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Human Studies Project

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Fitzwilliam, N.H.
July 27th.

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Dr. Karl Z. Morgan
Oak Ridge Laboratories
Union Carbide Corp.
Oak Ridge, Tenn.

Dear Dr. Morgan:

I got back to Boston, after an extended trip, on July 14th and took with me, unopened, considerable mail. Your committee letter was in the package and I am ashamed and mortified that I did not notice I was asked certain questions. I hope you will excuse my apparent rudeness and do me the favor of sending such excerpts from this letter to the rest of your committee as seems wise to you. I do not know the addresses of most of them although the names are known to me.

As was in Richland July 1-3 and discussed some of these things with Dr. Parker and his colleagues. On my return I wrote him further and intend supplementing my original letter with suggestions from various of my colleagues but I have no great hopes of giving you the kind of answers I know you seek.

On a few things I have very definite information. First, all experimental approaches to dust and fume retention studies on man or experimental animals have been done with dust and fume clouds measured in milligrams per cubic meter and a milligram of respirable dust or fume contains anything from 300 million and more particles. The possibility of working with concentrations much below this range has never been of practical interest because we had no way of measuring inhaled or exhaled suspensions save in heavy doses. Therefore I doubt if you'll find any decent or practical analogy to the problem which vexes you gentlemen -- what is a reasonable retention figure at concentrations such as a few particles per unit volume.

$1 \frac{mg}{m^3} = mg/10^6 cm$ $\frac{10^3}{10^6} = 10^{-3} \mu g/cc$

$\frac{10^{-3}}{3 \times 10^8} = 3 \times 10^{-12}$ gm/particle

(Corresponds to 1 micron particle of $\rho = 6$ or to particles 1.4 micron (spheres) diameter $\rho = 2$.)

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Secondly, in an attempt to answer the question on the bottom of your page 2, all our retention studies on man were done at concentrations of tobacco smoke, MgO, and $CaCO_3$ in the concentration ranges indicated. Particle size of smoke was about 0.25 microns, MgO probably from less than 0.1 micron to about 0.5, and $CaCO_3$ from about 0.3 to about 1.5. The tobacco smoke and MgO particles sizes are controlled by the method of generation which is simple combustion. The limestone was ground up, sieved through 300 mesh and blown up in a cabinet of about 10'x 10'x 10'. Afte r 20 or 30 minutes settlement the subjects breathed the air from the cabinet and exhaled through an electrostatic precipitator into a large spirometer. Concentrations were measured from time to time in the cabinet and values plotted against age of the cloud so that concentrations at any moment were known. Since we collected all the material expired we could determine total retention but we could not tell where the material lodged -- in nose, mouth, lungs, trachea, etc.

Thirdly, there was some suggestion that nose breathers were better prepared for exposures to harmful dusts like silica than were habitual mouth breathers. Extensive experiments on animals and on man gave no support to such an idea. At dilute concentrations I do not believe the nose gives any useful protection.

Fourthly, particle size of dusts retained in lungs of men have been measured. Obviously the measurements had to be made on lungs taken at autopsy. Results compare remarkably closely with size frequency distribution of the limestone dusts we breathed in our own experiments. Of possible interest to you gentlemen is the strong indication that the sizing of the particles is purely physical and not physiological -- it is done by simple settlement in the air breathed. The 50% size of silicotic particles is a little below 1 micron and the chances of retaining extremely small particles or particles over say 5 microns is extremely slight. The probability curves appear in Drinker & Hatch's

Industrial Dust (McGraw -Hill) and from them you can make a pretty respectable guess at your chances of retaining particles of any particular size.

Fifthly, the trend in our results indicated not much difference in retention with concentration providing particle size remained constant. Such constancy of particle size applied all right to tobacco smoke and magnesia but not to limestone of which particle size decreased as concentration of the air suspension decreased.

You'll find we have 3 classes of particulates to consider and not just 2, soluble and insoluble. Perhaps 2 will satisfy your problem, I can't say. By soluble we mean those carried off by bodily secretions in the ordinary common sense chemical meaning of solubility. That is how we get rid of inhaled limestone and of xxxx zinc oxide. I don't see how there can be any disagreement about that.

A second group of substances is typified by carbon -- it can accumulate and remain in lung tissue apparently indefinitely and cause no trouble at all, providing exposures are not overwhelming.

A third group is typified by free silica, especially quartz, which causes tissue proliferation, silicosis, and invites infection by tuberculosis. But silicosis does not cause trouble unless concentrations are of the order of those I cited --milligrams per cubic meter.

I am unable to imagine any problem you have which remotely resembles silicosis -- your concentrations are too low and always will be.

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Parker queried me on the possible movement of an inhaled inert particle (insoluble) once it had bumped into the walls of an alveolus and become xxxxx wetted. It probably will drift around via phagocytes until it gets to a lymph node and there it easily might remain fixed. Frankly I think the chances of this happening in your practical AEC problems is fantastically slight.

A small item which easily may escape your committee is the fact that particles chemists think are insoluble can be taken up by bodily processes and appear in blood or urine surprisingly quickly after being breathed. For instance, an extremely insoluble lead compound and a managanese compound appeared in urine within minutes after intravenous injection. I should think this fact easily could be of significance in your problems.

I would think that the travel of an inhaled radioactive particle could be followed experimentally. There are a number of labs where such studies could be made and they might be fruitful.

Sincerely yours,

Philip Drinker