Fixation and Microscopic Sizing of Aqueous Sodium Chloride Aerosols[1]

A new technique to fix tobacco smoke aerosols by methyl-2-cyanoacrylate vapor is applied to the study of the size distribution of sodium chloride droplets generated from a commercial inhalation nebulizer. The count mode diameter of the fixed droplets agrees well with the actual droplets calculated from known dried particles. The method allows direct visualization and measurement of droplets by light or electron microscopy, but it is limited to particles smaller than 2 μm in diameter. Further work is required to improve the fixation chamber design and sampling technique to ensure complete fixation and collection of droplets greater than 2 μm in diameter before the method can be used to characterize the polydisperse aerosol droplets from nebulizers.

INTRODUCTION

Accurate measurement of the droplet size distribution of medicinal aerosols is important in evaluating nebulizer performance, since the site of deposition of inhaled aerosol droplets is critically dependent upon particle size (1). Several sizing techniques have been applied to this problem, including use of the spiral centrifuge (2–4) and cascade impactor (5, 6). With these techniques, the droplet aerosol of a known solute concentration is initially dried. The aerodynamic size distribution of the sampled dry aerosol is then measured by comparison to calibration curves established by electron microscopy of dry particles or by sampling monodisperse microspheres of known aerodynamic diameter. From these data the size distribution of the initial droplets is calculated. Errors often arise in such determinations of droplet size from dry residue size, e.g., when the dried particles are hollow. Consequently, direct visualization and measurement of the droplet aerosol would be preferred. However, microscopic measurements have not been routinely applied to liquid droplets because evaporation or growth can occur during collection and measurement.

Recently, polymeric fixation with methyl-2-cyanoacrylate monomer vapor has been used to stabilize airborne tobacco smoke for electron microscopy (7–9). With this technique, good agreement was obtained between electron microscopy and cascade impactor measurements (7, 8). We have applied this technique to fix 0.9% (by weight) NaCl aerosol droplets generated from a commercial nebulizer used for inhalation therapy (Acorn Nebulizer, OEM Medical Incorporated, Madison, N. J., 08817).

[1] Supported by Grant 5RO1HL 19704 from the National Institutes of Health.

MATERIALS AND METHODS

Figure 1 shows the aerosol generation and fixation system. Compressed air (26 psig, 21°C, 48% relative humidity) was passed through the nebulizer at a flow rate of 9 liters/min. Part of the droplet aerosol stream was drawn through a 500-cm^3 flask containing methyl-2-cyanoacrylate monomer vapor at a flowrate of 100 cm^3/min. The fixation flask was held at 70°C by a water bath; at this temperature a few drops of methyl-2-cyanoacrylate provided the monomer vapor. When the monomer contacted the water of the aerosol droplet, it polymerized and fixed the droplets. Fixed aerosol was then collected on a platinum-coated carbon substrate electron microscope grid, using a point to plane electrostatic precipitator (10, Aries, Inc., Davis, Calif.), operated at 100 cm^3/min. Figure 2a shows an electron micrograph of the fixed NaCl droplets. Figure 2b shows an electron micrograph of NaCl crystals resulting from drying the NaCl droplets exiting the same generator with dilution air, and then sampling

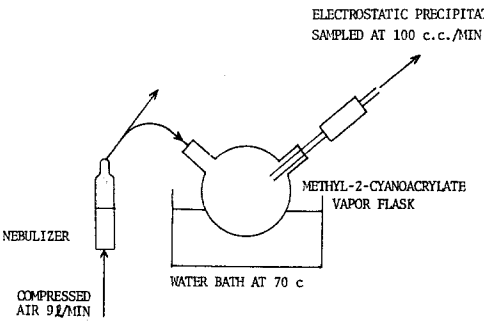

FIG. 1. System used for generation, fixation, and sampling of airborne droplets.

0021-9797/79/140351-07$02.00/0

by the electrostatic precipitator from a separate mixing–drying reservoir.

RESULTS AND DISCUSSION

Figure 3 shows the complete size distributions of the fixed droplets and the droplets before fixation. The particle size distribution of droplets before fixation was calculated from measurements of the size distribution of dried NaCl residue particles. The count median diameter (CMD) and geometric standard deviation (GSD) of these distributions are included with 99% confidence limits. These were calculated assuming the count data are log-normally distributed with respect to diameter (11). A Zeiss TGZ-3 particle size analyzer was used to measure the projected area diameter of these particles from electron micrographs (12). The projected area diameter data for the dry NaCl crystals were converted to cubical salt crystal dimensions (Fig. 2b) and a density of 2.17 g/cm^3 was assumed before calculating the diameter of 0.9% NaCl solution droplets having an equivalent mass of NaCl.

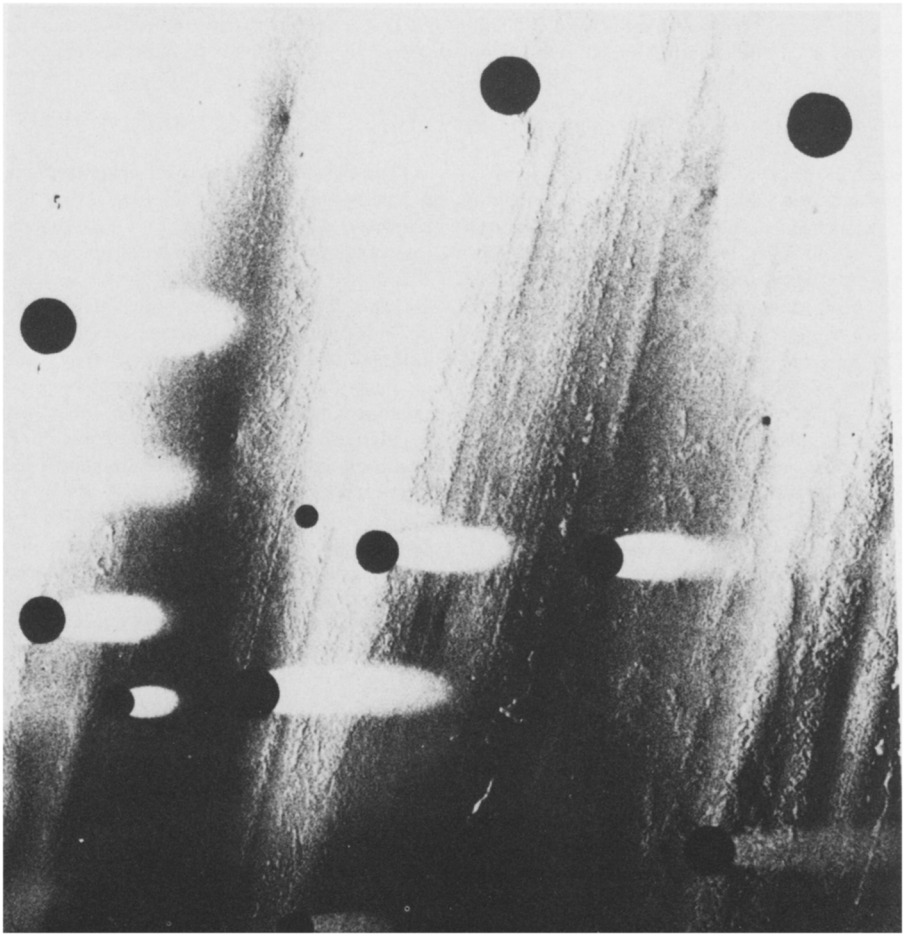

FIG. 2. (a) Transmission electron micrograph of sodium chloride particles generated from Acorn medical aerosol nebulizer. Droplets fixed by methyl-2-cyanoacrylate before electrostatic precipitator sampling ×4410. (b) Transmission electron micrograph of sodium chloride particles generated from Acorn medical aerosol nebulizer. Droplets dried by dilution air before electrostatic precipitator sampling. ×4410.

Figure 3 shows that the fixed droplet size distribution agrees fairly well with the calculated droplet distribution. The count mode diameter is 1.0 μm in both cases. However, the fixation and sampling process appears to cause a narrowing of the size distribution. Some of the droplets may be only partially fixed since the fixed CMD of 1.0 μm is 50% smaller than the calculated droplet CMD of 1.5 μm. Figure 3 also shows that most of the droplets larger than 2.0 μm are not found in the fixed aerosol samples. Some of these large droplets are lost by sedimentation and impaction in the fixation chamber and the sampling line before being collected in the electrostatic precipitator. Others may be only partially fixed with methyl-2-cyanoacrylate due to inadequate residence time in the fixation chamber; these may undergo further evaporation and be measured as smaller particles. The fixed particles seen between 0.2 and 0.6 μm that are not predicted from the dry NaCl measurements may be artifact particles formed by homogeneous condensation of monomer or

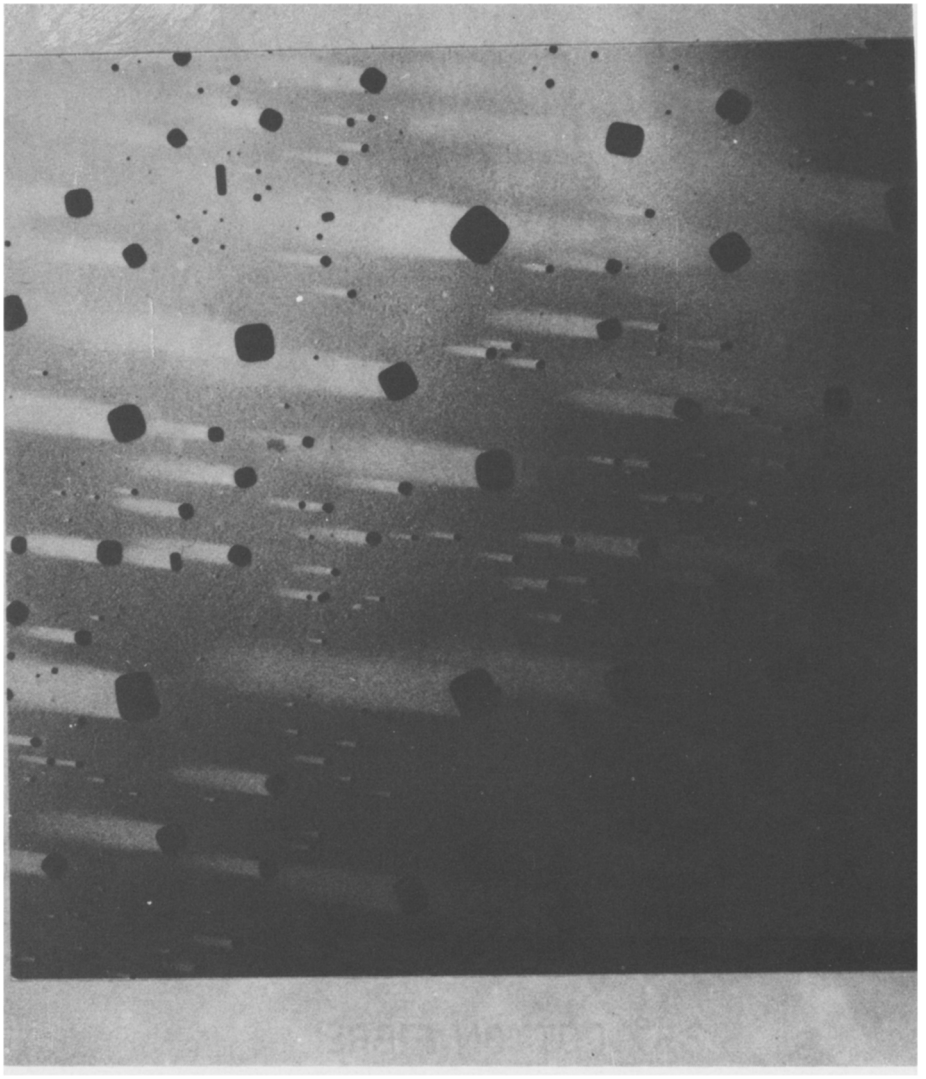

FIG. 2b. (*Continued*).

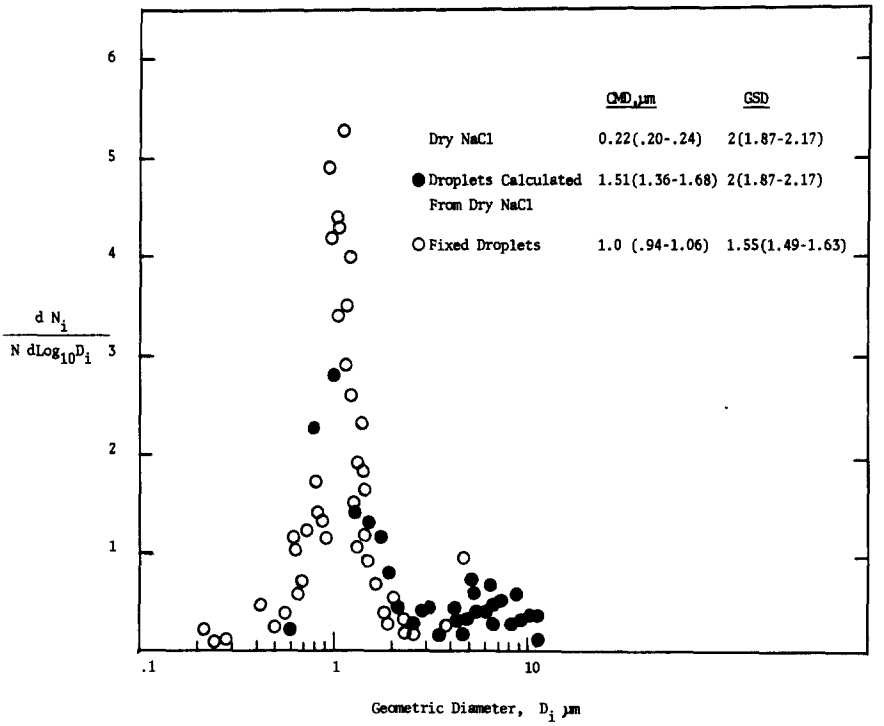

FIG. 3. The relative distributions of the number of fixed droplets and the number of droplets calculated from dry NaCl measurements, according to their geometric diameters. N_i = number of particles with diameter D_i. N = total number of particles measured. The 99% confidence limits of the CMD and GSD are given in parentheses.

heterogeneous condensation of monomer and H_2O vapor.

A separate test demonstrated that the fixation is complete for droplets of diameters up to 1.6 μm. Dry, monodisperse sodium chloride particles of 0.85 μm diameter (Fig. 4a) were produced from a vibrating orifice generator (13). This aerosol passed through a humidified chamber controlled at 75% relative humidity.

At this humidity the dry 0.85-μm sodium chloride particles grow in diameter by a known factor of 1.9 to form equilibrated saturated droplets of 1.62 μm (14). These droplets are then passed through the fixation flask. The resulting fixed spherical droplets were 1.59 μm in diameter (Fig. 4b). Small artifact particle formation was prevented in this test by controlling the quantity of monomer vapor.

We have also tested a range of fixation temperatures (20–80°C). In agreement with previous studies, 70°C was found to be the optimum temperature for obtaining the maximum degree of fixation. Below this temperature the 1.6-μm monodisperse saline droplets were not completely fixed and partial evaporation before fixation occurred at 80°C. We also found that by adding several drops of 3 N NaOH to the nebulizer solution, the fixing rate could be accelerated and we would obtain the maximum degree of fixation at 70°C.

These results show that the methyl-2-cyanoacrylate fixation method can determine the count mode of droplet aerosols from nebulizers which have a count mode less than or equal to 1 μm in diameter. Droplets larger than 2 μm in diameter cannot be completely fixed, which is in agreement with Carter and Hasegawa's (1975) results for tobacco smoke. The fixation method is still more complex and difficult to do than the conventional dry salt method for estimating droplet size. Much more work is required before it can be recommended for accurate characterization of polydisperse aerosol droplets from the ambient air or from nebulizers. Monodisperse aerosols should be used to study the fixation process over the range of sizes expected in polydisperse droplets.

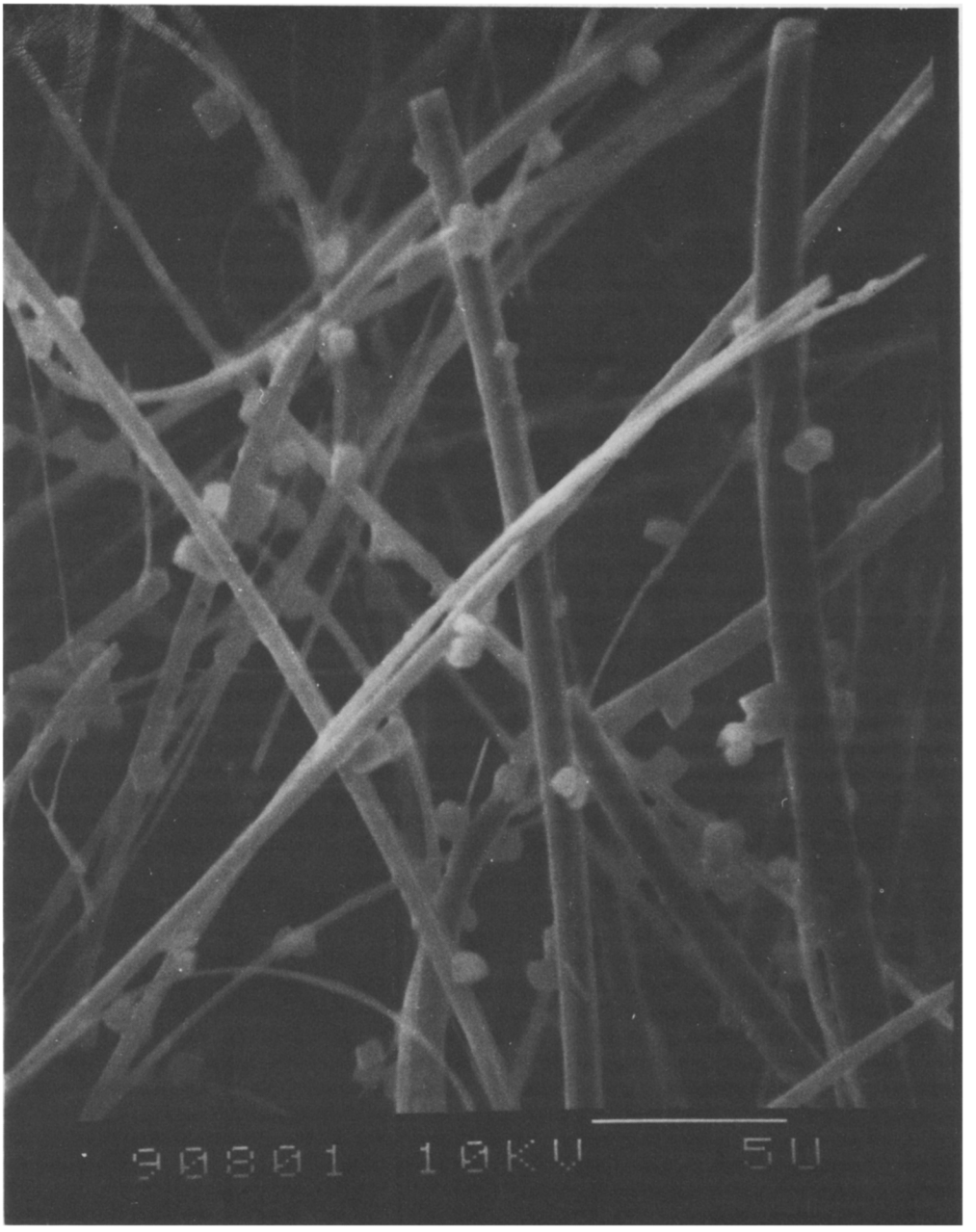

FIG. 4. (a) Scanning electron micrograph of 0.85-μm monodisperse sodium chloride particles generated from a vibrating orifice aerosol generator and collected on a fiber glass filter. $\times$3150.

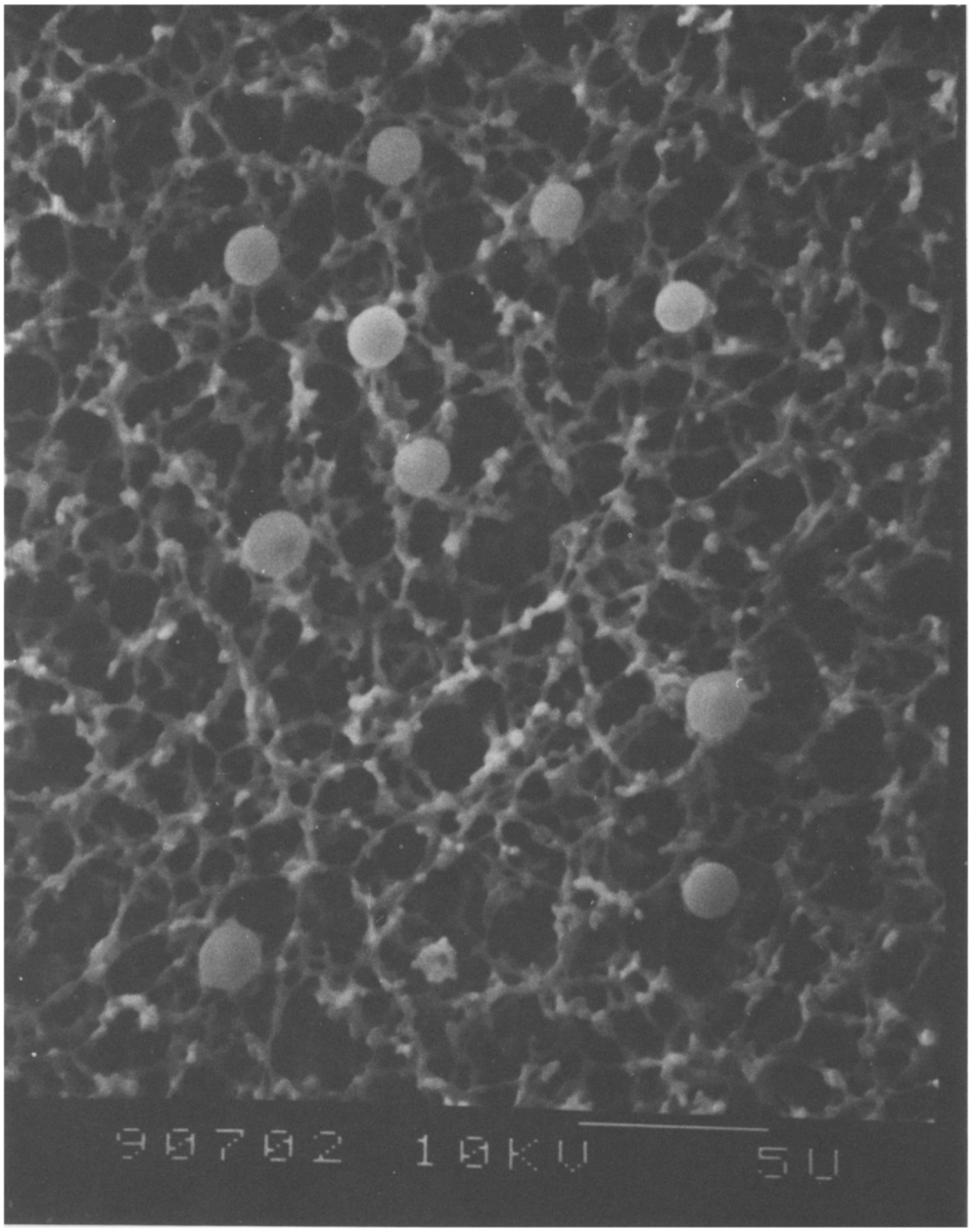

FIG. 4. (b) Scanning electron micrograph of 1.59-μm fixed saturated droplets grown from 0.85-μm dry NaCl crystals at 75% R.H. and collected on a membrane filter. $\times$3150.

REFERENCES

1. Morrow, P. E., *Amer. Rev. Resp. Dis.* **110,** 88 (1974).
2. Stober, W., and Flachsbart, H., *Atmos. Environ.* **7,** 737 (1973).
3. Ferron, G. A., Kerrebijin, K. F., and Weber, J., *Amer. Rev. Resp. Dis.* **114,** 899 (1976).
4. Porstendorfer, J., Gebhart, J., and Robeg, G., *J. Aerosol Sci.* **8,** 371 (1977).
5. Mercer, T. T., Tillery, M. I., and Chow, H. Y., *Amer. Ind. Hyg. Assoc.* **29,** 66 (1968).
6. Raabe, O. G., Fission Product Inhalation Program Annual Report, 1971–1972, LF-45, Lovelace Foundation, Albuquerque, New Mexico, p. 1.
7. Morie, G. P., Sloan, C. H., and Peck, V. G., *Beitr. Tabakforsch.* **7,** 99 (1973).
8. Phalen, R. F., Cannon, W. C., and Esparza, D., *in* "Fine Particles" (B. Y. H. Liu, Ed.), p. 732. Academic Press, New York, 1976.
9. Carter, W. L., and Hasegawa, L., *J. Colloid Interface Sci.* **53,** 134 (1975).
10. Morrow, P. E., and Mercer, T. T., *Amer. Ind. Hyg. Assoc.* **25,** 8 (1964).
11. Raabe, O. G., *Aerosol Sci.* **2,** 289 (1971).
12. Mercer, T. T., "Aerosol Technology and Hazard Evaluation," p. 66. New York, 1973.
13. Liu, B. Y. H., Berglund, R. N., and Agarwal, J. K., *Atmos. Environ.* **8,** 717 (1974).
14. Tang, I. N., Munkelwitz, H. R., and Davis, J. G., *J. Aerosol Sci.* **8,** 149 (1977).

ABRAHAM T. HO
KARL A. BELL
ROBERT F. PHALEN
ARCHIE F. WILSON

Departments of Medicine and Community and Environmental Medicine
University of California
Irvine, California 92717

Received June 18, 1979; accepted June 19, 1979