

centriacinar regions of the lung (*i.e.*, the portion of the lung where the region that conducts air and the region that exchanges gas are joined) are well established as one of the hallmarks of O₃ toxicity. Under certain conditions, some of the structural changes seen in these studies may become irreversible. It is unclear, however, whether ambient exposure scenarios encountered by humans result in similar "lesions" or whether there are resultant functional or impaired health outcomes in humans chronically exposed to O₃.

The epidemiologic lung function studies generally parallel those of the animal studies, but lack good information on individual O₃ exposure history and are frequently confounded by personal or copollutant variables. Thus, the Administrator recognizes that there is a lack of a clear understanding of the significance of repeated, long-term inflammatory responses, and that there is a need for continued research in this important area. In summary, the collective data on long-term exposure to O₃ garnered in studies of laboratory animals and human populations have many ambiguities. Nevertheless, the currently available information provides at least a biologically plausible basis for considering that repeated inflammation associated with exposure to O₃ over a lifetime may result in sufficient damage to respiratory tissue such that individuals later in life may experience a reduced quality of life, although such relationships remain highly uncertain.

c. Adversity of Effects for Individuals

Some population groups have been identified as being sensitive to effects associated with exposures to ambient O₃ levels, such that individuals within these groups are at increased risk of experiencing such effects. Population groups at increased risk include: (1) Active children and outdoor workers who regularly engage in outdoor activities;²⁶ (2) individuals with preexisting respiratory disease (*e.g.*, asthma or chronic obstructive lung disease);²⁷ and (3) some individuals, referred to as "hyperresponders," who

are unusually responsive to O₃ relative to other individuals with similar levels of activity or with a similar health status and may experience much greater functional and symptomatic effects from exposure to O₃ than the average individual response.

In making judgments as to when the effects discussed above become significant enough that they should be regarded as adverse to the health of individuals in these sensitive populations, the Administrator has looked to guidelines published by the American Thoracic Society (ATS) and the advice of CASAC. Based on these guidelines, with CASAC concurrence, gradations of individual functional responses (*e.g.*, decrements in forced expiratory volume (FEV₁), increased airway responsiveness) and symptomatic responses (*e.g.*, cough, chest pain, wheeze) were defined, together with judgments as to the potential impact on individuals experiencing varying degrees of severity of these responses.²⁸

In judging the extent to which such impacts represent effects that should be regarded as adverse to the health status of individuals, an additional factor considered is whether such effects are experienced repeatedly by an individual during the course of a year or only on a single occasion. While some experts would judge single occurrences of moderate responses to be a "nuisance," especially for healthy individuals, a more general consensus view of the adversity of such moderate responses emerges as the frequency of occurrence increases. Thus, EPA has concluded that repeated occurrences of moderate responses, even in otherwise healthy individuals, may be considered to be adverse since they could well set the stage for more serious illness.

2. Human Exposure and Risk Assessments

To put judgments about respiratory health effects that are adverse for individuals into a broader public health context, the Administrator has taken into account the results of human exposure and risk assessments.²⁹ This

broader context includes consideration, to the extent possible, of the particular population groups at risk for various health effects, the number of people in at-risk groups likely to be exposed to O₃ concentrations shown to cause health effects, the number of people likely to experience certain adverse health effects under varying air quality scenarios, and the kind and degree of uncertainties inherent in these assessments. These quantitative assessments add to our understanding of the overall body of evidence linking O₃ inhalation exposures to adverse health effects. The models used in these assessments were appropriate and the methods used represent the state of the art.

a. Exposure Analyses

The EPA conducted exposure analyses to estimate O₃ exposures for the general population and two at-risk populations, active children who regularly engage in outdoor activity (*i.e.*, "outdoor children") and "outdoor workers," living in nine representative U.S. urban areas.³⁰ Exposure estimates were developed for a baseline year (*e.g.*, 1993, 1994), using monitored O₃ air quality data (*i.e.*, the "as is" scenario), as well as for simulated air quality conditions reflecting attainment of the 1-hour NAAQS and various alternative standards. The exposure analyses provide: (1) Estimates of the number of people exposed in each of these population groups to various O₃ concentrations, and the number of occurrences of such exposures, under different regulatory scenarios,³¹ which are an important input to the risk assessment conducted for certain adverse health effects (summarized in the next section); and (2) estimates of the frequency of occurrences of O₃ "exposures of concern,"³² which help

standard proposed and alternative standards on which comment was solicited, as well as to refine the procedures used to simulate O₃ concentrations upon attainment of alternative standards (Richmond, 1997).

³⁰ The areas include a significant fraction of the U.S. urban population, 41.7 million people, the largest urban areas with major O₃ nonattainment problems, and two large urban areas that are in attainment with the 1-hour NAAQS.

³¹ Estimates of "people exposed" reflect the number of people who experience exposures to a given concentration of O₃, or higher, at least one time during the period of analysis, and estimates of "occurrences of exposure" reflect the number of times a given O₃ concentration is experienced by the population of interest.

³² "Exposures of concern" refer throughout to O₃ exposures at and above 0.08 ppm, 8-hour average, at moderate exertion. Such exposures are particularly relevant to a consideration of a number of health effects, discussed in section I.A.1 above, that have been observed in controlled human studies under these exposure conditions, but for which data were too limited to allow for

Paper describes and discusses these degenerative changes in more detail.

²⁶ Exertion increases the amount of O₃ entering the airways and can cause O₃ to penetrate to peripheral regions of the lung where lung tissue is more likely to be damaged.

²⁷ While not necessarily more responsive than healthy individuals in terms of the magnitude of pulmonary function decrements or symptomatic responses, these individuals may be at increased risk since the impact of O₃-induced responses on already-compromised respiratory systems may more noticeably impair an individual's ability to engage in normal activity or may be more likely to result in increased self-medication or medical treatment.

²⁸ These gradations and impacts are summarized in the 1996 proposal and discussed in the Criteria Document (Chapter 9) and Staff Paper (section V.F, Tables V-4 and V-5).

²⁹ See the 1996 proposal (61 FR 65723-6) and 1997 final rule (62 FR 38860-1) for a more complete summary of these assessments. A detailed description of the exposure and risk models and their application at the time of the 1996 proposal are presented in the Staff Paper and associated technical support documents (Johnson, 1994; Johnson *et al.*, 1996 a,b; Whitfield *et al.*, 1996). Following proposal, supplemental exposure and risk analyses were done to analyze the specific