

Assessing Potential Health Effects and Establishing Ozone Exposure Limits for Ozone-Generating Air Cleaners

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Technical Assessment for CPSC
Part I: Health Component of Ozone Review

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Submitted to Treye Thomas, PhD, CPSC Project Officer

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The Following tasks were outlined in the original work plan developed in October 2004 and submitted to CPSC to conduct the ozone review:

Work Plan

Work to be conducted based on statement of work provided to contractor by CPSC. Essentially this includes the following tasks as detailed in the Statement of Work:

- a) Conducting a comprehensive literature search and a critical review of the literature to independently assess the possible effects of low levels of ozone (representative of concentrations that may be expected resulting from the use of ozone generating air cleaners, throughout their operational and life cycles, intended for occupied spaces). Special emphasis will be placed on sensitive populations including the elderly, young children, and individuals with compromised pulmonary function.
- b) Evaluating whether the current 50 ppb exposure limit [maximum accumulation level] for ozone is adequate to protect consumers from potential adverse health effects. If the 50 ppb level is believed to be inadequate, contractor will recommend an alternative exposure limit [maximum accumulation level] for ozone concentrations.
- c) Recommending to CPSC staff the maximum emission rate of ozone from ozone-generating devices, and/or the maximum resultant concentration of ozone (ozone accumulation) from ozone-generating devices (within a space), based on the exposure limit [accumulation level] believed to be capable of reducing the occurrence of potential adverse health effects (based on literature review).

Introduction

The research team has compiled a detailed list of reference materials applicable to the objectives of the study. Due to the voluminous nature of the literature, the scope of the health effects portion of the review has been limited to papers that focus on health effects at or below the current 50 ppb maximum level recommended by the FDA. If there is evidence in the literature of adverse health effects reported from human exposure studies to ozone at levels below 50 ppb, then recommendations from this qualitative assessment will be used to propose an alternative maximum.

After further review of the Statement of Work the investigators raised the question to CPSC staff... “what section of the population are we developing a recommendation for maximum ozone concentration, (based on health considerations) from devices?” After further discussion with Dr. Treye Thomas of CPSC in April of 2005, it was determined that investigators would attempt to provide a "tiered" recommendation: one set of considerations addressing sensitive populations, and another set for the general population. This has accordingly been the direction in which investigators devoted their attention. In the event that a tiered recommendation is not warranted investigators feel it is essential that the final recommendation account for a margin of safety for potentially susceptible populations.

The primary component of the ozone review being conducted for CPSC pertains to the health effects of low level ozone exposure to consumers, including the general population and sensitive individuals. Using the information compiled through the literature review, investigators render, within this report, a summary of pertinent information to address this objective. ***Investigators were charged with formulating an opinion, based on the extensive literature review, as to whether the current 50 ppb indoor maximum accumulation limit for ozone is adequate to protect consumers from potential adverse health effects.***

A key question to be resolved is, once an acceptable accumulation level of ozone for a space is agreed upon, how will this recommendation then be applied to ozone generating devices? After

much consideration, thought, and detailed discussion with other notable peers in this subject expertise [names of those consulted with were provided to Project Officer Treye Thomas on a conference call on June 29, 2005], it appears that the most prudent approach would be based on the actual emission rate of ozone from the device itself. Using basic assumptions as to the environment where these devices may be used in (i.e. ventilation rate, outdoor conditions, deposition losses, potential reactions, etc), a maximum emission rate can be calculated based on the target level recommended for health reasons. In addition, it may be necessary to formulate a “maximum accumulation” level for certain devices that utilize some type of sensor technology which is purported to “limit the operation of the device to ensure that accumulation of ozone does not exceed a specific concentration within the space”. Assumptions for both types of recommendations, referred to above, would be for a typically sized room (devices would be used in 20-40 m³ space), and assuming a well-mixed environment.

Part 1: Background and Methods

1.0 Introduction

Ozone is a highly reactive toxic gas formed naturally in the upper atmosphere by photo-chemical reactions. Ozone is also formed in the lower atmosphere from the photochemical reaction of nitrogen oxides (NO_x) and volatile organic compounds (VOCs). Concentrations of ozone in the indoor environment vary as a function of outdoor contributions and indoor sources.

Indoor/outdoor ratios as a function of outdoor ozone contributions range from 0.05 in tightly sealed buildings (or those utilizing charcoal filters), to 0.85 in buildings with very high air exchange rates. Excluding extremes, the I/O ratio is more often in the range of 0.2-0.7 (Weschler, 2000). This may amount to ozone concentrations varying from 2-40 ppb added to the indoor environment based on outdoor-to-indoor transport (Sarwar, et al., 2004). In addition, indoor accumulation of ozone may also result from sources such as, copiers, laser printers, and electronic air cleaners, where electrical arcing occurs (formation by coronal electric discharge).

The primary question of this review is whether sufficient evidence exists in the published literature (search limited to English language articles) to determine whether ozone exposure to concentrations less than or equal to 50 ppb is likely to result in adverse health effects in healthy and/or susceptible populations. Human exposure to ozone, even at *relatively* low levels (80 to

160 ppb), has been found to cause a variety of adverse health effects including decreased measures of pulmonary function and increases in reported symptoms such as headache, eye irritation, and cough (US EPA, 1996). While these findings are consistent across human exposure studies and epidemiologic field studies of ambient ozone exposure, no articles in the published literature were found that evaluated adverse health effects from ozone produced by consumer ozone generating devices.

The oxidative properties of ozone have long been documented to cause adverse health effects in humans. Ozone is one of the 5 criteria air pollutants that the US Environmental Protection Agency (EPA) regulates under the Clean Air Act in response to the documented adverse effects to human health and welfare. The research compiled in EPA's air quality criteria documents detail the latest scientific information used in deriving National Ambient Air Quality Standards (NAAQS). The most recent published editions of the *Air Quality Criteria for Ozone and Related Photochemical Oxidants* (US EPA, 1996), the Canadian *National Ambient Air Quality Objectives for Ground-Level Ozone, Science Assessment Document* (Health Canada, 1999) and the recently released Staff Report, *Review of the California Ambient Air Quality Standard for Ozone, Initial Statement of Reason for Proposed Rulemaking* (CARB, 2005) provide an extensive review of the mechanisms of injury and an in depth analysis of the adverse health effects from ambient exposure to ozone. The US EPA recently released the *Air Quality Criteria for Ozone and Related Photochemical Oxidants, First External Review Draft* (accessible at: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=114523>). This first draft to the updated criteria document for ozone highlights the most recent scientific information intended for rule-making purposes for ambient ozone exposure [Note: at the time of this report's submission the Criteria Document had not been finalized and is therefore not formally cited in this literature review due to being in draft form at the time of this effort. The Final Report was released in March 2006].

Guidelines for occupational exposure limits for ozone have been published by the American Conference of Governmental Industrial Hygienists (ACGIH). The [Threshold Limit Values for Chemical Substances \(TLV[®]-CS\) Committee](#) was established in 1941. This group was charged with investigating, recommending, and annually reviewing exposure limits for chemical

substances. It became a standing committee in 1944. Two years later, the organization adopted its first list of 148 exposure limits (including ozone), then referred to as Maximum Allowable Concentrations. The term "Threshold Limit Values (TLVs[®])" was introduced in 1956. The first *Documentation of the Threshold Limit Values* was published in 1962 and is now in its seventh edition. In 1946 ACGIH recommended an 8 hour time weighted average of 1.0 ppm. In 1954 the level was reduced to 100 ppb and in 1989 this level was classified as a ceiling level (accessed at <http://www.acgih.org/About/history.htm>). ACGIH's current recommendations include a range of 8- hour Threshold Limit Values (TLV)-Time Weighted Average (TWA) values based on work load. The recommended TLVs are: 50 ppb for heavy work, 80 ppb for moderate work, and 100 ppb for light work. Exposures \leq 2 hours, for heavy, moderate or light workloads have an established TLV-TWA value of 200 ppb. The TLV-TWAs are intended to be protective of workers exposed continuously for an 8 hour work day, and a 40 hour work week (ACGIH Threshold Limit Values for Chemical Substances and Physical Agents, 2001). ACGIH TLV's and BEI's 2004 guidebook specifically states that these levels are to be used only for: *"guidelines or recommendations to assist in the evaluation and control of **potential workplace health hazards and for no other use** (e.g., neither for evaluating or controlling community air pollution; nor for estimating the toxic potential of continuous, uninterrupted exposures or other extended work periods; nor for proving or disproving an existing disease or physical condition in an individual). Further, these values are not fine lines between the safe and dangerous conditions and should not be used by anyone who is not trained in the discipline of industrial hygiene."* It is also worthy to note, as detailed in the ACGIH Documentation of the Threshold Limit Values and Biological Exposure Indices, "Ozone is injurious at relatively low concentrations and at short exposure periods...". It is further stated "...findings indicate that concentration has a greater effect than duration of exposure".

The National Institute for Occupational Safety and Health (NIOSH) has recommended a ceiling limit of 100 ppb that should not be exceeded at any time. NIOSH also recommends a 5.0 ppm ozone concentration that is immediately dangerous to life or health (IDLH). The IDLH concentration is the concentration to which a worker can be exposed and still be expected to escape without injury or irreversible health effects (NIOSH Pocket Guide to Chemical Hazards, 1997). NIOSH also has published the Registry of Toxic Effects of Chemical Substances

(accessed at: <http://www.cdc.gov/niosh/rtecs/rs7d80e8.html>). This registry contains references for toxicity for ozone exposures greater than the current FDA maximum accumulation level. The Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for ozone is 100 ppb. This standard is not to be exceeded in an 8-hour work shift over a 40 hour work week. These guidelines are useful as a reference yet they are not useful for estimating non-occupational exposures. The ACGIH TLV's and the OSHA PEL's are specifically designed for occupational exposures only.

A study by Tashiro et al. (2004) examined the concentrations of ozone in hotel rooms after one hour of generating ozone at a rate 500mg/hour for the purpose of compiling a health and safety manual for employees using ozone generators during hotel room housekeeping. The study was initiated in response to health complaints from employees. The authors report that the concentrations of ozone increased for 20 minutes immediately after ozone generation and then reached a plateau for 40 minutes. The peak levels of ozone post generation in a single hotel room was 10.5 times higher (2.1 ppm) than the recommended time weighted occupational limit for 2 hours of work (0.2 ppm). The ozone concentrations returned to baseline level in 30 minutes and the authors recommend that employees should wait at least 10-15 minutes when the levels reached 0.2 ppm, the recommended TLV for 2-hrs of work.

The recently published document, *Emergency and Continuous Exposure Limits for Selected Airborne Contaminants, Volume I* (National Research Council, 2000), provides some historical commentary regarding ozone standard setting. This report was commissioned to review and update previous recommendations that were made with regard to exposure limits (e.g., Emergency Exposure Limits (EELs) and Continuous Exposure Limits (CELs)) to a variety of airborne contaminants in enclosed environments, primarily of concern to the Department of Defense and to the National Aeronautics and Space Administration. These limits were specifically generated “...for narrowly defined occupational groups and are not intended for application in general industrial settings or as exposure limits for the general public.”

The document goes on to report that:

“A study that carried considerable weight in reaching the initial ozone ambient air quality standard of 80 ppb was based on the performance of cross country runners in California (Wayne et al., 1967). A significant relationship was observed between the oxidant concentrations during and 1-3 hours before the race and the percentage of runners whose performance decreased compared with that in the previous home meet. Deterioration began at concentrations around 30 ppb—appreciably lower than the national standard. A threshold concentration of 12 ppb was later suggested.” The authors of the document recommended an EEL of 1.0 ppm for 1 hour, which is less restrictive than the ACGIH TLV-STEL of 1.0 ppm for 15 minutes. However, the 24 hour EEL of 100 ppb is more restrictive than the ACGIH TLV/OSHA PEL of 100 ppb for a 40-hr workweek (assuming working shifts interspersed with periods of lower exposure). The 90-day CEL of 20 ppb was selected as it did not appear to pose a hazard.

Both USEPA and CARB have defined the policy-relevant background (PRB) ozone concentration as 40 ppb. The background concentration of ozone in surface air at sea level is reported to be 10-30 ppb (National Research Council, 2000) and that during the summer season the typical background daily maximum 1 hour level is between 30 and 50 ppb (EPA 1996). Policy Relevant Background has been defined by EPA as those concentrations that would occur in the US in the absence of North American anthropogenic emissions. The policy-relevant background concentrations define the level below which ambient ozone standards can not be set. Lefohn et al. (2001) report that levels of hourly averaged ambient ozone concentrations in the range 40-80 ppb are often measured as part of the "background ozone" burden and that average ozone concentrations greater than or equal to 50 and 60 ppb occur frequently during the winter and spring months challenging the EPA background estimate and implying that the current ozone standard is unattainable. Fiore et al (2003) find that the ozone background is generally 15-35 ppb with some instances of 40-50 ppb in the spring at high elevation western sites.

It is important to note that the current limit prescribed by the FDA does not discriminate between ozone contributed from an air cleaner as compared to that originating from outdoor infiltration of ozone from both anthropogenic and non-anthropogenic sources. *The FDA limit applies to the total accumulation of ozone in the space which ultimately must account for contributions from both the air cleaner and those from outdoor air.*

Controlled human exposure studies have documented responses to concentrations of ozone in the range of the ambient air quality standards, however these levels are still somewhat higher than the current FDA standard for ozone generating devices (21CFR 801.415). The recent published literature on controlled human exposure studies explores questions related to ambient exposures at or near the current **EPA** NAAQS for ozone of 80 ppb average 8-hour maximum for 18-35 year old healthy subjects. The Clean Air Act mandates that the NAAQS must protect human health and the environment from the adverse effects of exposure to ozone and account for a margin of safety (though undefined) to protect the most sensitive members of the population.

CalEPA's new 8-hour averaging time, not to be exceeded, standard of 70 ppb was derived from evaluating the multi-hour exposure studies documenting statistically significant mean group changes in pulmonary function on exposure to 80 ppb over 6.6 to 8-hours. In addition to the group mean decrements, a substantial number of subjects experienced particularly marked responses from exposure to 80 ppb and therefore should not be considered to be adequately protective of public health. CalEPA also noted that the controlled human exposure studies did not observe an effect for exposures of 40 ppb (Adams, 2000) and 60 ppb (from an unpublished study by Adams cited in CARB, 2005), thus arriving at a 70 ppb 8-hour exposure standard when including an undefined "adequate margin of safety."

1.1 Methods

This literature search and review is targeted specifically to low level ozone exposures in order to evaluate the adequacy of the existing FDA standard (21CFR801.415) of 50 ppb maximum level of ozone that is generated by or that results in an accumulation from ozone generating devices used in enclosed spaces intended to be occupied by people for extended periods of time. The FDA standard states that devices that generate ozone are considered mislabeled if they do not state the smallest area in which such device can be used so as not to produce an ozone accumulation in excess of 50 ppb.

Published literature on the adverse health effects from low level ozone exposure were reviewed with special consideration given to sensitive populations, including elderly, young children, and

those with compromised pulmonary function. By limiting this review to low level ozone exposure, investigators are attempting to assess the potential for health effects related to levels of exposure (at or near the 50 ppb maximum level) that may potentially be generated by ozone generating devices intended for use in occupied spaces, that are in compliance with the FDA standard (FDA limit includes total accumulation of ozone based on all sources including outdoors).

The research questions addressed in the Health section of this review are:

1. Is the 50 ppb FDA standard adequate to protect human health?
2. If not, propose an alternative exposure limit [accumulation level].

In assessing the potential toxicity of a chemical, establishing the presence of an adverse effect and identifying the mechanism of action constitute the initial stages of the evaluation. The qualitative assessment provides an overall picture of the literature and some level of confidence as to its underlying strength. For some purposes, the qualitative risk assessment may be sufficient, especially if data are lacking and the evidence to support interpretation is not well structured. The role of risk assessment in general is to broaden the basis of agreement, to reduce the degree of uncertainty in critical estimates, and to reduce the role of interpretation to the minimum necessary to support an informed judgment. The qualitative assessment should be able to evaluate the consistency of the database and whether or not there are irreconcilable contradictions or gaps that cannot effectively be bridged. The qualitative assessment is useful to provide a recommendation for future research which may provide clarification of uncertainties noted in the assessment.

One of the most commonly used guidelines in the United States for defining adverse health effects is the American Thoracic Society's 1985 *Guidelines as to what constitutes an adverse respiratory health effect, with special reference to epidemiologic studies of air pollution* (ATS, 1985). ATS defines an adverse health effect as medically significant physiologic or pathologic changes as evidenced by one or more of the following: 1) interference with the normal activity of

the affected person or persons, 2) episodic respiratory illness, 3) incapacitating illness, 4) permanent respiratory injury, and/or, 5) progressive respiratory dysfunction.

In 2000, ATS published an update titled, *What constitutes an adverse health effect of air pollution?* (ATS, 2000) which included consideration of biomarkers, quality of life, physiologic impact, symptoms, clinical outcomes, death, and population health versus individual risk as to whether a change in status is considered an adverse health effect. The 2000 update (ATS, 2000) goes into greater detail describing these criteria and notes that small, transient reductions in pulmonary function alone should not necessarily be regarded as adverse, however, reversible loss of lung function in conjunction with symptoms and permanent loss of lung function should be considered adverse.

This qualitative assessment was based on a search for documentation of adverse health effects associated with low level ozone exposure that is representative of concentrations that could be produced from ozone generating devices that are *in compliance* with the current 50 ppb accumulation standard. This study evaluated whether the current FDA maximum accumulation level of 50 ppb is believed to be adequate to protect human health and capable of reducing the occurrence of potentially adverse health effects.

The PubMed, Medline database (which includes the core toxicology journals from ToxNet) and Web of Science databases were searched. Different methods of key word searches and Medical Subject Headings (MeSH) searches were performed. Titles and abstracts were reviewed and literature was compiled, related to studies of respiratory exposure to ozone at or near concentrations ≤ 50 ppb ($\leq 98 \mu\text{g}/\text{m}^3$).

The search was limited for the health section of this review to English language publications, between 1994 and 2004. As there were so few studies addressing this low level of exposure, older pertinent literature (found through tree searches) is also cited. Published review articles were excluded from this review. The review included recent government documents which serve as reference documents for the rule making process in regulating ambient levels of ozone for the United States, the State of California, and Canada. Appendices include additional references

reviewed but not directly cited in this review (Appendix A) and health advisories/warnings from various government agencies and professional organizations regarding indoor ozone and/or ozone generating devices (Appendix B).

Epidemiology studies with respiratory outcomes, in which the mean background concentration of ozone was less than or equal to 50 ppb and the exposure variable was also less than or equal to 50 ppb were considered in the weight of evidence in this assessment. However, epidemiology studies with cardiovascular or mortality outcomes related to incremental increases in ambient ozone exposure were not included in the scope of this review. Recent research has indicated potential association with these outcomes, however, additional studies need to address methodological issues to ensure that: (1) ozone is not confounded by other pollutants including particulate matter (PM10 and PM2.5); (2) ozone is not confounded by temperature and season using parametric (versus non-parametric) generalized linear models; and specifically, (3) personal exposure to ozone is sufficiently related to ambient concentrations of ozone. Ozone-specific models must be subject to a thorough sensitivity analysis of predicted results similar to that undertaken for studies on particulate matter (CARB, 2005).

Part 2 Toxicology Studies: Mechanism of Injury

2.0 Introduction

Ozone (O₃) is a highly reactive gas. Ozone uptake occurs at the anatomic air-liquid interfaces, particularly the mucous membranes of the respiratory tract. Continuous ozone inhalation decreases the efficiency of ozone absorption in the central airways, facilitating increased delivery of ozone to the deep lung (Asplund et al. 1996).

It is notable that one does not have to look far to document the adverse health effects of ozone at levels of exposure at or near the current ambient air quality standards of 80 ppb, the current EPA 8-hour daily maximum average concentration, and 120 ppb, the current average hourly maximum concentration. The toxicological and medical literature is teeming with studies describing the adverse health effects of these “higher” concentrations of ozone exposure. This information is discussed at length in the Ozone Air Quality Criteria Documents (US EPA, 1996 and <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=114523>), the Health Canada

Scientific Assessment document (Health Canada, 1999), and the California Air Resources Board's Review of the one-hour ambient air quality standard for Ozone. Staff Report. (CARB, 2005).

There is, however, very little information in the literature pertaining to controlled animal and human exposure studies that investigates the adverse health effects associated with low concentrations of ozone exposure, specifically at or below the FDA maximum acceptable accumulation level of 50 ppb. In 1997 EPA concluded that the information on chronic adverse health effects was too uncertain to serve as the basis for establishing a more restrictive standard (EPA, 2002). In addition, a review of the literature for studies describing the health benefits of respiratory exposures to ozone did not identify any citations. EPA was required to consider the potential beneficial effects of ground-level ozone pollution in shielding the public from potentially harmful solar radiation. EPA concluded that the information on the potential indirect beneficial effects is too uncertain and not well enough understood to serve as a basis for establishing a less restrictive standard (EPA, 2002).

The 50 ppb maximum accumulation level set by FDA can not be interpreted as an exposure limit. It represents a concentration limit with no specified timeframe. The degree of response to ozone is related to two other factors besides concentration that contribute to the concept of dose: 1) V_E , the ventilation rate and 2) T , the duration of exposure (US EPA, 1996, Cal EPA, 2005). The effect of exercise or increased ventilation increases both the tidal volume and breathing frequency, thus it is expected to increase the tissue dose significantly. Many studies evaluating human exposure to ozone utilize exposure protocols that incorporate exercise regimens to simulate periods of moderate to heavy exercise and/or to achieve the target dose when comparing exposure protocols. These studies have been designed to simulate activity levels encountered daily outdoors, in an effort to evaluate the adverse health effects associated with ambient air quality exposures. Human exposure studies historically utilize "higher" ozone concentrations than the 50 ppb concentration considered for this review and the results may not be applicable to the low levels that are expected to be produced from compliant ozone generating devices.

A limited number of studies were identified with exposure to 40 and 60 ppb ozone. Controlled animal and human exposure studies reporting low level ozone exposure are summarized below.

2.1 Animal Exposure Studies

Animal studies have used a variety of exposure regimens to examine the effects of ozone on pulmonary function. Categories of exposure commonly include: 1) Acute (less than one day), 2) Short-term Repeated (less than a week), 3) Chronic Continuous, and 4) Chronic Intermittent (US EPA, 1996, CARB 2005). Animal studies are useful for obtaining information about responses to both long and short term exposures with “higher” levels of ozone that would be unethical to deliver to human subjects. They also have the advantage of being able to explore the pathologic and physiologic effects with invasive techniques that may not be acceptable in studies with human subjects. Though it is somewhat complicated and at times inappropriate to extrapolate the results from animal studies to quantitatively predict human health outcomes, these studies can be useful in providing a better understanding of the possible mechanisms and implications of health effects observed in human studies and contribute to a weight of evidence when applying a margin of safety for setting human exposure standards.

2.1.1 In Vitro

Investigators were unable to identify in vitro animal cell or tissue exposure studies that evaluated low levels of ozone exposure that would be consistent with exposure levels less than or equal to the FDA standard of 50 ppb.

2.1.2 In Vivo

Investigators were unable to identify in vivo studies on adverse health effects following acute ozone exposures to animals, with reported concentrations of ozone less than the 50 ppb threshold, applicable for this review.

One study of chronic low level ozone exposure to animals was identified for this review. Moss et al. (2001) studied the effects of ambient air pollution on the respiratory tract of rats exposed to Mexico City air for seven weeks. The comparison group was exposed to filtered ambient air. No significant changes were found in the nasal tissues of rats using quantitative morphological

methods. No inflammatory or epithelial lesions were identified. The authors suspect that the ambient air pollution concentrations were too low (18 ppb) to observe an effect. The authors also suggest that further research needs to be done to explore the validity of using bioassays of rat tissue to study the effects of air pollution on humans.

2.2 Human Exposure Studies

The principal advantage of controlled human exposure studies is that exposures to the pollutant(s) of interest can be precisely measured, and therefore exposure-response relationships can be determined with some degree of accuracy. Controlled exposure studies can, under some circumstances, identify a threshold exposure for certain outcomes on an individual subject basis. However, due to inherent limitations, as described below, controlled studies can not identify a threshold concentration on a population level with certainty, given the wide range of individual responses to ozone

Human exposure studies can only evaluate short-term responses to acute exposures under simplified exposure conditions. The experimental protocol may fail to capture effects that might occur in response to complex, real-world exposures. It remains unclear as to what factors account for the variability in pulmonary function test results among individuals. Identifying responses related to specific exposure conditions constitutes an important dimension of the standard-setting process. These studies, despite their limitations, provide the strongest and most quantifiable concentration-response data on the health effects of ozone.

2.2.1 In Vitro

Three studies in the literature were identified that evaluated the adverse health effects on human respiratory tract tissue from in vitro ozone exposures that approximate the low level of exposure expected from ozone generating devices in compliance with the current FDA standard (< 50 ppb).

Schierhorn et al (1999) exposed nasal mucosa collected from both atopic and nonatopic patients to concentrations of ozone ranging from 60 ppb to 2.0 ppm. Twenty-four tissue cultures were exposed to an ozone concentration of 60 ppb and the in vitro effects with respect to inflammatory

mediators and cytokines were measured. In addition Schierhorn et al (1999) evaluated whether these results are consistent with in vivo findings in bronchoalveolar lavage fluid (BALF), in nasal lavage fluid (NALF), or in animal studies. Findings in this study become significant at the 80 ppb exposure concentration. No significant increases of inflammatory mediators or cytokines were associated with 60 ppb exposures. However, cultures of isolated epithelial cells reflect only a partial picture of the inflammatory response in the mucosa because other inflammatory cells and processes present in vivo are not present in the in vitro model. This study was included, even though level of ozone exposure was slightly above the FDA standard, because so few studies were found at concentrations \leq 50 ppb.

Bayram et al (2001) looked at the release of inflammatory mediators in bronchial epithelial cells of nonatopic, non-asthma subjects and atopic asthma subjects. Bronchial biopsy specimens were collected from twenty-eight subjects. Human bronchial epithelial cell cultures were exposed to ozone concentrations of 0 to 100 ppb. This study demonstrates that cell cultures from both those with asthma and non-asthma subjects constitutively release proinflammatory mediators and that exposure to gaseous pollutants, such as ozone, even at concentrations as low as 50 ppb leads to significant differences in the amounts of inflammatory cytokines produced by cells from asthmatic subjects compared to cell from non-asthma subjects..

Bayram et al (2002) also demonstrated a significant increase in human bronchial epithelial cell permeability in asthmatic subjects as evidenced by decreased electrical resistance 24 hours following 10 ppb ozone exposure when compared to healthy subjects. A comparison between ozone-induced changes in asthma and non-asthma subjects' human bronchial epithelial cell cultures demonstrated that 10 ppb ($P < 0.01$) and 50 ppb ($P < 0.05$) ozone-induced decreases in the electrical resistance of cell cultures of subjects with asthma were significantly greater than the decreases in non-asthma patients 24 hours after exposure. These results suggest that ozone exposure may modulate airway disease by having a negative influence on bronchial epithelial cells and that subjects with asthma may be more sensitive to these effects.

2.2.2 In Vivo

Most human exposure studies have investigated responses to multi-hour exposures to ozone concentrations closer to those typically researched for the ambient air quality standards, ranging from 80 ppb to 160 ppb, for periods of 6.6 or 8 hours. One human exposure study was identified that utilized an exposure concentration of 40 ppb in its protocol.

Adams (2002) compared the responses of healthy adults who were exposed to ozone through a facemask system with those exposed in an environmental chamber while they completed a 6.6 hour protocol. Results with the facemask system were comparable to those obtained on the same subjects exposed in an environmental chamber. The change following the 40 ppb ozone exposure was not different from that with filtered air exposure. Although the group mean decrement following the 40 ppb exposure was not statistically significant, the degree of variation in FEV1.0 for the group ranged from +7.8% to -8.2%. Symptoms following the 40 ppb exposure were not different from those following exposure to filtered air.

No other controlled human exposure studies (either short term or long term) were identified with ozone concentrations ≤ 50 ppb. The California Initial Statement of Reason cites an unpublished study conducted by Adams for the American Petroleum Institute where subjects were exposed to 60 ppb ozone over several hours and no significant group mean changes were observed relative to clean air (CARB, 2005).

2.3 Conclusions

The lack of controlled exposure studies, on both animals and humans, at the low levels of exposure (≤ 50 ppb), limit the usefulness of these studies to predict health effects from ambient ozone exposure in a general population. Acute changes at the cellular level are indicative of potential for adverse effects in asthmatic individuals exposed to low levels of ozone acutely, however, whether long term, low level exposures produce similar adverse changes is a matter for future research. The few studies that we identified did not demonstrate significant group level adverse health effects at or below the 50 ppb accumulation level relevant to this review.

Research has not supported establishment of a Threshold nor a No Observable Adverse Effect Level (NOAEL) for ozone (McDonnell et al., 1993). Brauer et al. (2002) concluded that surrogate measures of exposure (i.e., those from centrally-located ambient monitors) were not highly correlated with personal exposures and obscured the presence of thresholds in epidemiologic studies at the population level, even if a common threshold exists for individuals within the population.

The lowest published concentrations demonstrating adverse health effects in human exposure studies is 120 ppb over 1-3 hours (Follinsbee et al, 1988) and 80 ppb over 6.6 hours while performing moderate to heavy exercise (Horstman et al, 1990; McDonnell et al, 1991). Findings from Hazucha et al. (1992) and Adams (2003) confirm that ozone concentration is the most important factor in determining responses to ozone exposure, compared to either exposure duration or ventilation. These studies as well as others (McDonnell et al, 1985a) have demonstrated that there is great intra-subject variability in measurement of lung function parameters as well as great inter-subject variability in human exposure studies involving healthy adults. Adams (2002) exposed subjects to several ozone concentrations compared to fresh air. Although the group mean decrement following exposure to 40 ppb was not different from that with fresh air exposure, the range of changes in the FEV1.0 for the group was +7.8% to – 8.2%. These studies are described in detail in EPA's Draft Criteria Document (accessed at <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=114523>). and CalEPA's Initial Statement of Reason (CARB, 2005).

It is important to note that controlled human exposure studies may be unlikely to see an effect at ozone exposures <50 ppb even if one had occurred, because the studies lack sufficient statistical power due to the small number of individuals that are tested and the high variability in both the inter and intra subject FEV1 outcome measurements. However, this assumption is difficult to make due to the lack of low level animal and controlled human exposure studies and the lack of studies with alternate exposure scenarios, such as episodic peak exposures followed by a plateau of elevated exposures as is seen during ozone generation in an enclosed space (Tashiro et al., 2004). This knowledge gap has been noted by authorities such as CARB (2005), National Research Council (2000), and US EPA (2006). More research is needed to begin to understand

the adverse health implications of low level ozone exposures and exposures from indoor sources in both healthy and asthmatic subjects.

Part 3 Epidemiology Studies: Likelihood of Health Effect and Extent of Injury

3.0 Introduction

The majority of human and animal exposure studies in the literature provide useful information on the acute and long-term effects for ozone exposures greater than the 50 ppb accumulation level being explored in this review. However there are a number of epidemiology studies which associate adverse health effects with low level increases in ambient concentrations of ozone. These studies provide limited insight for this review due to lack of consistency in established exposure metrics, modeling techniques (including different lag structures and assumptions), and an inability to adequately control for all known and potential confounders across the studies. These studies do however provide compelling evidence for the need for a margin of safety when setting exposure standards. Epidemiologic studies relying on ambient air quality data do not allow for exposure characterization in a precise manner and are best considered in conjunction with information from in vitro and in vivo controlled exposure experiments that support the observed association.

Epidemiologic studies of ambient ozone exposure must take into account the cyclic nature of ambient ozone, with ozone concentrations usually highest in the mid afternoon and dropping to lowest in the pre-dawn hours. In addition, ambient ozone concentrations show both daily and seasonal variation. To fully understand the effects of long term ozone exposure on observed respiratory health, it is also critical to consider the length of time between exposures and the observed lags in adverse health outcomes. As the lag interval approaches the time necessary for repair to be complete, (7 days), the pattern of injury changes. Near-continuous exposure for a significant period of time (measured in months) fundamentally alters both the pattern of toxic cellular injury and the nature of the inflammatory response. The periodicity of the exposure and the duration of inter-exposure intervals also appear to affect the biological response. Several risk factors exhibit variation across published studies, including the presence and levels of co-pollutants, the relationships between ambient measures of ozone and exposure-related factors,

factors related to sensitive subpopulations, and climatic and meteorological conditions. While, multi-pollutant models are often used to assess and account for confounding variables, there are many limitations with these models including uncertainty in assessing the independent health effects of pollutants that are correlated (US EPA, 1996; Health Canada, 1999; CARB, 2005).

It should also be noted that the epidemiologic concept of exposure differs from the toxicologic concept. In epidemiology one must relate the exposure variable or index of exposure to the outcome variable and define the odds or risk that associates one with the other. In toxicology the concept of exposure implies dose, which is dependent on concentration, ventilation rate, and time. The use of ambient ozone measurements as exposure variables introduces another level of uncertainty. Epidemiologic studies on the health effects of ambient ozone exposures use different averaging times (metrics) of ozone for their exposure indices. Some studies use a 1-hour maximum while others use an 8-hour maximum, and still others use 8-hour, 12-hour, or 24-hour average concentrations. This contributes to the difficulty in characterizing the ozone exposure (US EPA 1996; Health Canada, 1999; CARB, 2005).

Exposure characterization in epidemiology studies suffers from three types of measurement error: (1) the use of average population rather than individual exposure data; (2) the difference between the average personal ambient exposure and the ambient concentrations; and (3) the difference between the true and measured ambient concentrations (US EPA, 2004). Use of ambient exposure measurements (assuming subjects are outdoors 100% of their time), will tend to overestimate true personal ozone exposure. The general population spends > 90% of their time indoors on the average, equating to a significantly lower personal exposure to ozone.

Given the significant amount of time spent indoors, in combination with the type of buildings (homes, office buildings, hospitals), and the number of devices that generate ozone either intentionally or as a byproduct, it is conceivable that an individual's exposure to ozone may be more influenced by indoor sources than previously considered.

A few health effects studies have looked at measured ozone concentrations in indoor environments (Navidi et al, 1999), including homes (Lee et al, 2004), schools (Linn et al, 1996),

and the workplace (Liu et al, 1995), however, specific contributions of indoor sources were not included.

Few published epidemiology studies have attempted to account for personal exposure, and none have adequately addressed the contributions of indoor sources of ozone whether deliberately generated or generated as a by-product. In addition, with the high variability in individual lung function responses and symptom exacerbations that have been documented in both controlled exposure studies and ambient exposure studies (US EPA, 1996; CARB, 2005), it is unknown as to what extent potential confounders affect the results of epidemiologic field studies. While it is tempting to argue that epidemiologic studies have found associations between incremental increases in ambient ozone measurements (as low as 10 ppb) and morbidity and mortality endpoints, it is difficult to use these studies with their limitations as a predictor of adverse health effects caused by exposure to levels of ozone ≤ 50 ppb.

Models exploring mortality endpoints with incremental increases in ambient ozone have also been published. Increases in ambient pollution have been associated with increased risk of mortality. The biologic plausibility and coherence of these findings need to be supported and while toxicological findings and other Hill criteria fulfill this need, answers to exposure issues are equally important. Bell et al. (2004) using data and methods from the National Morbidity, Mortality, and Air Pollution Study, found an increase in both daily all cause and cardiovascular and respiratory mortality in 95 US urban communities following days with an increase in ambient ozone concentration of 10ppb when compared to a national average relative rate of mortality. This model although robust to the adjustment for particulate matter (PM₁₀) may not account for the risk associated with the other hazardous pollutants produced by atmospheric photochemistry. Bell et al. (2004) conclude that increases in this widespread pollutant “adversely affects mortality” and propose the usefulness of their model in tracking the consequences of public health control strategies.

The question remains as to what ozone concentration or low level exposure scenario can be associated with adverse health effects. Without controlled human exposure studies in the low level range, investigators are limited in their use of the epidemiologic studies for evidence of

causation of adverse health effects from low level ozone exposure. Rather, at this point in time we can view the results as one piece of the puzzle in assessing the adverse health effects from exposures <50 ppb. Appendix A contains references (evaluated for this review, but not elaborated on) that describe adverse health effects associated with levels of ozone exposure in the ambient air quality range and incremental increases in these levels. The epidemiologic studies with respiratory outcomes, in which the mean background concentration of ozone was less than or equal to 50 ppb and the exposure variable was also less than or equal to 50 ppb, were included.

Despite the aforementioned shortcomings related to a lack of toxicological data, epidemiology studies do provide some weight of evidence for demonstrating the potential for adverse health effects (morbidity endpoints) from incremental increases in low level ozone concentrations (Appendix A) and may be pertinent to considerations regarding sensitive populations while future low level exposure research is conducted.

Part 4: Integrative Summary -- Is 50 ppb adequate to protect human health?

4.0 Introduction

Using the ATS Guidelines (ATS, 1985, ATS 2000), many of the health outcomes associated with low level ozone exposure could be considered “adverse”, but a definitive dose-response at concentrations less than 50 ppb has not been established. California Air Resources Board (2005) has reviewed the ozone literature in their recent standard setting effort and concluded that “many of these effects, including pulmonary function changes accompanied by symptoms, pulmonary function changes and respiratory symptoms that reduce quality of life, large changes in pulmonary function, clinical outcomes such as emergency department visits for asthma, hospitalization for respiratory and cardiovascular disease, and death, are related to acute ozone exposures. In addition, outcomes such as increased airway reactivity and inflammation may be considered adverse if they signify increases in the potential risk of the population profile for disease exacerbation or initiation. Animal studies showing tissue changes with repeated or chronic ozone exposures raise concern as to possible subclinical effects of repeated and long-term exposure to elevated ozone concentrations.”

Despite their limitations, numerous toxicological and epidemiologic studies over the past decade have shown positive associations between ozone levels and adverse health effects (Appendix A). Given that numerous studies with different study designs and different outcomes do have positive associations for adverse respiratory health effects with increases in ozone exposure, it is difficult to dismiss that both short-term and chronic exposures to low concentrations of ozone, may be posing a health risk.

4.1 Indoor vs. Outdoor Ozone Exposure

The concept of indoor ozone production presents challenges for the both the toxicologic and epidemiologic assessment of the risk of adverse health effects at low levels of ozone exposure. Ozone is introduced into enclosed spaces through the use of products that either generate ozone intentionally or as a byproduct. Over the past decade a significant increase in the use of desktop laser printers and ozone generating devices marketed as air cleaners in homes, office buildings, schools and hotels has been observed.

Some of the epidemiologic studies accounted for, or alluded to, the amount of time spent outdoors as contributing to the exposure level. Also of note is the degree of exertion, hence increased ventilation rate, as with outdoor work for adults or participation in sports for children. Whereas some populations may have a greater risk for respiratory effects due to activity level it has also been pointed out that many Americans spend a large proportion of their time indoors and that this in turn may limit the observed effect for subpopulations with less exposure than indicated by ambient measurements. Indoor ozone concentrations in closed air conditioned homes have been documented to be less than ambient outdoor concentrations (I/O ratios of 0.2-0.7). This assumption, however, does not take into consideration ozone generated from indoor sources including, air cleaning devices that intentionally generate ozone, and other products that produce ozone as a by-product.

With the increased availability and use of ozone generating devices used as air cleaners, it is no longer prudent to make this assumption. An unknown proportion of the population may be exposed to elevated indoor exposures of ozone, yet the magnitude of the exposure and hence the

influence on the observed effect has not been defined, which again requires that a qualitative margin of safety be considered when evaluating the current FDA ozone standard.

Alternative exposure scenarios that consider indoor exposure from anthropogenic sources with varied ozone concentrations, ventilation rates (activity level), and durations of exposure need to be evaluated that would provide information on the adverse health effects associated with low levels of ozone exposure in indoor environments. Although it is not clearly linked to observed health effects at low levels of exposure below 50 ppb, ozone may serve to potentiate adverse health effects from other byproducts due to indoor ozone reactions (Weschler, 2004). These potential adverse health effects would stem from response to secondary by-products resulting from the reaction of ozone with other chemicals in the indoor environment (Fan, 2003; Morrison and Nazaroff, 2002; Clausen, 2001).

It is only in recent years that more in-depth studies have been conducted regarding subsequent reaction products, and ultra fine particulates being introduced as a function of the presence of ozone indoors (Weschler, et al., 1996, 1997a, 1997b, 1999, 2000; Shaughnessy, et al., 1998, 1999a, 1999b, 2001; Sawar, et al., 2004). According to the USEPA website (US EPA, 2003): “These experiments investigate the chemical reactions that take place when an ozone-generating air cleaner is operated in the presence of emissions from a typical source of VOCs, such as an air freshener or cleaning product. Results demonstrate that the ozone-generating air cleaners have little impact on airborne concentrations of solvents used in consumer products, but do impact concentrations of many of the fragrance compounds emitted by this type of product. Reaction products include formaldehyde and other oxygenated organics. The interaction between ozone and some of the product emissions, such as terpenes, triggers formation of ultra fine particles”.

Epidemiologic and related studies have linked fine particle exposure to increases in mortality and morbidity (Pope, A., et al., 1996; USEPA, 1997). Based on these studies the US EPA revised their current Particulate Matter National Ambient Air Quality Standard (NAAQS) to focus on fine particles less than 2.5 microns in size (in the past, focus was on particles < 10 microns). While the aforementioned NAAQS is set for outdoor air, it is well known that the average American spends 15-18 hours indoors (in homes, schools, workplace, etc.) for every hour spent outdoors. Sawars, et al. (2004), in a recent publication demonstrated that indoor reactions of

ozone with terpenes emitted from a broad cross section of common consumer products (air fresheners (liquid and solid), general all-purpose cleaners, wood floor cleaners, perfumes) can lead to elevated concentrations of particles with diameters less than 1 micron in size. The authors recommend “Such exposure could be reduced by avoiding indoor sources of ozone (e.g., from ozone generators marketed as “air purifiers”)”.

The above cited studies concur with other ongoing research efforts that demonstrate the resultant effects of ozone in the indoor environment. The subsequent byproducts in the indoor environment pose an additional risk related to ozone that is not even considered in the formulation of ambient standards. Whereas this additional risk has yet to be quantitatively determined, continued research on these aspects of ozone and indoor chemistry are being furthered. It is evident that epidemiological studies have found associations between ozone concentrations measured at outdoor monitoring stations and adverse health outcomes. Weschler (2004) recently hypothesized “that exposure to the products of ozone-initiated indoor chemistry is more directly responsible for the health effects observed in the epidemiology studies than is exposure to outdoor ozone itself”.

In summary, few published observational field studies have looked at personal exposure, and none have adequately addressed the contributions of indoor sources of ozone whether deliberately generated or generated as a by-product and the additional risk from secondary by-products has not been adequately explored. These issues are important to fully understand the public health impact from ozone deliberately generated indoors.

4.2 Sensitive Populations

The one in vivo animal study that was identified in this review did not observe adverse health effects at levels below 50 ppb; nor did the one in vivo human study that exposed healthy adult subjects to 40 ppb ozone delivered via facemask system.

The three in vitro human studies of low level ozone exposure had mixed effects with some adverse findings in both healthy and asthma subjects.

Ozone exposure at levels slightly above the 50 ppb FDA standard has been shown to influence immune system mediators (Peden, 1997), and to sensitize or potentiate concomitant exposures in susceptible populations (Kehrl et al, 1999).

Both the California Health and Safety Code and the Federal Clean Air Act require that a standard protect public health with an adequate margin of safety, although neither includes a specific legislative definition of this term. Ambient air quality standards are formulated to protect identifiable subgroups, as well as the general population.

Given the available information from chamber studies which are conducted primarily on healthy young adults, the evidence from animal toxicology studies (demonstrating pathophysiologic mechanisms) and epidemiology studies (demonstrating decreases in pulmonary function endpoints, and increases in symptoms, emergency room visits) there is evidence that should be considered in addressing an adequate margin of safety for protecting sensitive subgroups.

4.2.1 Infants and Children:

Children have a higher ventilation rate relative to body weight at rest and during activity than adults. Children also tend to spend more time outdoors in conjunction with being more active than adults. Given these factors, their exposure to ozone is intuitively greater than the general population. This greater exposure is factored in when considering a margin of safety. However, there is limited data addressing age-related responsiveness to ozone. Children or adolescents have not been found to be either more or less responsive than young adults who have undergone similar exposure protocols, although children tend to report fewer symptoms (Avol, 1987; Koenig, 1987; Koenig 1988). In summary, chamber studies of exercising children at levels greater than 50 ppb suggest they have responses generally similar to adults and epidemiologic studies that have examined both children and adults do not show clear evidence for greater sensitivity in children (McDonnell et al. 1985b). However, children are considered to be potentially more sensitive than adults given their increased ventilation rate and amount of time spent outdoors. McConnell et al. (2002) found that children who were exposed to higher ozone concentrations and participated in three or more outdoor sports exhibited a higher rate of asthma induction.

4.2.2 Pre-Existing Lung Disease:

The range of responses to ozone exposure in people with compromised health status is largely unknown. Human exposure studies addressing the responses of mild to moderate asthma populations have shown changes in symptoms, lung function and inflammation in the same range as those without asthma but larger increases in airway reactivity than healthy people (EPA, 1996; CARB, 2005). Some results, particularly those indicating increased inflammation (Calderon-Garciduenas, 2000) and potentiation (Koenig, 1990), may help explain the epidemiological findings of an association between ambient ozone levels and increased indicators of exacerbation of disease (symptoms, medication usage) and decreased lung function (FVC, FEV1, PEFr) (Appendix A).

Studies involving individuals with COPD indicate that, even at concentrations substantially higher than the current ambient air quality standard, they are unlikely to experience marked respiratory effects (Gong, 1997; Linn, 1983; Solic, 1982).

Epidemiological studies taken as a whole indicate an association between incremental increases in ambient ozone levels and increased indicators of exacerbation of disease (as indicated by increases in immune system mediators, symptoms, medication usage) and decreased lung function (as measured with FVC, FEV1, PEFr) (Appendix A). Individuals with pre-existing lung disease tend to have decreased lung function and chronic airway inflammation to begin with. Even small decrements in lung function or small increases in inflammation may be a cause for greater concern than those same effects in healthy individuals. Hence, this should be considered when applying a margin of safety to proposed standards.

4.3 Existing Health-based Warnings and Advisories

Appendix B contains warning and advisories published by various health authorities that have recognized the potential for adverse effects from the use of ozone generating devices.

4.4 Recommendations

4.4.1 FDA Standard

At this time there is insufficient evidence (very few studies) in the form of in vitro studies and controlled exposure studies (animal and human) in the toxicological and medical literature to fully assess the adverse health effects of low level ozone exposure, at or near the FDA standard of 50 ppb. Much of the epidemiologic research on ozone is referential to ambient monitoring data and the research protocols favor exposures in the range of 80 to 120 ppb, the concentrations specified in the EPA NAAQS.

The evidence from epidemiologic studies is limited as well because of: 1) the lack of low level controlled exposure studies, and 2) the use of different exposure indices (average or maximum average ambient ozone concentrations). Ambient ozone monitoring data is most useful for examining aggregate health effects associated with an aggregate population whose exposure is assumed to be outdoors. Many confounders in ozone health effects research have been identified and the epidemiologic models do attempt to account for this (CARB, 2005). However, very few studies actually account for the time spent indoors when calculating an exposure index (Neas et al, 1995; Kunzli et al 1997, Tager et al, 1998). Indoor environments are unique and exposure patterns to ozone generated in indoor environments may not be similar at all to ambient exposure patterns. Therefore it is possible that the ozone exposure scenarios that have been developed for human exposure studies to answer questions about ambient ozone exposure in the outdoor environment would not be helpful in evaluating adverse health effects from low levels (≤ 50 ppb) of ozone in the indoor environment. These findings (in conjunction with the recent attention focusing on indoor chemistry and the contribution of ozone reaction byproducts which may be just as harmful as ozone itself) reflect a definitive need to further investigate the resultant effects of low level ozone exposure in the indoor environment. Additional studies are needed to address the adverse health effects of low level ozone exposure. As previously stated by EPA, more research is needed to assess adverse health effects of ozone using various exposure scenarios. Investigators submit that new models need to consider the effects of not only time spent indoors, but also of the indoor sources of ozone, the ozone reaction byproducts, and their relative contributions to personal exposure.

The FDA standard is not expressed as a true exposure limit, as with EPA ambient air quality standards and OSHA and ACGIH occupational exposure limits. Rather the FDA standard, acknowledging that ozone is a known respiratory irritant, placed limits on devices based on emission levels and accumulation levels. We are unable to apply a time frame to the 50 ppb accumulation limit. There is simply not enough data from human exposure studies to extrapolate the potential for adverse health effects at such low levels of exposure.

Ozone exposures have been demonstrated to cause adverse health effects in controlled human exposure studies (CARB, 2005, Health Canada, 1999, EPA 1996), and epidemiologic studies have associated incremental increases (as low as 10 ppb) in ambient ozone with adverse health effects (Appendix A). The current FDA standard for accumulation of ozone from devices used in occupied, enclosed spaces is greater than the 20 ppb Continuous Exposure Limit recommended for assessing the habitability of particular enclosed environments (submarines and spacecrafts) (National Research Council, 2000) and less than the 70 ppb 8-hour ambient air quality standard set by CalEPA (CARB, 2005). The authors of this report believe that the 50 ppb maximum accumulation level set by the FDA (although less than the current outdoor standard of 70 ppb set by CalEPA) is appropriate in light of the published evidence to date. In other words, although the FDA standard is less than any set limit for outdoor air, one must consider the weight of the epidemiologic data and the unknown impact of ozone-generated indoors and their byproducts due to secondary reactions when considering potential for long term exposure in enclosed spaces.

Given the limited data available, the current FDA standard of 50 ppb accumulation level from ozone generating devices used in enclosed spaces is considered to be adequate to protect consumers from adverse health effects related to ozone exposure. Evidence to recommend raising or lowering the FDA standard is not compelling, and given the lack of substantial data (at the current time) to the contrary, the current standard is considered sufficient for the consumer at this time. This recommendation relies on the assumption that ozone generating devices are able to operate within the accumulation level of the FDA standard. If the accumulation level is exceeded, there is the potential to have exposures in the range demonstrated to induce adverse health effects.

Consideration of implications of indoor chemistry related to ozone and byproducts was beyond the scope of this project and authors were requested by CPSC to specifically limit the references to these issues until further quantitative evidence is available of the outcomes related to these reactions. *However, the continued research in this field as to the impact of indoor chemistry (primarily ozone reactions with indoor terpenes) and resultant adverse byproducts may warrant more stringent ozone limits in the near future beyond the current FDA limit. This would be based not only on the harmful effects from breathing ozone, but also the combined synergy related to the byproducts of indoor reactions resulting in irritants such as aldehydes, ketones, organic acids, and ultrafine particles.*

The Statement of Work requested that a comprehensive literature review be conducted to assess the potential for adverse health effects associated with ozone exposures that would be expected from the use of ozone-generating air cleaners. The literature was limited to exposure time frames and concentrations that are applicable to evaluation adverse health effects with respect to exposures typical for ambient air quality standards. We did not conduct a formal quantitative risk assessment and therefore can not discuss the 50 ppb standard in terms of quantitative risk or exposure limit. While we can not assign a time frame and discuss this in terms of exposure, the current FDA maximum accumulation limit of 50 ppb, is believed to be an adequate level to reduce the occurrence of potential adverse health effects in consumers, based on the best available knowledge in ozone exposure research and the caveats discussed above.

4.4.2 Sensitive Populations

At this time a separate recommendation for a specific accumulation level for potentially sensitive subpopulations is not recommended. There is however limited information from low level human exposure studies that supports that either children, elderly, those with asthma, or those suffering from allergic rhinitis or COPD have a greater response to low level ozone exposures. There are however epidemiological findings that do find an association between incremental increases in ambient ozone levels and increased indicators of exacerbation of disease (as indicated by increases in immune system mediators, symptoms, medication usage) and decreased lung function (as measured with FVC, FEV1, PEFr) (Appendix A). Individuals with pre-

existing lung disease tend to have decreased lung function and chronic airway inflammation to begin with and even small decrements in lung function or small increases in inflammation may be a cause for greater concern than those same effects in healthy individuals. Infants and children are also potentially more susceptible and these populations should especially be considered when weighing the potential for adverse health effects from ozone *and* ozone-initiated chemistry byproducts. Adverse health effects such as decreases in pulmonary function, alterations in the respiratory tract, and declines in lung function have been observed in epidemiologic studies with ozone levels close to background concentrations. Ozone levels below U.S. EPA regulations have been associated with increased frequency of respiratory symptoms in children with asthma (Gent et al. 2003).

When looking at the evidence in total, the lack of low level human exposure data and the lack of an established threshold level do not support recommending a specific change to the FDA standard for sensitive populations at this time. However, given the recent flourish of epidemiologic evidence that shows sensitive populations do have the *potential* to exhibit adverse health effects at low levels of ozone exposure (at or below background levels), it would be prudent to consider a margin of safety to protect these groups from the unquantified risk associated with exposure to ozone intentionally generated indoors. The question remains as to whether sensitive populations should be advised to avoid exposure to intentionally generated ozone until a margin of safety can be determined (or suggested) using quantitative risk assessment, or whether empirical prevention guidance is warranted at this time.

4.5 Best Available Information

Because we are unable to define the level of indoor ozone exposure where health effects are expected, because of the amount of variability in consumer and commercial use of ozone generating devices, and because personal exposure is influenced by time spent indoors and outdoors, it may be improbable to set an indoor exposure limit in relation to ozone generated indoors. The authors of this report agree with CPSC that a maximum emission rate and resultant concentration (accumulation level) should be determined using health based criteria. While we can not assign a time frame and discuss the accumulation limit in terms of exposure, the current FDA maximum accumulation limit of 50 ppb represents a level below which the occurrence of adverse health effects, have not been demonstrated in healthy subjects in controlled ozone

exposure research. However, evidence from toxicological and epidemiologic studies support that further research is needed on adverse effects from low level ozone exposures.

This recommendation is based on currently available information and may be subject to change as new research findings on long term low level exposure to ozone and exposure to ozone in indoor environments are published. Ongoing research on ozone-initiated reactions and subsequent byproducts must be considered as results become more quantifiable and useful in risk assessment models.

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APPENDIX A

Note: Appendix A contains references (evaluated for this review) that did not provide explicit pertinent information regarding the potential for adverse health effects at levels ≤ 0.05 ppm.

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APPENDIX B

Existing Health Advisories and Warnings

Ozone Generators and Indoor Air Quality
Health Advisories

US EPA. *Ozone-Generating Air Cleaners and Indoor Air Chemistry.*
<http://www.epa.gov/appcdwww/iemb/ozone.htm>

US EPA. *Ozone Generators that are Sold as Air Cleaners: An Assessment of Effectiveness and Health Consequences.*
<http://www.epa.gov/iaq/pubs/ozonegen.html>

CalEPA. *ARB Warns, Danger from Popular “Air Purifying” Machines.*
<http://www.arb.ca.gov/newsrel/nr012005.htm>

Cal EPA. *ARB Health Update: Ozone Generators Sold as Air Purifiers.*
<ftp://ftp.arb.ca.gov/carbis/research/health/healthup/jan05.pdf>

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http://www.dhs.ca.gov/ehlb/IAQ/Indoor%20Ozone/o3_fact.htm

State of Alaska Epidemiology. Bulletin Number 36. *Ozone Generators-Warning-Not for Occupied Spaces.*
http://www.epi.hss.state.ak.us/bulletins/docs/b1997_36.htm

North Carolina Public Health. Epidemiology. *Indoor Ozone.*
<http://www.epi.state.nc.us/epi/oeo/ozone/indoor.html>

Health Canada. *Air Cleaners Designed to Intentionally Generate Ozone (Ozone Generators) – Questions and Answers.*
http://www.hc-sc.gc.ca/hecs-sesc/cps/publications/ozone_qa.htm

American Lung Association. *Ozone Generators.*
http://alaw.org/air_quality/indoor_air_quality/ozone_generators.html

The Hartford Loss Control Department. *Ozone Generators and Indoor Air Quality*
<http://www.thehartford.com/corporate/losscontrol/CFLC/56ozone.pdf>

Technical Assessment for CPSC
Part II: Ozone Devices
Modeling Considerations

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Peer review comments incorporated

May 19, 2006

The following tasks were outlined in the original work plan developed in October 2004 and submitted to CPSC to conduct the ozone review:

Work Plan

Work to be conducted based on statement of work provided to contractor by CPSC. Essentially this includes the following tasks as detailed in the Statement of Work:

- d) Conducting a comprehensive literature search and a critical review of the literature to independently assess the possible effects of low levels of ozone (representative of concentrations that may be expected resulting from the use of ozone generating air cleaners, throughout their operational and life cycles, intended for occupied spaces). Special emphasis will be placed on sensitive populations including the elderly, young children, and individuals with compromised pulmonary function.
- e) Evaluating whether the current 50 ppb exposure limit [maximum accumulation level] for ozone is adequate to protect consumers from potential adverse health effects. If the 50 ppb level is believed to be inadequate, contractor will recommend an alternative exposure limit [maximum accumulation level] for ozone concentrations.
- f) Recommending to CPSC staff the maximum emission rate of ozone from ozone-generating devices, and/or the maximum resultant concentration of ozone (ozone accumulation) from ozone-generating devices (within a space), based on the exposure limit [accumulation level] believed to be capable of reducing the occurrence of potential adverse health effects (based on literature review).

This supplement to the health component review which has already been submitted is intended to cover the recommendation to CPSC pertaining to options to address emissions from ozone-generating devices.

INTRODUCTION

Based on the health component discussion previously submitted, the 50 ppb FDA limit (buildup within the space) for ozone was considered to be adequate based on current literature, or lack thereof of sufficient evidence below this value. *The continued research in this field may warrant more stringent ozone limits in the near future based not only on the harmful effects from breathing ozone, but also from the effects of the byproducts of indoor reactions resulting in irritants such as aldehydes, ketones, organic acids, and ultrafine particles.* It is important to note that the 50 ppb concentration limit is based on all sources which may contribute to the resultant indoor ozone concentration. This would include not only contribution from the use of the ozone generating device but also (primarily) that from outdoor air. It is well-established in the literature that typical indoor/outdoor ratios of ozone range from 0.2 to 0.7 (Weschler, 2000). The modeling proposed herein describes an approach that centers on the accumulation of ozone within the space based on air cleaners alone. To fully evaluate the indoor accumulation of ozone, one must consider not only contributions from indoor sources but also that from the outdoor environment. This may amount to ozone concentrations varying from 2-40 ppb added to the indoor environment based on outdoor-to-indoor transport (Sarwar, et al., 2004). This is discussed briefly, however due to variance in outdoor ozone concentrations throughout the U.S. and the various assumptions that must accompany the model, the basic approach presented here focuses solely on the ozone accumulation based on indoor ozone sources (ozone generators or ozone-emitting air cleaning devices). The broader scenario of including outdoor air sources must be considered in the final evaluation as to resultant indoor ozone accumulation and whether or not it is below the 50 ppb level.

The question remains as to what approach may be most suited to ensuring that these devices are compliant with such a recommendation. Basic choices for limiting emissions through a performance standard are to monitor maximum concentration accumulated within a standardized chamber, or to focus on emission rates related to the specific device. It is important to develop an index that is measurable and can be used to judge what contribution an air cleaner will make to

the overall room ozone concentration in its actual application condition. Niu et al. (2001) have stated that the emission rate is a more useful emission index than the maximum concentration measured in a test chamber. They base this on the premise that the most relevant concern is that the 50 ppb limit will not be exceeded in actual use conditions rather than in a standard testing chamber. The approach of focusing on the device emission rate has many merits as opposed to regulating a given environment.

MODELING OZONE EMISSIONS FROM AIR CLEANERS

Recent and past work have demonstrated that many ozone-generating devices on the market produce room ozone concentrations that exceed health-based standards (California Air Resources Board, 2006). This section focuses on basic modeling that can be utilized to determine the resultant ozone concentration within a given space, based on the emission rate from the air cleaning device.

Concentrations of contaminants in indoor air are dynamic and result from the competition between various source and removal processes. These processes can be described by a simple mass-balance model, where the key assumption is that the indoor space is “well-mixed”. For most residential environments and for the time scales of interest (of order hours), this is a reasonable assumption well borne out by the many model-measurement comparisons of indoor pollutant behavior since this approach was first introduced (Traynor et al. 1982; Dockery and Spengler 1981). It is recognized that spatial variation in concentrations can occur, especially when contaminant species are emitted from localized sources. The characteristic mixing time, τ , (defined as the period required for an instantaneous point release in an unventilated room to disperse such that the standard deviation among local concentrations is less than 10%) can be used to examine the “well-mixed” assumption. Measured values for τ ranged from 10 minutes, under natural convective flow conditions, up to 90 minutes, under thermally quiescent conditions in a study conducted by Baughman et al. (1994). Dreschler et al. (1995) measured τ to be 2-15 min in the same room for a variety of forced flow conditions, representative of what may be observed in homes throughout the U.S. Under the forced flow conditions described above, where $\tau \ll (\text{ventilation rate})^{-1}$, the well mixed approximation should describe exposure conditions reasonably well (Nazaroff and Weschler, 2004). Although the well-mixed approximation is used

in the modeling below, it is of use to note that from a regulatory standpoint, consideration may be given to developing a test protocol to measure ozone at set distances from the device under normal room conditions. This might be applied in addition to the proposed method in this document and would add an additional margin of safety.

To base a proposed performance standard on an ozone emission rate, several parameters contributing to ozone accumulation must be defined. The factors which determine the buildup within an indoor environment include ozone generation rate, ozone decomposition rate, leakage/penetration, ventilation and degree of mixing. Mathematically, the 'well-mixed box' equation is:

$$\frac{dC_i}{dt} = S/V + P\lambda_v C_o - \Lambda C_i \quad (1)$$

where:

C_i = The indoor concentration of ozone (mass per unit volume)

S = Source strength (emission rate in mass per unit time)

V = Volume of indoor space of interest

P = Penetration fraction for species entering from outside the volume of interest (unitless)

λ_v = Ventilation rate (units of inverse time)

Λ = sum of all first order removal processes (units of inverse time)

C_o = outdoor concentration of ozone (mass per unit volume)

The first order removal processes can be broken down into their constituent parts as follows:

$$\Lambda = \lambda_v + \lambda_d \quad (2)$$

The first order decay model provides an excellent representation of the ozone decay processes in an indoor environment (Mueller et al. 1973), and it has been further analyzed that the decay is mainly due to heterogeneous deposition/reaction at room surfaces (Sabersky et al. 1973). In the above Equation 2, the removal processes are described as the sum of removals afforded by ventilation, λ_v , and by surface removal rate, λ_d (units of inverse time). The surface removal rates are typically reported as first order rates, or as deposition velocities which must be multiplied by the surface to volume ratio to obtain the first order rate. Thus, the surface removal rate, λ_d , can be described by:

$$\lambda_d = k_d (A/V) \quad (3)$$

Where: k_d = ozone deposition velocity, and A/V is the effective surface to volume ratio for the given space.

Note that this discussion has ignored the contribution of homogeneous reactions to ozone decay. In general, the impact of homogeneous chemistry would be minor compared to removal by ventilation (air exchange rate) and heterogeneous removal, provided the steady state ozone concentration is approximately 5 to 10 times greater than the sum of reactive VOCs prior to the introduction of ozone (Weschler 1992).

Substituting the values for the composite removal, Λ , into equation 1 yields:

$$\frac{dC_i}{dt} = S/V + P\lambda_v C_o - \lambda_v C_i - k_d (A/V) C_i \quad (4)$$

For an experiment in which the concentration of ozone reaches an equilibrium value within a space (i.e. where $\frac{dC_i}{dt} = 0$ in equation 4, or equivalently when t (time) is long enough that the exponential terms in the solution to equation 4 approach zero), the equation for steady state becomes:

$$S = V [C_i (\lambda_v + k_d (A/V)) - P\lambda_v C_o] \quad (5)$$

Here C_i is the equilibrium (steady state) concentration of ozone in the space.

Assumptions/final criteria for determination of emission rate limit for devices

Outdoor air penetration

To examine the *sole* contribution from an ozone-emitting device to the resultant concentration within a space, one must assume a zero penetration fraction for ozone entering from outside sources. This is logical considering that the end effect of outdoor infiltration on indoor concentrations has two possibly conflicting outcomes. On the one hand, ventilation air is considered, in the analysis of the estimation of indoor ozone buildup from air cleaners, to be

ozone free and therefore helps to remove ozone (Viner et al. 1991). Conversely, during peak ambient air pollution episodes, outdoor air infiltration of ozone can be significant (Shair and Heitner 1974). Normal usage of an air cleaner would typically be under closed room conditions, reducing the rate of infiltration and subsequent effect of outdoor air. The zero infiltration rate postulation is a compromise between both extremes and is a reasonable assumption for purposes herein. The authors recognize that dependent on a number of variables including air exchange rate and the outdoor ozone concentrations, the outdoor contribution may be significant to be considered in the final determination of resultant ozone within the space. Under such conditions the ozone infiltration rate and outdoor ozone concentrations could be used to establish the emission parameters and design the system for a near worst case scenario (if CPSC desires to provide this margin of safety). Further development of the potential contribution from outdoor air is presented later in this report on pages 14-16.

For purposes of examining the contribution of ozone based primarily on the air cleaning device alone, the outdoor penetration factor will be neglected here. Equation 5 is reduced to the final form (equation 6, below) useful to determine the source term necessary to comply with a 50 ppb concentration limit (based on air cleaner emission alone) within a given space:

$$S = V[C_i (\lambda_v + k_d (A/V))] \quad (6)$$

Using equation 6, an air exchange rate and surface removal rate must be assigned to enable calculation of acceptable source term (emission rate) for a given volume of indoor space.

Ventilation Rate (Air exchange)

The determination of an appropriate ventilation rate to encompass air exchange in homes, must take into account the range of values that are found in homes throughout the U.S. Murray and Burmaster (1995) provided analysis on a set of 2,844 measurements of residential ventilation rates in U.S. houses. These data are reasonably well described by a log normal distribution. When considering all climate zones and seasons the geometric mean ventilation rate was 0.53 h^{-1} . There are large variations based on season and climatic zones. It was observed that during the winter the 25th percentile value was 0.29 h^{-1} and the 75th percentile value was 0.67 h^{-1} . During the summer the 25th and 75th percentile values are 0.53 and 1.92 h^{-1} respectively. As one

would anticipate, ventilation rates are also higher when windows are open (often greater than 5 ach) than when they are closed (Alevantis and Girman 1989). It is worthwhile to note that approximately one-third of the measurements in the winter season fall short of the recommended 0.35 h^{-1} ventilation rate for homes recommended by ASHRAE (ASHRAE 2004). In addition, in the coldest climate zone, approximately 55% of the measured ventilation rates, from all seasons, are less than 0.35 h^{-1} . Persily and Martin (2000), in a study of modeled ventilation rates, found that predicted infiltration rates on an annual basis are below 0.25 h^{-1} in modern manufactured housing. The study indicated that infiltration rates vary as much as 5 to 1 based on variations in weather conditions alone. In specific areas of the country, they found that the air change rate is below 0.25 h^{-1} for about one-third of the year in Albany and Seattle and for 70% of the year in Miami. These results are consistent with an earlier study by Persily (1998) which also modeled residential ventilation rates and found air exchange rates are often below 0.35 h^{-1} , again corresponding to underventilation relative to the outdoor air ventilation recommendation for homes by ASHRAE.

In light of these studies, selection of an appropriate ventilation rate for the ozone emissions model should be based on a lower common denominator value to account for homes with lower ventilation rates (the lower the ventilation rate, the greater the ozone concentration accumulation within the space based on a set emissions rate limit). Such an assumption of ventilation rate must be protective of homes at worse case times of the year (winter cold climate areas of the U.S.). The studies by Murray and Burmaster (1995) and Persily (1998; 2000) indicate that home air exchange may fall well below the 0.35 h^{-1} ventilation rate recommended by ASHRAE at specific times of the year. However, given the mean (geometric) value of 0.53 h^{-1} for ventilation rates encompassing all climate zones and seasons, one may argue that selecting a ventilation rate lower than 0.35 h^{-1} would be biased to account for the lower fraction of homes in the U.S. alone. In addition, given that the 0.35 h^{-1} ventilation rate value is also cited by the International Mechanical Code (2003), and the International Residential Code (2003) as a minimum that should be provided by windows or mechanical means within a home, this may be most reflective of a representative value to use for modeling purposes. Thus, the assumed ventilation rate of 0.35 h^{-1} shall be used for λ_v in equation 6 above. It can be argued that a lower air exchange rate should be selected to reflect a protection factor for a broader cross section of homes in the U.S. This is an issue that ultimately lies with CPSC in developing a margin of safety related to the

modeling assumptions. Further discussion as to effect of varying air exchange rates on a prescribed emission rate limit is provided later in this report on pages 14-16.

Surface Removal Rate

Knowledge of the surface removal rate for ozone within a space is essential if one is to calculate generation rates from monitored concentration data. Reasonable values for the decomposition rate must be known for various residential situations if reliable concentration predictions are to be made (Mueller et al. 1973); however as Nazaroff et al. state (1993) “As a scientific topic, the issue of air pollution interaction with indoor surfaces is at a juvenile stage of development” . They go on to spell out a number of shortcomings that must be resolved in order to better characterize contaminant removal by indoor surfaces.

Most data presented in the literature report on the surface removal rate, λ_d , obtained by observed decay of ozone within a given environment. From this information, the deposition velocity, k_d , is inferred based on estimates of surface to volume, A/V , ratios (Equation 3). The surface to volume ratio, A/V , varies with the indoor dimensions, surface coverings and furnishings. As expected, this suggests that the decay rate is different in each home, and is determined by variables such as the quantity and types of furnishings and finishes, and the dimensions/layout of each home (Lee et al. 1999). All else being equal, smaller rooms have higher surface to volume ratios as compared to large rooms. This, in effect, results in an accelerated ozone removal by surfaces in smaller rooms than larger rooms (Weschler 2000). In addition, fleecy surfaces provide an extended surface area as compared to smooth surfaces. Rooms with fleecy surfaces such as carpeting, drapes, upholstered furnishings, etc. tend to have larger surface removal rates for ozone, than rooms without such accommodations (Mueller et al. 1973; Sabersky et al. 1973). This would account for why bedrooms typically display higher surface removal rates as compared to other indoor settings. A recent study by Hodgson et al. (2004) focused on quantifying object and material surface areas in typical residences. The study involved evaluating 33 rooms in nine California residences consisting of bathrooms, bedroom/offices and common areas. Total surface area-to-volume was determined for each room. Total surface area-to-volume ratios for the 12 bedrooms ranged from 2.3 to 4.7 $m^2 m^{-3}$, again, highly dependent on the size of the room. Bedrooms generally had higher surface to volume ratios as compared to

other rooms in the house. Surface to volume ratios for bedrooms of different sizes varied by about a factor of two.

A compilation of studies on surface removal rates are presented in Table 1 on the following page:

Table 1: Summary of literature: Removal of Ozone by Surfaces in Different Indoor Environments

Indoor Setting	Surface area (m ²)	Vol (m ³)	A/V nominal	A/V reported; (effective ratio) (m ² m ⁻³)	surface removal rate (h ⁻¹) λ _d	deposition velocity (m/h) k _d	Reference	Comments	
Bedroom	42.7	19	2.25	5			Singer et al. 2005		
Bedroom	47.4	22	2.15	4.5			Singer et al. 2005		
Bedroom	54.4	27	2.01	4.2			Singer et al. 2005		
Bedroom	60.2	31	1.94	3.6			Singer et al. 2005		
Aluminum room	31.25	11.9	2.62	3.3	3.24	0.972	Mueller et al. 1973		
Stainless steel room	36.21	14.9	2.43	2.7	1.44	0.54	Mueller et al. 1973		
Bedroom	73.47	40.8	1.80	3.3	7.2	2.18	Mueller et al. 1973		
Office home (no forced air)	91.87	55.2	1.66	2.8	3.96	1.41	Mueller et al. 1973		
Home (forced air)				3.3	2.88	0.90	Sabersky et al. 1973		
department store				3.3	5.4	1.66	Sabersky et al. 1973		
Office	50.46	24.1	2.09	2.8	4.32	1.54	Thompson et al. 1973		
Office	45.24	20.7	2.19	2.8	4.32	1.54	Allen et al. 1978		
Homes (43 homes located in S California)				1.56 +/- 0.32	2.80 +/- 1.30	1.76 +/- .612	Allen et al. 1978	Lee et al. 1999	measurements from living rooms/family rooms (high ceilings, resulting in very low surface to volume ratios)
12 bedrooms S California data				2.3 to 4.7 (m ² /m ³)			Hodgson et al. 2004	Data function of varying room sizes; as room size increased, A/V decreased	

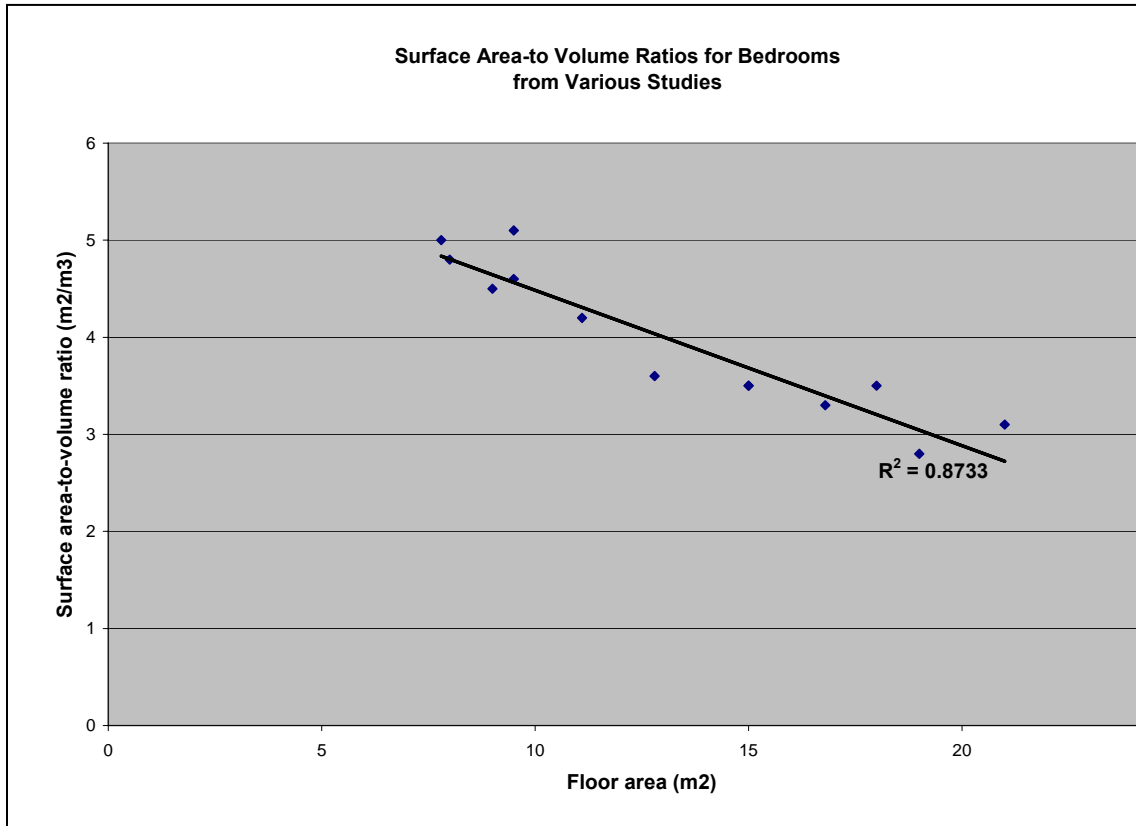
Based on the surface removal rate information it is clear that the removal rates vary significantly dependent on the room type, materials, and size. Due to the variance in room-to-room ozone removal rates, it is useful to select a room that is representative of where the devices may be used in the majority of homes. Bedrooms have been selected as a basis for determining a suitable surface removal rate since these rooms are commonly chosen by the occupants for placement of air cleaning devices. In a recent survey by the Association of Home Appliance Manufacturers (AHAM, 2003), it was found that over 1/3 of homeowners place the devices in bedroom areas, with another 1/3 placing them in the living room areas, and the remaining distributed in various other locations within the home. A further examination of composite representative data of surface area-to-volume ratios, compiled from three of these studies, specific to bedroom areas alone, is shown below in Table 2:

Table 2: Representative surface area-to-volume ratios

type of room	floor area (m²) room ht = 2.43m	Surface area-to- volume ratio reported (m² m⁻³)	Reference
Bedroom	7.8	5	Singer et al. 2005
Bedroom	9	4.5	Singer et al. 2005
Bedroom	11.1	4.2	Singer et al. 2005
Bedroom	12.8	3.6	Singer et al. 2005
Bedroom	16.8	3.3	Mueller et al. 1973
Bedroom	8	4.8	Hodgson et al. 2004
Bedroom	9.5	4.6	Hodgson et al. 2004
Bedroom	9.5	5.1	Hodgson et al. 2004
Bedroom	15	3.5	Hodgson et al. 2004
Bedroom	15	3.5	Hodgson et al. 2004
Bedroom	18	3.5	Hodgson et al. 2004
Bedroom	19	2.8	Hodgson et al. 2004
Bedroom	21	3.1	Hodgson et al. 2004

Figure 1 on the next page graphically provides an approximate representation the data from Table 2.

Figure 1: Reported surface area-to-volume data from bedrooms as a function of floor area (all values based on room height of 2.43 m)
 (Source: Mueller et al. 1973; Singer et al. 2005; Hodgson et al. 2004)



In addition to the surface area-to-volume ratio, the deposition velocity, k_d , must be considered to formulate a final surface removal rate. Table 1 lists the deposition velocities calculated using estimated values for the surface to volume ratio in the various indoor settings. These values vary across the board yet are not as diverse as might be expected. Sabersky et al. (1973) demonstrated that different surfaces scavenge ozone at markedly different rates, which begs the question as to why the deposition values are so similar from site to site and study to study. Nazaroff et al. (1993) hypothesized that the likeness in values may be more a function of many materials being found in buildings, and since these materials tend to be similar from structure to structure, then the “average” deposition velocity will be similar from structure to structure. In their study of 43 homes, Lee et al. (1999) calculated a value of 1.76 +/-

.612 m/h. The range of values determined by Lee is consistent with other deposition velocities reported in Table 2, from the literature.

For our purposes in modeling the indoor environments, the deposition velocity presented by Lee of 1.76 m/h will be used in the determination of surface removal rates. Here again, a more protective value could be selected for the deposition velocity, depending on how conservative a position is assumed by CPSC. The surface area-to-volume ratios will be estimated as a function of room size (use of Figure 1) and shall be based on bedroom space. For typical bedroom sizes ranging from 25 m³ up to 40 m³ the surface removal rate (product of surface-to-volume ratio and deposition velocity) corresponds to values of 7.9 to 6.2 h⁻¹ respectively.

SUMMARY: Determination of O₃ Emission Rate Limit for Air Cleaning Devices

Based on the preceding discussion, the following values will be used in the calculation of an ozone emission rate limit (source term, S, in mg/h) for air cleaning devices (Use of Equation 6, above):

Ventilation rate: $\lambda_v = 0.35 \text{ h}^{-1}$

Deposition velocity: $k_d = 1.76 \text{ m/h}$

Surface area-to-volume ratio: A/V (being a function of room size, assuming a room height of 2.43 m) determined based on use of Figure 1

Steady state ozone concentration: $C_i = 50 \text{ ppb}$; for equation for proper units, $C_i = .098 \text{ mg/m}^3$

Volume: based on room size, m³

For purposes of establishing an emission rate limit for ozone-generating air cleaning products, a representative room size should be established. As previously discussed, the site within the home selected for the use of the air cleaning device (for these calculations) is the bedroom area. Size of room may vary depending on the individual home. Accordingly the surface area-to-volume ratio would change as a function of room size based on Figure 1. Sizes of bedrooms in the United States may vary depending on housing stock characteristics for different parts of the country. The Department of Housing and Urban Development construction standards detail that all bedrooms shall

have a minimum of at least 70 square feet (~ 6.5 m²) of floor area (HUD 1995). Beyond this number bedroom sizes may range up to 40m² and above for master bedrooms in large homes.

Emission rate limits are provide in Table 3 based on varying room sizes. These limits are based on the assumptions provided within this report.

Table 3: Calculations for determination of Source term (to adhere to 50 ppb accumulation in space based on air cleaning device alone); $k_d=1.76$; $C_i=.098\text{mg/m}^3$; vent rate= 0.35 h^{-1}

Volume (m3) (2.43m height)	A/V ratio (reported) m ² /m ³	S term (mg/h)
15	5.1	14
20	4.8	17
25	4.5	20
40	3.5	26

Table 3 provides a reference base for estimating emission rates (S) relating to the 50 ppb limit based solely on air cleaner device contribution. The emission rates are the result of calculations based on the assumed values for ventilation rate and surface removal rates (based on room size). Equation 6 has been used for calculation of source terms related to air cleaners. Discussion of the various assumptions in the model has been included in this report.

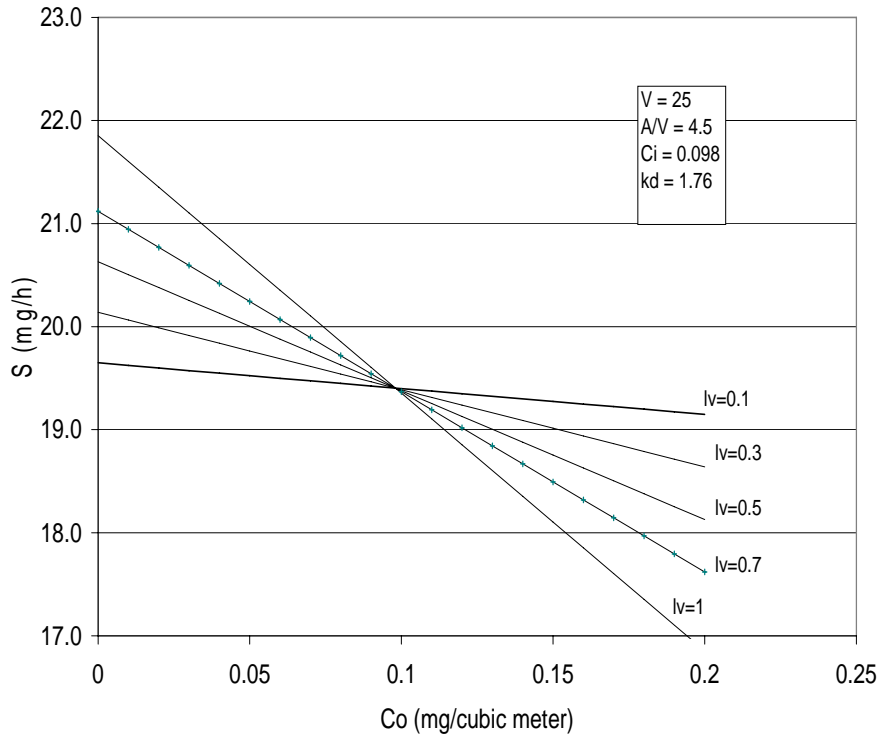
As previously noted the values presented in Table 3 are based on assumptions related to representative air exchange rates and surface removal rates in homes throughout the U.S. In addition the contribution of outdoor ozone penetration has been neglected in the calculations. To fully evaluate the indoor accumulation of ozone (and compliance with a 50 ppb limit), one must consider not only contributions from indoor sources but also that from the outdoor environment. Even though the effect may be minor in some cases, outdoor concentrations can play a role, as they *do* influence the final indoor levels. If the CPSC wishes to protect consumers from being exposed to indoor levels over 50 ppb, then the outdoor contribution may need to be considered. For example, if the final emission rate terms given above are used, with Houston mid-day summer ozone levels

of 100 ppb, and a penetration factor of 1, the final indoor concentration is greater than 50 ppb.

$$C_i = \frac{S/V + P\lambda_v C_o}{\lambda_v + k_d(A/V)} = \frac{14\text{mg/h} / 15\text{m}^3 + (1)(0.35\text{h}^{-1})(0.2\text{mg/m}^3)}{(0.35\text{h}^{-1}) + (1.76\text{m/h})(5.1\text{m}^{-1})} = 0.108\text{mg/m}^3 = 54\text{ppb}$$

Figure 2 plots S vs Co (outdoor ozone concentration) for various air exchange rates. Note that homes, in urban areas, in summer that experience higher ventilation rates will require a substantially lower emission rate (S) than recommended in Table 3 if the final accumulation of ozone in the space is to be less than or equal to 50 ppb.

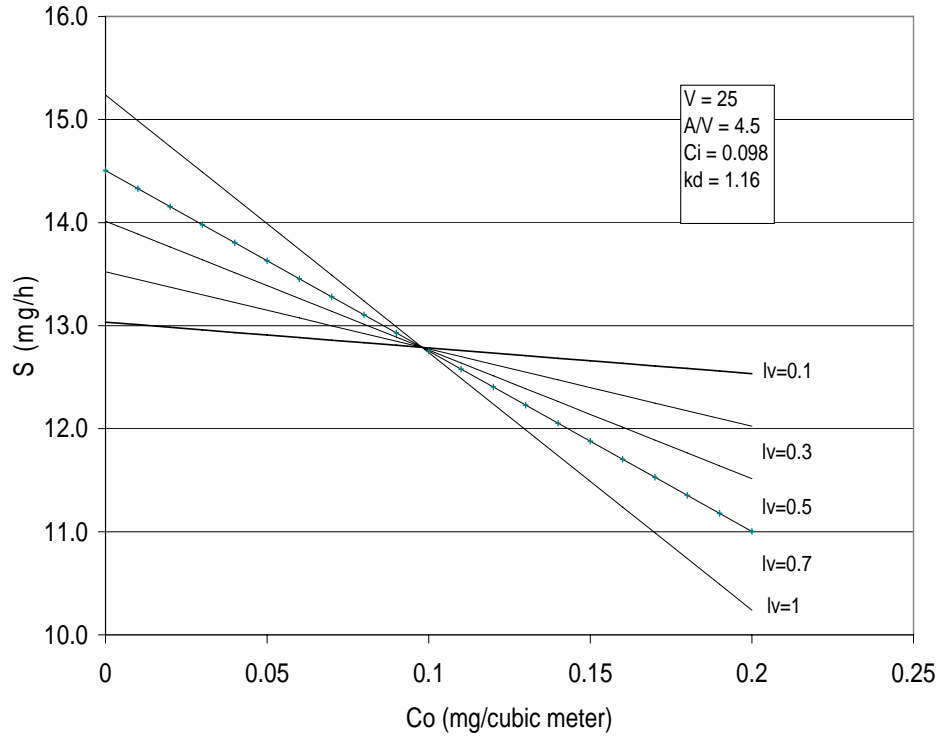
Figure 2: Maximum Source Term, S, (emission rate, mg/hr) vs Outdoor Ozone Concentration, Co, (to result in ≤ 50 ppb within the space)



In addition, as previously noted the assumption of surface removal rate (specifically deposition velocity) will have a significant impact on resultant indoor ozone accumulation. The final value utilized depends on the margin of safety that CPSC elects

to build into their final analyses. Lee et al. (1999) calculated a deposition velocity, k_d , value of 1.76 +/- .612 m/h. Noting that the arithmetic standard deviation for k_d is 0.6 m h⁻¹, then 16% of homes have a k_d less than 1.16. Reproducing Figure 2 for houses with $k_d = 1.16$ provides a much more conservative estimate of S as displayed in Figure 3.

Figure 3: Maximum Source Term, S, (emission rate, mg/hr) vs Outdoor Ozone Concentration, C₀, (to result in ≤ 50 ppb within the space) for k_d = 1.16



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