of 0.05 to 1.0 ppm and eye irritation at 0.05 to 2 ppm. The rather cryptic first line of the table, however, shows a range of 0.05 to 1.5 ppm at which 50 to 75% may report no effects, implying that a substantial fraction of exposed individuals may respond to very low concentrations. The Consensus Workshop (Hart et al. 1984) and the review by the National Research Council (1981) discuss human experience extensively.

It is of importance to understand something of the interaction of formaldehyde in cells because this information provides some insights into the way the molecule may exert its irritant effects.

There is sound evidence that indicates that formaldehyde binds to macromolecules, which probably accounts for its carcinogenic and mutagenic activity, and may also be the mechanism by which it exerts sensory and inflammatory effects. Formaldehyde can bind reversibly to RNA and DNA, as well as protein, and establishes crosslinks in both nucleic acids and protein. The potent allergenic activity of formaldehyde derives from its ability to react with endogenous protein, to cause it to be then recognized as foreign.

Heck et al. (1986) have summarized the work at the Chemical Industry Institute of Toxicology (CIIT) on the mechanism of nasal toxicity of formaldehyde. Formaldehyde clearly forms a covalent bond with DNA of cells in the respiratory tract. In one series of studies, exposures of rats to formaldehyde labeled with both ^{3}H and ^{14}C produced a dose-related cross linking of DNA with protein. Physical evidence of cross linking had been obtained earlier, but this work clearly established that formaldehyde itself participated in the binding. At air concentrations above 6 ppm, the effect diminished because of cell toxicity; at 0.3 ppm the effect was measurable but very slight. It is interesting that this level of sensitivity corresponds to the irritancy thresholds observed in humans. Very recently, Casanova et al. (1988) reported DNA-protein cross linking in nasal mucosa of monkeys to be nearly six-fold less than in rats at 2 ppm and nearly eight-fold less at 6 ppm. The anatomy of the primate is much more respresentative of that of humans, and it is probable that the biology of the nasal mucosa is similarly a better model of the human.

It is likely that cross linking caused by formaldehyde is transient. Cosma et al. (1988) have shown a dose-response in extent of cross linking in primary cultures of rat tracheal epithelium at concentrations between 50 and 400 μM formaldehyde. Crosslink removal was evident four hours later and nearly complete at 16 hr. Incidence of single strand breaks was also dose-related, with repair complete in 2 hr. In cultured human bronchial cells, Grafstrom

et al. (1983) observed a similar response and repair, noting that the epithelial cells and fibroblasts behaved similarly.

The cell toxicity noted above at concentrations of 6 ppm and higher is reflected in work by Swenberg et al. (1986), who exposed rats to 0.5 to 15 ppm formaldehyde. Cell turnover was evaluated by measuring incorporation of ^{3}H labeled thymidine into DNA that is being synthesized for newly formed cells of the nasal mucosa of exposed animals. The label was administered intraperitoneally after exposure, and the extent of selective incorporation into nasal mucosa served as an index of increased cell turnover. When thymidine was administered 18 hr after a 6-hr exposure to 0.5 ppm formaldehyde, a slight but detectable increase in incorporation was evident, but after 3 daily 6-hr exposures, the rate of incorporation was the same as controls. This finding indicates that recovery from the low-level impact occurs rather readily.

These findings lead one to wonder whether acute reversible effects are based on direct and reversible reactions with protein and possibly DNA in cells of contract surfaces. In spite of the known immunologic response in skin, the question of true allergic response of the respiratory tract is not well answered. It appears that some individuals acquire a formaldehyde sensitization, but few seem to respond to an immunological inhalation challenge (Hendrick and Lane 1977; Hendrick et al. 1982). However, it is likely that asthmatics would be more responsive to formaldehyde as an irritant, as they are to other irritants (National Research Council 1981) although Sheppard et al. (1984) evaluated asthmatic subjects under 10-min exposures to concentrations up to 3 ppm formaldehyde during exercise and quiescence, and found no bronchio-constrictive influence in any group.

The mechanism for disposition of formaldehyde is very well established. Formaldehyde is a ubiquitous endogenous metabolite and is oxidized by an aldehyde dehydrogenase. The reaction is very fast, perhaps, because formaldehyde is so common in normal metabolic processes; half-time in blood is apparently less than 1.5 min. In fact, experimental respiratory exposure of humans to 100 ppb formaldehyde for 40 min does not lead to increased levels in blood (Heck et al. 1985). A study of inhalation exposure to ^{14}C-labeled formaldehyde, with the intent of determining distribution into the central nervous system, showed a very small fractional deposition of label in brain compared to contact tissues such as esophagus and lung. The very heavy circulation and short circulatory pathway to the brain would be expected to provide a greater deposition than in other tissues. In addition, because of the rapid metabolism of formaldehyde and resultant rapid incorporation of carbon into other molecules, it is doubtful that the brain labeling represented intact formaldehyde.

Such rapid disposition is probably the reason that systemic effects of formaldehyde have not been observed. The product of this metabolic activity

is formic acid, however, which is removed very slowly. While metabolism of endogenous formic acid is adequate, the question of the effect of an added burden imposed by exogenous formaldehyde must be asked, particularly when formic acid produced in metabolism of methanol is so destructive. Given that all effects of formaldehyde so far observed appear to be at sites of environmental contact, it seems safe to assume that at exposures that are likely under conditions of interest in this report, systemic injury by formaldehyde or its metabolites will not be a factor. Possible impacts of environmental formic acid will be discussed below.

Formaldehyde apparently does not cause reproductive impairment or birth defects, even at doses sufficient to cause maternal toxicity. These findings are accompanied by evidence that hexamethylenetetramine (HMT), which is metabolized to formaldehyde, also does not cause fetal responses. The rationale in such a study is that the very rapid disposition of formaldehyde prevents it from reaching the fetus, whereas HMT should distribute to the fetus and be metabolized to formaldehyde there as in other organs of the dam, which would increase concentration at any sensitive site.

Formaldehyde also shows no evidence of causing germ cell mutations, even though it causes mutagenic activity in in vitro systems. This is not surprising, because whether or not a chemical is mutagenic in vitro, it must be able to reach or penetrate the germ cells to cause hereditable mutation; exogenous formaldehyde does not reach any systemic target in significant amounts.

Although there are adequate data to indicate sensory and irritation thresholds for formaldehyde, these boundaries do not give a clear index of the limits of non-carcinogenic effects in humans. To quote the conclusion of the Workshop: "Available animal and human studies provide information to qualitatively establish various toxic effects of formaldehyde exposure, but quantitative assessment is not indicated at this time for biological effects other than carcinogenicity."

One problem in developing an assessment of non-carcinogenic health impact for compounds carried in smoke is estimation of the thresholds that might obtain for humans. Odor and irritation sensitivity studies are necessarily partly subjective, and also are dependent in part on prior abuses of the olfactory sense and the respiratory tract generally.

C. Toxicology of Formic Acid

If future studies indicate that formic acid is indeed present in significant amounts in the immediate emissions from fires, there is little available toxicologic data from which to infer its biological importance.

Toxicological study of formic acid has been limited to evaluation of its role as a persistent metabolite in methanol poisoning. The pathway includes

a relatively easy oxidation of methanol to formaldehyde, which is converted to formic acid very rapidly, as has already been discussed. The latter is further oxidized very slowly in humans, and the accumulation of formic acid results in a general acidosis, which is considered responsible for the sometimes disastrous consequences of methanol ingestions for the optic nerve.

Formic acid is sometimes used to create the acid medium necessary in preparing silage, which can result in vapor phase exposures to agricultural workers. A Finnish study of this practice (Liesivuori and kettunen 1983) found exposures as high as 99 mg/m^3 (about 45 ppm). This paper indicated that one asthmatic farmer was adversely affected by inhalation of the formic acid vapors, and another study was quoted as finding irritation of mucous membranes and respiratory difficulty in 40% of exposed farmers. Rats exposed to 20 ppm 6 hr/d for 2 wk developed central nervous and kidney effects, (Savolainen and Zitting 1980) possibly because such high exposures over the extended period of the experiment resulted in sustained levels that exceeded the rate of metabolic turnover or excretion.

D. Exposure and Potential for Acute Health Effects

If emission factors of 7 g of formaldehyde and 8.5 g particulate/kg fuel are used, the working ratio for formaldehyde/particulate would be about 0.82 mg/mg. At 100 m visibility, estimated particulate concentration would be 5 mg/m^3 and formaldehyde concentration would be 4.1 mg/m^3 (3.1 ppm). If the factors based on fuel wood combustion were used, the concentration would be about seven-fold lower or about 0.58 mg/m^3 (0.44 ppm).

It seems unlikely that formaldehyde will remain intact during the down plume dilution process, given its reactivity and the processes known to affect it at higher altitudes. However, it can be argued that the photochemical removal may not be effective in the altered light access of the plume, and that the free radical chemistry known to form formaldehyde from methane may also react the methane produced in a fire. We are left with no useful additional information, and the assumption for the present will be that no degradation of formaldehyde occurs in the plume.

Concentrations of 0.4 to 3 ppm appear likely near a fire, although better measurements must be made to verify this prediction. A concentration of 0.1 ppm can be expected to cause a muscosal and upper respiratory irritant response in some people, and it is to be expected that 1.0 ppm or more almost certainly will do so. The higher concentrations could reflexly decrease ventilation, unless the reflex can be overridden. Decreased ventilation could reduce the physical capacity of an individual who is at a high exertion level. It is likely that formaldehyde contributes significantly to the mucosal irritation caused by smoke.

E. Exposure to Formic Acid

It is not possible to judge exposures to formic acid on the basis of existing data. There is also a scarcity of data describing the impact of formic acid in the breathing atmosphere. It is possible that formic acid could represent a significant fraction of the respiratory irritancy of smoke, particularly as a co-irritant, and study of its formation and disposition in smoke should be undertaken. The only study of human exposure suggests that exposures in the realm of 25 to 40 ppm do not produce great responses, but it is difficult to judge the meaning of that work.

III. Acrolein

A. Formation and Environmental Behavior

It has been recognized for a long time that acrolein is a more potent irritant than formaldehyde, and there is a rather extensive literature on its toxicology, including reviews by Beauchamp et al. (1985), Carson et al. (1981) and U.S. EPA (1980). Unfortunately, there has apparently been no impetus for seeking and measuring it in the general atmosphere, as there has been for formaldehyde; the literature describing the sources and environmental behavior of acrolein is limited. The review by Carson et al. (1981) under an U.S. EPA contract mentions several measurements of ambient air, all in urban settings. Concentrations of acrolein ranged from 0.005 to 0.025 mg/m^3, which presumably arises from engines and other fossil fuel combustion. Most other non-occupational exposure information relates to cigarette smoke, and some measurements of acrolein as an emission from fuel wood combustion have been made.

The absence of general environmental data is not surprising, because acrolein apparently does not arise in many natural processes other than combustion, whereas formaldehyde seems involved in a variety of pathways for one-carbon compounds and substituents. Also, with the carcinogenic potential for formaldehyde, and its massive use in consumer products, it is expected that its environmental characteristics should be well studied.

Like formaldehyde, acrolein is also found in the emissions from open fireplace burning of firewood, to the extent of roughly one-tenth of the output of formaldehyde (Lipari et al. 1984). These studies suggested that aldehyde emissions in general are greater in less efficient burns. A very crude relationship between aldehyde output and fuel consumption through the entire period of the experiments indicated that total aldehydes represented from 0.6 to 2.3% of the fuel weight, and formaldehyde was found to comprise about 20 to 40% of the aldehyde total. The time course measurements showed that in the very early stages of the burn, acrolein concentrations approached

or even exceeded those of formaldehyde, but dwindled to very small outputs in the next few minutes. A prescribed or wild fire can be expected to correspond to the early phase described by Lipari et al. (1984) as long as it progresses through new fuel; the following smoldering phase may produce limited acrolein. However, the data gathered by Reinhardt (1989) on individual firefighter exposures to acrolein and formaldehyde suggest that formaldehyde is usually more abundant than acrolein, but there is little consistency in the ratios. In fact the report cautions that as yet, neither can be used as a surrogate measure of the other. A limited number of measurements also suggest that differences between emissions of either formaldehyde or acrolein during work attacking the fire or mopping up may be little more than a range between unity and about two. 'Attack' means actively trying to check the flames from moving further. Mopping up is work in the smoldering areas after the fire has subsided. As mentioned earlier, there were at least transient exposures to both substances in excess of short-term exposure limits.

Kleindienst et al. (1986) also measured acrolein and formaldehyde in combustion products, before and after irradiation with artificial sunlight. At the beginning of irradiation the acrolein concentration was about 11% of the formaldehyde level, but unlike the 17% increase in formaldehyde in the chamber, acrolein decreased 37%. The consistency of this change is not known because, of the three experiments, only one followed acrolein. In a study of smoke exposure effects on reflex activity in rats, Farrar (1980), measured CO, CO_2 and acrolein in non-flaming combustion of Douglas fir, finding that acrolein levels were about two orders of magnitude lower than CO and three orders below CO_2 levels. The study was of no value in identifying specific responses, because smoke concentrations were overwhelming.

One area of environmental study of acrolein is the investigation of cigarette smoke. It is considered here because cigarettes are, after all, foliage, and the emissions, at least, have potentially a qualitative relationship to those from forest and agricultural waste. The principal difference is probably in the temperature of combustion, because a burning cigarette tip may exceed 800°C, which is probably not characteristic of an open forest slash or grass burn. Kensler and Battista (1963) found acrolein to be about ten times as plentiful as formaldehyde in the smoke of machine smoked cigarettes. Guerin et al. (1987) found acrolein to be present in mainstream smoke in amounts roughly similar to those of formaldehyde, per cigarette. Sidestream smoke, which probably is more representative of open burning than that of the mainstream because of the lower temperatures, was found to contain about 12-fold more acrolein than the mainstream smoke. The correspondence of passive burning and that during 'drawing' on the cigarette, and rapid and smoldering open fires is not clear, however. Calculated amounts of acrolein

were from 0.1 to 1.7 mg/cigarette. Other estimates, reviewed by Izard and Libermann (1978) were closer to the lower end of this range.

Such studies usually measure emissions as a function of smoke puffs or total cigarettes, not as a function of amount of fuel consumed. The information 'per puff' is then translated to dosage as a function of presumed lung ventilation. It is unclear how much of the combustion is really sidestream rather than mainstream, and the effect of very hot gases moving across the tobacco just prior to combustion is not discussed.

For purposes of estimation and possible comparison with forest fuel combustion, a cigarette weight of 1.0 g is assumed. We weighed a cigarette with filter removed at about 700 mg. Whether this is representative is not known. No one in this organization smokes and it was not convenient to sample several brands. If the emission of acrolein is 0.1 mg/cigarette the acrolein/fuel ratio is roughly 1/10,000, or about 100 mg/kg. When compared with the lower end of the range of 1 to 7 g formaldehyde/kg fuel, as discussed earlier, this figure is not inconsistent with the estimates by Lipari et al. (1984) and Kleindienst et al. (1986) of acrolein/formaldehyde ratios of approximately 1/10.

B. Toxicology of Acrolein

In 1985 a group from the CIIT published an extensive review of the toxicological literature on acrolein (Beauchamp et al. 1985). It is a good general source and is the basis for the next several paragraphs. Where appropriate, other literature, particularly that published more recently, is also discussed. The reviews by Carson et al. (1981) and by US EPA (1980) were mentioned earlier.

Acrolein is intercepted primarily in the upper respiratory tract, causes irritation and ciliary stasis, and potentially may cause more severe cellular toxicity. Effects on mucociliary activity are difficult to evaluate on an air concentration basis, because the studies have either utilized in vitro aqueous epithelial preparations or cigarette smoke inhalation. Reflex depression of respiratory rate associated with irritation of the respiratory tract has been observed. It has been suggested that the irritant properties of acrolein are a function of its reaction with sulfhydryl groups in the receptors of the nasal mucosa. In fact, acrolein is so reactive with thiols such as glutathione that it is quickly trapped irreversibly in the cells of contact. Not surprisingly, various evidence indicates that glutathione is protective. While the binding to proteins through their sulfhydryl groups is well established, it is unclear whether acrolein can bind to nucleic acids as does formaldehyde.

Murphy et al. (1963) reported dose-related impairment of guinea pig respiratory function at a concentration as low as 0.2 ppm, for two hours. The primary functional change seemed to be bronchio-constriction, which

caused increased airway resistance and decreased respiratory rate. Kane and Alarie (1977) found that 1.0 ppm acrolein over a 10-min exposure caused a 40% reflex decrease in respiratory rate; 0.5 ppm resulted in about a 30% lower rate. At a concentration of 8.1 ppm the respiratory rate dropped from approximately 250 cycle/min to about 50 cycle. Repetitive exposures to 0.5 ppm for 3 hr/d for 4 d resulted in the further depression of respiratory rate by 60% compared with 30% on the first day.

Subacute exposure effects are most pronounced in the upper tract, which is to be expected from the efficient interception and reaction at surface of first contact. Dose-response studies indicate that in the hamster and rabbit the threshold is at about 0.4 ppm, for prolonged exposures (13 wk, 6 hr/d, 5 d/wk). Comparative inhalation studies suggest that dogs and monkeys are slightly more sensitive than rats and guinea pigs with most parameters negative at 0.7 ppm, over 5 8-hr d/wk for 6 wk.

Nielsen et al. (1984) used a tracheotomy to bypass the nasal passage in an effort to learn where the reflex response to acrolein originates. A concentration of acrolein that caused at a 50% depression in respiratory rate in intact animals had no such effect on animals exposed only by way of the trachea. The response is therefore considered to require a sensory mechanism rather than irritant tissue damage alone. In this system, 0.79 ppm for 20 min caused a 70% depression in intact animals, but 3 ppm caused no change when the nasal passage was not exposed.

Eye irritation is well-known. In rabbits, exposure to 2 ppm acrolein caused lacrimation, with no evidence of either biochemical or ophthalmologic effects.

Kane and Alarie (1977) have prepared a table based on studies of irritant potential in humans. The lowest concentration reported to have an effect was 0.06 ppm, which caused eye irritation in some individuals. Generally, it appears that 0.5 ppm for a period of 5 min or more is likely to be irritant, and 1.0 ppm may be tolerable for no more than 10 or 15 min. A precise statement may be impossible due to great individual variation in background, sensitivity, and differences in measurement precision. As an example of the great sensitivity of humans, men exposed to 0.8 and 1.2 ppm acrolein for 10 and 5 min, respectively, began to lacrimate within 20 sec in the first group and in 5 sec in the second. These findings are not inconsistent with animal observations, and it would be expected that lower concentrations for slightly longer periods would be as irritant.

Kane and Alarie (1978) also have considered the nature of combined effects of acrolein and formaldehyde, which is the situation to be expected in exposures to smoke. Rather than a purely additive effect, the effects of the two components are less than additive, possibly indicating a tendency to compete for sites of action.

A concentration of 0.09 ppm (lowest observed) caused detectable reflex lowering of respiratory rate (Weber-Tschopp et al. 1971), and 0.3 ppm caused

irritation in as little as 10 min. The odor threshold for acrolein is reported by Leonardos et al. (1969) to be 0.21 ppm, and that of formaldehyde is 1.0 ppm. For comparison, hydrogen sulfide (rotten egg) is detectable at 0.0005 ppm.

The metabolism of acrolein is probably not of significance at the concentrations expected as a consequence of smoke exposure for two reasons. As noted already, most of the acrolein contacted is probably tightly sequestered in cells of contact. It is known that acrolein is converted to glycidaldehyde and acrylic acid, both of which are oxidized to CO_2 in the body. Both are quite toxic, but the low levels that would result from the exposures of concern here do not pose a danger. Nonetheless, it must be recognized that unlike formaldehyde, high doses of inhaled acrolein can produce systemic responses.

High or prolonged exposures have caused hepatic effects. Continuous 90-d exposure to 1.0 ppm caused focal hepatic necrosis. Hepatic enlargement has been seen at an exposure of 2.1 ppm over 10 hr, and slight decreases in liver weight accrued in rats exposed to 0.55 ppm for 2 to 3 wk. Kidney inflammation has been observed in rats, guinea pigs, monkeys and dogs at concentrations of 0.22 ppm continuously for 90 d and at 3.7 ppm over 6 wk of 8-hr exposures, 5 d/wk. In the former study, the results as observed were not dose related. All species but the dog were affected at the lowest level but no effects were observed at the next higher level of 1.0 ppm. In the dogs, there was no indication of a graded response with increasing dose. The intermittent exposures caused no response at 0.7 ppm.

Cardiovascular effects have been seen in exposures such as those described above, and in intensive exposures over shorter periods. These exposures are much more pertinent to the problems associated with cigarette smoking, which can produce much higher levels of acrolein, and which are not mitigated by dilution with ambient atmosphere.

Clinical chemistry and hematology were affected slightly at the higher exposures, but appeared not to be adversely altered at levels that might be encountered in the atmosphere associated with a vegetation fire.

Inhaled acrolein is unlikely to directly cause teratogenic effects or fetal toxicity. In the only reported inhalation study male and femal rats were exposed at 55 ppm for 4-d mated, and the females were exposed throughout gestation, which was stated to cause no changes in fertility or fetal development. Most of the other research in this area has employed various routes of injection rather than inhalation, however, which bears no relation to exposures in the field. Even then the effects appear to be due to fetal toxicity; virtually all chemicals are fetotoxic if maternal toxicity can be bypassed in some fashion.

The acrylic acid metabolite of acrolein has been shown to cause a related dose increase in teratogenicity in rats after intraperitoneal injection (Singh

et al. 1972). It is unlikely that these have significance to the concerns of this report, because there will be little opportunity for formation of the metabolites due to the reactivity of acrolein at sites of contact in the respiratory tract.

A rather large number of mutagenicity assays of various kinds have been conducted, but data are contradictory and tend to suggest that at worst, acrolein has limited ability to interact with genetic material in the systems tested. Direct chemical studies of the ability of acrolein to react with nucleic acids suggest also that such reactions are unlikely in intact animals. This absence of effect is of interest because the greater irritancy of acrolein compared with formaldehyde might suggest either that the formaldehyde effect is not related to its reaction with macromolecules, or that these two aldehydes act by differing mechanisms.

The acrolein epoxide, glycidaldehyde, is a potent mutagen in vitro, and has been shown to be carcinogenic. As already stated, it is unlikely to be formed in significant quantities, if at all, from inhaled acrolein, so it can not be expected to result in cell injury. The absence of evidence for acrolein carcinogenicity would suggest that formation of carcinogenic metabolites that might cause acute effects is not significant.

An effect that must be considered for any pulmonary irritant is the ability of exposed individuals to repel respiratory infection. Acrolein has been identified as a cause of the interference with macrophage phagocytosis (ability of scavenger cells in the lung to engulf foreign material or bacteria) noted in smokers, which may indicate an effect on antibacterial activity (Green et al. 1977). Jakab (1977) found that 1.0 ppm acrolein for 24 hr would interfere with resistance to inhaled bacteria by mice, but found a no-effect period of 4 hr. Eight-hr exposure to 3 ppm and higher levels decreased the destruction of *Staphylococcus aureus* in the lungs of mice, in a dose-dependent pattern. In mice with a viral pneumonia infection as well, the effect was sharply accentuated (Astry and Jakab 1983). Aranyi et al. (1986) found no increase in mortality among mice exposed to 0.1 ppm acrolein for 3 hr nor was in vivo bactericidal activity (clearance of ^{35}S-labeled *Klebsiella pneumonia*) of alveolar macrophages decreased. Five successive daily 3-hr exposures caused some increase in mortality and a slight decrease in bactericidal activity.

Acrolein as a metabolite of allyl alcohol is not pertinent to the present discussion, because it is formed at other organ sites in metabolism of the alcohol. The lung would participate in that activity, but cell surface damage is not a consequence of systemic exposure.

While the focus of this review is on acute exposure and responses, data from some chronic exposures is instructive, particularly where good dose response information has emerged. Histopathology, DNA, elastin and collagen content of the lung was assessed in rats exposed to 0.4, 1.4 and 4 ppm acrolein for 62 d, on a 6-hr/d, 5-d/wk schedule. Effects were limited in the middle dose, with only 3 of 31 rats showing lesions, and at 0.4 ppm

there were no detectable responses, including animal weight and organ weight. One interesting observation was that in the animals at higher exposures, after several weeks the rate of weight gain rose to normal, although absolute weight did not catch up (Kutzman et al. 1985). Leach et al. (1987) also examined pathological changes, and several immunologic parameters after 3 wk of exposure 6 hr/d, 5 d/wk to measured concentrations of 0.17, 1.07 and 2.98 ppm. The immunologic indices measured were not affected at any treatment, and only the highest concentration produced observable pathology.

C. Exposure and Potential for Acute Health Effects

Data on emission of acrolein from burning vegetation suggest a wide range of possible concentrations in smoke. Neither firewood nor smoking tobacco appears representative of the foliage and fine fuels of many prescribed fires, but they suggest that acrolein levels may be from ten-fold less to ten-fold more than formaldehyde levels in the same burn. Data provided by Reinhardt (1989) on formaldehyde/acrolein ratios generally show figures between 5 and 10, with a few at 2 or below, a few at 15 to 20, and 3 of 109 above 35. Although acrolein is degraded by sunlight, its fate in smoke is not clear. The working assumption of this paper is that it remains intact and dilutes with other smoke components downplume. Based on estimates of formaldehyde concentration, acrolein levels could range from 0.1 to 10 ppm near a fire. The lower end of the irritancy scale is on the order of 0.1 ppm.

It is highly likely that acrolein makes a discernable addition to the irritant character of smoke near the fire line. If the concentration is 10- or 100-fold higher the response would be substantial. If acrolein survives in the smoke plume, at the highest proposed emission level, it could evoke irritant responses at a considerable distance downplume.

IV. Ozone

A. Formation and Environmental Behavior

Ozone is not an immediate product of fire, but forms in dispersing smoke plumes. As a significant acute intoxicant under certain exposure conditions, it bears attention here. The function of ozone as an upper atmosphere shield against ultraviolet radiation has no relation to its air pollutant activity, although some ozone may circulate downward from the stratosphere. It is reasonable to expect that if a plume containing significant ozone is at ground level, human intoxication might occur. In fact such an ozone transport event has apparently been recorded (Schjoldager et al. 1978). To show why smoke may play a role in pollution by ozone which is already ubiquitous, it is useful to review briefly the formation and behavior of ozone. The reactions are

rather complex, but may be summarized according to the very readable article by Seinfeld (1989) who describes the process from the end, rather from the beginning:

> Ozone (O_3) is produced by reaction between atomic and molecular oxygen ($O + O_2 \rightarrow O_3$). The reaction is very energetic and is stabilized by any of several third molecules, such as N_2 or another molecule of O_2, so the reaction does not immediately reverse. The atomic oxygen (O) needed arises from photochemical reaction of NO_2 to $NO + O$. If, O, O_2, O_3, NO and NO_2 were the only species present, most of the NO and O_3 would quickly form NO_2 and O_2 and at equilibrium there would be at most about 20 ppb ozone, a level that is probably of little consequence.

At this point hydrocarbons enter, which arise from industrial and transportation activities concentrated in urban areas (anthropogenic sources), from natural hydrocarbons emitted by vegetation (biogenic), or formed in combustion of vegetation. The molecules of concern here range from 2 to 9 or 10 carbons in all possible configurations. Hydrocarbons react with hydroxyl (OH) radicals in the atmosphere to form very reactive organic peroxy radicals that scavenge NO, preventing it from removing ozone. The net effect in general is that increased hydrocarbons in the atmosphere are accompanied by increased ozone.

It has been assumed that the primary source of hydrocarbons is anthropogenic, or urban, and in fact, urban areas produce as much as 20 times as much reactive hydrocarbon per unit area as do forest lands (Lamb et al. 1987). On a regional basis, however, natural hydrocarbons volatilized from vegetation are at least as important (Chameides et al. 1988), and nationally, vegetation produces about two-thirds of the non-methane hydrocarbons (Lamb et al. 1987).

Vegetation combustion produces large quantities of hydrocarbons, and sufficient concentrations of nitrogen oxides (NO_x) for the reactions (Westberg et al. 1981) even though the amounts of NO_x are not toxicologically significant. In fact, Altshuller (1987) suggests that at very low NO_x concentrations the reaction to ozone may be more efficient. (Altshuller gives an excellent discussion of natural non-urban ozone formation.) Some lower level atmospheric ozone may circulate down from the stratosphere.

There has been extensive research into the relation between fire and smoke, and ozone. Evans et al. (1974) showed that ozone is not detectable in the fire zone, presumably because of reaction with other combustion products. Benner et al. (1977) burned pine needles in a combustion chamber, and found that even ambient ozone was depleted by the fire. The smoke was retained in an irradiation chamber and exposed to artificial sunlight, which caused production of ozone in the study atmosphere. A number of field studies have also shown that ozone is produced photochemically in the smoke plume.

Evans et al. (1977) collected atmospheres from smoke of prescribed fires and irradiated the samples with artificial sunlight. Maximal production of ozone appeared at about 70 min after illumination. Down-plume samples at the point of highest concentration contained 60 to 75 ppb ozone 15 to 30 km from the source. Acknowledging the absence of data on vertical mixing and ultraviolet intensity, they suggest that the upper limit for ozone derived from forest smoke at ground level, will be about 80 ppb. A similar down-plume ozone enhancement was observed by Radke et al. (1978).

Westberg et al. (1981) describe the ozone pattern and the presumed mechanism of ozone production in the vicinity of a slash fire. They discuss formation 'directly above' the fire, but since the observations were made from an aircraft it is clear that the burning zone as such was not meant. Hydrocarbon and NOx levels were sufficient to serve as substrates for the photochemical formation of ozone throughout the measurement zones. They found that ozone concentrations at 3, 24 and 48 km down-plume were 55, 40 and 40 ppb above ambient levels, giving totals of smoke-derived and ambient ozone on the order of 90 ppb.

These numbers indicate a problem with our assumption that all components of a smoke plume remain in constant proportion. In this case, it appears that dilution is offset by continuing ozone formation as radiation penetrates the plume, increasing ozone production relative to the total amount of reactants available in the plume. Similar plume characteristics were found by Stith et al. (1981) in three prescribed burns, who found that the increased concentrations were associated with more intense ultraviolet intensities at the top of the plumes. The absorption of ultraviolet radiation by smoke is profound; Altshuller et al. (1967) found that reductions in radiation reduce ozone production sharply. There is other evidence to suggest that smoke plumes may not remain homogeneous. Radke et al. (1978) remark that their measurements showed the NO_2 plume to be narrower than the visible smoke plume as defined by cloud condensation nuclei. This finding as well as the constancy of the ozone plume under dilution should reflect the reactivity of components at the fringe of the plume where radiation is strongest.

Large tropical forest fire smokes were found to contain about 40 to 60 ppb ozone, mixed through out the air column from atmospheric pressures of 1000 mbars at the surface to about 200 mbars at altitude (Delany et al. 1985). The authors estimated a physical mixing time in the atmospheric layer on the order of 30 min. The area studied probably includes little in the way of urban sources of pollution, so it may be assumed that the measured levels may be corrected by the 25 to 30 ppb observed over the ocean by the same group (Routhier et al. 1980). The net concentration resulting from fire may be somewhat lower than observed in temperate zone forest burns, but there are a variety of factors that might account for the difference, including humidity,

fuel type, and the contribution of hydrocarbons volatilizing from vegetation (Chameides et al. 1988; Grimsrud et al. 1975).

Forested areas also serve as a sink for ozone, whether by contact with surfaces, or by interaction with volatile hydrocarbons produced by foliage (Lenschow et al. 1982). In the same work, the role of oceans as a sink for ozone is also discussed. The importance of the oceans is evident when considering the levels of about 90 ppb ozone in air that had apparently flowed down the Mississippi Valley over the Gulf of Mexico, where the measurements were made.

B. Toxicology of Ozone

The literature of ozone toxicity is quite broad and should afford an unusual opportunity to relate experimental studies in animals to studies of humans exposed to ozone under controlled or measured conditions. Unfortunately, much of the animal work has been done at levels that are higher than ranges that might be encountered in any but a localized industrial setting or an extreme urban pollution. In that group of studies, in many cases, there is not enough dose-response information to allow even speculation about low-dose effects that are pertinent to smoke exposure. There seems to be little point in reviewing most of these studies here. Menzel (1984) has prepared a quite comprehensive review of animal and human studies to that time. The scarcity of usable dose-response data is somewhat strange, in view of numerous findings that adverse responses to ozone can be seen in humans at concentrations that are within or not far removed from non-emergency, ambient levels or air quality health standards.

Avol et al. (1984) assessed some respiratory function indices in well conditioned bicyclists exercising at 50% of maximal oxygen consumption, and a nominal ventilation rate of 55 L/min, which is about 6 to 8 times the resting rate. The exposures were for 1 hr, to filtered and scrubbed air containing 80, 160 and 320 ppb ozone, and ambient urban (Los Angeles) air containing 150 ppb ozone and 295 μg particulate/m^3. In the clean air with added ozone, there was no effect at 80 ppb, but at 160 and 320 ppb, there was a dose-related decrease in expiratory function and increase in symptoms, observable at least 1 hr after the end of exposure. The authors observed that the effects at 160 ppb may be compared with the National Ambient Air Quality Standard (NAAQS) of 120 ppb. No exposures were done between 80 and 160 ppb.

It appeared that coexisting particulates did not influence the ozone effect. The question of effects of co-pollutants is quite important, and not well answered. Spektor et al. (1988a) studied respiratory functional response to ambient O_3 in a group of boys and girls aged 8 to 15 yr at a summer camp away from urban pollution sources. Daily maximum ozone concentrations ranged upward from about 40 ppb to occasionally in excess of 100 ppb.

Several findings are of interest. There is high variability among individuals, as others have observed; modest average decrements in function can be projected to occur at the ambient standard of 120 ppb; the data do not suggest a threshold above 60 ppb and there appears to be no difference in response compared with chamber exposures to ozone only.

In contrast to their own study in children and the work of Avol et al. (1984), Spektor et al. (1988b) concluded that there was as much as a ten-fold magnification of effect in adults exposed in an ambient atmosphere when compared with a 'clean' chamber atmosphere at equivalent ozone concentration. Their subjects in this case were adults, divided into three ranges of physical activity at a full range of ozone concentrations up to 124 ppb. This paper is interesting because it includes calculations of the decrement in standard function tests *per ppb* ozone, and the conclusion that while a threshold concentration could not be identified, it is below 80 ppb. A very useful tabular comparison with other related research is also included in the paper.

Kulle et al. (1985) examined the effects of 2-hr exposures to 100, 150, 200, and 250 ppb ozone on pulmonary ventilation in 20 non-smokers. Exercise was required at intervals during the exposure. Dose-response data suggested to the authors that a threshold exists at or below 150 ppb, which is consistent with the estimates by Avol et al. (1984). In a similar study, McDonnell et al. (1983) found that coughing was induced at a concentration of 120 ppb, and that functional deficits appeared in a dose-related manner through the range of exposures to 400 ppb. These studies suggested that the dose-response slope may be quite steep, requiring several narrowly separated concentrations for better definition. Linn et al. (1986) used a design of 2-hr exposures to concentrations of 80, 100, 120, 140 and 160 ppb, with exercise 15 min every 0.5 hr. The only general response was irritation at 160 ppb. However, two individuals responded to lower levels in a clearly dose-responsive fashion. In one individual who had developed an upper respiratory infection, forced expiratory volume was depressed 6% at 120 ppb, 17% at 140 ppb, and 35% at 160 ppb. The other subject showed measurable change at 140 ppb.

Longer exposures, as might be expected, seem to produce responses at lower levels. Under moderate exercise over a 6.6 hr exposure period, forced expiratory volume decreased about 13% by the end of the observation period (Folinsbee et al. 1988). Decrements with time appeared progressively through the six measurements, suggesting that even though not measurable in early stages, change begins immediately with beginning exposure. Other functions decreased as well, and subjective assessment of respiratory distress was also dose-related. Response to methacholine-induced increase in airway resistance doubled following exposure.

Vigorous exercise produced conditions in which 2.5 hr exposure at 120 ppb produced a response (McDonnell et al. 1985). The exercise was intermittent

over 2 hr at a rate that produced a minute ventilation of 35 L/min/m^2 body surface. The forced expiratory volume in 1 sec declined in ozone-exposed subjects and the decrement persisted up to 20 hr. There is also a demonstrable difference between men and women in response to ozone, according to findings corrected for differences in ventilation rate (Lauritzen and Adams 1985).

As should be expected, pre-existing differences in respiratory function influence response to ozone. This is of importance in the context of worker or public health, because our concern is with the most sensitive segment of the community. Asthma is a natural candidate for investigation because asthmatics are known to be quite sensitive to sulfur dioxide. Koenig et al. (1985) studied adolescents exposed to 120 ppb ozone for 30 and 60 min at rest, and found no significant differences in standard functions between tests after clean air and after ozone, and no differences between asthmatics and normal children. A later study at 120 and 180 ppbs for 30 min followed by 10 min of light exercise also disclosed no differences.

Other factors also influence ozone effects. A study of 2-hr exposure to 500 ppb, with 30 min of rest, then 30 min of exercise each hour showed decrements just after the exposures, and a still larger decrease in function after exercise. The effects of temperature variation indicated that heat stress may contribute to the primary response to ozone (Follinsbee et al. 1977). Unfortunately, no dose-response information was obtained. Pulmonary function response to ozone relative to age was observed by Reisenauer et al. (1988) in subjects aged 55 to 74. The ozone exposures were for 1-hr at 200 and 300 ppb during light exercise, and changes were observed only in women at 300 ppb, and those alterations were slight.

Plopper et al. (1979) suggest that differences in response between humans and rats are not large. They found slight morphological changes in the lungs of rats exposed to 100 ppb for 7 d, and macrophage accumulation and other changes in lungs of rats exposed to 200 ppb. Glutathione peroxidase and reductase, glucose-6-phosphate dehydrogenase and non-protein sulfhydryls were all increased in a dose related manner that suggested a threshold considerably below 100 ppb for the prolonged exposure of the study. Lung histamine concentrations of guinea pigs exposed to 100 ppb for 2, 4, and 8 hr were increased without evidence of cellular toxicity.

As with other respiratory irritants, the possibility of altered susceptibility to infectious disease following ozone exposure is an important question. Most animal work has been on direct bacterial or viral infection. Ozone has increased responses to becteria after exposures of mice as low as 100 ppb over a 3-hr period (Ehrlich et al. 1977; Miller et al. 1978). Effects on bacterial disease may be related to depressed alveolar macrophage activity, irritant responses with consequent cellular vulnerability, and decreased mucociliary clearance.

Viral infection seems to be less influenced by ozone. Fairchild (1977) reported that influenza virus growth in the nasal passages of mice increased after exposure to 600 ppb ozone for 3 hr, but vesicular stomatitis virus infectivity was not increased at even higher exposures. The behavior of both viruses was unaffected in the lungs. Selgrade et al. (1988) evaluated the effect of several concentrations of ozone on influenza infection in mice. Exposures were 3 hr/d for 5 successive d, at concentrations of 250, 500, and 1000 ppb. Virus titers and survival were not affected at any exposure, but there was some amplification of typical viral pathology by ozone at 1000 ppb and wet lung weight in infected mice was increased at 500 and 1000 ppb.

Studies in humans usually have evaluated the potential for infection indirectly, i.e., the populations of polymorphonuclear neutrophils (PMN) that scavenge bacteria in the respiratory tract. Irritant and infectious agents increase populations of PMN in the nasal and bronchial passages. Graham et al. (1988) found that exposure of human volunteers to 500 ppb ozone for 4 hr on 2 successive d induced a several-fold recruitment of PMN, detected in the nasal washings at a level which approaches that at which a major smog alert would be called.

In a similar study to that of Graham et al. including some of the same investigators, males were exposed to 400 ppb for 2 hr, with intermittent exercise (Korent et al. 1988). Eighteen hr after exposure, bronchio-alveolar lavage showed a more than eight-fold increase in PMN and decreased numbers of macropahges, which is an inflammatory response. Free protein from the circulation increased, indicating greater permeability of pulmonary vasculature. Seltzer et al. (1986) observed a similar increase following a 2-hr exposure to 400 and 600 ppb, accompanied by intermittent exercise. None of these studies projected a no-effect concentration. Substantial increases in prostaglandins E_2 and $F_2\alpha$ also resulted. It would be most useful to learn whether these changes occur in some degree at more reasonable levels.

Rabbits exposed to 500 ppb ozone for 3 hr produced increased numbers of PMN in the alveoli and bronchi (Alpert et al. 1971), as distinguished from the nasal washings of the human subjects discussed by Graham et al. (1988) indicating that the response occurs in the entire tract. The latter studies were unilateral lung exposures and showed that the responses were local, not systemic. At higher exposures, the PMN production increased correspondingly, and the activities of hydrolytic enzymes in the cells decreased with dose. It is not likely that vegetation smoke would produce levels approaching 500 ppb.

The mechanism of ozone effects on the lung is still an open question; considerable information about specific biochemical changes is available, but which mechanism predominates is not known. For the purposes of this review an exhaustive discussion is not necessary; thorough reviews are available elsewhere (i.e., Menzel 1984). Among identified responses are alterations in

prostaglandin production. Prostaglandins are produced in each cell and mediate cellular responses to other regulators. They also tend to amplify inflammatory responses. Madden et al. (1987) exposed cultured endothelial cells to 1.0 ppm ozone and observed inhibited prostacyclin synthesis (prostaglandin PGI_2), which they concluded was the result of increased hydrogen peroxide formation. An increase in prostaglandin PGD_2 was observed in canine lung by Kleeberger et al. (1988) after 5-min exposure to 1.0 ppm ozone, along with other indices of inflammation, including increased airway resistance. Whether prostaglandins play some mediating role, or these changes simply indicate a transient change in membrane integrity as suggested below is not known. No dose-response data were obtained, but 4 such short exposures at about 1-hr intervals showed similar responses; no tolerance to the responses developed (Kleeberger et al. 1988).

The Kleeberger et al. study showed that recovery appears rapid after ozone exposure, even to concentrations as high as 1.0 ppm, and that very short exposure will produce a response. It seems that both recovery and short-term cumulation occur simultaneously; the idea of a constant exposure factor that includes concentration X pulmonary ventilation X time is probably not applicable beyond short periods. The inflammatory response is accompanied by decreased lung histamine concentration in guinea pigs exposed to 1.0 ppm ozone for 2 hr, presumably as the result of release from mast cells (Shields and Gold 1987).

In a similar set of exposures, Foulke et al. (1988) placed baboons in 500 ppb ozone for 5 min, which caused increased airway resistance. In a second set of exposures, cromalyn sodium cut the ozone response by half. Cromalyn has an effect of stabilizing cell membranes, which led Foulke et al. to the hypothesis that ozone damages cell membranes.

Another primate study raised questions about the recovery from ozone. Tyler et al. (1988) exposed young male monkeys to 250 ppb ozone 8 hr/d daily for 18 mon, or daily on alternate mon. The discontinuous exposure caused less effect on inspiratory capacity, but resulted in greater collagen content in the lung, and greater biochemical change.

C. Exposure and Potential for Acute Health Effects

The data indicate that ozone is not a concern at the fire line, but that the down-plume addition of smoke-derived ozone to the existing burden, particularly that arising from urban activity, should be examined. It is obviously necessary to relate existing research on health effects of various concentrations of ozone to the levels that may be presumed to be present in smoke at some distance from the burn. Some dilution will occur, and some deposition or reaction at surfaces. At the same time formation continues, and the data of Westberg et al. (1981) suggest that even with dilution as a

function of distance from the source, ozone concentration remains roughly the same.

It appears that ozone levels derived from smoke together with other sources probably do not exceed about 90 ppb, but for the purpose of comparison, this analysis will assume that the total ozone levels from forest slash combustion and other sources could produce down-plume levels of 100 ppb over distances of several km, and that non-urban levels without a prescribed fire contribution would not exceed 50 ppb.

Studies of ozone effects on various physiological and biochemical functions suggest that there is a threshold for acute responses, and that it is close to the 100 ppb figure. It seems clear that smoke as such may produce as much as one-half of the threshold concentration at certain times, which represents a very small safety factor. The published studies of ozone effects on physically well-conditioned humans are germane to the exposure of fire fighters. *Given the potential for down-plume expsoure of individuals with serious respiratory impairment, ozone from forest burning should be considered as a potential threat to some individuals away from the fire site.*

It is obviously inappropriate to make a blanket assessment of the potential for smoke-derived ozone to affect the health of people in any given area. The effects of terrain and weather are complex and may well create pockets of high or negligible ozone levels. Until better predictive models exist, however, it seems necessary to make empirical measurements of ozone concentrations at down-plume ground-level sites, and to assume that health may be affected at considerable distance from a fire.

V. Free Radicals

A. Occurrence of Free Radicals in Combustion Processes

Consideration of free radicals as a possible cause of smoke derived health effects is rather recent, and probably results from convergence of two different lines of research. The extensive biological research into intracellular free radicals arising from activity of foreign chemicals, and their metabolites have led to curiosity about the cellular impact of exogenous free radicals, of which those associated with tobacco smoke probably produce the most intense exposures. The extensive study of tobacco smoke, and its pathology has in turn stimulated parallel examination of smokes from industrial and dwelling fires (Lachocki et al. 1988, 1989).

Free radicals are molecular species that contain an odd number of electrons; as a consequence they are quite reactive, and very short lived. Such great reactivity confers the potential to cause damage to essential molecules within cells, including both proteins and nucleic acids, if the radical or its precursor can reach such sites. It should be expected that the cell membrane of contact surfaces such as that of the lung is highly vulnerable.

The existence of free radicals in tobacco smoke was reported in 1971 by Bluhm et al., and a variety of evidence has suggested an association between free radicals of smoke and respiratory toxicity (Pryor 1986). We may intuitively expect that in the case of tobacco smoke, free radicals or any toxic species formed might persist long enough to reach the respiratory tract because of the initial proximity. We might also expect that wood combustion radical products would not survive long enough to reach a fire worker, let alone a bystander 100 or 1000 m distant. It seems clear now, however, that there are precursors of free radicals produced from burning wood and other cellulosic materials that may persist long enough to reach human targets and produce free radicals in the lung (Lachocki et al. 1988, 1989).

The knowledge about free radicals from wood is not yet at a stage that permits valid predictions of the contribution of this class of emissions to the health impact of smoke. However, the existing work suggests strongly that these substances play a significant role, a supposition that is supported by the existing information about the impact of endogenous free radicals on respiratory and other cellular pathology.

Lachocki et al. (1988) pyrolyzed several organic materials commonly found in households, and trapped the smoke in a phenyl-*N*-butyl nitrone (PBN) solution. PBN reacts with oxygen and carbon-centered free radicals to form a stable nitroxide radical, which is detected by electron spin resonance techniques. The reactions were carried out in an air stream with temperatures rising to 500°C in 3 min. Cellulosic substances (pine, birch plywood, research tobacco, cellulose) produce nitroxide radicals of undetermined structure. Of particular interest, it was found that free radicals arising from cellulose continued to form for more than 20 min in the dodecane solution used to trap the smoke. Production of radicals from tobacco smoke continued for less than 30 sec after trapping. The difference was considered to be related to the higher NOx levels produced by tobacco combustion.

In subsequent work (Lachocki et al. 1989) the same workers pyrolyzed yellow pine and oak to determine if the radicals known to arise from wood combustion would persist in the same manner as those from cellulose in the earlier work. Persistence was observed. It must be recognized that in these studies the smoke was trapped in solvent immediately after leaving the combustion train, and then added to the spin trapping medium after several minutes. Finding of radicals in the solution after some time has elapsed indicated the survival of the reactive precursor species in the trapping sovlent, compared to those from other sources such as tobacco, which survived a relatively short time. Pryor et al. (1983) have reported that radicals in tobacco smoke would continue to arise in the gas phase after several minutes, apparently driven by NOx reactions. That kind of experiment was apparently not done in the studies of wood combustion just discussed. Lachocki et al. (1989) concluded, however, that the observed radicals arose from metastable

intermediates that continued to decay in the trapping solution. They further believe that the same intermediates may persist in the smoke plume to be inhaled by persons in the vicinity. Whether the precursor substance is volatile enough to be transported in the gas phase, or whether it is in solution in the organic condensate of the particulate phase is not known, but it would seem likely that the physical state could influence its persistence.

There have been no measurements of radicals in smoke from burning of forest or agricultural materials.

B. Toxicology of Free Radicals

Pryor (1986) has written a brief but very useful review of the nature, and biological importance of free radicals, from which several points necessary to this discussion have been extended.

There are a variety of sources of free radicals to which cells might be exposed. First, it must be remembered that radicals are produced by normal physiological processes in energy metabolism. As long as they remain in the intended reaction sequences they should not produce observable adverse effects, although such products are believed to cause considerable repairable damage in normally functioning cells. If in excess of trapping or repair capacity, or if for some reason there is 'leakage' into parts of the cell that may be vulnerable, injury could result. Environmental sources such as combustion may lead to direct exposure of cells to free radicals at surfaces of contact, particularly the lung. On the other hand, foreign chemicals of natural origin such as ozone, or those made synthetically like chlorinated pesticides, or that may arise either naturally or by human activity, such as NO_2 or benzo(a)pyrene may also, through the processes of their metabolism, cause free radical production within cells.

Intracellular free radicals have been implicated in a variety of general conditions, but in the context of smoke inhalation, we probably need not be concerned with systemic effects because it is not likely that exogenous radicals such as those of smoke will progress beyond the cells of contact of the lung. By the same token, however, it is likely that exogenous free radicals, or more likely their precursors, can enter surface cells, and produce responses similar to those of intracellular origin.

Free radical pathology is believed to contribute to lung cancer and emphysema, and there is evidence to suggest that the Adult Respiratory Distress Syndrome (ARDS) results in part from activity of endogenous free radicals. ARDS is a disease in which the eventual pathological manifestation is increased capillary permeability, and accumulation of fluid in the alveoli, with the expected respiratory deficiency. As yet, the etiology is unknown; the disease is characterized by a very complex web of immunological and other factors (Rinaldo and Rogers 1986). There are a variety of in vitro and in vivo

studies of tobacco smoke effects on lung tissue, and isolated biochemical systems. The relation of these observations to effects of smoke components, particularly free radicals, in a breathing atmosphere can only be speculated upon.

C. Health Impact of Free Radicals Formed in Fire

At present it is not possible to predict exposures or responses, if any, that might be produced by free radicals in smoke from prescribed fire. However, it seems likely that relatively stable precursors of radicals are produced in combustion of cellulosic materials, which in turn generate radicals at more or less constant concentration. The life time of this process is such that it seems possible that human exposure to smoke less than an hour old may include exposure to such substances.

VI. Health Impact of Particulate Matter

Particulate matter in smoke plumes is the most visible manifestation of combustion, but the effect of inhaled smoke particles as such is not at all clear. Smoke particulates are in large part condensed volatile organics which serve as aggregations, as solvents, and as surfaces of attachment for any and everything else in the atmosphere. That complexity is an obstacle to study, and the mix will differ from fire to fire and within zones of a given fire and plume. It is therefore not surprising that there is no description of the effects of particulates of smoke as independent causes of adverse response without respect to whatever organic or inorganic material they contain.

There is an allusion to an absence of particulate effects in a report by Kensler and Battista (1963) on tobacco smoke. They introduced a charcoal filter into the smoke stream that stopped the gases, and allowed particulate matter to pass. Most of the depression of the activity of the cilia of the upper respiratory tract of animals was caused by substances in the gas phase, and particulates passing into the tract were not very active. One study of humans exposed to ozone noted that the observed responses were not modified by co-pollutants (Avol et al. 1984).

In spite of the absence of knowledge about particulate matter, much of smoke-related regulatory activity is based on the amount of particulate material of respirable size in the air, not on any discrete health effects of the visible material. Perhaps this is because it is not only visible but easily measured. Most major epidemiological studies of populations exposed to possibly adverse atmospheres relate disease characteristics, and incidence to particulate levels as the primary index of air pollution, with no information about the total character of the atmospheres in question.

There is a wealth of information about many other specific components of smoke. Formaldehyde, ozone, acrolein, polynuclear aromatic hydrocarbons, and free radicals are among the numerous specific substances in smoke. Particulates alone are simply not the subject of such study, and a separate toxicological assessment of particulates cannot be done at this time. It may not be possible to study particulates of smoke alone. Similarly it is not presently possible to examine the role of the equilibrium of volatile pollutants between particulate and gas phases.

The weakness of the data has led to such strange exercises as using the fairly extensive urban epidemiological data that associate high particulate levels with disease, to predict effects of specific other sources of particulates such as forest or agicultural smokes. In other words, rural air or air into which a single smoke type has intruded is considered to have the same health impact as urban air with the same particulate level.

Urban pollution and that derived from single sources of vegetation smoke have been studied by numerous investigators, and it is clear that they are not likely to be similar. Ozone and nitrogen oxide concentration are particularly different, with much greater levels in an urban atmosphere, and they in turn lead to a variety of reaction products not seen in rural smokes. Ketone and nitro derivatives of the polynuclear aromatics scarcely appear in vegetative smoke. Similarly, the various chlorodioxins and furans, when found, are usually from urban combustion sources.

The character of non-volatile components, such as soil, masonry dust, fly ash, asbestos, machinery wear products, bacteria, and so on is also much different in the urban matrix. This issue is given considerable attention in a review, and discussion by Matanoski et al. (1986). Their concern is with cancer incidence, and its relation to particulate air pollution, but their conclusions apply as well to short term effects. They believe pollution should not be described in terms of suspended particulates, but that the focus should be on specific contaminants. It is interesting that in their review of existing data, and opinions on the carcinogenic impact of particulates and organics, they conclude that outdoor air pollution plays a limited role in either urban or rural lung cancer.

It seems reasonable to assume that particulate matter from vegetation fires will be mostly condensed organic compounds. There may be a small amount of mineral elemental material entrained from the normal content of the vegetation, plus a certain amount of fine mineral soil captured in updrafts.

If we are to try to develop some idea of the toxicology of particulates from wood combustion, it is obviously necessary to establish some information about their nature. That they are of respirable size is unquestioned. According to Sandberg and Martin (1975), 82% of the mass of particulate in forest smoke was in particles $< 1.0\ \mu m$ aerodynamic diameter, and 69% of the mass was

$< 0.3\ \mu m$. The physical nature of the particles is very well described by Thomas et al. (1968), even to the orientation of the polynuclear aromatics in the particle in a quasi-crystalline organization. These particles in aggregate are what we commonly call soot, the term also used in the chemistry literature.

Among the differences between urban, and more remote atmospheres are levels of nitrogen oxides, which have a direct influence on the fate of organic constituents of the pollutant pattern, particularly the polynuclear aromatic hydrocarbons (PAH). Phtotochemical reactions in the presence of very low concentrations or absence of NOx deplete the total indirect mutagenicity of wood smoke particles, and deplete PAH bound to particles (Bell and Kamens 1986). Higher concentrations of NOx (10 ppm) result in formation of nitro derivatives of PAH, which, curiously, seem to be not carcinogenic (Butler and Crossley 1981), but are potent mutagens (Mermelstein et al. 1981; Rosenkranz and Mermelstein 1983). This difference suggests that the greater NOx burden of the urban atmosphere confers greater biological activity on at least some parts of the pollutant mix.

The inorganic matter characteristic of the urban aerosol not only has its own toxicologic profile (lead has been used as a marker for urban atmospheres), but may modify the behavior of organic constituents. Fly ash will serve as an adsorption surface for the PAH, and unlike the effect of soot on the behavior of constituent PAH, fly ash interferes with photochemical decomposition (Korfmacher et al. 1980), leaving the PAH in a biologically active form for longer periods. Effects upon acute irritants can scarcely even be speculated upon.

It is a justifiable presumption that on the basis of comparable particulate loading, urban atmospheres contain a greater variety of known toxic materials than atmospheres contaminated by vegetation smoke also, and therefore convey greater risk. Unfortunately, there is not as yet enough information to show certainly that such single sources as agricultural or forestry fires produce less hazard than particulate laden urban air. Those sources can be distinguished, if necessary, by greater NOx and inorganic particulate levels, and lower radiocarbon content in urban air.

Should there be motivation to differentiate the health impact of urban particulate pollution, and that of specific rural combustion products, then the methodology for sorting the respective air loading components exists clearly.

For reasons explained earlier, effects of particulates as such and independent of their varied content of other combustion products cannot be judged. Exposure is easily estimated, but exposure without discreet toxicology data provides no information on risk.

VII. Collateral Issues

A. Toxicologic Interactions Among Chemicals in Smoke

Whenever two or more chemicals with toxic potential exist together there is a question whether some combination of the substances is more or less toxic than the sum of the individual effects. There are also potential qualitative differences. One chemical may modify the manner in which another affects a biological system. Unfortunately, the available information about interactions of the various components of smoke is extremely limited, but rational qualitative estimates are possible.

It takes little intuition to recognize that experimental determination of all possible interactions of the hundreds of substances in smoke is unthinkable. A mathematical determination of the number of experiments needed for, let us say, 10 tests on 100 different interacting materials is entertaining but of no utility. Ten tests won't tell us a great deal, and 100 components is a gross underestimation.

This is not to say that the whole question should be abandoned in despair. There is a good deal known about the subject of biological interaction in general, and the application of some basic principles can provide us with a reasonably reliable concept of the effect of biologically interacting smoke constituents. There is a massive literature on the interaction of pharmaceuticals, because interaction of prescription and over the counter drugs is an obvious concern in clinical medicine. This work is vital to the question asked here because a number of generalities have emerged, and because the dosages that demonstrate these generalities are enormous by the standards of exposure that characterize contact with smoke.

The first issue that should be addressed is the potential for some kind of reactions between components to produce new, and exotic products. Once out of the immediate zone of reactivity where temperatures and concentrations of combustion products are high, chemical interactions other than those driven photochemically are not likely. Many of the known products of combustion are in fact products of interactions in close proximity to the fire. It is neither possible nor sensible to consider them as other than combustion products.

The real question of concern is whether unknown and remarkable products form at sites where exposure is likely. Certain reactions leading to secondary products in emissions are well-known, such as the interactions of hydrocarbons in sunlight and subsequent reactions of free radicals with aldehydes, or the formation of ozone through the reaction of other constituents of the smoke plume and sunlight. Most such reactions include free radical reactions, a well studied field, and it is doubtful that formation of unknown exotic toxic substances will occur. The con-

tinuing effort to identify airborne contaminants, and follow their history is sufficiently effective that such substances have probably not escaped detection.

Interactions of combustion products in target organisms is a different kind of question. Chemicals may increase effects of other chemicals by adding the same kind of response, with the total response being purely additive ($1 + 1 = 2$). The mechanism may involve changing the extent of detoxication reactions or excretion, thereby prolonging the residence of the first chemical, and increasing its effect. If the second chemical alone is not able to contribute to the toxic response, the effect would be potentiation, in which the sum of effects might be something like $1 + 0 = 3$. If both chemicals alone have a related effect, and the sum of responses are greater than the expected additive response, the effect is synergistic ($1 + 1 = 3$).

Such changes in response are rarely, if ever, massive. Synergism or potentiation do not produce effects hundred- or thousand-fold greater than eiher can achieve alone. Changes are more likely to be in the small whole number range. In the body, the interactions will be mediated through the biological systems involved, and will not include direct interactions between chemicals after they are absorbed.

It is to be expected that such interactions will be threshold dependent. With the exception of a very low potential for carcinogenic response due to heavy exposure to PAH or formaldehyde, there is little likelihood that the kind of effects produced by smoke constituents will not be threshold-based. Not only do threshold based effects require some level of the chemical to be present in order than an effect will occur, the interacting chemical must also be present in an amount sufficient to trigger its response. If the effects are not physiologically similar, and thereby subject to simple addition, both thresholds would have to be exceeded substantially before an effect could be detected. Because of the often non-specific effect of irritants, it is likely that they are additive in their effect on the respiratory mucosa.

An argument might be made that the irritants would serve as promoters of carcinogenic response, causing exposures that represent trivial cancer risk to become significant. It is not likely that irritants will amplify the risk associated with PAH exposure because the responses occur in different parts of the respiratory tract. Theoretically, coexisting irritants might increase the potency of formaldehyde as an upper respiratory genotoxic carcinogen, but the primary cancer risk relating to formaldehyde exposure from smoke of prescribed burning is truly trivial compared to that of other sources of the same chemical. It is doubtful that even a massive amplification would have significance.

The conclusion must be, then, that while our knowledge of toxic interactions of smoke components as such is not adequately studied, it is not likely that it is a significant part of the smoke toxicity problem.

B. Combustion of Herbicides Applied to Vegetation Prior to Burning

The perception is widespread that when chemicals burn, products of extraordinary toxicity may be produced. This belief also applies to herbicides or insecticides that have been used on forest, and agricultural land that is later burned, whether intentionally or accidentally. There is enough information on combustion of organic compounds in general, and on herbicides in particular, from which worst-imaginable-case estimates of combustion products can be prepared. It is clear that the amounts in the atmosphere do not approach levels sufficient to produce responses.

In a report to the Bonneville Power Administration, Dost (1982) considered whether combustion of applied herbicides might produce substances with significant potential for helath impacts. Several studies have shown a limited number of terminal combustion products of herbicides, of which carbon dioxide and carbon monoxide predominate, as would be expected. Almost all of the chlorine in such chemicals will be oxidized to hydrogen chloride. Very small amounts of chlorine gas and phosgene can be produced under forced laboratory conditions, so it was assumed, for purpose of the analysis, that they were also possible products in the field. It was also assumed that ammonia and cyanide, and in some cases acetonitrile, could arise from nitrogenous herbicide compounds. In the case of the herbicide glyphosate, the phosphorus present was known to form some phosphorus pentoxide, which then formed phosphoric acid.

By calculating the amount of herbicide assumed to be present, following either aerial application or injection by hack-and-squirt methods, a relation was established with fuel loading, which in turn related to smoke production, visibility limits, and a volume of distribution, which therefore defined atmospheric concentration.

The calculations showed that even when it was assumed that all of the chlorine in a herbicide formed phosgene, chlorine gas, or hydrogen chloride, the amounts were trivial when compared with known toxicology or with established federal workplace standards. The same conclusion was reached with respect to herbicides containing nitrogen or phosphorus. All of the potential products are common industrial chemicals with well-established allowable levels for workplace exposure. When it was assumed that the herbicides simply volatilized and distributed in the smoke cloud, exposures were again well below no-effect-levels.

C. Estimates of Exposure to Smoke Components

No method other than direct measurement can provide reliable information about the atmospheric concentration of smoke constituents. However, it is possible to make estimates on the basis of visibility limits, which is reasonably well related to particulate loading.

Estimates of the concentration of a given smoke constituent can be based on the relation between particulate and constituent loading, or on the less direct relation of both constituent, and particulate to fuel consumed.

Particulate emission measurements have ranged from a high of 40 g/kg fuel to 8.5 g/kg (Imhoff and Manning 1983; Dasch 1982; Sandberg and Martin 1975; Radke et al. 1978; Lim and Lips 1981). Most of the ratios fall between 8.5 and 15 g/kg fuel. If such numbers are used to draw a relation between smoke density, and concentration of any smoke constituent in the air to estimate human exposure, the lower particulate output/unit fuel implies a higher concentration of the material of interest in the atmosphere if the output/kg fuel remained the same. In our estimates we therefore used the low figure of 8.5 g particulate.

The light extinction for smoke is about 0.5 g/m^2. A square column 1 m on each side containing 0.5 g of smoke would block all light, whether the column was very long or so short the particulates were spread in a layer. If the column is 100 m long, the volume would be 100 m^3 and the concentration of particles would be at a concentration of 0.005 g or 5 mg/m^3.

VIII. Research Needs

1. Exposure assessment is perhaps the most critical need. The idea of using a visibility limit to estimate exposure is attractive but must be approached with caution. It assumes a uniform smoke plume, with no gradations of concentration at the edges, which is satisfactory for visualizing the concept of dilution. However, a heavy plume between an observer and a distant point may totally obscure vision of a landmark 1000 m away, with no exposure to the observer, because the plume was across the viewing axis. Also, some pollutants do not have a constant ratio with visibility. At present, however, visibility is the only easily observed general index. Further efforts should be made to correlate visibility or some other accessible index with other components of interest, and with fire characteristics. A heavy emphasis on personal monitoring is needed, exploring ways of measuring exposure, and biological monitoring, such as measuring metabolites or macromolecule repair products that will give a clear idea of target cell dosage.
2. Acrolein is a very potent irritant. It is necessary to learn more about its production in fires. Its fate in time and space is not understood, and should be an important research objective.
3. With all irritants there appears to be a need to learn whether the reflex respiratory shutdown that follows irritant exposure can be overridden to maintain necessary oxygen exchange, or whether there is some middle ground where the response exists, and function is consciously maintained despite the inhibition.

4. It seems important to learn whether formic acid is a significant emission from vegetation fires.
5. The question of free radical formation and toxicity could be the most important set of problems in smoke toxicology. Research to first determine the extent of free radical formation, and then to study their character seems critical, after which their biological responses should be studied.
6. Because of the approach to undesirable levels of ozone in typical smoke plumes, research should concentrate on ground level ozone concentrations at various distances, and times from sources of vegetation smoke, with attention to modulation by terrain and meteorological factors. The photochemical reactions within the upper reaches of smoke plumes should be examined in more detail to learn whether a critical smoke component level might be modified by the manner in which the burn is managed. Particularly, the formation of ozone as the plume is diluted is interesting and important. Some evidence suggests that the rate of formation increases as more light is admitted to the distribution volume, and it is imaginable that light availability is the rate limiting factor through a wide range of precursor concentrations. It is becoming clear that the naturally occurring unsaturated hydrocarbons that volatilize from foliage are more reactive as precursors in photochemical ozone formation than are saturated compounds liberated in human activity. It seems quite important to learn the extent to which fire volatilizes these natural compounds without otherwise reacting them, thereby increasing the potential for atmospheric ozone formation.
7. The role of condensed organic and other particulate material in modulating the effect of other specific components of smoke should be evaluated.

Summary

Only in recent times, systematic attention has been paid to the occupational health of forest firefighters and workers who manage prescribed fire. Two parts of the effort to learn the impact on worker health are medical observation of those workers, and study of occupational hygiene. It is also necessary to learn what components of smoke are most likely to affect firefighters, and to learn something of the manner in which those substances might compromise health; this review is a step toward that end.

The number of possible products of vegetation combustion is almost limitless, and every fuel and condition of burning produces a unique pattern.

Nonetheless, it is possible and practical to select a limited number of products that are most likely to be involved in the acute toxicity of smoke. Two products that are almost certainly important are formaldehyde and acrolein. Both appear to occur in all smoke. The toxicology of both is well studied; in particular both are powerful mucosal irritants. Estimates of

exposure suggest strongly that concentrations are high enough in smoke to contribute some or all of the irritant activity.

There seems to be a reasonable prospect that free radical precursors with half-lives in the tens of minutes are produced when cellulosic materials burn. If so, they will reach the respiratory tract, and liberate free radicals that react immediately on or in pulmonary cells.

Ozone is not produced in the fire, but the various hydrocarbons of smoke are substrates for reactions that eventually produce ozone, and that production may continue for miles down-plume. Some measured plume concentrations approach the threshold for human health effects.

The effects of the best known component, the particulate material, are unknown in isolation from all of the other substances in smoke. In spite of that ignorance, particulate loading is the principal index of smoke pollution for regulatory purposes, and sometimes is incorrectly used to represent smoke emissions regardless of source.

The need to understand health impacts of these components of smoke seems obvious. Perhaps less obvious is the need to use such knowledge in management of both prescribed burning and wildfire. To some extent, it is possible to either manage fire itself to alter emission patterns, or control exposures in certain situations. Whether that should be done to protect worker health can only be judged if enough is known about health effects to direct the management decisions.

References

Adewuyi YG, Cho S, Tsay R, Carmichael GR (1984) Importance of formaldehyde in cloud chemistry. Atmos Environ 18:2413–2420.

Alpert SM, Gardner DE, Hurst DJ, Lewis TR, Coffin DL (1971) Effects of exposure to ozone on defensive mechanisms of the lung. J App Physiol 31:247–252.

Altshuller AP (1987) Estimation of the natural background of ozone present at surface rural locations. J Air Pollution Control Assoc 37:1409–1417.

Altshuller AP, Cohen IR, Purcell TC (1967) Photooxidation of hydrocarbons in the presence aliphatic aldehydes. Science 156:937–939.

Appleman LM, Woutersen RA, Feron VJ, Hooftman RN, Notten WRF (1986) Effect of variable versus fixed exposure levels on the toxicity of acetaldehyde in rats. J Appl Toxicol 6:331–336.

Aranyi C, O'Shea WJ, Graham JA, Miller FJ (1986) The effects of inhalation of organic chemical air contaminants on murine lung host defenses. Fund Appl Toxicol 6:713–720.

Astry CL, Jakab GJ (1983) The effects of acrolein exposure on pulmonary antibacterial defenses. Toxicol Appl Pharmacol 67:49–54.

Avol EL, Linn WS, Venet TG, Shamoo DA, Hackney JD (1984) Comparative respiratory effects of ozone and ambient oxidant pollution exposure during heavy exercise. JAPCA 34:804–809.

Barrow CS, Buckley LA, James RA, Steinhagen WH, Chang JCF (1986) Sensory irritation: studies on correlation to pathology, structure-activity, tolerance develop-

ment, and prediction of species differences to nasal injury. In: Barrow CS (ed) Toxicology of the nasal passages, Hemisphere, Washington, DC. pp 101–122.

Beauchamp RO Jr, Anjelkovich DA, Kligerman AD, Morgan KT, Heck Hd'A (1985) A critical review of the literature on acrolein toxicity. CRC Crit Rev Toxicol 14:309–377.

Bell DA, Kamens RM (1986) Photodegradation of wood smoke mutagens under low NO_x Conditions. Atmos Environ 20:317–321.

Benner WH, Urone P, McMahon CK, Ryan P (1977) Photochemical potential of forest fire smoke. Proc Air Pollut Control Assoc 77–5.3, 15 pp.

Bernstein RS, Stayner LT, Elliott LJ, Kimbrough R, Falk H, Blade L (1984) Inhalation exposure to formaldehyde: An overview of its toxicology, epidemiology, monitoring, and control. Am Ind Hyg Assoc J 45:778–785.

Bluhm AL, Weinstein J, Sousa JA (1971) Free radicals in tobacco smoke. Nature 229:500.

Butler JD, Crossley P (1981) Reactivity of polycyclic aromatic hydrocarbons adsorbed on soot particles. Atmos Environ 15:91–94.

Carson BL, Beall CM, Ellis HV III, Baker LH, Herndon BL (1981) Acrolein health effects. Report by Midwest Research Institute to US. EPA on contract #68-03-2928, 121 pp.

Casanova M, Deyo DF, Heck Hd'A, Steinhagen WH, Everitt JI, Monticello TM, Morgan KT, Popp JA (1988) Comparative studies of the covalent binding of inhaled [^{14}C]formaldehyde in rhesus monkeys and fischer rats. Abstract #60 Twelfth Ann Scientific Evening for Chemical Industry Ins Toxicol.

Chameides WL, Davis DD (1983) Aqueous-phase source of formic acid in clouds. Nature 304:427–429.

Chameides WL, Lindsay RW, Richardson J, Kiang CS (1988) The role of biogenic hydrocarbons in urban photochemical smon: Atlanta as a case study. Science 241:1473–1475.

Cooper JA, Currie LA, Klouda GA (1981) Assessment of contemporary carbon combustion source contributions to urban air particulate levels using carbon-14 measurements. Environ Sci Technol 15:1045–1050.

Cosma GN, Jamasbi R, Marchok AC (1988) Growth inhibition and DNA damage induced by benzo[*a*]pyrene and formaldehyde in primary cultures of rat tracheal epithelial cells. Mutat Res 201:161–168.

Costa DL, Kutzman RS, Lehmann JR, Drew RT (1986) Altered lung function and structure in the rat after subchronic exposure to acrolein. Am Rev Respir Dis 133:286–291.

Dasch JM (1982) Particulate and gaseous emission from wood-burning fireplaces. Environ Sci Technol 16:638–645.

DeAngelis DG, Ruffin DS, Reznik RB (1980) Preliminary characterization of emissions from wood-fired residential combustion equipment. U.S. EPA 600/7-80-040. U.S. EPA, Office of Research & Dev, Research Triangle Park, NC.

Delany AC, Haagensen P, Walters S, Wartburg AF, Crutzen PJ (1985) Photochemically produced ozone in the emission from large-scale tropical vegetation fires. J Geophys Res 90:2425–2429.

Dost FN (1982) Combustion of herbicides. Report (unpublished) to Bonneville Power Administration, Vancourer, WA. (Also presented at Society for Envir Toxicol & Chem Meeting Nov 2–5, 1986).

Dost FN (1986) An estimate of carcinogenic risk associated with polyaromatic hydrocarbons in smoke from prescribed burning in forestry. Report to Bureau of Land Management. 16 pp.

Ehrlich R, Findlay JC, Fenters JD, Gardner DE (1977) Health effects of short-term inhalation of nitrogen dioxide and ozone mixtures. Environ Res 14:223–231.

Evans LF, King NK, Packham DR, Stephens ET (1974) Ozone measurements in smoke from forest fires. Environ Sci Technol 8:75–76.

Evans LF, Weeks IA, Eccleston AJ, Packham DR (1977) Photochemical ozone in smoke from prescribed burning of forests. Environ Sci Technol 11:896–900.

Fairchild GA (1977) Effects of ozone and sulfur dioxide on virus growth in mice. Arch Environ Hlth, Jan/Feb 28–33.

Farrar DG (1980) The effect of the sensory irritant component of a combustion atmosphere derived from douglas fir on the leg-flexion avoidance response of the rat. J Combust Toxicol 7:3–23.

Folinsbee LJ, Horvath SM, Raven PB, Bedi JF, Morton AR, Drinkwater BL, Bolduan NW, Gliner JA (1977) Influence of exercise and heat stress on pulmonary function during ozone exposure. Exer Physiol 43:409–413.

Folinsbee LJ, McDonnell WF, Horstman DH (1988) Pulmonary function and symptom responses after 6.6-h exposure to 0.12 ozone with moderate exercise. JAPCA 38:28–35.

Foulke JM, Delemos RA, McFadden ER Jr (1988) Airway response to ulta short-term exposure to ozone. Am Rev Respir Dis 137:326–330.

Grafstrom RC, Fornace AJ Jr, Autrup H, Lechner JF, Harris CC (1982) Formaldehyde damage to DNA and inhibition of DNA repair in human bronchial cells. Science 220:216–218.

Graham D, Henderson F, House D (1988) Neutrophil influx measured in nasal lavages of humans exposed to ozone. Arch of Environ Hlth 43:228–233.

Green GM, Jakab GJ, Low RB, Davis GS (1977) Defense mechanisms of the respiratory membrane. Am Rev Resp Dis 115:479–514.

Grimsrud EP, Westberg HH, Rasmussen RA (1975) Atmospheric reactivity of monoterpene hydrocarbons, NOx photooxidation, and ozonolysis. Int J Chem Kin 7:183–195.

Guerin MR, Higgins CE, Jenkins RA (1987) Measuring environmental emissions from tobacco combustion: sidestream cigarette smoke literature review. Atmos Environ 21:291–297.

Hart RW, Terturro A, Neimeth L (eds) (1984) Report on the Consensus workshop on formaldehyde. Environ Hlth Perspec 58:323–381.

Heck Hd'A, Casanova M, McNulty MJ, Lam C (1986) Mechanisms of nasal toxicity induced by formaldehyde and acrolein. In: Toxicology of the Nasal Passages, Barrow CS (ed), Hemisphere, Washington, DC. pp. 235–247.

Heck Hd'A, Casanova M, Dodd PB, Schachter EN, Witek TJ, Tosun T (1985) Formaldehyde (CH_2O) concentrations in the blood of humans and Fisher-rats exposed to CH_2O under controlled conditions. Am Ind Hyg Assoc J 46:1–3.

Hendrick DJ, Lane DJ (1977) Occupational formalin asthma. Brit J Ind Med 34:11–18.

Hendrick DJ, Rando RJ, Lane DJ, Morris MJ (1982) Formaldehyde asthma: challenge exposure levels and fate after five years. J Occup Med 24:893–897.

Imhoff RE, Manning JA (1983) Comparison of measured and modeled ambient concentrations of residential wood combustion emissions. USDA. Proceedings: Air Pollut Cont Assoc 83-54.10. 16 pp.

Izard C, Libermann C (1978) Acrolein. Mutat Res 47:115–138.

Jakab GJ (1977) Adverse effect of a cigarette smoke component, acrolein on pulmonary antibacterial defenses and on viral-bacterial interactions in the lung. Am Rev Resp Dis 115:33–38.

Kamens RM, Rives GD, Perry JM, Bell DA, Paylor RF Jr, Goodman RG, Claxton LD (1984) Mutagenic changes in dilute wood smoke as it ages and reacts with ozone and nitrogen dioxide: An outdoor chamber study. Environ Sci Technol 18:523–530.

Kane LE, Alarie Y (1977) Sensory irritation to formaldehyde and acrolein during single and repeated exposures in mice. Am Ind Hyg Assoc J 38:509–522.

Kane LE, Alarie Y (1978) Evaluation of sensory irritation from acrolein-formaldehyde mixtures. Am Ind Hyg Assoc J 39:270–274.

Kensler CJ, Battista SP (1963) Components of cigarette smoke with ciliary-depressant activity. New Eng J Med 269:1161–1166.

Kleeberger SR, Kolbe J, Adkinson NF Jr, Peters SP, Spannhake EW (1988) The role of mediators in the response of the canine peripheral lung to 1 ppm ozone. Am Rev Resp Dis 137:321–325.

Kleindienst TE, Shepson PB, Edney EO (1986) Wood smoke: measurement of the mutagenic activities of its gas- and particulate-phase photooxidation products. Environ Sci Technol 20:493–501.

Koenig JQ, Covert DS, Marshall SG, Van Belle G, Pierson WE (1987) The effects of ozone and nitrogen dioxide on pulmonary function in healthy and asthmatic adolescents. Am Rev Resp Dis 136:1152–1157.

Koenig JQ, Covert DS, Morgan MS, Horike M, Horike N, Marshall SG, Pierson WE (1985) Acute effects of 0.12 ppm ozone or 0.12 ppm nitrogen dioxide on pulmonary function in health and asthmatic adolescents. Am Rev Resp Dis 132:648–651.

Koren HS, Devlin RB, Graham DE, Mann R, Hortsman DH, Kozumbo WJ, Becker S, McDonnell WF (1988) Cellular and biochemical changes in the lower airways of subjects exposed to ozone. US Health Effects Research Lab, Research Triangle-Park, NC.

Korfmacher WA, Wehry EL, Mamantov G, Natusch DFS (1980) Resistance to photochemical decomposition of polycyclic aromatic hydrocarbons vapor-adsorbed on coal fly ash. Environ Sci Technol 14:1094–1019.

Kulle TJ, Sauder LR, Hebel JR, Chatham MD (1985) Ozone response relationships in healthy nonsmokers. Am Rev Resp Dis 132:36–41.

Kutzman RS, Popenoe EA, Schmaeler M, Drew RT (1985) Changes in rat lung structure and composition as a result of subchronic exposure to acrolein. Toxicology 34:139–151.

Lachocki TM, Church DF, Pryor WA (1989) Persistent free radicals in woodsmoke: An ESR spin trapping study. Free Rad Biol Med 00:000–000.

Lachocki TM, Church DF, Pryor WA (1988) Persistent free radicals in the smoke of common household materials: Biological and clinical implications. Environ Res 45:127–139.

Lamb B, Guenther A, Gay D, Westberg H (1987) A national inventory of biogenic hydrocarbon emissions. Atmos Environ 21:1695–1705.

Lauritzen SK, Adams WC (1985) Ozone inhalation effects consequent to continuous exercise in females: Comparison to males. J Appl Physiol 59:1601–1606.

Leach CL, Hatoum NS, Ratajczak HV, Gerhart JM (1987) The pathologic and immunologic effects of inhaled acrolein in rats. Toxicol Lett 39:189–198.

Lenschow DH, Pearson R Jr, Stankov BB (1982) Measurements of ozone vertical flux to ocean and forest. J Geophys Res 87:8833–8837.

Leonardos G, Kendall D, Barnard N (1969) Odor threshold determinations of 53 odorant chemicals. JAPCA 19:91–95.

Liesivuori J, Kettunen A (1983) Farmers' exposure to formic acid vapor in silage making. Ann Occup Hyg 27:327–329.

Lim KJ, Lips HI (1981) Overview of emissions from wood combustion. Proceedings: Conference on Wood Combustion Environmental Assessment. U.S. EPA-600/9-81-029. PB81-248155. pp 39–54.

Linn WS, Avol EL, Shamoo DA, Spier CE, Valencia LM, Venet TG, Fischer DA, Hackney JD (1986) A dose-response study of healthy, heavily exercising men exposed to ozone at concentrations near the ambient air quality standard. Toxicol Ind Hlth 2:99–112.

Lipari F, Dasch JM, Scruggs WF (1984) Aldehyde emissions from wood-burning fireplaces. Environ Sci Technol 18:326–330.

Lipfert FW (1982) A national assessment of the air quality impacts of residential firewood use. In: Proceedings of Residential Wood and Coal Combustion Speciality Conference. Air Poll Cont Assoc, East Central Section, Louisville, KY.

Madden MC, Eling TE, Friedman M (1987) Ozone inhibits endothelial cell cyclooxygenase activity through formation of hydrogen peroxide. 34:445–463.

Matanoski G, Fishbein L, Redmond C, Rosenkranz H, Wallace L (1986) Contribution of organic particulates to respiratory cancer. Environ Hlth Perspec 70:34–49.

McDonnell WF III, Chapman RS, Leigh MW, Strope GL, Collier AM (1985) Respiratory responses of vigorously exercising children to 0.12 ppm ozone exposure. Am Rev Respir Dis 132:875–879.

McDonnell WF, Horstman DH, Hazucha MJ, Seal E Jr, Haak ED, Salaam SA, House DE (1983) Pulmonary effects of ozone exposure during exercise: Dose-response characteristics. Appl Physiol: Respir Environ Exer Physiol 54:1345–1352.

McGinnis GD, Prince SE, Biermann CJ, Lowrimore JT (1984) Wet oxidation of model carbohydrate compounds. Carbohy Res 128:51–60.

Menzel DB (1984) Ozone: An overview of its toxicity in man and animals. J Toxicol Environ Health 13:183–204.

Mermelstein R, Kiriazides DK, Butler M, McCoy EC, Rosenkranz HS (1981) The extraordinary mutagenicity of nitropyrenes in bacteria. Mutat Res 89:187–196.

Miller FJ, Illing JW, Gardner DE (1978) Effect of urban ozone levels on laboratory-induced respiratory infections. Toxicol Lett 2:163–169.

Morrison BM Jr, Heicklen J (1979) The photooxidation of CH_2O at 33130 Å in the absence and presence of NO. J Photochem 11:183–196.

Murphy SD, Klingshirn DA, Ulrich CE (1963) Respiratory response of guinea pigs during acrolein inhalation and its modification by drugs. J Pharmacol Exp Therap 141:79–83.

National Research Council (1981) Formaldehyde and other aldehydes. National Academy Press, Washington, DC.

Nielsen GD, Bakbo JC, Holst E (1984) Sensory irritation and pulmonary irritation

by airborne allyl acetate, allyl alcohol, and allyl ether compared to acrolein. Acta Pharmacol et Toxicol 54:292–298.

Platt V, Perner D, Pätz H (1979) Simultaneous measurement of atmospheric CH_2O, O_3, and NO_2 by differential optical absorption. J Geophys Res 84:6329–6335.

Plopper CG, Dungworth DL, Tyler WS, Chow CK (1979) Pulmonary alteractions in rats exposed to 0.2 and 0.1 ppm ozone: A correlated morphological and biochemical study. Arch Environ Hlth 34:390–395.

Pryor WA (1986) Oxy-radicals and related species: their formation, lifetimes, and reactions. Ann Rev Physiol 48:657–667.

Pryor WA, Prier DG, Church DF (1983) Electron spin resonance study of mainstream and sidestream cigarette smoke: Nature of free radicals in gas-phase smoke and in cigarette tar. Environ Hlth Perspect 47:345–355.

Radke LF, Stith JL, Hegg DA, Hobbs PV (1978) Airborne studies of particles and gases from forest fires. J Air Pollut Cont Assoc 26:30–34.

Ramdahl T, Alfheim I, Rustad S, Olsen T (1982) Chemical and biological characterization of emissions from small residential stoves burning wood and charcoal. Chemosphere 11:601–611.

Reinhardt TE (1989) Firefighter smoke exposure at prescribed burns. A study and action recommendation, Draft Report to USDA Forest Service, PNW Research Station, Seattle, WA.

Reisenauer CS, Koenig JQ, McManus MS, Smith MS, Kusic G, Pierson WE (1988) Pulmonary response to ozone exposures in healthy individuals aged 55 Years or Greater. JAPCA 38:51–55.

Rinaldo JE, Rogers RM (1986) Adult respiratory distress syndrome. New Eng J Med 315:578–580.

Rosenkranz HS, Mermelstein R (1983) Mutagenicity and genotoxicity of nitroarenes. All nitro-containing chemicals were not created equal. Mutation Res 114:217–267.

Routhier F, Dennett R, Davis DD, Wartburg A, Haagenson P, Delany AC (1980) Free tropospheric and boundary-layer airborne measurements of ozone over the latitude range of 58°S to 70°S. J Geophys Res 85:7307–7321.

Sandberg DV, Martin RE (1975) Particle sizes in slash fire smoke. USDA For Serv Res Pap PNW-199. 7 pp.

Savolainen H, Zitting A (1980) Glial cell effects of subacute formic acid vapour exposure. Acta Pharmacol Toxicol 47:239–240.

Schjoldager J, Sivertsen B, Hanssen JE (1978) On the occurrence of photochemical oxidants at high latitudes. Atoms Environ 12:2461–2467.

Schulam P, Newbold R, Hull LA (1985) Urban and rural ambient air aldehyde levels in Schenectady, New York, and on Whiteface Mountain, New York. Atmos Environ 19:623–626.

Seinfeld JH (1989) Urban air pollution: State of the science. Science 243:745–752.

Selgrade MK, Illing JW, Starnes DM, Stead AG, Ménache MG, Stevens MA (1988) Evaluation of effects of ozone exposure on influenza infection in mice using several indicators of susceptibility. Fund Appl Toxicol 11:169–180.

Seltzer J, Bigby BG, Stulbarg M, Holtzman MJ, Nadel JA, Ueki IF, Leikauf GD, Goetzl EJ, Boushey HA (1986) O_3-Induced change in bronchial reactivity to methacholine and airway inflammation in humans. J Appl Physiol 60:1321–1326.

Sexton K (1983) Photochemical ozone formation in urban and point-source plumes. Environ Sci Technol 17:224–227.

Sheppard D, Eschenbacher WL, Epstein J (1984) Lack of bronchomotor responses to up to 3 ppm formaldehyde in subjects with asthma. Environ Res 35:133–139.

Shields RL, Gold WM (1987) Effect of inhaled ozone on lung histamine in conscious guinea pigs. Environ Res 42:435–445.

Singh AR, Lawrence WH, Autian J (1972) Embryonic-fetal toxicity and teratogenic effects of a group of methacrylate esters in rats. J Dent Res 51:1632–1638.

Singh HB, Salas LJ, Stiles RE (1982) Distribution of selected gaseous organic mutagens and suspect carcinogens in ambient air. Environ Sci Technol 16:872–880.

Spektor DM, Lippmann M, Lioy PJ, Thurston GD, Citak K, James DJ, Bock N, Speizer FE, Hayes C (1988a) Effects of ambient ozone on respiratory function in active, normal children. Am Rev Respir Dis 137:313–320.

Spektor DM, Lippmann M, Thurston GD, Lioy PJ, Stecko J, O'Conner G, Garshick E, Speizer FE, Hayes C (1988b) Effects of ambient ozone on respiratory function in healthy adults exercising outdoors. Am Rev Respir Dis 138:821–828.

Stith JL, Radke LF, Hobbs PV (1981) Particle emissions and the production of ozone and nitrogen oxides from the burning of forest slash. Atmos Environ 15:73–82.

Su F, Calvert JG, Show JH (1979) Mechanism of the photooxidation of gaseous formaldehyde. 83:3185–3191.

Swenberg JA, Gross EA, Randall HW (1986) Localization and quantitation of cell proliferation following exposure to nasal irritants. In: Toxicology of the Nasal Passages, Barrow CS (ed) 291–300 pp.

Thomas JF, Mukai M, Tebbens BD (1968) Fate of airborne benzo[*a*]pyrene. Environ Sci Technol 2:33–39.

Tyler WS, Tyler NK, Last JA, Gillespie MJ Barstow TJ (1988) Comparison of daily and seasonal exposures of young monkeys to ozone. Toxicology 50:131–144.

U.S. Environmental Protection Agency (1980) Ambient water quality critiera for: Acrolein, U.S. EPA-440/5-80-016. Office of Water Regulations and Standards.

Veyret B, Rayez J, Lesclaux R (1982) Mechanism of the Photoxidation of formaldehyde studied by flash photolysis of $CH_2O—O_2—NO$ mixtures. J Phys Chem 86: 3424–3430.

Ward DE, Hardy CC (1984) Advances in the characterization and control of emissions form prescribed fires. Proceedings Air Poll Cont Assoc presentation 84-36.2. 32 pp.

Ward DE, Rothman N, Strickland P (1989) the effects of forest fire smoke on firefighters: A comprehensive study plan. Prepared for Congressional Committee on Appropriations for Title II-Related Agencies, and the National Wildfire Coordination Group by USDA—Forest Service and The John Hopkins University. 48 pp.

Weber-Tschopp A, Fischer T, Gierer R, Grandjean E (1977) Experimentelle Reizwirkungen von Akrolein auf den Menschen. Int Arch Occup Environ Hlth 40:117–130.

Westberg H, Sexton K, Flyckt D (1981) Hydrocarbon production and photochemical ozone formation in forest burn plumes. J Air Pollut Cont Assoc 31:661–676.

Woutersen RA, Appelman LM, Van Garderen-Hoetmer A, Feron VJ (1986) Inhalation toxicity of acetaldehyde in rats. III. Carcinogenicity study. Toxicol 41:213–231.

Zitting A, Savolainen H (1980) Biochemical effects of subacute formic acid vapor exposure. Res Comm. Chem Path Pharmacol 27:157–162.

Manuscript received March 27, 1990; revised version accepted May 29, 1990.