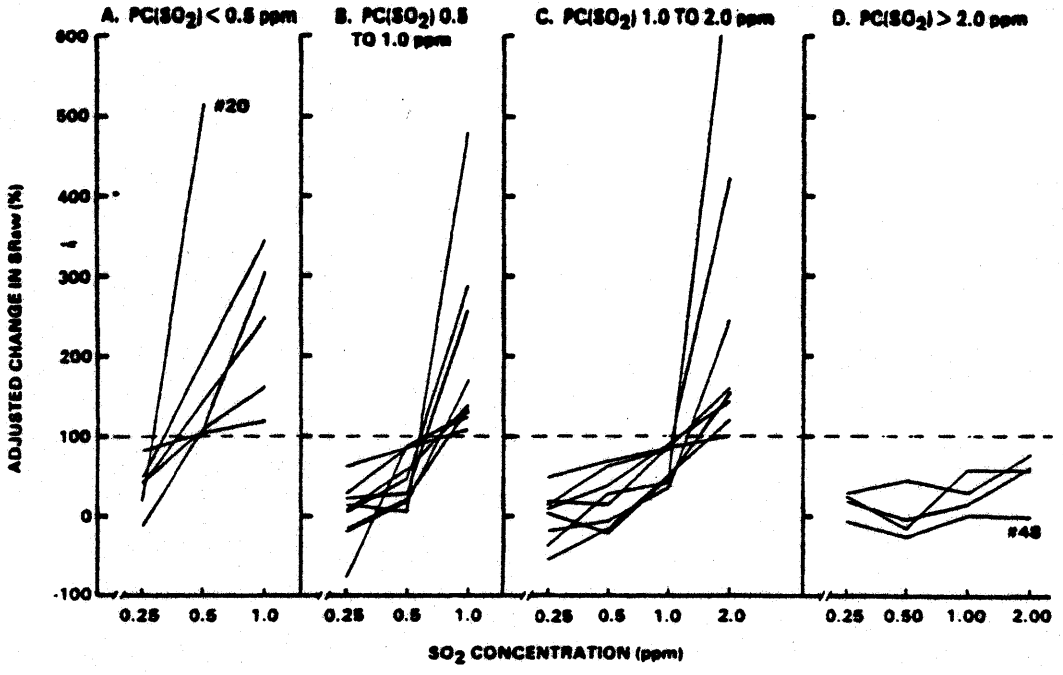
REVIEW OF THE NATIONAL AMBIENT AIR QUALITY STANDARDS FOR SULFUR OXIDES: UPDATED ASSESSMENT OF SCIENTIFIC AND TECHNICAL INFORMATION

DRAFT ADDENDUM TO THE 1982 OAQPS STAFF PAPER



Strategies and Air Standards Division
Office of Air Quality Planning and Standards
U.S. Environmental Protection Agency
Research Triangle Park, N.C. 27711

September 12, 1986

Cover Illustration. Individual dose-response curves of percentage (normalized) changes in airway resistance (SRaw), adjusted for response to clean air exposure, as a function of SO_2 exposure for asthmatic subjects. (A) 6 subjects with response at < 0.5 ppm, (B) 9 subjects with response between 0.5 and 1.0 ppm, (C) 8 subjects with response between 1.0 and 2.0 ppm, and (D) 4 subjects with response at > 2.0 ppm SO_2. Data are not included for 0.0 ppm since they were used to adjust for exercise-induced bronchoconstriction. The interrupted horizontal line represents 100% increase in SRaw and the SO_2 concentration corresponding to its point of intercept with each subject's curve was defined as $PC(SO_2)$ (Horstman et al. 1986). The substantial variability in sensitivity to peak SO_2 exposures among asthmatics is an important consideration in the review of the sulfur oxides standards.

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ADDENDUM TO THE 1982 OAQPS STAFF PAPER

I. INTRODUCTION

A. Purpose

This paper evaluates and interprets the most relevant scientific and technical information reviewed in the draft EPA document, Second Addendum to Air Quality Criteria for Particulate Matter and Sulfur Oxides (1982): Assessment of Newly Available Health Effects Information (EPA, 1986d) and represents an update of the 1982 sulfur oxides Staff Paper (EPA, 1982a). This staff paper addendum is intended to help bridge the gap between the scientific review of recent health effects information contained in the criteria document addendum and the judgments required of the Administrator in setting primary national ambient air quality standards (NAAQS) for sulfur oxides. As such, particular emphasis in this paper is placed on conclusions, recommendations, and uncertainties regarding the averaging times and levels for the primary standards. While the paper should be of use to all parties interested in the standards review, it is written for those decision makers, scientists, and staff who have some familiarity with the technical discussions contained in the criteria document addendum.

B. Background

1. Legislative Requirements

Since 1970 the Clean Air Act as amended has provided authority and guidance for the listing of certain ambient air pollutants which may endanger

public health or welfare and the setting and revising of NAAQS for those pollutants. Primary standards must be based on health effects criteria and provide an adequate margin of safety to ensure protection of public health. As several recent judicial decisions have made clear, the economic and technological feasibility of attaining primary standards are not to be considered in setting them, although such factors may be considered to a degree in the development of state plans to implement the standards (D.C. Cir., 1980, 1981). Further guidance provided in the legislative history of the Act indicates that the standards should be set at "the maximum permissible ambient air level . . . which will protect the health of any (sensitive) group of the population." Also, margins of safety are to be provided such that the standards will afford "a reasonable degree of protection . . . against hazards which research has not yet identified." (Committee on Public Works, 1974). In the final analysis, the EPA Administrator must make a policy decision in setting the primary standard, based on his judgment regarding the implications of all the health effects evidence and the requirement that an adequate margin of safety be provided.

2. Original Sulfur Oxides Standards and Review to Date

The current primary standards for sulfur oxides (to protect public health) are 0.03 parts per million (ppm) or 80 micrograms per cubic meter ($\mu g/m^3$), annual arithmetic mean, and 0.14 ppm (365 $\mu g/m^3$), maximum 24 hour concentration not to be exceeded more than once per year. The current secondary standard for sulfur oxides (to protect public welfare) is 0.5 ppm (1300 $\mu g/m^3$), maximum 3-hour concentration, not to be exceeded more than once per year. For both primary and secondary standards, sulfur oxides are measured as sulfur dioxide (SO_2). Thus, SO_2 is the current indicator for the sulfur oxides standards.

The formal review of the original SO_2 criteria and standards was initiated in 1978. The Clean Air Scientific Advisory Committee (CASAC) closed on the criteria document (which also addressed particulate matter) in January 1982. The first addendum to the criteria document, which summarized the recent controlled human studies on the health effects of SO_2, was issued the same year. A staff paper, which identified critical issues and summarized the staff's interpretation of key studies, received verbal closure at a CASAC meeting in August 1982 and formal written closure in August 1983 (See Appendix A for Executive Summary of staff paper). The decision to produce a second addendum to the combined PM/SO_2 criteria document and this sulfur oxides staff paper addendum was taken in context of the recommendations to review certain new studies on the effects of particulate matter and announced on April 1, 1986 [51 FR 11058].

C. Approach

The approach in this paper is to address the newly available health effects information in the second criteria document addendum (CD addendum or CDA; EPA, 1986a) in the context of those critical elements which the staff believes have implications for previous conclusions reached on the primary sulfur oxides standards. Particular attention is drawn to judgments related to the ranges of interest for the primary standards. Previous staff conclusions related to the secondary standard, and the form of the standards will not be addressed here.

Because sulfur oxides are often studied in combination with particulate matter, much of the more important literature has already been assessed in the companion staff paper and staff paper addendum on particulate matter (EPA, 1982c; 1986b). Where possible, pertinent references are made to those papers, with only summaries presented in this paper.

The principal focus of this paper is on the effects of SO_2, alone and in combination with other pollutants. Other sulfur oxide vapors (e.g., SO_3) are not commonly found in the atmosphere. The effects of the principal atmospheric transformation products of SO_2 (i.e., sulfuric acid and sulfates) are discussed in the companion staff paper on particulate matter (EPA, 1982c) and will be further examined in a forthcoming document on acid aerosols.

Section II provides an update of air quality information on sulfur oxides to support discussions of the primary standards. Section III addresses those essential elements that require re-examination in light of the new information reviewed in the CD addendum; these elements include identification of possible mechanisms of toxicity and discussion of controlled human and community studies relating level(s) and duration(s) of exposure to indicators of health effects.

Drawing from the discussion in Sections II and III, Section IV identifies and assesses the factors the staff believes should be considered in selecting the averaging times and levels of primary standards. Updated staff findings and recommendations on the alternative policy options in these areas are also presented.

II. AIR QUALITY CONSIDERATIONS

The major chemical and physical properties of SO_2 in the atmosphere and characterization of ambient concentrations at U.S. sites are presented in the 1982 staff paper ("SP"; EPA 1982a) and discussed in more detail in Chapters 2 and 5 of the criteria document ("CD"; EPA, 1982b). Because most of the recently available health effects information on SO_2 is related to short-term (5 to 10 minute) exposures, this section will update information on short-term peak-to-mean ratios and related issues. This information is relevant in estimating human exposures and examining relationships among different standard averaging times.

A. Peak to Mean Ratios

The shortest averaging period retained in many monitoring data banks and produced by atmospheric models is one hour. The 1982 staff paper summarized the available information on the variance of 5 to 10 minute peak concentration within particular hourly periods. That assessment concluded that, based on typical distributons, the 5 to 10 minute peak is likely to be within a factor of 1.4 to 2.4 times the hourly average (Larsen, 1968; Burton and Thrall, 1982).

Recent work (Thrall et al.; 1982, Rote and Lee, 1983; Armstrong, 1985, 1986) on peak-to-mean ratio appears consistent with the earlier assessment. Thrall et al. (1982) analyzed monitoring data taken from a dense (18 site) network around the Kincaid (Illinois) power plant. The network was established as a part of an Electric Power Research Institute (EPRI) model validation study. Kincaid is an isolated 1300 MWe, base load, coal-fired plant with a single 187 meter stack. A 23-week sample (March-August 1980) was examined. The maximum hourly value in this sample was approximately 0.34 ppm and the maximum 5-minute value was 0.56 ppm. Thrall

et al. found that the peak-to-mean ratios tend to fall as the hourly average increases. Thus, although the overall ratio of 5-minute peak to hourly mean was 2.3 ± 1.3* for all hours, the ratio for hours over 0.1 ppm was only 1.8. The overall 10-minute peak to hourly mean ratio was 2.0 ± 0.96*, dropping to 1.6 for hours over 0.1 ppm.

Thrall and coworkers considered the situation of an isolated fuel combustion source. Rote and Lee (1983) provides a similar analysis for urban areas. In this case, the Regional Air Pollution Study (RAPS) data base was used. RAPS was a two year (1975-1976) study of air pollution in St. Louis which included 13 SO_2 monitoring sites. Unfortunately, the instruments were spanned to 1.0 ppm and for 10 sites, as many as 6% of the 1-minute values exceeded 1.0 ppm. Analyzing a large random sample of station hours (40,000), Rote and Lee found that the overall ratio of 5 minute peak to hourly mean concentration was 1.5 ± 0.48* while the 10-minute peak-to-mean ratio was 1.4 ± 0.39*. These ratios for all hours combined were found to be unaffected by hours containing out-of-range 1-minute values. At higher mean concentrations, the ratios also tended to be lower. However, in this case Rote and Lee found evidence that, for hours > 0.5 ppm, the apparent decline in ratio with increasing mean concentration was in part due to the spanning of the instruments.

Recent air quality analyses of sites near two primary copper smelters in Arizona estimated six minute peak-to-one-hour mean ratios (Armstrong, 1985, 1986). Although the ratios found at the Magma - San Manuel smelter were in the range of those found at Kincaid and other sites, the ratios at a second smelter (Phelps-Dodge, Douglas) were higher, with a 6 minute peak to hourly mean ratio of 3.3.

*Standard deviation

B. Factors Affecting Assessment of Peak Air Quality Levels

The 1982 staff paper concluded that short-term peak levels in excess of 0.5 ppm were most likely in the vicinity of major SO_2 point sources. Recent theoretical work on low persistance meteorological events (Huber and Pooler, 1985) as well as analyses of ambient data (Kilkelly and Roberson, 1985) have raised questions regarding both the impact of smaller sources of SO_2 and the adequacy of monitoring data to assess such impacts. A staff assessment of these issues found that small sources with less than Good Engineering Practice (GEP) stack height may also produce SO_2 peaks in excess of 0.5 ppm (EPA, 1986c). Most of these peaks are due to building downwash, are of limited area and extent (usually within 0.5 km of the stack), and are of very short duration (usually 30 seconds to 2 minutes). Based on the analyses noted above, it appears that very short duration peaks in excess of 0.5 ppm may occur on the order of 1000 per year at a fixed location. No accurate determination of how many sources may be subject to downwash appears feasible. Preliminary, but very rough, calculations indicate that the numbers may be quite significant. In addition, small sources regardless of stack height, may also produce comparable short duration peaks due to looping plumes. These exceedances would likely be found within 3 km of the stack and occur on the order of 10 times per year (EPA, 1986c).

A review of Kilkelly and Roberson (1985) and related strip charts permits several insights regarding the monitoring of very short-term (2-3 minute) peak SO_2 concentrations. The data in question were recorded near facilities with short stacks and are reported to show evidence of building downwash (Docket No. A-83-49, Item IV.H.39). Staff examination showed that the instruments were spanned to 1 ppm and frequently hit this limit for short-time periods. This means that the true peaks can not be readily

estimated but were presumably in excess of 1 ppm. This "peak lopping" does not appear to affect significantly the hourly averages at the sites in question because the area under the curve at the peak is quite small. Clearly, for peaks of longer duration ($\geq$ 5-10 minutes), peak lopping would lead to a significant underestimate of the hourly average. Peaks in excess of the spanned value for 5-10 minutes were seen at some of the facilities in the Kilkelly set and around some TVA facilities (Lott, 1985). In such cases, it is possible that hourly averages may be underestimated due to spanning. Peak lopping, if it occurs, would also bias any analysis of peak to mean ratios. EPA monitoring guidance calls for SO_2 instruments to be spanned to 0.5 ppm with a requirement that they be respanned if the limit is reached.

A related concern examined by the recent staff assessment (EPA, 1986c) is instrument response time. Many SO_2 instruments now in wide use require 4-5 minutes to reach 95% of scale. Thus, if the actual peak lasts only 30 seconds to 1 minute, most instruments would not respond fast enough to register the true peak.

In summary, the recent staff assessment of short-term peaks and smaller sources prompts the following conclusions:

1) Peaks well in excess of 0.5 ppm appear likely to occur around numerous small sources of SO_2. Although of very limited duration and areal extent, they can occur with relatively high frequency. None of the recently published assessments of the health effects of SO_2 has addressed exposures of such limited duration (< 30 seconds to 2 minutes); and

2) It appears that, due to spanning and instrument response time, most monitored data are not accurately measuring very short-term peaks. It is therefore not presently possible to assess the extent to which such peaks may be occurring.

III. CRITICAL ELEMENTS IN THE REVIEW OF THE PRIMARY STANDARDS

This section summarizes relevent aspects of recent information in the CD addendum on the mechanisms by which SO_2 may cause airway reactions and concentration/response relationships derived from controlled human and community studies of SO_2 effects. A comprehensive discussion of these and other critical elements including mechanicms of toxicity, effects of concern, and sensitive populations is contained in Section V of the 1982 staff paper (EPA, 1982a). The present summary provides a basis for later discussions of the implications of the more recent studies for the standards review.

A. Mechanisms

The previous staff assessment found that the most striking acute response to SO_2 for asthmatics and others with hyper-reactive airways is rapid bronchoconstriction (airway narrowing), usually evidenced in increased airway resistance, decreased expiratory flow rates, and the occurrence of symptoms such as wheezing and shortness of breath. Several of the more recent studies discussed in the CD addendum contribute further to understanding the mechanisms and factors that affect these responses (CDA, Section 4.4). The discussion below highlights insights from the CD addendum with respect to the impact of breathing mode, temperature/humidity conditions, and the time course of exposure and recovery.

1. Inhalation Patterns; and Airway Cooling/Drying

The penetration of SO_2 to sensitive portions of respiratory tract is largely determined by the efficiency of the oral or nasal mucosa in absorbing SO_2, which in turn depends on the mode of breathing (nasal, oral, or oronasal) and the rate of airflow. Newly published controlled SO_2 exposure studies on asthmatics confirm previous findings that at

comparable SO_2 concentrations, bronchoconstriction effects increase with both increased ventilation rates and as the relative contribution of oral ventilation to total ventilation increases, as seen by comparing oral-only (i.e., mouthpiece) breathing with oronasal breathing (Bethel et al., 1983b, 1985; Roger et al., 1985; Koenig et al., 1985).

The CD addendum notes that increased oral ventilation not only allows more direct penetration of SO_2 but may also result in airway drying and alterations in airway surface liquid that further affects SO_2 absorption and penetration (CDA, pp. 4-36). Evaporation of airway surface liquid and perhaps convective cooling of the airways caused by cold, dry air can act as direct bronchoconstrictive stimuli in asthmatics (Deal et al., 1979; Strauss et al., 1977; Anderson, 1985). Recent studies indicate that the combined effect of SO_2 and cold, dry air further exacerbates the asthmatic response (Bethel et al., 1984; Sheppard et al., 1984; Linn et al., 1984a,b, 1985a). It has been suggested that reduced water content and not cold per se could be responsible for much of this effect. This is consistent with other recent findings that the bronchoconstrictive effects of SO_2 are reduced under warm, humid conditions (Linn et al., 1985a). It appears that the interactive effects of breathing SO_2 and dry (or cold) air range from less than additive to synergistic depending on whether oral airway geometry is altered by use of mouthpieces, preventing any initial conditioning of inspired air in the mouth (e.g., warming, humidifying) (CDA, p. 4-37).

2. Time Course of Response, Recovery and Adaption

The time required for SO_2 exposure to elicit significant bronchoconstriction in exercising asthmatics is brief. Exposure durations as short as 3 minutes have produced significant responses in a mouthpiece study (Sheppard et al., 1984)

with the majority of studies using 5-10 minute exposure durations. Little enhancement of response is apparent on prolonged exposure beyond 5 minutes, although some suggestion of an increase is seen with continuous exercise between 10 and 30 minutes (Kehrl et al., 1986). On mechanistic grounds, it would appear possible for some response to occur with exposures of less than 5 minutes with high enough concentrations. The relationship between concentration, time and response for such periods has not, however, been systematically examined.

Following a single SO_2 exposure during exercise, airway resistance in asthmatics appears to require a recovery period of 1-2 hours (Hackney et al., 1984). A reduced response is observed if SO_2 exposure is repeated within 15-30 minutes, but not with subsequent exposures 5-24 hours later (Sheppard et al., 1983; Roger et al., 1985; Kehrl et al., 1986; Linn et al., 1984c; Snashall and Baldwin, 1982). Similar attenuation of airway constriction, induced by exercise or hyperventilation of cold, dry air, is observed when the exercise exposure is repeated at short-time intervals, with a refractory period that persists for 2-4 hours (Stearns et al., 1981; Bar-Yishay et al., 1983). Significantly, while repeated short exercise periods over a 1-hour period result in reduced response, 30 minutes of continued exercise results in responses that equal or exceed those observed after a single 10 minute period (Kehrl et al., 1986).

The CD addendum discusses several possible mechanisms that might account for the mitigated responses to SO_2 over time (e.g., decreased responsiveness of airway smooth muscle or vagal reflex pathways due to mediator depletion or inhibition of SO_2-receptors) (CDA, pp. 4-37, 38). Since continuous exercise apparently prevents a recovery period, Kehrl et al. (1986) suggest that the mechanism for "adaptation" to rapidly

repeated SO_2 exposures may be increased production and/or secretion of airway surface liquid during recovery following an SO_2 challenge. This would act to decrease relative SO_2 penetration in subsequent exposures.

B. Concentration/Response Information

The following review summarizes key results from those recent studies cited by the CD addendum as providing the most reliable quantitative information as well as some that provide reasonable evidence of concentration-response relationships without allowing derivation of specific levels. Responses to SO_2, alone or in combination with other pollutants, are examined in three time scales: 1) peak exposures (minutes-hours), 2) short-term exposures (hours-days) and 3) long-term exposures (months-years). A further assessment of these studies as applied to selecting alternative levels for air quality standards is presented in Section IV.

1. Peak Exposures

Information on the effects of relatively brief (minutes-hours) peak exposures to SO_2 is derived from studies of humans under controlled laboratory conditions. The importance and limitations of controlled human exposure studies are discussed in the CD and CD addendum as well as the 1982 staff paper (EPA, 1982a,b; 1986a). Recent controlled exposure studies confirm that "normal", healthy subjects, even at moderately heavy exercise, do not experience significant effects on pulmonary function due to peak SO_2 exposures in the range of 0.25 to 2 ppm (CDA, pp. 4-8 to 4-9). A single recent chamber study of chronic obstructive pulmonary disease patients was conducted under conditions that the CD addendum states are unlikely to produce effects even in sensitive individuals. Thus, the preponderance of newly available exposure-response information on peak SO_2 exposures is for exercising asthmatic subjects.

The results of the recent studies of asthmatic subjects are summarized in Table 4-4 of the CD addendum which organizes the data according to concentration. Most of the data reflect 5 to 10 minute exposures. The following discussion of anticipated responses associated with particular concentrations is drawn from that tabular summary.

a) 1.0 to 2.0 ppm

Recent studies by 3 separate research laboratories of the effects of 1 ppm SO_2 on freely breathing, mild asthmatics at moderate exercise are qualitatively consistent with each other as well as with previous studies that administered exposures through mouthpieces. All found statistically and potentially clinically significant* changes in respiratory mechanics, most pronounced within minutes after exercise had ceased, followed by gradual recovery (within 1 hour). When reported, associated symptoms (e.g., shortness of breath, chest discomfort) also increased significantly (Schacter et al., 1984; Roger et al., 1985). Group mean functional changes were in SRaw (+ 170 to 230%) and FEV_1 (- 14 to - 23%) (CDA, Table 4). Individual variability is illustrated by the Roger et al. results. One subject could not be tested at 1.0 ppm because of reaction at a lower concentration. Another was removed after the second exercise due to pronounced wheezing and chest tightness and a 10-fold increase in SRaw. Two other subjects had a greater than 500% increase. The responses in asthmatics observed by Kehrl et al. (1986) appear to be greatest after 30 minutes of continuous exercise although the increase in airway resistance was statistically no greater than the changes observed after 10 minute

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*Unless otherwise modified (as in this case), the use of "significant" with respect to measured changes should be understood as"statistically" significant, and not necessarily clinically or medically significant.

exposure (233% vs. 172% increase over baseline). Successive exercise periods separated by 15 minute intervals resulted in attenuated responses even to 1 ppm SO_2 (Roger et al., 1985; Kehrl et al., 1986).

Horstman et al. (1986) report that 12 (of 27) subjects in the Roger et al. (1985) study, whose SRaw values did not increase by 100% at 1 ppm or lower levels, were also exposed to 2 ppm using the same protocol. At this level, 7 of these less sensitive asthmatics had SRaw increases of 100 to over 600%.

b) 0.75 ppm

Recently published studies of moderately exercising asthmatics exposed to 0.75 ppm SO_2 for 10 minutes (Linn et al., 1983a; Hackney et al., 1984; Schacter et al., 1984) replicate earlier results, finding significant increases in airway resistance (group mean SRaw increase was 186 to 263%), substantial decreases in $FEV_{1.0}$, and significantly increased reports of lower airway symptoms. In contrast to functional measurements, the increase in symptom scores were not significantly greater when SO_2 was administered through mouthpieces compared to freebreathing in a chamber.

c) 0.6 ppm

Highly consistent and significant bronchoconstrictive responses have been observed in freely breathing mild asthmatics exposed to 0.6 ppm for 5 minutes while exercising at fairly high levels (minute ventilation, V_e, ~ 50 L/min) under a wide range of temperature and humidity conditions (Linn et al., 1983b; 1984a,b; 1985a). Increases in airway resistance and symptom scores were most pronounced (~ 207% over control) in either cold or dry air (-6°C, 20% RH) compared with more humid warmer conditions (e.g., 39% increase in SRaw in 38°C, 80% RH). Even under moderate conditions (~ 22°C, 85% RH), Linn et al. (1984a) found that

typical respiratory symptoms were sufficient to impair subjective well-being and "normal performance capabilities." Three of the 23 subjects in this study required medications to relieve symptoms following exposures and four had SRaw increases of in excess of 250%. In this and a subsequent study (Linn et al. (1984c), these investigators examined symptoms during the week after SO_2 exposures. In the latter study, they reported a tendency toward less favorable clinical states (i.e., increased symptoms) in the week following exposures on two succesive days to 0.6 ppm and that three (of 14) subjects reported experiencing an asthma attack during the week after SO_2 exposure; whereas no subject reported such an attack after clean air exposure. Comparable findings have not been noted in other studies.

d) 0.5 ppm

Recent studies of airway responses in free breathing mild asthmatics exposed at exercise to 0.5 ppm SO_2 for durations of 5, 10, and 20 minutes indicate significant bronchoconstriction occurs at moderate to heavy exercise rates (V_e ~ 40-60 L/min) (Bethel et al., 1983a, b; Koenig et al., 1983; Roger et al., 1985) but not at lower exercise rates (V_e ~ 27-40 L/min) (Schacter et al., 1984; Bethel et al., 1983b).

Roger et al. (1985) examined both repeated exposures and subject variability. Responses to SO_2 were mitigated after repeated, free-breathing exposures separated by 15-minute intervals, although they remained significant. Elevations in airway resistance over baseline averaged 93% after the first exercise period and 52% after the third exercise period. Cumulative frequency distributions of the subjects' SRaw values at rest and at exercise in clean air and after 10-minute exercise in 0.5 ppm SO_2 indicate that exercise and SO_2 each contributed about equally to the overall increase in SRaw. As in other studies, there was a wide range in the magnitude of

the induced bronchoconstriction in various subjects. For example, after exercise in 0.5 ppm SO_2, 25% of the subjects had a SRaw increase of ~ 170% over baseline compared to the mean of 93%, while 25% had negligible changes. In addition, while significant increases in symptoms were not reported for the group as a whole, three subjects had SRaw increases of over 320% and one, who was removed before completion of the full protocol, had an eight-fold SRaw increase after 10-minutes of 0.5 ppm and an 11-fold increase after the 2nd exposure, with audible wheezing and chest tightness.

e) 0.4 ppm

Mild asthmatics performing moderately heavy exercise (V_e = 48 L/min) while freely breathing 0.4 ppm SO_2 for 5 minutes had statistically significant increases in SRaw (group mean 69% increase vs. 35% in clean air) and mild increases in several symptoms (e.g., cough, wheeze, chest tightness) after 5 minute exposure (Linn et al., 1983b). One subject (of 23) was reported to have experienced "clinically significant bronchoconstriction" after this exposure and required medication to relieve asthma symptoms. As part of another study discussed previously, a group of mild asthmatics exercising at a similar level (~ 50 L/min) at a much colder temperature (5°C), responded with apparent increases in airway resistance and respiratory symptoms at 0.4 ppm SO_2 under both high and low humidity (Linn et al., 1984a).

f) 0.1 - 0.3 ppm

Most recent chamber exposures found no clearly significant increases in airway resistance among freely breathing mild asthmatics exercising at moderate to high levels (35-50 L/min) below 0.4 ppm (Linn et al., 1984a, b; 1983b; Roger et al., 1985; Schacter et al., 1984). The one exception was at 0.25 ppm with heavy exercise (60 L/min) (Bethel et al., 1985). Even here, a significant increase over exercise control was not observed with

0.25 ppm in the same study at an even higher ventilation rate (80-90 L/min), suggesting that the bronchoconstriction induced by exercise alone overshadowed any effects of SO_2 (Bethel et al., 1985). Although some minimal increases in symptom scores were reported even as low as 0.2 ppm, the clinical significance of these changes is questionable (Linn et al., 1983b; 1984a). The fact that some hyper-reactive individuals may be responsive to such low SO_2 levels cannot be dismissed, however, given that an SO_2 concentration of 0.25 ppm was sufficient to nearly double SRaw over baseline in the most sensitive subject (1985).

g) Combined Relationships/Subject Variability

A number of the more recent studies developed exposure/response relationships over various concentration and ventilation ranges while others examined the influence of various subject-related and environmental factors. Although individual studies fix various important factors to permit within study comparisons, it is more difficult to compare directly the results from different investigations. One approach suggested in an earlier staff assessment (Cohen, 1983) and used by Kleinman (1984) and Linn et al. (1983b) normalizes studies according to effective oral dose rate. The results of such an analysis applied to both recent and earlier SO_2 studies are shown in Figure 3-1. As illustrated, reasonably consistent results are derived from the various controlled SO_2 asthmatic studies when adjustments are made for differences in ventilation rates and oral/nasal breathing patterns by expressing the results in terms of the oral dose rates of SO_2. Earlier analyses also found a good consistency among then available studies using similar surrogates of "effective dose" (Kleinman, 1984; Linn et al., 1983b).

This relationship can be used to estimate responses for exposures of interest not yet tested. For example, it is of interest to determine whether large responses might occur in asthmatics at high concentrations,

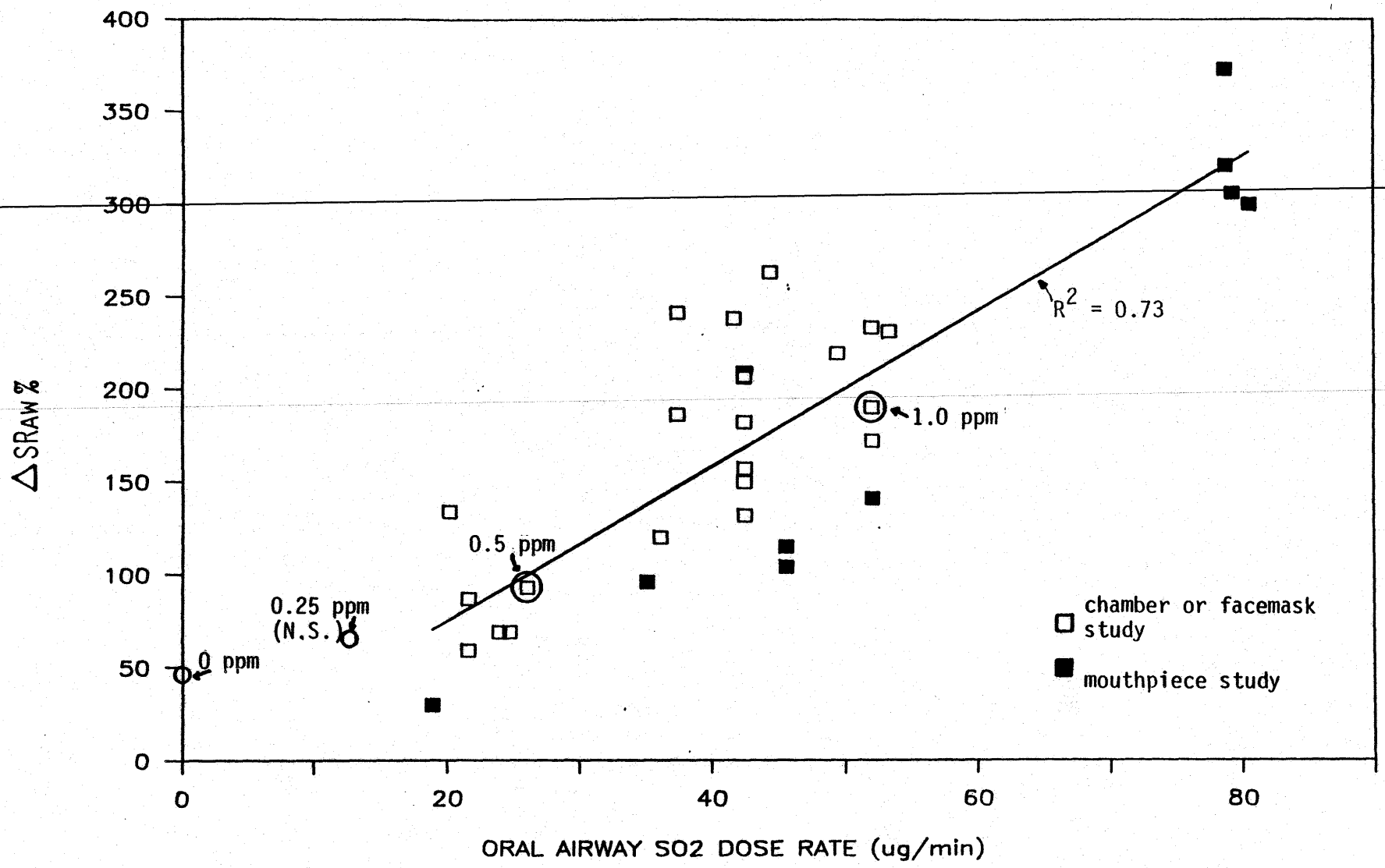

Figure 3-1. Combined SO_2 dose/response relationships. Includes recent and earlier controlled studies of exercising or hyperventilating asthmatics with SRaw reported. Points respresent group mean responses significantly different from baseline vs. normalized oral-dose rate (SO_2 concentration x oral V_e). Oral V_e estimates for freebreathing from Niinimaa et al. (1981). The results of Roger et al. (1985) are highlighted at specific concentrations (V_e total = 42 l/min) for orientation. Despite uncertainties in estimating the oral V_e the results suggest reasonably good consistency among three laboratories with no apparent difference between 5 and 10 minute exposures and no tendency for mouthpiece studies to overstate response when appropriate adjustments for ventilation are made.

e.g., 2 ppm while at more typical activity levels. Assuming oronasal ventilation for "mouth" breathers (Niinamaa et al., 1981), oral V_e would be about 4 to 7 L/min at rest to light activity and the predicted mean increase in SRaw would be approximately 0 to 70%.

The consistency among group mean responses represented in Figure 3-1 masks the substantial variability among individual asthmatics, both within and among studies. Among the most useful studies for examining this variability is the work of Roger et al. (1985) and companion analysis by Horstman et al. (1986). The study covers a wide range of concentrations (0.25 to 2 ppm), includes a substantial number of subjects (28) who were not pre-selected for SO_2 sensitivity, and presents individual exposure-response data. The highlighting in Figure 3-1 shows that the group mean results are representative of the range of values for all SO_2/asthmatic studies. The range of subject response from this work is illustrated in Figure 3-2, reproduced from the Horstman et al. (1986) report. The points represent an interpolation of exposure-response relationships for each subject to determine the SO_2 exposure producing a 100% increase in SRaw over exercise in clean air (termed PC [SO_2]). The resulting cumulative plot is useful in estimating the likelihood of a possibly clinically significant response (doubling of SRaw) in mild asthmatics exposed at moderate exercise (or ventilation) to particular SO_2 concentrations.

2. Short-term Exposures

The principal basis for developing quantitative assessments of acute effects of ambient exposures of SO_2 on a daily basis remains community epidemiological studies. Such studies can provide strong evidence for the existence of pollution effects resulting from community exposures. The major limitations of the epidemiological studies are discussed in the CD, CD addendum as well as the 1982 staff paper.

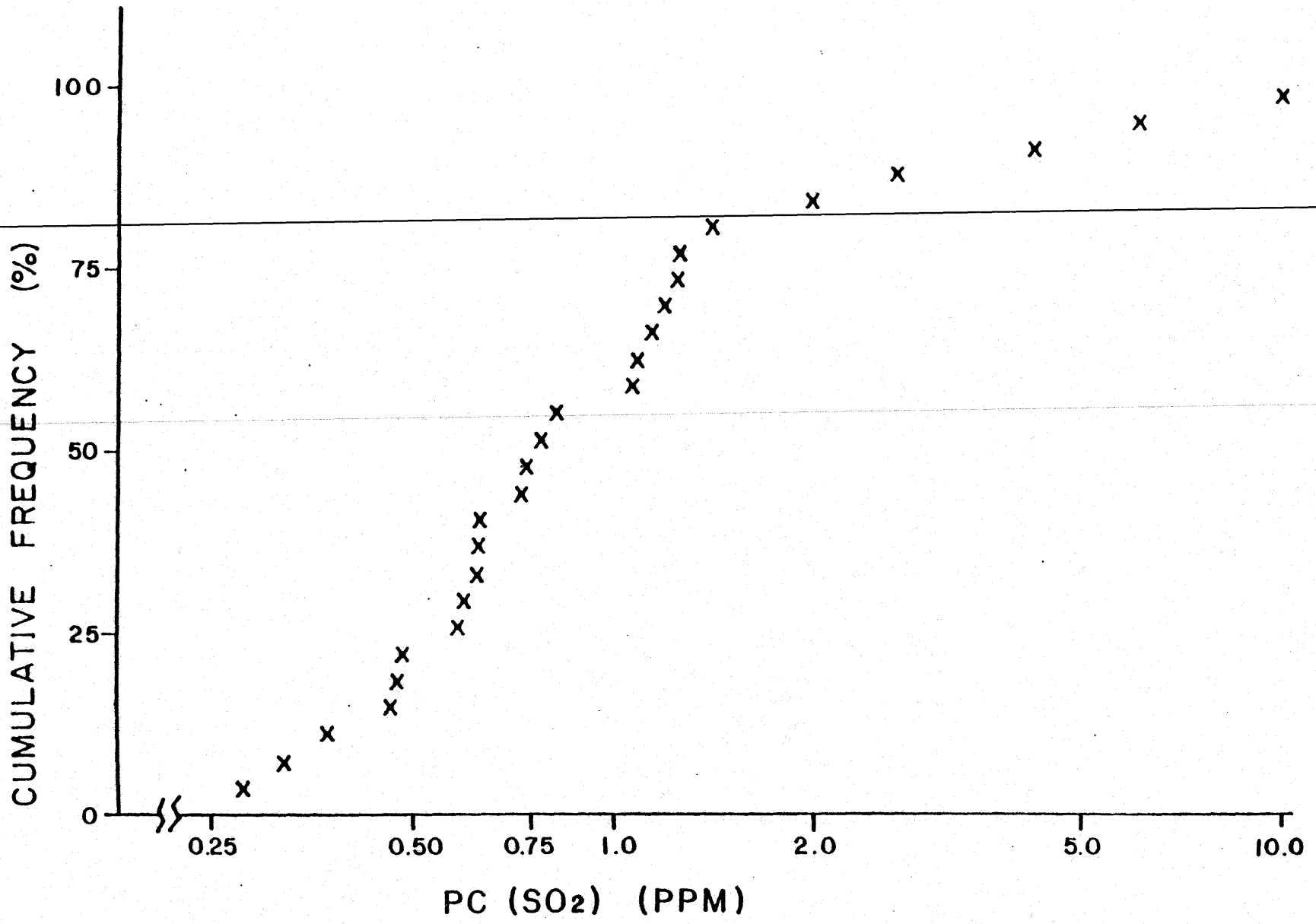

Figure 3-2. Distribution of individual airway sensitivity to SO_2 (Horstman et al., 1986). PC (SO_2) represents concentration of SO_2 that in combination with exercise (V_e = 42 l/min) resulted in a 100% increase in sRaw. Cumulative percentage of subjects is plotted as a function of PC (SO_2) and each data point represents PC (SO_2) for an individual subject. These data show substantial variability in sensitivity among mild asthmatics volunteers not selected for responsiveness to SO_2.

Recognizing these limitations, the discussion in the 1982 staff paper outlined those studies cited by the CD as providing the most reliable quantitative information as well as other studies that provide useful information on the relative importance of SO_2 without allowing derivation of specific levels. These included a set of British studies of mortality and morbidity. The CD addendum identifies several more recent analyses of the London mortality data and one U.S. morbidity study as providing the most useful new information on the short-term SO_2 exposures. These studies are summarized in Table 3-1. The more full description and evaluation of these studies contained in Section III of the companion draft PM staff paper addendum (EPA, 1986b) will not be repeated here. The discussion will focus on the relative importance of SO_2 as compared with particulate matter in producing the observed effects.

With respect to the daily mortality studies, the CD addendum states that:

> "the following conclusions appear warranted based on the earlier criteria review (U.S. EPA, 1982b) and present evaluation of newly available analyses of the London mortality experience: (1) markedly increased mortality occurred, mainly among the elderly and chronically ill, in association with BS and SO_2 concentrations above 1000 $\mu g/m^3$, especially during episodes when such pollutant elevations occurred for several consecutive days; (2) the relative contributions of BS and SO_2 cannot be clearly distinguished from those of each other, nor can the effects of other factors be clearly delineated, although it appears likely that coincident high humidity (fog) was also important (possibly in providing conditions leading to formation of H_2SO_4 or other acidic aerosols); (3) increased risk of mortality is associated with exposure to BS and SO_2 levels in the range of 500 to 1000 $\mu g/m^3$, clearly at concentrations in excess of 700 to 750 $\mu g/m^3$; and (4) less certain evidence suggests possible slight increases in the risk of mortality of BS levels below 500 $\mu g/m^3$, with no specific threshold levels having yet been demonstrated or ruled out at lower concentrations of BS (e.g., at 150 $\mu g/m^3$) nor potential contribution of other plausibly confounding variables having yet been fully evaluated." (p. 3-8)

Besides the uncertainties that remain in separating the effects of SO_2 and PM, various issues are still unresolved regarding these London data

TABLE 3-1. SUMMARY OF RECENT (1982-86) EPIDEMIOLOGICAL STUDIES PROVIDING MOST USEFUL CONCENTRATION/RESPONSE INFORMATION FOR SHORT-TERM SO_2 EXPOSURES

Observed Effects	Time	Observed Concentration Range PM($\mu g/m^3$)	SO_2($\mu g/m^3$)	Comments	Study
Increases in daily mortality in metropolitan	1958-1972 winters	500-1000 BS* 24-hr average	500-1000	Ranges reflect judgment as to "effects likely levels" from 1982 assessment; indications of small increases at lower BS levels (CDA, Table 1). Recent studies reinforce 1982 CD conclusions. Nature of relationships vary significantly with model. Mazumdar et al. infer no association < 700 $\mu g/m^3$ SO_2, but methodology for separating pollutants questioned in CDA.	Mazumdar et al, 1982, 1983; Shumway et al. 1983
Short-term reductions in lung function in 330 school children, Steubenville, OH	Four separate study periods of 3 weeks following pollution "episodes" in 1978-1980	1) 420 TSP 2) 270 TSP 3) 220 TSP 4) 160 TSP (max 24 averages for "alert" or "sham" episodes)	280 460 170 190	First 3 episodes: small (2%-3%) but significant reversible declines in FVC up to 2-3 weeks after peak. Less consistent results for FEV. No significant effects after 4th "sham" episode. SO_2 levels in 3rd episode lower than in 4th. Baseline measurements for 1st 4th taken on days with high pollution. Linear regression of pooled data for 330 children indicate significantly more negative slopes in functions vs. TSP and SO_2 across ranges (10-270 $\mu g/m^3$, 0-280 $\mu g/m^3$, respectively). Higher response in some children.	Dockery et al, 1982
Short-term reduction in lung function in 179 school children in the Netherlands (Ijmond)	Before, during, after pollution episode Nov. 1984-Feb. 1985	200-250 TSP and RSP (D_{50} < 3.5 μm) 24-hr average	200-250	Small (3-5%) reversible declines in several measures of airway function (FVC, FEV_1, MEF) during episode and 5 days later. No effect after 26 days or shortly after a day when TSP, RSP and SO_2 levels all averaged 100-150 $\mu g/m^3$. Separate sub-groups of children tested on each day. Peak TSP levels possibly understated.	Dassen et al., 1986

including a possible threshold for PM-mortality associations, varying coefficients obtained with different subsets of data and models, the effects of unmeasured variables such as demographic change over time and indoor air pollution, and the appropriate statistical methods to account for long-term seasonal trends in mortality (Wyzga et al., 1985).

While the possibility of small increases in the risk of mortality at SO_2 levels less than the "likely effects level" (500 $\mu g/m^3$ or 0.19 ppm) cannot be dismissed conclusively, the published analyses of London mortality data provide little basis to determine whether 24-hour concentrations of SO_2 below this level may have accounted for any of the observed association between mortality and pollution. Because significant quantities of SO_2 are unlikely to penetrate to the tracheobronchial region at lower concentrations without increased ventilation, the mechanisms by which SO_2 could contribute to excess mortality in ill or otherwise sensitive populations are limited. Peak levels in London at the time of these studies were undoubtedly well in excess of the 24-hour values, but at lower daily concentrations were less likely to affect even individuals with hyperreactive airways. The capacity of fog particles to "carry" untransformed SO_2 is limited. At present, it appears more likely that the role of SO_2, in the presence of smoke, involved transformation products such as acidic fine particles.

Other recent studies discussed in the CD addendum and in the PM staff paper addendum examined pollutant/mortality relationships in more contemporary atmospheres in New York City, Pittsburgh, and Athens, Greece. The Ozkaynak et al. (1985) reanalysis of 14 years of N.Y.C. data (1963-76) found significant associations between excess daily mortality and PM, SO_2 and temperature. Differences in the rate of change of SO_2 and PM indicators during the study period allowed estimation of their separate effects. In joint regression

analysis across all years, PM indicators (coefficient of haze and visibility extinction coefficient) together accounted for significantly greater excess mortality than did SO_2.) As the CD addendum notes, however, these findings must be considered preliminary for risk assessment purposes.

The work of Mazumdar and Sussman (1983) in Pittsburgh and that of Hatzakis et al. (1986) in Athens, however, found conflicting results. The first found a significant association between particulate matter and excess deaths in Pittsburgh, but no effect of SO_2, while the Athens study found an association with SO_2 but not with smoke measurements. The CD addendum points out that limitations in both studies with respect to measurement of particulate matter as well as methodological difficulties prevent drawing meaningful conclusions from these studies with respect to the effects of particulate matter and SO_2.

b) Morbidity

Previous conclusions regarding morbidity effects of short-term PM/SO_2 exposures were primarily based on studies of bronchitic subjects in London from the 1950's through the early 1970's. Findings related to more contemporary conditions are presented by Dockery et al. (1982) and Dassen et al. (1986)* and summarized in Table 3-1. The CD addendum concludes that the repeated measurements of lung function by Dockery et al. showed statistically significant but physiologically small and apparently reversible declines of FVC and $FEV_{0.75}$ levels associated with short-term increases in PM and SO_2 air pollution (p. 3-14, 3-18). The small, reversible decrements appear to persist for up to 3-4 weeks after episodic exposures

*The June, 1986 draft of the CD addendum did not include a discussion of Dassen et al., which was accepted for publication later that month. The revised CD addendum will incorporate this study.

to these pollutants across a wide range of concentrations with no clear delineation of a threshold defined by the authors or by the CD addendum. A staff assessment of that study is contained in the draft PM staff paper addendum (EPA, 1986b). The following additional points are relevant in assessing the implications of Dockery et al. (1982) for SO_2 concentration/response relationships.

1) Of the 4 study periods in Steubenville, the most significant declines in $FEV_{0.75}$ (4% on average) were observed following the episode with the highest SO_2 level (455 $\mu g/m^3$, 24 hr. avg). This observation is, however, confounded because pollution levels during baseline measurements for this period were among the lowest for any of the four study periods.

2) No significant effects on lung function were reported in the Fall 1980 study, when 24-hr. SO_2 levels reached 190 $\mu g/m^3$. In the Spring 1980 study, which had significant lung function declines following a pollution episode, SO_2 was lower (169 $\mu g/m^3$ maximum) suggesting any pollution related effect was more attributable to particles.

3) When data for all 4 study periods were pooled and lung function was regressed on TSP and SO_2 levels - assuming the relationship was linear across all studies - similar results were obtained for both pollutants.

A similar study of the effects on children of episodic exposures to particulate matter and SO_2 conducted in the Netherlands by Dassen et al. (1986) produced results similar to those of Dockery et al. Pulmonary function values measured during an air pollution episode in which both 24-hr average PM (as TSP or RSP) and SO_2 levels reached 200 to 250 $\mu g/m^3$ were significantly lower (3-5%) than baseline values measured 1-2 months earlier in a group of Dutch school children. Lung function parameters that showed significant declines included FVC and FEV, as well as measures of small airway function

(e.g., maximum mid-expiratory flow, maximum flow at 50% of vital capacity). Declines from baseline were observed 2 weeks after the episode in a different subset of children, but not after 3 1/2 weeks in yet a third subgroup. Before the last set of measurements 24-hr average of both PM (as TSP or RSP) and SO_2 ranged between 100-150 $\mu g/m^3$, suggesting that these levels were not associated with observable functional effects.

In comparing these results to those of Dockery, it is notable that the absolute magnitude of response in the Netherlands episode was greater than that for any of the four Steubenville episodes, although the peak SO_2 levels (200 to 250 $\mu g/m^3$) were lower than two of those episodes. The relative magnitude of the effect appears to be better related to the concentration of small particles (EPA, 1986b).

In summary, the more quantitative epidemiological evidence from London suggests that effects may occur at SO_2 levels at or above 0.19 ppm (500 $\mu g/m^3$), 24-hour average, in combination with elevated particle levels. Additional evidence suggests the possibility of short-term, reversible declines in lung function at SO_2 levels above approximately 250-450 $\mu g/m^3$ (0.10-.18 ppm). Whether any of these effects are due (in part) to SO_2 alone, formation of sulfuric acid or other irritant aerosols, particles alone, or peak SO_2 values well above the daily mean cannot be determined unequivocally.

3. Chronic Exposures

Table 3-2 summarizes the most useful of the recent studies that have examined the long-term effects of exposures to SO_2, in the presence of particles, on respiratory mechanics, symptoms, and illness. Other, less reliable, studies are evaluated in Appendix B of the PM staff paper addendum (CEC, 1983; Muhling et al., 1985; Wojtyniak et al., 1986). Several cross-sectional studies report significant associations between long-term SO_2

Table 3-2. SUMMARY OF RECENT (1982-86) EPIDEMIOLOGICAL STUDIES PROVIDING MOST USEFUL CONCENTRATION/RESPONSE INFORMATION ON LONG-TERM EXPOSURES TO SO_2

Observed Effects	Time	Population	Observed Concentration Range SO_2 ($\mu g/m^3$)	PM ($\mu g/m^3$)	Comments	Study
a) Communities Dominated by Large Point Sources						
Increased prevalence of chronic phlegm, cough	1976	~ 5,600 adults in 4 Utah towns at varying distances from large copper smelter	115 (5 yr average - 1971-76)	70 TSP/14 SO_4	3 cleaner communities had 5-yr. SO_2 between 11-35 $\mu g/m^3$, 5-8 $\mu g/m^3$ SO_4; little gradient across towns in TSP (50-70 $\mu g/m^3$). Results more consistent in non-smokers, women; consistent with previous 1970 survey. No lung function measurements. Any effects of SO_2 likely attributable to high short-term peaks.	Chapman et al., 1985
Increased prevalence of cough	1979-82	~ 700 3rd-6th graders in 2 smelter and 2 control communities in Arizona	103 (3 yr average)	52 TSP/9-10 SO_4	High short-term peaks in 1 smelter town (repeated 3-hr. avgs. ~ 1.0 ppm), as well as 2nd smelter area with elevated cough (avg. 24 hr max ~ 440 $\mu g/m^3$; 3 yr avg. SO_2 ~ 50 $\mu g/m^3$, 28 $\mu g/m^3$ TSP). 2 control areas had 3-yr SO_2 < 14 $\mu g/m^3$, 4-7 $\mu g/m^3$ SO_4, 58-60 $\mu g/m^3$ TSP. No trend with pollution in shortness of breath, wheeze, sputum production, lung function (FEV_1).	Dodge, 1983; Dodge al., 1985
b) Multiple Urban Area Comparisons						
Increased prevalence of cough, expectoration, lower respiratory illness in men. Upper respiratory disease in children. Reduced lung function in adults and children.	1974-76	~ 20,000 adults and children in 20 areas of 7 cities and 1 industrial region in France	13-127 (3 yr average)	20-150 Smoke 45-240 "Dust"	Significant effects found only with SO_2; PM measurements of questionable comparibility (CDA, p. 3-43). Inconsistent trends within cities. No control for parental smoking in children; uncertain control for season; apparently incomplete statistical analysis.	PAARC 1982a,b

exposures and effects in populations of adults and children (PAARC, 1982a,b; Chapman et al., 1985; Ware et al., 1986; Dodge, 1983; Dodge et al., 1985).

The CD addendum (p. 3-45) concludes that these new studies provide evidence for: 1) increased respiratory symptoms among young adults in association with annual average SO_2 levels of 115 $\mu g/m^3$ (Chapman et al., 1983); 2) increased prevalence of cough in children (but not lung function changes) being associated with intermittent exposures to mean peak 3-hr SO_2 levels of $\sim$1.0 ppm or annual average levels of $\sim$103 $\mu g/m^3$ (Dodge et al., 1985); and 3) symptoms of lower respiratory disease and decrements in lung function in adults associated with annual average SO_2 levels ranging without evident threshold from about 25 to 130 $\mu g/m^3$ (PAARC, 1982a,b). In addition, the PAARC study suggests that upper respiratory disease and lung function decrements in children may also be associated with annual average SO_2 levels across the above range.

Some questions must be raised regarding the PAARC analysis, however: (1) SO_2 and PM indices were only tested in separate regressions resulting in potentially confounded results, especially given the remarkably low collinearity in the 2 pollutants; (2) The positive associations between SO_2 and lung function were significant for only one of the two SO_2 measurement methods used and are apparently dominated by a large difference in Rouen (an industrial city) between the SO_2 levels as measured by the two methods; (3) The large within-city and between-city differences as separate sources of variability were not assessed, possibly greatly reducing the statistical significance of estimated effects in this very large study. These and other uncertainties related to aerometry, the lack of control for parental smoking (for children), in controls for seasonal effects, and the counter-intuitive results for NO_2 further limit the confidence to be placed in the present results.

Correlations, and conclusions, from the Ware et al. (1986) study are weakened by the relatively low illness rates in one area (Carondolet, St. Louis) during periods of relatively high SO_2 levels and by the fact that after SO_2 levels declined there (from 184 $\mu g/m^3$ in 1976 to 88 $\mu g/m^3$ in 1977) and TSP dropped only slightly (125 $\mu g/m^3$ to 104 $\mu g/m^3$), illness rates increased slightly. Otherwise, reduced ventilatory function has been found to be significantly related to elevated SO_2 levels in only the PAARC study and possibly in the recent van der Lende et al. (1986) report, although the latter findings are considered too preliminary for risk assessment purposes. Similarly, the Schenker et al. (1983) study suggests increased risk of wheeze (but not cough or phlegm) associated with elevated SO_2 concentrations but specific effect levels are difficult to identify (CDA, p. 3-37).

Many of these studies in which high long-term SO_2 concentrations have been measured and correlated with health effects were conducted in areas around major point sources of SO_2 emissions (e.g., copper smelters, coal-fired power plants). It is therefore likely that the populations studied were exposed to repeated high short-term peak concentrations of SO_2, primary sulfuric acid, and other stack related particles. In light of the controlled human and animal exposure studies on SO_2 and sulfuric acid discussed previously in this paper and in the 1982 PM staff paper (EPA, 1982c), it appears likely that the effects associated with SO_2 in these studies were at least in part related to intermittent, acute bronchial insults. None of these studies, however, have attempted to separately analyze those individuals expected to be most responsive to short-term SO_2 or other exposures, i.e., asthmatics and atopics.

IV. FACTORS TO BE CONSIDERED IN SELECTING PRIMARY STANDARDS FOR SULFUR OXIDES

This section, drawing upon the previous summary of newly available scientific information, enumerates key factors that should be considered by the Administrator in decisions on the primary standards for sulfur oxides. The staff conclusions and recommendations on the most appropriate policy options update and supplement those made in the 1982 staff assessment. Where the original conclusions and recommendations and supporting rationale are unchanged by the newly available information, they are summarized without restating the supporting discussion. Particular emphasis is placed on aspects of the new information that amend or revise the original assessment. The key standard components discussed are the levels and averaging times for the primary standards. In addition, a summary assessment of the relative protection afforded by alternative standard combinations is presented.

A. Levels and Averaging Times of the Standards

1. General Considerations

The major scientific basis for selecting SO_2 standards that have an adequate margin of safety comes from controlled human exposures and community epidemiological studies, with mechanistic support from toxicological, deposition, and air chemistry investigations. The limitations of available controlled human studies for quantitative evaluation of ambient exposures of populations are summarized in the CD and in the CD addendum. Such studies provide accurate measurements of specific pollutant exposures, but are limited in exposure regimes, numbers and sensitivity of subjects, and severity of effects tested, and may involve artifacts not representative of ambient exposures. Community epidemiological studies, while representing real world conditions, can only provide associations between a complex

pollutant mix and a particular set of observable health endpoints. It follows that, although the scientific literature provides substantial information on the potential health risks associated with various levels and exposure patterns of SO_2, selection of appropriate levels, form, and averaging times remains largely a public health policy judgment.

The following sections present a brief staff assessment of how the concentration/response relationships suggested by the most significant controlled human and epidemiological studies in the CD addendum supplement the quantitative information previously assessed in the 1982 staff paper, and indicate how these studies may be applied in decision-making on standards for SO_2. The presentation also outlines a qualitative assessment of the key factors that affect the margin of safety associated with the ranges of standards derived from these studies. This assessment includes identification of those aspects of the qualitative literature that should be considered in establishing standards that provide an adequate margin of safety. Peak (< 1-hour), short-term ($\leq$ 24-hour), and long-term (annual), exposures are discussed separately.

2. Peak (< 1-hour) Exposures

a) Derivation of Ranges of Interest from Controlled Human Exposure Studies

Table 4-1 presents an updated staff assessment of the controlled human studies most useful in developing a range of interest for selecting a 1-hour SO_2 standard. Both recently published studies and those assessed in the 1982 staff paper are included. The table focuses on those studies involving free breathing (chamber) or facemask exposures, which provide the closest approximation of natural breathing. Studies in which subjects breathed through mouthpieces are also used. Although caution is necessary

Table 4-1. UPDATED STAFF ASSESSMENT OF KEY CONTROLLED HUMAN STUDIES

SO_2 Concentration (5-60 minutes)	Observed Effects[1]	Comments/Implications
1-2 ppm	Substantial changes in 8 of 12 subjects (Δ SRaw 100-600%) exposed to 2 ppm. At 1 ppm, functional changes (Δ SRaw 170-200%), symptoms in free breathing asthmatics at moderate exercise[2]	Effects indicative of clinical significance. At 2 ppm, 80% of mild asthmatics could experience at least a doubling of SRaw. Some might not tolerate exposure at moderate exercise. Approx. 60% at 1 ppm could experience at least a doubling of SRaw.[3] Some asthmatic mouth breathers may have significant bronchoconstriction at 2 ppm even at light activity.
0.6-0.75 ppm	Functional changes (Δ SRaw 120-260%), symptoms in free breathing asthmatics at light-moderate exercise[4]	Effects indicative of clinical significance; 25-50% of mild, free-breathing asthmatics at moderate exercise could experience at least a doubling of airway resistance.[3]
0.5 ppm	Significant functional changes (Δ SRaw 50-100%), symptoms in oronasal (facemask) and free breathing asthmatics at moderate, but not at light exercise.[5] At heavy exercise, Δ SRaw 220-240%.[6]	At moderate or higher exercise, symptoms possibly of clinical significance. About 20-25% could experience at least a doubling in airway resistance.[3]
0.4 ppm	Functional changes (Δ SRaw 70%), symptoms in free breathing asthmatics at moderate-heavy exercise[7]	Lowest level of clinically significant response for free breathing. Approx. 10% of mild, free breathing asthmatics could experience a doubling in airway resistance.[3]
0.1-0.3 ppm	No effects in free breathing asthmatics at light exercise. Slight but not significant functional changes in free-breathing subjects at moderate-heavy exercise (0.25)[6], but not at lower levels.[7]	Significant effects unlikely at moderate exercise. Effects of SO_2 indistinguishable at heavy exercise. Possibility of more significant responses in small percentage of sensitive asthmatics at 0.28.[3]

[1]Unless otherwise noted, (Δ SRaw__%) reflects group mean increase over clean air control at rest. Light, moderate, heavy exercise refers to ventilation rates approximating $\leq$ 35 L/min, 40-45 L/min, and $\geq$ 50 L/min, respectively. Effects reflect results from range of moderate temperature/humidity conditions (i.e., 7-26°C, 36-90% RH). Studies at 0.5-0.6 ppm indicate that exercise-induced bronchoconstriction associated with cold and/or dry air exacerbates response to SO_2 while warm, humid air mitigates asthmatic responses relative to moderate conditions.

[2]Schacter et al. (1984); Roger et al. (1985); Horstman et al. (1986).

[3]Horstman et al., (1986).

[4]Hackney et al. (1984); Schacter et al. (1984); Linn et al. (1983a,b, 1984a,b,c, 1985a).

[5]Kirkpatrick et al. (1982); Linn et al. (1984b); Roger et al. (1985); Schacter et al. (1984).

[6]Bethel et al. (1983a,b; 1985).

[7]Linn et al. (1983b, 1984a).

in extrapolating mouthpiece study results to ambient conditions, it does not appear that substantial differences exist in SO_2-induced responses for the different breathing modes when account is made for the partitioning of oral and nasal airflow components in oronasal breathing (see Appendix A). Inferences made in the "implications" column are derived from observations made by the investigators or in the CD addendum. The percentage of asthmatics showing a potentially clinically significant increase in airway resistance (100%) is derived from Horstman et al. (1986) (See Figure 3-2).

The table indicates that functional changes and symptoms are likely in a large percentage of freely breathing asthmatics exposed to 5 to 10 minute peaks of SO_2 between 1 and 2 ppm while involved in light to moderate exercise (V_e ~ 30-50 L/min), comparable to daily activities such as climbing stairs and light bicycling or jogging. At comparable exercise rates (V_e ~ 40 to 48 L/min), Linn et al. (1983a,b) found "clinically and physiologically significant responses" in free breathing young adult asthmatics exposed to 0.75 ppm and to 0.6 ppm SO_2. Several studies report significant asthmatic responses at 0.5 ppm with oronasal (free or facemask) breathing at moderate-heavy exercise (V_e ~ 40-60 L/min) (Kirkpatrick et al., 1982; Bethel et al., 1983b; Roger et al., 1985) but no substantial symptomatic or functional effects at lower ventilation rates (27-40 L/min) (Linn et al., 1982; Bethel et al., 1983b; Roger et al., 1985; Schacter et al., 1984).

Asthmatics exposed to 0.4 ppm SO_2 at a moderate to heavy exercise rate (V_e ~ 48 L/min) showed a moderate increase in SRaw and a mild increase in group mean symptom score, with one subject requiring medication to relieve symptoms (Linn et al., 1983b). Studies of free breathing exposures at lower

concentrations (0.1 to 0.3 ppm) suggest marginal, if any, group responses only with 0.25 ppm at heavy exercise (50-60 L/min). Any effect of SO_2 is negligible compared to exercise at these levels (Linn et al., 1984b; Bethel et al., 1985). The CD addendum concludes from these observations that "some SO_2-sensitive asthmatics are at risk of experiencing clinically significant (i.e., symptomatic) bronchoconstriction requiring termination of activity and/or medical intervention" (p. 4-41) when exposed to SO_2 concentrations of 0.4 ppm or greater when this exposure is accompanied by at least moderate activity.

The 1982 staff paper outlined several considerations that are important in evaluating these results in the context of decision making on a standard to limit peak (5-10 minute) SO_2 exposures. The following discussion represents an update of those considerations.

1) Health Significance of the Observed or Anticipated Effects

Although little controversy exists that a full asthma attack represents an adverse health effect, the relative significance of some of the less severe responses observed in the above controlled human studies is open to question. Based on the 1982 CD discussion of these matters, the staff paper concluded that the results of these studies begin to be of some concern when bronchoconstriction is accompanied by noticeable symptoms. This is an imprecise criterion, however, as not all studies report symptoms and symptom reports are not always a reliable indicator of clinical status. Based on the current assessment, an increase in airway resistance of 100% is also a useful benchmark for functional changes of concern (Horstman et al., 1986). The scientific literature does not, however, provide sufficient information to specify an SO_2 concentration at which the observed effects can themselves be considered adverse or serve as indicators of potentially more serious

consequences. In making such a judgment, the Administrator should consider, among other factors, the following:

a) In almost all cases, the bronchoconstriction and symptoms observed appear to have been transient and reversible. Sheppard et al. (1983), however, reported that for two subjects, exposure to SO_2 with hyperventilation produced severe bronchoconstriction that lasted longer than 45 minutes. In several other studies, asthmatic subjects have required removal from exposure at 0.5-0.6 ppm and higher (Linn et al., 1983b; Roger et al., 1985). Although direct evidence of long-term consequences from repeated peak exposures is not available, the possibility of such effects cannot be ruled out.

b) At concentrations less than 0.4 ppm with free breathing, group mean functional changes were moderate to small (Δ SRaw ~ 0 to 70% over baseline) and within the range of variability observed for day to day changes in many asthmatics. At 0.6-0.75 ppm, group mean effects were more substantial (Δ SRaw ~ 200% over baseline).

c) Most studies utilized mild, young adult or adolescent, non-smoking asthmatic volunteers. Furthermore, the subjects were exposed only when they were asymptomatic and without apparent respiratory tract infections or allergic responses. Even among the otherwise well defined groups of relatively mild asthmatics studied, there was great variability in the magnitude of bronchoconstriction induced by SO_2. As illustrated by the data derived from Roger et al. (1985) in Figure 3-2, the SO_2 concentration necessary to increase SRaw by 100% or more in freely breathing asthmatics at 42 L/min was 0.75 ppm for 50% of the subjects, and ranged between approximately 0.3 and 1.4 ppm in 80% of the subjects. Even more sensitive individuals may exist in the population of "mild" asthmatics; those with more severe asthma may also be more sensitive to SO_2 induced bronchoconstriction.

d) Although the reported responses are not generally interpreted as overt asthma attacks, the combination of bronchospasm and symptoms might be perceived by some subjects as a "mild" attack; this could result in discomfort, the need for medication, and curtailment of desired physical activities. According to Linn et al. (1983b), the responses of their subjects at 0.6 ppm "might be judged to show adversity in that the subjects sense of well being was clearly diminished, their degree of air-flow obstruction seemed to impair physical performance meaningfully, and drug treatment was clinically indicated in a few. On the other hand, possibly arguing against a judgment of adversity, are the observations that the effects were quickly reversible, were similar to effects produced by exercise even in clean air, and did not prevent the subjects from carrying out their duties (completing the exposure protocol)."

The staff obtained additional guidance on the physiological or health significance of asthmatic responses in the controlled exposure studies through discussions with a number of experts in the field (Cohen, 1984). Some experts felt that the relatively mild, transient, and reversible effects are not of physiological significance given the current widespread use of effective medication. In contrast, others felt that despite asthmatics' sensory accommodation and learning to manage attacks through medication or altered activity, even subtle functional changes are significant and potentially serious especially when accompanied by symptoms. Several pointed out that there may be persistent, undetected effects (e.g., residual obstruction) associated with even "mild" episodes which may increase airway reactivity and predispose the individual to further insults (e.g., infections, other bronchoconstrictive agents).

Furthermore, these experts agreed that any asthmatic experience is alarming and in different degrees, disabling. They felt that the effects observed at 0.5 ppm SO_2 would, at a minimum, affect an individual's lifestyle by causing discomfort, an increase in their medication usage, or discontinuance or restriction of their activity.

2) Relative Effect of SO_2 Exposure Compared to Exercise, Other Stimuli;

Consistent with previous findings discussed in the 1982 staff paper, recent studies find that SO_2 enhances the bronchoconstrictive effects due to exercise. Roger et al. (1985) report that the effects of moderate exercise ($V_e \sim 42$ L/min) in inducing bronchoconstriction is roughly equal to that of 0.5 ppm SO_2 while the effects of 0.25 ppm SO_2 on asthmatics are insignificant compared to those caused by moderate-heavy exercise. The exercise rate in this study is roughly equivalent to light jogging or climbing several flights of stairs (SP, Appendix A).

Cold (< 6°C) and/or dry air has been found to exacerbate the effects of SO_2 in exercising asthmatics, producing effects greater than those seen at normal temperatures. SO_2 at concentrations as low as 0.3 ppm may measurably potentiate the effect of cold air (Linn et al., 1984b) which may be possible in ambient winter conditions in the U.S.. On the other hand, effects with warm, humid temperatures are less than those seen in conditions typical of most laboratory studies.

3) Exposure Considerations

Peak 1-hour SO_2 levels in excess of 0.5 ppm are rare with current U.S. air quality, and almost always occur only in the vicinity of major point sources. Shorter term (5 to 10 minute) peaks at these levels are somewhat more common, but no systematic data exist. Moreover, indoor SO_2 levels are almost always substantially lower than outdoor levels (EPA,

1982b; pp. 5-117). Thus, effects appear likely for situations involving asthmatics undergoing light to moderate exercise outdoors relatively near (< 10 km) sources of SO_2 in conditions resulting in peak (> 0.5 ppm, 5 to 10 minutes) SO_2 levels. Staff estimates of the probability of such exposures near large sources under alternative standards are summarized in the next section (C). Asthmatics may also be exposed to more frequent peaks of limited durations (< 30 seconds to 2 minutes) around numerous smaller industrial and commercial sources (Section IIB). It is not currently possible to determine whether exposures of such limited duration would produce effects approaching those seen at the 5 to 10 minute exposures used in most of the studies to date.

To the extent such sources produce repeated frequent short-term peaks, the findings of temporary adaptation response may be of some significance. Within a single day, repeated episodes of exercise with elevated SO_2 concentrations would be expected to produce mitigated responses. Since tolerance appears to be short-lived (<5 hrs.), however, it would not afford protection against SO_2 on subsequent days, nor necessarily on the same day.

Some data suggest that rapid rises in SO_2 levels, such as those involved in many of the controlled studies, are more likely to produce effects than are more gradual rises. As discussed in the 1982 staff paper, however, a rapid rise could result from a) movement from indoors to outdoors, b) onset of exercise resulting in a rapid rise in SO_2 at sensitive respiratory tract receptors, c) movement into an area of peak levels (by vehicle or otherwise), as well as, d) an actual rapid increase in ambient levels at a point.

4) Variance about the 1-hour average

The controlled studies discussed in Section III indicate that effects occur within 5-10 minutes but do not necessarily worsen with continued

exposure to SO_2 over the course of an hour. Five and ten minute averages will vary about the 1-hour mean. Thus, for an area just attaining a 1-hour standard of 0.5 ppm, 5 or 10 minute peaks will be higher. Analyses of recent data (Section II), indicate that the peak is likely to be within a factor of 2 (1.5 to 1.8 of the mean) or less than 1.0 ppm.

Based on the above evaluation of the more recent studies and related factors, the staff revises its original recommended range of interest for a possible 1-hour SO_2 standard to 0.2 to 0.5 ppm. The lower bound of 0.2 ppm represents a 1-hour level for which maximum 5 to 10 minute peak exposures are not likely to exceed 0.4 ppm, the lowest level at which the CD Addendum indicates a risk of clinically significant responses for asthmatics engaged in moderate (or higher) activity levels. Based on normal air quality variations, a 1-hour standard at the upper bound of the range of 0.5 ppm would permit 5-10 minute peaks as high as 1.0 ppm during the peak hours, and would permit multiple hours in which the 5-10 minute peak would exceed 0.5 ppm, even when the 1-hour average is within this range. The risk of substantial effects with such exposures is higher.

Independent of frequency of exposure considerations, 1-hour concentrations at the high end of the above range may not provide a substantial margin of safety for exercising asthmatics. The low frequency with which such peak values would occur in the presence of active sensitive subjects is, however, a mitigating factor that should be examined in determining the margin of safety provided by alternative standards.

b) Additional Factors to be Considered in Evaluating Margin of Safety and Risks-Peak Exposures

The data do not suggest other groups that are more sensitive than asthmatics and atopics to single peak exposures. To the extent that the

suggested range is protective of asthmatics and atopics, the risk of functional effects in other sensitive individuals appears small. Other effects of concern (aggravation of bronchitis, increased respiratory illnesses) have not been evaluated adequately in controlled human studies, but epidemiological evidence suggests that they may result from repeated peak exposures over longer time periods. Potential interactions of SO_2 and ozone have not been investigated in the more recent literature.

The potential pollutant interactions and other considerations listed above should be considered in determining the need for and evaluating the margin of safety provided by alternative 1-hour standards.

3. Short-Term (24-hour) Exposures

a) Derivation of Ranges of Interest from Epidemiological Studies

An updated staff assessment of the most useful epidemiological studies for deriving ranges of interest for 24-hour standards is summarized in Table 4-2 and discussed below.

The "effects likely" row in Table 4-2 is unchanged from the 1982 assessment. The CD addendum relies on the original London mortality and bronchitic studies as those most appropriate in concluding that notable increases in excess mortality and exacerbation of bronchitic symptoms may occur above 500 $\mu g/m^3$ BS and SO_2. With regard to increased mortality, greater certainty with respect to effects occurs when both pollutants exceed about 750 $\mu g/m^3$. These estimates represent judgments of the most scientifically reliable "effects levels" for daily smoke and SO_2 at least in the context of historical London pollution episodes.

Because of the severity of the health endpoints in these studies, and the need to provide an adequate margin of safety in standard setting, it is important to determine whether the data suggest the possibility of health risks below these "effects likely levels". As discussed in the

criteria document addendum, the London mortality studies and reanalyses support the possibility of effects due to particles below 500 $\mu g/m^3$ - with no obvious threshold.

The situation with respect to SO_2, however, is less clear. The 1982 CD notes that results from a selected group of subjects suggested that 500 $\mu g/m^3$ SO_2 (and 250 $\mu g/m^3$ BS) may not be absolute thresholds for the most sensitive bronchitis patients, although the lead author of the study strongly objects to this interpretation (Lawther, 1986). On the other hand, the 1982 staff assessment previously concluded that the available evidence on daily mortality did not suggest a significant risk of increased mortality for exposures to SO_2 alone at concentrations below the likely effects levels.

Table 4-2. UPDATED STAFF ASSESSMENT OF SHORT-TERM EPIDEMIOLOGICAL STUDIES

Effects/ Study	Measured SO_2 - $\mu g/m^3$ (ppm) - 24 hour mean			
	Daily Mortality in London[1]	Aggravation of Bronchitis[2]	Small, Reversible Declines in Children's Lung Function[3]	Combined Effects Levels
Effects Likely	500-1000 (0.19-0.38)	500-600 (0.19-0.23)	-	500 (0.19)
Effects Possible	-	<500 (0.19)	250-450 (0.10-0.18)	250 (0.10)
No Effects Observed	-		100-200 (0.04-0.08)	<200 (.08)

[1]Deviations in daily mortality during London winters (1958-1972). Early winters dominated by high smoke and SO_2, principally from coal combustion emissions, and with frequent fogs (Martin and Bradley, 1960; Ware et al., 1981; Mazumdar et al., 1981, 1982).
[2]Examination of symptoms reported by bronchitics in London. Studies conducted from the mid-1950's to the early 1970's (Lawther et al., 1970).
[3]Studies of children in Steubenville (1978-80) and in the Netherlands (1985-86) before, during, and after pollution episodes characterized by high particle and SO_2 levels (Dockery et al., 1982; Dassen et al., 1986).

The two recent London mortality reanalyses provide differing results regarding the effects of SO_2. Mazumdar et al. (1982) found no consistent trend in mortality with increasing SO_2 below 700 $\mu g/m^3$ (0.27 ppm) and that the component of London mortality explained by pollution in the 1958-72 winters is almost entirely due to smoke across all levels considered. For days with BS and SO_2 below 500 $\mu g/m^3$, the association between mortality and pollution persisted for smoke and not SO_2. Shumway et al. (1983) did not attempt to separate the effects of the two pollutants and found that their association with daily increases in mortality were nearly identical with no apparent threshold. While the effects of SO_2 and BS cannot clearly be separated due to the high degree of their covariance, it does not appear that the recent published analyses suggest a revision to the previous assessment, which concluded there was not a significant risk of increased daily mortality with SO_2 alone below the effects likely levels.

The studies of school children in Table 4-2 exposed to peak SO_2 and particle concentrations during pollution episodes suggest small, but significant, reversible declines in lung function. The studies suggest the possibility of effects below the low end of the original range of interest (365 $\mu g/m^3$ or 0.14 ppm) down to levels as low as approximately 250 $\mu g/m^3$ (0.10 ppm) with more certainty at levels around 450 $\mu g/m^3$ (0.18 ppm). Again, it is difficult to distinguish the effects of the two pollutants though a more consistent trend of reduced lung function with higher TSP, and not SO_2, was reported by Dockery et al. (1982). Given that SO_2 alone has not been observed to cause altered clearance or lung function in animals or humans in controlled laboratory conditions without very high short-term peaks (> 1-5 ppm) (EPA, 1982a,b), it may be that the observed declines in lung function during and after the pollution episodes were due to the elevated particulate levels (including the transformation products of SO_2) either

acting alone or in the presence of SO_2, rather than SO_2 alone. Alternatively, very high peak SO_2 concentrations on the order of minutes may have accounted for the lung function decrements though this does not seem likely.

Therefore, caution should be applied in using the recent episode studies in the context of evaluating the range of interest for SO_2 alone. While effects may be associated with levels between 250-450 $\mu g/m^3$ (0.10-0.18 ppm), it is questionable to what extent SO_2 was a factor in causing the observed responses.

In summary, the available data indicate that the upper bound for the range of interest for 24-hour SO_2 standards remains at 500 $\mu g/m^3$ where effects appear to be likely. Although consideration should be given to a lower bound of 250 $\mu g/m^3$ (0.10 ppm), it is not clear whether important effects are caused by SO_2 at levels below the current standard level (365 $\mu g/m^3$, 0.14 ppm) which was previously judged - and still appears - to provide adequate protection.

b) Summary of Factors to be Considered in Evaluating Margin of Safety -- Short-Term Exposures

The 1982 staff paper identified a number of factors to be considered in developing a 24-hour standard with a margin of safety. The staff finds that this original discussion (SP, pp. 75-78) is still appropriate. In summary, the factors include:

1) Interaction with ozone, particles, and other pollutants as well as fog.
2) Relative exposure in the U.S. compared to the British studies.
3) Risk for other sensitive groups and effects not evaluated in the more quantitative data, and
4) Whether the 24-hour standard acts alone or in concert with a new one-hour standard.

4. Long-Term (Annual) Exposures

Based on the 1982 assessment, the staff concluded that although the possibility of effects from continuous low-level exposures to SO_2 could not be ruled out, no quantitative rationale could be offered to support a specific range of interest for an annual standard given the inconclusive nature of the available epidemiological data. As discussed in Section III, several recent community studies suggest increased risk of respiratory symptoms (cough, phlegm production, wheeze) in populations (children and adults) exposed to high (>100 $\mu g/m^3$) long-term levels of SO_2, with and without high particle concentrations. The majority of these studies were conducted in areas subjected to intermittent short-term peak SO_2 concentrations resulting from point source emissions (Chapman et al., 1985; Dodge, 1983; Dodge et al., 1985; Schenker et al., 1983). A major concern, therefore, is whether repeated SO_2 peaks permitted by 24-hour or 1-hour standard ranges in area-source dominated population centers might, after some long time period, result in increased risk of the effects noted, along with other effects suggested by animal data (EPA 1982a,b).

One recent study (PAARC, 1982a,b) demonstrating associations between SO_2 and respiratory health effects did not focus on point-source dominated exposures. Increased respiratory symptoms and disease in adults and children were associated with SO_2, but not particles, across a range from 25 to 130 $\mu g/m^3$ with no apparent threshold (CDA, p. 3-45). In addition, unlike in any other study, associations between SO_2 and reduced lung function were detected. As noted in Section III, a number of questions regarding the aerometry, statistical analyses, and interpretation of this work argue against placing great reliance on the conclusions at present.

While no single study may provide strong evidence for substantial risks, there does appear to be some consistency across results indicating a possibility of respiratory impacts associated with either low-level, long-term exposures to SO_2 or, more certainly, with repeated exposures to peak SO_2 levels over long periods. In essence, the recent studies do add some support to previous staff recommendations to retain an annual primary standard. This recommendation was in part based on the finding that elimination or substantial relaxation of the current annual standard would result in increased exposures to large numbers of people in several heavily populated urban centers (Frank and Thrall, 1982). Pending resolution of the issues raised by the new studies, the staff recommends maintaining an annual standard at about the current level of 0.03 ppm (80 $\mu g/m^3$).

B. Analysis of Relative Protection Afforded by Alternative Standards

An essential consideration in evaluating potential standards is the relative protection afforded by standards with different averaging times and levels. A preliminary staff assessment of this issue is presented in the 1982 SP (pp. 79-83, Appendix D). This assessment, based on analysis of air quality data (Frank and Thrall, 1982; Johnson, 1982), air quality modeling (Burton et al., 1982), and source/population information (Anderson, 1982), found that no single averaging time (annual, 24 hr, 3 hr, 1 hr) would provide the same degree of protection and control afforded by the other averaging time in all situations. The current 24-hour standard would prevent 1-hour peaks in the range of interest from occurring in most population oriented sites, but would allow multiple exceedances of these values in many point source oriented sites. Similarly, the 24-hour standard limits high annual values in most, but not all sites of interest. The current 3-hour secondary standard limits 1-hour peaks even more than the 24-hour

standard, but does not materially affect long-term urban values. In essence, based on that preliminary analysis of alternative averaging times, the staff concluded "that implementation of the current suite of SO_2 standards (annual, 24-hour, 3-hour) provides substantial protection against the direct effects of SO_2 identified in the scientific literature" (SP, pp. 82-83).

Since closure on the 1982 staff paper, the staff has continued to analyze relationships among averaging times and relative protection afforded. Based on the above updated assessment of effects associated with both 24-hour and annual exposures, the staff finds that the above conclusions concerning protection provided by the current standards remain demonstrably valid. The staff has found the most critical aspect of examining the relative (or alternative) standards to be in relation to peak exposures associated with effects in asthmatics. Over the past several years, the staff has developed tools to permit analysis of substantially greater detail than previously possible. These tools and the results of their application to examine 1) current standards, 2) emissions typical of current conditions, and 3) alternative standards are presented in detail in separate reports (EPA, 1986c; 1986d). The following discussion summarizes the major findings from these reports.

Population exposure simulations require detailed analyses of both air quality and population patterns. EPA (1986d) describes a population exposure study around four utility power plants each located in or near an urban area. The decision to focus that analysis on power plants was guided by earlier studies (Frank and Thrall, 1982; Burton et al. 1982) which showed they were the source category most likely to produce high short-term levels of SO_2 in populated areas. Other large sources, such as smelters or Kraft pulp mills, however, can also produce such peaks.

A complete risk assessment would combine exposure results with detailed exposure-response functions. To reduce the complexity of this analytic problem to a manageable size, the staff developed a benchmark called an Exposure of Concern (EOC). This benchmark permitted fixing a concentration, averaging period and exercise rate above which effects of concern could be expected in some fraction of asthmatics. Based on the health studies and analyses described above, the benchmark EOC most often used was defined as an asthmatic exposed at or above 0.5 ppm SO_2 for 5 minutes while at an activity level associated with a ventilation rate at or above 35 L/minute. At these levels, on the order of 25% of asthmatics might experience a doubling of airway resistance (Figure 3-2). In some of the work, other concentration levels and averaging periods were also examined. The EOC defined above is not intended to define a threshold of response, but rather as a level where a significant fraction of individuals so exposed might experience potentially adverse effects.

The combined models estimated the probability that the 5-minute peak equalled or exceeded 0.5 ppm. These probability estimates of exceeding a target level (0.5 ppm) provided the air quality basis for the exposure calculation. EPA's NAAQS Exposure Model (NEM) (Biller et al., 1981) was modified to incorporate these probability estimates. NEM is designed to simulate daily population movement around an urban area accounting for travel patterns, activity levels, and microenvironment (e.g., indoor vs. outdoor). The population and travel data were specific to the urban areas being studied. The activities which are defined in NEM as "High" correspond to ventilation $\geq$ 35 L/minute. The use of air quality probability

estimates meant that it was possible to express the exposure results as a probability weighted distribution and allowed estimation of the expected number of exposures.

The findings of the exposure analysis are subject to a number of uncertainties inherent in both air quality modeling and large population simulations. The results are conditioned by the analytic assumptions made. The exposure analysis identifies some 16 separate sources of uncertainty and error. Among the more significant are: 1) Lacking activity pattern and residential location data for asthmatics, it was assumed that the geographic distributions, and activity patterns and ventilation rates for asthmatics are the same as for the general population. Although this may not be an unreasonable assumption for most mild asthmatics, it undoubtedly overstates the time spent at elevated ventilation rates for more severe cases; 2) Power plants were assumed to operate at 100% capacity. Sensitivity analyses indicate that exposures are overestimated because of this assumption; and 3) Although care was taken to select a representative sample of plants/exposure regimes, only four power plants were modeled. Nonetheless, despite the caveats noted above as well as others in the reports, the results do provide an indication of both current exposures and those which might occur under alternative standards around large utility power plants.

The exposure analysis results in EPA (1986d) include air quality levels, the expected number and percent of asthmatics living in the vicinity of each plant that experiences one or more EOC per year, and the highest probability of an EOC for any single asthmatic. Because of variations in population around plants and the tendency for the maximum probability of exposure to approach one under a variety of scenarios, the fraction (%) of asthmatics with one or more EOC/yr is the most useful metric for comparing

results around different plants. This number, is, however, somewhat sensitive to the size of the area modeled (EPA, 1986d).

The results of the analysis of the fraction of asthmatics with an EOC under 1) current emissions, and 2) maximum emissions assuming the current standards are just met, are displayed in Figure 4-1. With current emissions, approximately 0.2 to 13% of resident asthmatics are predicted to experience at least one 5 minute exposure to 0.5 ppm per year while at moderate or higher exercise. With the exception of Eddystone, this represents on the order of one to four thousand asthmatics (assuming 4% of the population is asthmatic) for each plant. With the exception of Eddystone, the maximum probability of an EOC for "most exposed" individual approaches unity at all plants. The results for just meeting the current standards are comparable to the "current" case but with 3 of 4 plants showing increases in predicted EOC fraction. In part, such increases are due to assumptions regarding implementation, which reflect current practice in some areas of the country, but are less restrictive than more strict compliance requirements in practice in other areas. The 3-hour standard tends to be controlling for large more isolated plants, while the 24-hour standard controls in more urban locations.

The results of the exposure analysis for alternative one hour standards selected from the range of interest are illustrated in Figure 4-2. Standards in this range would reduce the EOC fraction to under 4% for all plants modeled, but still do not eliminate all such exposures. A standard of 0.4 ppm, for example, would protect over 98% of potentially exposed asthmatics from an EOC. The maximum probability of an individual EOC for the range illustrated is 0.1 to 0.9.

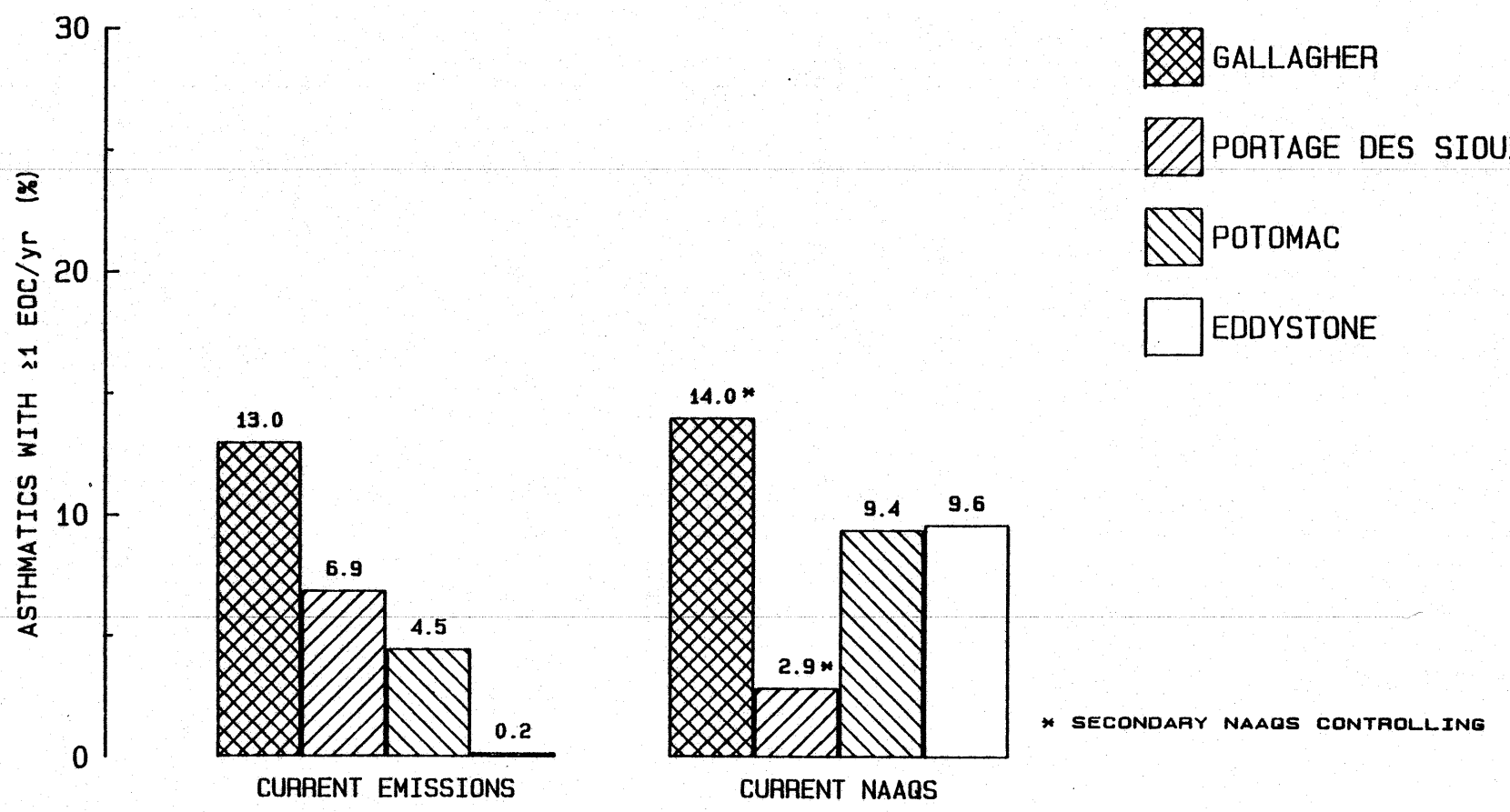

Figure 4-1. Expected percentage of asthmatics with one exposure of concern ($\geq$ 0.5 ppm SO_2 for 5 minutes, "high" activity) per year in vicinity of four selected power plants. For 1) current emissions and 2) just meeting current SO_2 NAAQS assuming a 30 day emission limit (EPA, 1986d). The degree of protection varies significantly with implementation approach.

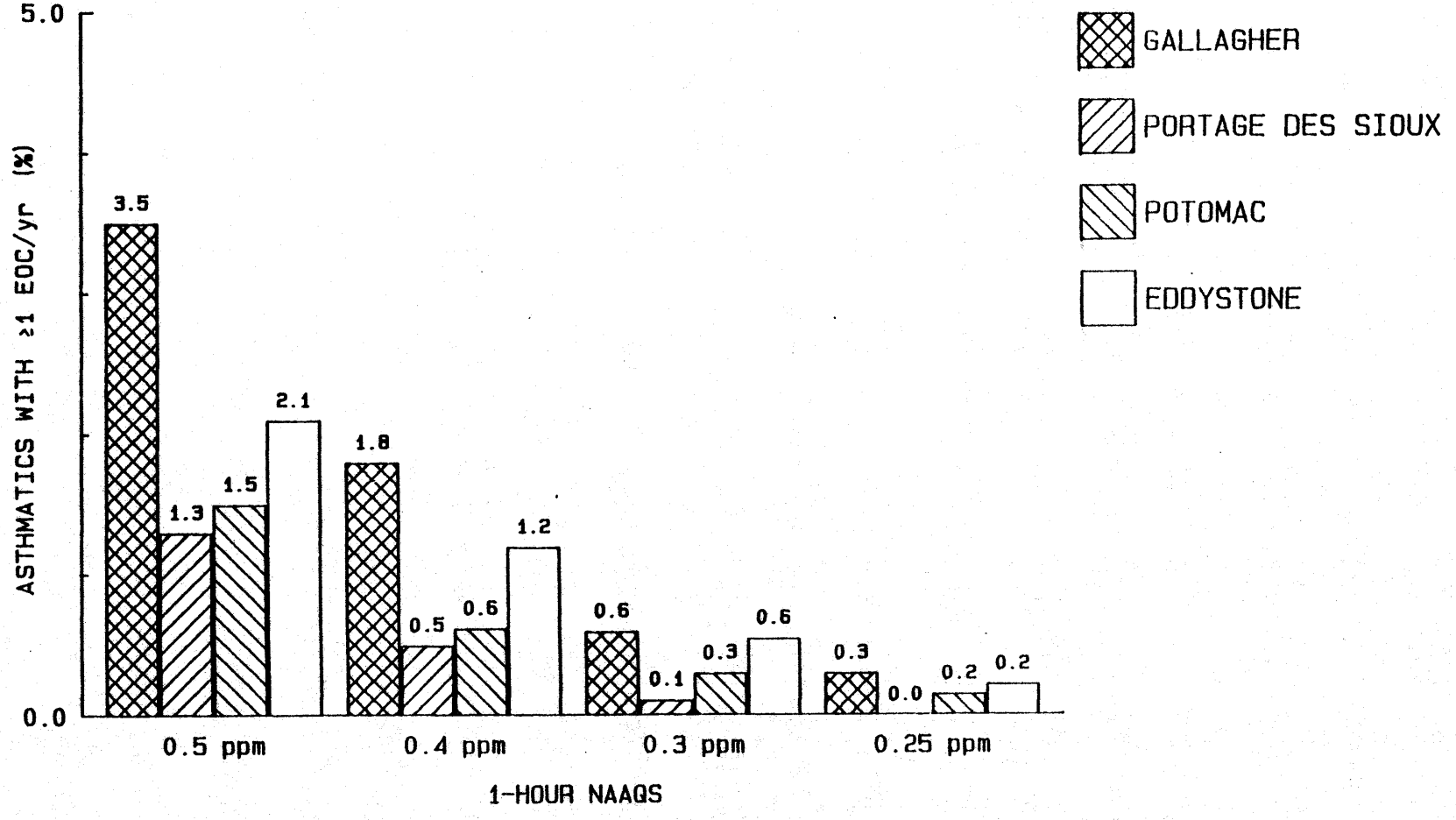

Figure 4-2. Expected percentage of asthmatics with one exposure of concern ($\geq$ 0.5 ppm SO_2 for 5 minutes, "high" activity) per year in vicinity of four selected power plants. For just meeting alternative one hour standards (EPA, 1986d).

The results of the exposure analysis for utilities should be viewed in light of the assumptions and uncertainties noted above. In addition, although utility power plants account for the majority of SO_2 emissions in the U.S., recent work has shown that other smaller sources may also produce peak exposures (Section II). Around smaller sources (e.g., industrial or commercial boilers), limited duration peaks in excess of 0.5 ppm are due either to low persistance meteorological events or, if the facility has a short stack, may be due to the phenomenon of building downwash. In either event, the peaks are likely to be of very short duration (less than 30 seconds to two minutes). Because the meteorological events causing the peaks are not well characterized and are not normally addressed in standard EPA dispersion models, a complete analysis of the situation around smaller plants is not feasible. Very rough estimates indicate that the populations at risk of an exposure in such situations may be large. However, given the very short duration of most such peaks, their health significance for exercising asthmatics is uncertain.

In summary, the staff analysis of relative protection afforded by alternative standards results in the following conclusions:

1) The current standards provide substantial protection against the effects identified as being associated with 24 hour and annual exposures.

2) The current standards - as reflected by current emissions or emissions when the standards are just met with somewhat less restrictive implementation assumptions - also provide some limit on peak SO_2 exposures of concern for asthmatics. In some cases, however, up to 10 to 15% of the sensitive population could be exposed once

a year to levels $\geq$ 0.5 ppm for 5 minutes, while at elevated ventilation.

3) The range of 1-hour standards analyzed (0.25 to 0.5 ppm) provides increased protection against such exposures, limiting the fraction of asthmatics exposed to less than 4%.

C. Summary of Staff Conclusions and Recommendations

The major updated staff conclusions and recommendations made in Section IV, A-B are briefly summarized below:

1) The more recent data provide additional support for the earlier staff recommendations regarding consideration of a new 1-hour SO_2 standard. Based on an updated staff assessment of controlled human exposures to peak (minutes to hours) SO_2 concentrations, the staff has revised the range of potential 1-hour levels of interest to 0.2 to 0.5 ppm (525 to 1300 $\mu g/m^3$). The lower bound represents a 1-hour level for which the maximum 5 to 10 minute peak exposures are unlikely to exceed 0.4 ppm, which is the lowest level where potentially significant responses in free (oronasal) breathing asthmatics have been reported in the criteria document addendum. The upper bound of the range represents a 1-hour level for which 5 to 10 minute peak concentrations are unlikely to exceed 1 ppm, a concentration at which the risk of significant functional and symptomatic responses in exposed sensitive asthmatics and atopics appears high. In evaluating these laboratory data in the context of decision making on possible 1-hour standards, the following considerations are important: (a) the significance of the observed or anticipated responses to health, (b) the relative effect of SO_2 compared to normal day to day variations in asthmatics from exercise and other stimuli, (c) the low probability of exposures

of exercising asthmatics to peak levels, and (d) five to ten minute peak exposures may be a factor of two greater than hourly averages.

Independent of frequency of exposure consideration, the upper bound of the range contains little or no margin of safety for exposed sensitive individuals. The limited geographical areas likely to be affected and low frequency of peak exposure to active asthmatics if the standard is met add to the margin of safety. The data do not suggest other groups that are more sensitive than asthmatics to single peak exposures, but qualitative data suggest repeated peaks might produce effects of concern in other sensitive individuals. Potential interactions of SO_2 and O_3 have not been investigated in asthmatics. The qualitative data, potential pollution interactions, and other considerations listed above should be considered in determining the need for and evaluating the margin of safety provided by alternative 1-hour standards.

2) Based on a staff assessment of the recent short-term epidemiological data, the original range of 24-hour SO_2 levels of interest - 0.14 to 0.19 ppm (365 to 500 $\mu g/m^3$) - still appears appropriate, although some consideration could be given to the findings of physiological changes of uncertain significance at levels as low as 0.1 ppm. Earlier staff conclusions and recommendations concerning a 24-hour standard (SP, pp. 85-86) remain appropriate.

3) The previous staff assessment concluded that although the possibility of effects from continuous lower level exposures to SO_2 cannot be ruled out, no quantitative rationale could be offered to support a specific range of interest for an annual standard. The more

recent epidemiological data provide additional support for the original recommendation for retaining an annual standard at or near the current level 0.03 ppm (80 $\mu g/m^3$). This recommendation was based in part on a finding that alternative short-term standards would not prevent annual levels in excess of the current standard in a limited number of heavily populated urban areas. Given the additional information and the possibility of effects from a large increase in population exposure, the staff recommends maintaining the primary annual standard at its current level.

4) Analyses of alternative averaging times and population exposures suggest that:

   a) The current standards provide substantial protection against the effects identified as being associated with 24 hour and annual exposures.

   b) The current standards - as reflected by current emissions or emissions when the standards are just met with somewhat less restrictive implementation assumptions - also provide some limit on peak SO_2 exposures of concern for asthmatics. In some cases, however, up to 10 to 15% of the sensitive population in the vicinity of major sources could be exposed once a year to levels at or above 0.5 ppm for 5 minutes, while at elevated ventilation.

   c) The range of 1-hour standards analyzed (0.25 to 0.5 ppm) provides increased protection against such exposures, limiting the fraction of asthmatics exposed to less than 4%.

The relative protection afforded by current vs. alternative standards as indicated by current and ongoing exposure analyses is an important consideration in determining what, if any, standard revisions may be necessary.

APPENDIX A. ANALYSIS OF DOSE-RESPONSE RELATIONSHIPS FROM CONTROLLED SO_2 EXPOSURE STUDIES ON ASTHMATICS

The following discussion describes the analyses used to generate Figure 3-1, which plots results from the various controlled SO_2 exposure studies on mild asthmatics.

1) The studies used are summarized in Table A-1. To standardize comparisons, only studies that reported changes in specific airway resistance (SRaw). Unfortunately, several studies reporting significanct declines only for other lung function parameters could not be not represented (e.g., Koenig et al., 1983b, 1985a; Schacter et al., 1984). Studies involving unusual temperature and/or humidity conditions (i.e., < 6°C, RH < 40% or > 90%) were also excluded to avoid the interactive effects of airway drying or cooling in contributing to bronchoconstriction. In addition, results at low SO_2 exposure levels (generally $\leq$ 0.25 ppm) where changes in SRaw were not statistically different from changes due to exercise alone were eliminated from the analysis. This would not be expected to bias the analysis in the domain where SRaw increases significantly with increased SO_2 exposure. The regression line in Figure 3-1 should not be extrapolated to zero dose, since at SO_2 levels below 0.25 ppm (~ 20 µg/min, oral airway dose rate) exercise-induced constriction dominates.

2) The studies involved either 5 or 10 minute exposure periods with one exception. Although total dose is a less satisfactory predictor of response than dose rate when considering longer exposure times (e.g., 1-hour) (Linn et al., 1982), no consistent trend can be seen in comparing responses to 3 vs. 5 minute vs. 10 minute exposures, which supports findings of Linn et al., (1983b).

Table A-1. Summary of Data from SO_2 Controlled Asthmatics Studies Used in Dose-Response Analysis

CONC. (ug/m^3)	CONC. ppm	DURATION MINUTES	TEMP C/RH	N	EXPOSURE	Ve M^3/min.	ORAL Ve M^3/min. ORONASAL	ORAL Ve M^3/min. MOUTH	ORAL SO2 ug/min. ORONASAL	DOSERATE ug/min. MOUTH	% SRaw EXERCISE	% SRaw SO2/ EXERCISE	INCREASE SO2 OVER CLEANAIR	REFERENCE
1300	0.5	5	23/80	6	M	0.04	0.04	0.04	52	52	15	141	126	KIRKPATRICK (1982)
1300	0.5	5	23/80	7	M	0.041	0.041	0.041	53.3	53.3	5	231	225	BETHEL (1983b)
1970	0.75	10	23/80	23	M	0.04	0.04	0.04	78.8	78.8	52	373	321	LINN (1982b)
630	0.25	10	23/80	7	M	0.03	0.03	0.03	18.9	18.9	0	30	30	SHEPPARD (1981a)
2600	1	5	23/80	6	M	0.031	0.031	0.031	80.6	80.6	0	300	300	SHEPPARD (1981a)
1300	0.5	3	23/82	8	M	0.035	0.035	0.035	45.5	45.5	0	104	104	SHEPPARD (1983)
1300	0.5	10	23/80	7	M	0.035	0.035	0.035	45.5	45.5	0	115	115	SHEPPARD (1981a)
1300	0.5	10	22/85	24	M	0.027	0.027	0.027	35.1	35.1	35	96	61	LINN (1982a)
1300	0.5	5	23/80	9	M	0.061	0.061	0.061	79.3	79.3	25	306	281	BETHEL (1983b)
1970	0.75	10	23/90	14	M	0.04	0.04	0.04	78.8	78.8	54	321	267	LINN (1983a)
1300	0.5	5	23/80	6	F	0.04	0.019	0.026	24.7	33.8	15	69	54	KIRKPATRICK (1982)
1300	0.5	5	23/90	9	F	0.061	0.038	0.042	49.4	54.6	25	219	194	BETHEL (1983b)
2600	1	10	26/70	27	C	0.042	0.02	0.027	52	70.2	47	190	143	ROGER (1985)
2600	1	10	26/70	10	C	0.041	0.02	0.027	52	70.2	48	172	124	KEHRL (1986)
1570	0.6	5	22/85	24	C	0.05	0.027	0.033	42.39	51.81	27	132	105	LINN (1984a)
1300	0.5	10	26/70	28	C	0.042	0.02	0.027	26	35.1	47	93	46	ROGER (1985)
1570	0.6	5	21/80	24	C	0.05	0.027	0.033	42.39	51.81	28	150	122	LINN (1984b)
1040	0.4	5	23/85	23	C	0.048	0.023	0.032	23.92	33.28	35	69	34	LINN (1983b)
800	0.3	5	7/80	24	C	0.05	0.027	0.033	21.6	26.4	59	87	28	LINN (1984b)
800	0.3	5	21/80	24	C	0.05	0.027	0.033	21.6	26.4	28	59	31	LINN (1984b)
1570	0.6	5	21/20	22	C	0.05	0.027	0.033	42.39	51.81	20	206	186	LINN (1985a)
1570	0.6	5	21/80	22	C	0.05	0.027	0.033	42.39	51.81	10	157	147	LINN (1985a)
630	0.25	5	23/36	19	C	0.06	0.032	0.042	20.16	26.46	77	134	57	BETHEL (1985)
1570	0.6	5	5/85	24	C	0.05	0.027	0.033	42.39	51.81	38	182	144	LINN (1984a)
1300	0.5	5	23/41	10	C	0.06	0.032	0.042	41.6	54.6	39	238	199	BETHEL (1983a)
2600	1	30	26/70	10	C	0.041	0.02	0.027	52	70.2	50	233	183	KEHRL (1986)
1570	0.6	5	7/80	24	C	0.05	0.027	0.033	42.39	51.81	58	207	149	LINN (1984b)
1570	0.6	5	23/85	23	C	0.048	0.023	0.032	36.11	50.24	36	120	84	LINN (1983b)
1970	0.75	10	23/90	23	C	0.04	0.019	0.026	37.43	51.22	54	186	132	LINN (1983a)
1970	0.75	10	22/85	23	C	0.04	0.019	0.026	37.43	51.22	55	241	186	LINN (1982b)
1970	0.75	10	22/85	17	C	0.045	0.0225	0.03	44.325	59.1	?	263	-	HACKNEY (1984)

[1] M = mouthpiece, F = facemask, C = chamber (freebreathing)

[2] V_e = total ventilation rate. Oral V_e is oral component of ventilation for normal oronasal augmentors or habitual mouthbreathers. Oral SO_2 dose rate calculated separately for these 2 populations (see text).

3) Given the almost complete absorption of SO_2 that occurs in the moist surfaces of the nasal airways, the oral component of ventilation is critical in determining the SO_2 dose that penetrates to the airways where bronchomotor responses are triggered (Kleinman, 1984). Data on the partitioning between oral and nasal breathing under different exercise levels (Niinimaa et al., 1981; see 1982 staff paper, Appendix A) were used to estimate the oral component of ventilation given the ventilation rates (V_e) reported by the investigators. For example, Kirkpatrick et al. (1982) exposed asthmatics via mouthpiece to 0.5 ppm while exercising at about 40 L/min. Because a mouthpiece forces inspired air through the oral cavity thereby bypassing the nasal airways, it can be assumed that the oral V_e was 40 L/min resulting in an estimated SO_2 dose delivered via the oral airways of [1300 $\mu g/m^3$ (0.5 ppm) x 0.04 m^3/min (40 L/min)], or 52 µg/min. The asthmatics in the Kehrl et al. (1986) study were exposed free-breathing 1.0 ppm SO_2 while exercising at a ventilation rate of approximately 41 L/min. At this exercise level, most normal healthy individuals breathing unencumbered augment the amount of air entering the nasal passages by inhaling some air via the mouth so that the oral V_e would be approximately 20 L/min (Niinimaa et al., 1981). The oral airway SO_2 dose is estimated as [2600 $\mu g/m^3$ (1.0 ppm) x 0.02 m^3/min (20 L/min)], or 52 µg/min, which is identical to that in the Kirkpatrick study. Interestingly, the increases in airway resistance over clean air/exercise control in these studies were almost identical (126% vs. 124%).

For all calculations on free breathing experiments, typical oral/nasal breathing patterns were used as determined by Niinimaa et al., (1981) (see 1982 staff paper, Appendix A). By assuming that all of the freebreathing subjects were normal augmentors, some underestimation of SO_2 dose likely

results, especially given indications of increased frequency of allergic rhinitis and nasal congestion in asthmatics resulting in obligatory mouth breathing. Variability in such conditions between different groups of subjects may explain observed differences in responses between studies, as evidenced by the failure to fully replicate the Kirkpatrick et al. (1982) results under the same conditions but with fewer subjects with nasal disorders (Bethel et al., 1983b). An alternative approach is taken by Kleinman (1984) who estimates population-weighted oral V_e at different activity levels. A separate analysis (not illustrated), which used the same group of data assuming subjects were habitual mouthbreathers, produced no apparent improvements ($r^2 = 0.76$).

For the facemask experiment included in Bethel et al. (1983b), actual measurements of oral airflow through the masks were provided and roughly matched Niinimaa et al.'s prediction for oronasal breathing. In the Kirkpatrick et al. (1982) facemask study, it was assumed that free, oronasal breathing was simulated.

5) Changes in SRaw in response to SO_2 exposure while at exercise over baseline measurements were used as opposed to changes in SRaw over increases due to exercise alone in clean air. Again, separate analysis (not shown) using the latter measure yielded nearly identical results.

6) A simple linear regression was fit to the data. As mentioned, the linear relationship should not be extended to lower SO_2 exposure levels down to zero.

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