Commentary

Low-Toxicity Dusts: Current Exposure Guidelines Are Not Sufficiently Protective

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Exposure to low-toxicity dusts, which have previously been viewed as ‘nuisance dusts’, can cause chronic obstructive pulmonary disease or other nonmalignant respiratory disease. In Britain, the ‘de facto’ airborne exposure limits for these dusts have remained unchanged for >30 years; currently, they are 10 mg m\(^{-3}\) for inhalable dust and 4 mg m\(^{-3}\) for respirable dust. During this time, exposures in industry have decreased and although in the past, many occupational dust exposures may have exceeded these limits, today this is less likely. However, there is good evidence from epidemiology and toxicology studies that current dust exposures may still present a risk to workers and that for some of those who are affected, there are devastating health consequences. Numerous researchers and others have drawn attention to the necessity to control dust exposures to levels lower than are currently accepted in Britain. It is proposed that until regulators agree on the safe occupational exposure limits for low-toxicity dusts, health and safety professionals should consider 1 mg m\(^{-3}\) of respirable dusts as a more appropriate guideline than the value of 4 mg m\(^{-3}\) currently used in Britain.

Keywords: COPD; COSHH; inhalable dust; lung function; OEL; respirable dust

INTRODUCTION

Dusts are invariably complex mixtures with variable composition. Even materials that are often described as if they are homogeneous, for example, coalmine dust, are actually highly variable in composition. Some components in these airborne dusts are known to be toxic to humans when inhaled; the prime example of this is perhaps crystalline silica—most commonly found in the form of quartz. For more than a century, inhalation of high concentrations of fine (respirable) crystalline silica has been known to cause silicosis in stonemasons, miners, and other similar groups of workers (Corn, 1980). However, in the past, exposure to dusts with low crystalline silica content was not linked with toxicity and many were characterized as ‘nuisance’ dusts, whose effects were thought to be a mere irritation. The US Bureau of Mines explained:
Nuisance dust, or inert dust, can be defined as dust that contains less than 1% quartz. Because of its low content of silicates, nuisance dust has a long history of having little adverse effect on the lungs. Any reaction that may occur from nuisance dust is potentially reversible. However, excessive concentrations of nuisance dust in the workplace may reduce visibility (e.g., iron oxide), may cause unpleasant deposits in eyes, ears, and nasal passages (e.g., portland cement dust), and may cause injury to the skin or mucous membranes by chemical or mechanical action.

Mody and Jakhete (1987)

It has long been known that in coalminers, a population exposed to high levels of dust that has low toxicity, a form of parenchymal lung disease, coal workers’ pneumoconiosis, develops. This is characterized by large-scale dust accumulations in the terminal bronchiolar walls, with minimal fibrosis (macules) and occasional nodule formation. In addition, research over the past 20 years has shown that many, perhaps all, dusts previously considered inert can produce chronic obstructive pulmonary disease (COPD) or other chronic lung conditions from long-term exposures (Soutar et al., 1997). The term COPD encompasses the diseases chronic bronchitis and emphysema, which are characterized by the lung airways becoming narrowed, leading to limitation of lung airflow and dyspnea. A diagnosis of COPD is often based on lung function tests, measured as forced expiratory volume in 1 s (FEV₁) and the ratio of FEV₁ to forced vital capacity (FVC). COPD tends to be progressive and is poorly reversible.

Although by far the greatest burden of COPD is a consequence of cigarette smoking, the British Health and Safety Executive (HSE) says, ‘There is increasing research evidence that COPD can be caused or made worse by dusts, fumes and irritating gases at work’. They suggest that in Britain, ‘around 15% of COPD may be linked to work; 4000 COPD deaths every year may be related to work exposures; 40% of COPD patients are below retirement age; a quarter of those below retirement age are unable to work at all’. (HSE, n.d.) Work-related COPD is therefore linked to hundreds of deaths and much suffering, along with economic loss. These data are supported by a number of review publications, e.g. Blanc (2012).

Low-toxicity dusts include all poorly soluble, nonfibrous dusts that, at low levels of exposure, have negligible toxic effect on the body but if inhaled in sufficient quantity, accumulate and cause injury in the terminal airways and proximal alveoli, leading to inflammation with subsequent development of COPD and, in coalminers at least, pneumoconiosis. By this definition, low-toxicity dusts include a wide range of materials, some of which, such as barium sulphide dust, have occupational exposure limits (OELs) but many that do not. Low-toxicity dusts include mixtures containing amorphous silica, silicon, silicon carbide, pulverized fuel ash, limestone, gypsum, graphite, aluminium oxide, titanium dioxide, other mineral dusts with low crystalline silica content, and organic dusts free of harmful bacteria or biological toxins such as endotoxin, unless they are considered to be hazardous because of their biological component, e.g. flour dust. Soluble dusts are excluded from this definition because of their short residence time in the lung.

We suggest that the term ‘nuisance’ dust should not be used in relation to low-toxicity dusts as it erroneously implies that there are no health problems that might arise from exposure. This has already been implemented in many countries, with terms such as ‘particles not otherwise specified’ (PNOS) being substituted.

In this commentary, we argue that current limits for low-toxicity dust in Britain and elsewhere are not sufficient to protect health. We particularly highlight studies of coal dust because these low-toxicity dusts have been widely studied and we consider these data informative of the toxicity of low-toxicity dust more generally.

**EXPOSURE TO LOW-TOXICITY DUSTS AND HOW THESE EXPOSURES HAVE CHANGED OVER TIME**

In 1943, the British Medical Research Council published a monograph on Chronic Pulmonary Disease in South Wales Coalmines, in which Thomas Bedford and Clifford G Warner contributed a chapter on the airborne dust concentrations in the mines (Bedford and Warner, 1943). They made measurements with a range of instruments, including konimeters and thermal precipitators, and counted the number of particles collected using microscopic methods. From their data, they were able to estimate the particle exposure levels in air as number, mass, and surface area concentrations, with the latter two metrics calculated using size-distribution data. At the coalface in the five collieries they investigated, the average estimated mass concentration of particles >0.4 μm in diameter ranged from 23 to 230 mg m⁻³ and the corresponding values for particles 0.4–5 μm (respirable) were 12–43 mg m⁻³ (based on 20–118 samples each collected over a period of 10–20 min).
Today, airborne dust is often measured as the inhalable and/or respirable dust fraction [where the inhalable aerosol is the mass fraction of particles that can be inhaled into the nose or mouth, and the respirable aerosol is the mass fraction of particles that may reach the alveoli when inhaled, both formally defined in EN481 (CEN, 1993)]. Using internationally agreed sampling criteria, inhalable dust being the successor to the poorly defined ‘total’ dust. The relationship between these two measures depends on the size distribution of the aerosol. Okamoto et al. (1998) found that inhalable dust levels were on average 2.6 times the respirable dust levels (correlation coefficient = 0.78, on the log-transformed data), with inhalable-to-respirable dust ratios for specific dust types ranging from 2 (welding) to 5.1 (foundry work).

During the past ~40 years, the OELs for low-toxicity dusts have changed. In 1969, in Britain, the government adopted the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLVs®) for ‘Inert or nuisance particulates’, which was either 15 mg m\(^{-3}\) or 50 million particles per cubic foot (mppcf) of total dust containing <1% crystalline silica. By 1974, the limit was reduced to 10 mg m\(^{-3}\) or 30 mppcf, and by 1980, the TLV was expressed as the previous total dust limit and an additional respirable dust limit of 5 mg m\(^{-3}\). Today, ACGIH recommends guidelines (not TLVs) of 10 mg m\(^{-3}\) inhalable and 3 mg m\(^{-3}\) respirable for insoluble or poorly soluble particles not otherwise specified (PNOS) and although no sampling period is stated, it is assumed that the Committee intends these guidelines to be 8-h time-weighted average (TWA) exposures. These guidelines apply only to substances that do not have an applicable TLV, are insoluble or poorly soluble in water or aqueous lung fluid, and have low toxicity, i.e. do not cause toxic effects other than inflammation or the mechanism of ‘lung overload’ (ACGIH, 2012). In 1984, the HSE started to publish its own limits, and for these, it provided a limit for ‘dust not otherwise specified’ as 10 mg m\(^{-3}\) of total dust or 5 mg m\(^{-3}\) of respirable dust.

From 1988, the definition of a ‘substance hazardous to health’ within the new Control of Substances Hazardous to Health (COSHH) regulations in Britain included airborne dust of any kind at >10 mg m\(^{-3}\) of total inhalable dust and >5 mg m\(^{-3}\) of respirable dust, both as TWAs over an 8-h period (HSE, 1988) There was no specific OEL for these dusts and these values acted as a ‘trigger’ for the application of the Regulations. In 1997, the sampling criterion for respirable dust was revised and the value in the Regulations was reduced from 5 to 4 mg m\(^{-3}\); the change in number was intended simply to compensate for the change in sampling criterion and was not intended to be a real change in the ‘trigger’ value. The values 10 and 4 mg m\(^{-3}\) still apply and so the ‘exposure limits’ for most low-toxicity dusts have remained essentially unchanged since the early 1980s.

**EPIDEMIOLOGICAL EVIDENCE FOR THE RISKS ASSOCIATED WITH LOW-TOXICITY DUST**

Studies of British and US coal miners have consistently shown that chronic exposure to respirable dust is associated with outcomes linked to COPD, including loss of lung function, the development of respiratory symptoms, and COPD mortality (US National Institute for Occupational Safety and Health, NIOSH, 2011a). For example, data from British coalminers showed that chronic exposure to respirable dust was associated with impaired FEV\(_1\), with the effects being found among both smokers and nonsmokers (Soutar and Hurley, 1986). The effect was equivalent to a decline in average FEV\(_1\) of about 70 ml for an exposure to 3 mg m\(^{-3}\) for 20 years, although the magnitude of the effect on lung function was much greater in some groups of men, i.e. former miners aged <65 years with chronic bronchitis.

There has been increasing evidence from the epidemiological literature of impaired lung function associated with relatively low-level exposures to other low-toxicity dusts. For example, Soutar et al. (1979) carried out a cross-sectional study of workers exposed to polyvinyl chloride (PVC) dust at a large manufacturing site in England. The highest respirable dust levels were ~2.5 mg m\(^{-3}\). The study showed statistically significantly lower FEV\(_1\) among men with higher PVC dust exposure. The total loss was equivalent to 52 ml of FEV\(_1\) for the mean cumulative respirable dust exposure, equivalent to 0.7 mg m\(^{-3}\) for 20 years.

Gardiner et al. (2001) studied the respiratory health of carbon black production workers in seven European countries. The mean exposure to inhalable dust among the participants in the study was estimated to be 0.77 mg m\(^{-3}\) (range: 0.07–7.41 mg m\(^{-3}\)), although the levels were higher during the first phase of the research, which occurred 5–8 years earlier. Working for 40 years with a mean exposure of 1 mg m\(^{-3}\) was predicted to increase the prevalence of cough by almost 70% and the prevalence of cough and sputum production by 60%. The same 40-year exposure was predicted to result in an estimated loss of average FEV\(_1\) of 142 ml.
Other epidemiological studies have shown reduced lung function and COPD among workers exposed to a wide range of low-toxicity dusts. For example, Jaén et al. (2006) identified an association between symptoms of chronic bronchitis and airflow obstruction with employment in the textile industry. Bailey et al. (2007) found association of COPD with agricultural exposures and Harber et al. (2007) observed that self-reported exposure to fumes (not further specified), but not dusts, was associated with an increased rate of decline of lung function in workers with COPD.

The average reduction in lung function reported in most of these studies is relatively modest when compared with the effects of aging or cigarette smoking, but there will be a range of effects among an exposed population and some individuals will be more seriously affected. The HSE estimated that workers exposed to 4 mg m⁻³ of low-toxicity dust for 40 years would, on average, experience an additional 178-ml reduction in FEV₁ over and above the 1000- to 1200-ml change due to aging (Meldrum, 2006). However, at least 12% of those exposed in this way are considered to have a more marked loss in FEV₁ (627 ml) and they would be twice as likely as controls to report breathlessness. For the same exposure, 7% of people would suffer sufficient loss in FEV₁ (993 ml) for them to be three times more likely to report ‘walking slower than other people on the same level because of my chest’.

TOXICOLOGICAL EVIDENCE FOR THE NATURE OF THE HAZARD

Inhalation studies in laboratory animals using low-toxicity dusts have shown that at some critical dose, the normal clearance mechanisms involving alveolar macrophages breaks down and there is a linear accumulation of dust with no effective clearance. As a consequence, dust rapidly accumulates in the lung, causing inflammation, cell proliferation, fibrosis, and possibly cancer (Cullen et al., 2000). This phenomenon has been termed ‘rat lung overload’ to delineate it from any human effect because there is no human equivalent. Among other rodents, hamsters do not show overload and although mice show evidence of overload, the responses, especially in terms of pathological change, are quantitatively less than those shown by rats (Bermudez et al., 2002, 2004).

The phenomenon of rat lung overload was first described by Morrow, who posited that the particle volume burden was the key and that high volumes of particles within macrophages caused impairment of the ability of the macrophages to migrate and clear the particles from the lungs (Morrow, 1988). Evidence, however, quickly began to accumulate that the total particulate surface area in the lung was in fact the metric that determined the onset and extent of ‘overload inflammation’ (Oberdörster, 1996). For example, Tran et al. (2000) investigated the recruitment of polymorphonuclear leukocytes into the alveolar region and the rate of dust translocation to the lymph nodes for two low-toxicity dusts (barium sulphate and titanium dioxide). They showed that using mass or particle number to characterize the lung dose gave divergent dose–response relationships, but if particle surface area was used as the dose metric, then similar dose–response was seen for both dusts. The data suggested a threshold of the total surface area of particles in the lung of ~200–300 cm², i.e. below this dose, there was little or no effect. The authors concluded that a surface area dose metric ‘provides a unified, generic explanation of the behavior of “low toxicity” dusts across a wide range of size distributions’ (Tran et al., 2000). However, the phenomenon of rat lung overload has little relevance for human lung response at high lung burden of low-toxicity dust. As discussed herein, high lung burdens of low-toxicity dust in humans cause COPD primarily and pneumoconiosis only in the very highly exposed coalmining populations (Kuempel et al., 2001a, b). There is some evidence for increased retention of dust in the alveolar interstitial compartment in the lungs of coalminers at the very high lung burdens they experience (Kuempel et al., 2001a, b, Gregoratto et al., 2010). However, this is in contrast with the virtual cessation of clearance and subsequent rapid buildup of dust that accompanies rat lung overload, nor do we see the pathological consequences of rat lung overload—plication, fibrosis, and cancer—in humans. Recent reports have shown an association between increased risks of lung cancer in coalminers linked to their quartz exposures (Miller and MacCalman, 2010). Additionally, the International Agency for Research on Cancer (1997) concluded that there was inadequate evidence to classify the carcinogenic potential of coal dust (Group 3).

The difference in the response of rats and humans to high lung burdens of low-toxicity dust may be related to the very different handling methods of low-toxicity dust by human lungs compared with rat lungs, where humans tend to internalize low-toxicity dust in interstitial tissue throughout ongoing exposure, whereas rats do not (Nikula et al., 1997a, b); at the point of overload in rats, there is sudden internalization in the lung interstitium with profound pathological consequences. Monteiller et al. (2007) used an in vitro system involving epithelial cells to investigate whether the surface area of low-toxicity dust was a better measure
than mass for predicting inflammation. They tested a range of dusts, both fine particulates (carbon black, titanium dioxide, and barium sulphate) and nanoparticles (carbon black, titanium dioxide, nickel, and cobalt), in comparison with a highly active sample of quartz. Chemokine markers of an inflammatory response from epithelial cells were measured. In each case, the response from the quartz was substantially greater than that with the other particles. The nanoparticle titanium dioxide and carbon black both produced much stronger inflammatory responses than the same mass dose of the fine particulates of the same composition. However, when the dose was expressed in terms of surface area, all of the low-toxicity particles, including the two metal nanoparticles, produced a similar response. These data suggested a threshold, measured as surface area of particles relative to the surface area of the exposed cells, between ~1 and 10 cm² cm⁻².

Pauluhn (2011) recognizes that there is a common mode of action for low-toxicity dusts based on a chronic inflammatory response linked to lung overload, but he considers the particle displacement volume to be the most appropriate exposure metric. Based on an analysis of data from six different types of poorly soluble particles (i.e. ultrafine and pigmentary titanium dioxide, synthetic iron oxide (Fe₃O₄, magnetite), two aluminum oxyhydroxides, and multiwalled carbon nanotubes), he identifies a gravimetric threshold level for adverse effects of 0.5 ml m⁻³ (respirable) × agglomerate density.

The data and the discussion of the underlying mechanisms suggest that if dose is measured appropriately, such as using the surface area of dust, then all low-toxicity dusts will produce a similar biological response, which ultimately could result in chronic lung disease.

**IDENTIFICATION OF A SAFE LEVEL**

The epidemiological and toxicological evidence suggests that COPD or other lung injury may occur at levels of exposure below the present-day OELs (or COSHH trigger values). This is not a new observation; for example, >10 years ago, Cullen et al. (2000) highlighted that some ‘low toxicity dusts may have adverse effects at relatively low exposure concentrations . . . less than the United Kingdom (UK) occupational exposure limit’.

Given the diversity of dust mixtures that may be encountered, there is a need for a generic OEL; and from the discussion of the toxicological evidence, the OEL for low-toxicity dusts would ideally be expressed in terms of surface area of dust per unit volume of air inhaled (e.g. cm² m⁻³). In the 1940s, Bedford and Warner estimated exposure to coalmine dust using this metric based on the airborne number concentration and the size distribution of the aerosol, although in this case in relation to pneumoconiosis. Furthermore, although there have been considerable developments in measurement technology since then (e.g. LeBouf et al., 2011), it is still impractical to directly measure personal exposure to dust in terms of surface area.

Schulte et al. (2010) discussed the development of OELs for engineered nanoparticles, which have similar toxicity as other low-toxicity dusts when dose is assessed by surface area. The authors present the derivation of exposure limits for fine and nanoparticle titanium dioxide by the NIOSH. These suggested limits were based on the available animal toxicological data extrapolated to humans. The proposed limit for the fine (respirable) material was 1.6 mg m⁻³, based on the 95th percentile of the concentration predicted to give a 1 in 1000 excess risk of lung cancer, and for the nanoparticle, the corresponding limit was 0.19 mg m⁻³. They further suggested that titanium dioxide may be considered representative of a ‘whole class’ of poorly soluble low-toxicity dusts ‘where the risk for inflammation and cancer . . . is related to particle size and surface area’. Note that the final limits published by the NIOSH were 2.4 mg m⁻³ for fine titanium dioxide and 0.3 mg m⁻³ for the ultrafine material (NIOSH, 2011b). [In the NIOSH documents, ‘fine’ is defined as all particle sizes that are collected by respirable particle sampling and ‘ultrafine’, as the fraction of respirable particles having primary particle diameter <0.1 μm (<100 nm).]

In 1983, the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) set a limit value for occupational exposure to inhalable dust of 4 mg m⁻³ and, in 1997, a limit of 1.5 mg m⁻³ for respirable dust (Greim and Ziegler-Skylakakis, 2007). In 2012, the limit for respirable dust was reduced to 0.3 × A mg m⁻³ for dusts, where ‘A’ is the density of the dust in g cm⁻³ (Deutsche Forschungsgemeinschaft, 2012). To obtain the limit for a specific dust with different density, it is necessary to multiply by the dust density, giving, for example, a limit of ~0.6 mg m⁻³ for graphite, 0.7 mg m⁻³ for bauxite, 0.8 mg m⁻³ for many silicates, 1.3 mg m⁻³ for titanium dioxide, and 1.7 mg m⁻³ for hematite, all as respirable dust. The limit is intended to prevent inflammation from impaired clearance of particles from the lung and, thus, to exclude risks of more serious lung disease, such as lung cancer or pulmonary
A WAY FORWARD

We consider that research during the past >20 years has shown that many, perhaps all, dusts previously considered inert can produce serious health effects at long-term average exposures well below the British trigger values of 10 and 4 mg m\(^{-3}\). In many countries, exposure limits for coal dust and some other low-toxicity dusts are already less than these values. It therefore seems unwise to regard exposure to low-toxicity dusts below the COSHH trigger levels as safe. We believe it would be prudent to consider that such dusts should be covered by the COSHH Regulations because they represent a risk to health even though they have not been assigned Workplace Exposure Limits (WELs) or hazard classifications within the Registration, Evaluation, Authorization and Restrictions of Chemicals (REACH) Regulations of the European Union.

Exposure levels in workplaces have undoubtedly been decreasing over time and for low-toxicity dusts, the risk decreases as exposure decreases, and there is probably some threshold below which the risk is zero. However, the trigger for inclusion of these dust exposures within the COSHH Regulations has remained unchanged and so there is a danger that efforts to reduce exposure will be seen as unnecessary and the impetus for further improvements in exposure control may diminish.

A number of stakeholders in Britain and elsewhere have recently expressed concern about the current regulatory regime for these dusts. The Institute of Occupational Medicine (IOM) has suggested that, ‘until safe limits are put in place, employers should aim to keep exposure to respirable dust below 1 mg m\(^{-3}\) and inhalable dust below 5 mg m\(^{-3}\)’ (IOM, 2011). The British Trade Union Congress (TUC) has advised trade union health and safety representatives that they ‘should try to ensure that employers follow a precautionary standard of 2.5 mg m\(^{-3}\) for inhalable dust . . . and 1 mg m\(^{-3}\) for respirable dust’ (TUC, 2011). In Germany, the MAK commission has adopted a limit equivalent to 0.3 \(A\) mg m\(^{-3}\) respirable, where \(A\) is the density of the substance in g cm\(^{-3}\), which is equivalent to \(\sim 1.3\) mg m\(^{-3}\) for titanium dioxide. All three bodies, therefore, regard 1 mg m\(^{-3}\) for respirable dust as a more appropriate guideline than the 4 mg m\(^{-3}\) COSHH trigger. It would be prudent for health and safety professionals to take this information into account while giving advice.

We urge regulators in Britain and elsewhere to move to develop new, safe OELs for poorly soluble low-toxicity dusts.

REFERENCES


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