June 2023

The SCOEL recommendation document covers the following substances:

Substance name	EC number	CAS RN
Calcium oxide	215-138-9	1305-78-8
Calcium dihydroxide (Calcium hydroxide)	215-137-3	1305-62-0

This text is not part of the official SCOEL Recommendation and is provided to give additional helpful information to the reader as regards chemicals addressed by the SCOEL Recommendation. The list is non-exhaustive and is presented for information purposes only.

Recommendation from the Scientific Committee on Occupational Exposure Limits for Calcium oxide (CaO) and calcium hydroxide ($Ca(OH)_2$)

8-hour TWA:	1 mg/m^3 respirable dust
STEL (15 min):	4 mg/m^3 respirable dust

1. SUBSTANCES

Calcium oxide

Synomyms	Quick lime, quicklime, lime, unslaked lime
CAS no	1305-78-8
Mwt	56.08
Solubility in water	Disintegrate on contact with water in a strongly exothermal reaction (~1140 kJ/kg CaO)
Classification	Not classified in the EU

Calcium hydroxide

Synonyms	Hydrated lime, slaked lime, lime milk, milk of lime
CAS no	1305-62-0
Mwt	74.10
Solubility in water	1.85 g/L at 0˚C and 0.71 g/L at 100˚C
The pH of the aqueous solution is	At 25˚C, pH=11.3 at 0.1g/L and 12.7 at 1.8 g/L
Classification	Not classified in the EU

2. OCCURRENCE AND USE

The term lime refers to quicklime and, less frequently, to hydrated or slaked lime. Sometimes it is incorrectly used to describe limestone. Quicklime is produced by thermal decomposition (calcination) of limestone ($CaCO_3$) in shaft or rotary kilns at temperatures ranging from about 1100 to 1300˚C. Calcium oxide is used in the production of iron and steel, glass, calcium carbide, aerated concrete, and for soil stabilization (Oates 1990) as well as for a thermochemical reaction with industrial wastes (Cheong et al. 2007). About half of the CaO production is used for preparing $Ca(OH)_2$ (Oates 1990).

Hydrated lime refers to a dry $Ca(OH)_2$ powder, while slaked lime refers to an aqueous suspension of $Ca(OH)_2$ particles in water, which is also the case with milk of lime. Hydrated lime is used in the production of sodium carbonate (soda ash) by the Solvay (ammonia-soda) process. It is used in metallurgy, in refining of sugar beet extract, in lime-cement-sand mortars and for water treatment to remove hardness, for sewage treatment where it precipitates phosphates, for neutralization of acids in industrial waste, for flue gas desulphurization, for production of bleaching powder (calcium hypochlorite), for soil stabilization and a wide range of other purposes (Oates 1990). In humans, $Ca(OH)_2$ is used in endodontic root canal filling materials (e.g. Geurtsen and Leyhausen 1997).

Commercial lime can contain hexacalent water-soluble chromate (Cr(VI)). A German study found a median content of about 2 mg/kg with a range from 0.3 to 10 mg/kg with raw materials from different geographic locations (Weiler and Rüssel 1974).

Alkaline effects of cement as surrogate for alkaline effects of calcium oxide and hydroxide.

Due to the limited data on CaO and $Ca(OH)_2$, this document reports data on cement effects on the similar endpoints as for CaO and $Ca(OH)_2$ due to the approximately similar alkalinity; the pH is determined by the hydroxyl ion concentration.

Cement is a mixture of clay and limestone that has been calcinated at about 1400˚C (Prodan and Bachofen 1998); a small amount (~3%) of quartz sand, sandstone or limestone may be added as raw material (Jakobsson et al. 1993). The calcinated clinker is milled to Portland cement that formally consists of CaO (65%), SiO_2 (~20%), Al_2O_3 (~5%), Fe_2O_3 (~4%) and MgO (< 5%), but is a mixture of tricalcium silicate, bicalcium silicate and CaO. Normally, Portland cement does not contain free (crystalline) silica, but raw materials containing diatomaceous earth may change the amorphous silica into the crystalline SiO_2, cristobalite, during the calcination (Prodan and Bachofen 1998).

Portland cement is by far the most used type of cement. Its two main components are tricalcium silicate (alite, $CaSiO_5$) and dicalcium silicate (belite, $CaSiO_4$) comprising about 55 and 20%, respectively. Both compounds react with water and form the same calcium silicate hydrate and $Ca(OH)_2$:

$2CaSiO_5 + 6H_2O \rightarrow 3CaO{\bullet}2SiO_2{\bullet}3H_2O + 2Ca(OH)_2 + heat$

$2CaSiO4 + 4H_2O \rightarrow 3CaO{\bullet}2SiO_2{\bullet}3H_2O + Ca(OH)_2 + heat$

The reaction with water causes a rapid increase in alkalinity due to saturation or supersaturation with $Ca(OH)_2$. Also, the minor content of alkali metal (Na^+/K^+; Me) sulphate (low percentage) will increase the alkalinity of the mixture due to the reaction:

$Ca(OH)_2 + Me_2SO_4 \rightarrow CaSO_4{\downarrow} + 2MeOH$

Additionally, the content of Na_2O (< 1%) in cement causes an increase in alkalinity:
$Na_2O + H_2O \rightarrow 2\ NaOH$

Overall, addition of water to cement can raise the pH which may exceed 13, and thus a more alkaline mixture than that from CaO and $Ca(OH)_2$ (Helmuth et al. 1979). Using the alkaline effect of cement as proxy for effects of CaO and $Ca(OH)_2$ may be considered a worst-case scenario and thus if an exposure effect is absent with a certain exposure level of cement an effect is not expected at the same exposure level of CaO and $Ca(OH)_2$.

With water, cement forms a highly alkaline mixture as is the case with CaO and $Ca(OH)_2$. However, if reactions from cement and its products are used to predict the effects of CaO and $Ca(OH)_2$ effects other than from alkalinity have to be taken into account in the interpretation of the results.

Cement contains hexavalent chromium. Until the addition of ferrous sulphate became a common procedure, cement contained about 5-10 mg Cr(VI)/kg of cement (Prodan and Bachofen 1998); a content of 20 mg Cr(VI)/kg has also been reported (Jakobsson et al. 1993). After the addition of ferrous sulphate, the level of Cr(VI) decreased to less than 2 mg/kg (Prodan and Bachofen 1998). Cement is used as a binding agent in mortar and concrete which is the mixture of cement, gravel and sand (Prodan and Bachofen 1998).

Sand (crystalline silica) is used in preparation of ready-to-use mixtures (Sacharov 1998) and, previously, cement was used in asbestos-cement products where fibre concentrations were substantial prior to the 1960s (Weill 1994).

Examples of exposures to CaO and cement are shown in Table 1. Only few quantitative exposure data were retrieved on CaO from occupational settings. More data are available on exposure to Portland cement, where exposure levels are highly dependent on the geographic areas. Due to the differences in cement exposures, this allows construction of exposure-response relationships that will be used as proxy for CaO exposures.

3. HEALTH EFFECTS

The systemic effects of CaO and $Ca(OH)_2$ are negligible at normal occupational exposures, i.e. excluding accidental exposures. Thus, 1 mg/m^3 of CaO or $Ca(OH)_2$ contain 0.71 and 0.54 mg Ca/m^3, respectively. Assuming an exposure level of 1 mg/m^3 and an inhalation of 10 m^3 during an 8-hour workday, this result in an inhaled dose of 7.1 and 5.4 mg calcium per day, respectively. Overall, occupational exposures add a negligible body burden of calcium as the Tolerable Upper Intake Level is 2500 mg/day (Flynn et al. 2003).

Calcium oxide reacts with water on the external surfaces of the body and is converted to $Ca(OH)_2$, which liberates OH^- ions, affecting the skin and the mucous membranes. In consequence, effects on internal organs (including i.a. reproductice effects) are not relevant for the setting of an occupational exposure limit (OEL) due to the tightly regulated pH of the body. Where cement exposures are used for evaluation of respiratory effects of CaO and $Ca(OH)_2$ the major confounders may be exposure to asbestos, crystalline silica and smoking. For example, asbestos and smoking can accelerate loss of lung function (e.g. Siracusa et al. 1988).

Accidental oral ingestion of alkalis causes the most severe corrosive effects on the oesophagus, rather than the stomach, except at deliberate ingestion of a large quantity. In this case both the stomach and the small intestine may be involved. Such injuries increase the risk of oesophagal cancer. Thus, the incidence of carcinoma following oesophagal injury from sodium hydroxide ranges from 0.8 to 4% (IPCS 1998). This suggests that the modest inhalation of CaO and $Ca(OH)_2$ by occupational airborne exposures is less likely to affect the stomach. Also in healthy individuals, it is not biologically plausible that low level exposures to CaO or $Ca(OH)_2$ cause effects in or below the stomach as CaO and $Ca(OH)_2$ are expected to be neutralised by the acidic gastric juice; the gastric hydrochloric acid secretion is regulated by neuronal, hormonal, and paracrinic pathways (Geibel and Wagner 2006; Hou and Schubert 2006; Martinsen et al. 2005), where the pH is kept below 4.0 in healthy individuals (Geibel and Wagner 2006; Martinsen et al. 2005). The daily HCl production is 1-2 litres with a concentration of about 0.15mol/L (Geibel and Wagner 2006).

Hexavalent chromium (Cr(VI)) can cause skin allergy and cancer (SCOEL/SUM/86). The low level of Cr(VI) in lime (10 mg/kg=10 μg/1000 mg is used as the upper limit) and the current low level of airborne exposures (set to 1 mg lime/m^3) suggest an exposure concentration of about 10^{-2} μg/m^3 of Cr(VI). Excess lung cancer in 1000 male workers exposed for a working life is 0.1-0.6 at 1 μg Cr(VI)/m^3 (SCOEL/SUM/86). This predicts an expected life-time excess number of cases of 1 to 6 per 1 million exposed individuals (i.e. a life time risk of 10^{-6} to $6 \cdot 10^{-6}$) from a 1 mg lime/m^3 exposure at the maximum chromate content. This low risk indicated from the worst-case scenario is not considered relevant in the further evaluations undertaken for setting an OEL.

Where effects of cement, due to its content of compounds with alkalinity similar to that of CaO and $Ca(OH)_2$, is used as a proxy for effects of CaO and $Ca(OH)_2$, other effects of cement not related to effects of CaO and $Ca(OH)_2$ need to be taken into account. The previous level of Cr(VI) in cement (~10 mg/kg) and the current low level (2 mg/kg) suggest neither a substantial carcinogenic effect from the Cr(VI) content in cement as long as the evaluations are limited to a few mg/m^3 of cement, which is seen from the above calculations. Overall, using low level cement exposures as a proxy for elucidation of carcinogenic effects of CaO and $Ca(OH)_2$ are not expected to be biased by content of Cr(VI).

Where cement exposures are used for evaluation of carcinogenic effects of CaO and $Ca(OH)_2$, the effects should be limited to the respiratory tract, the oral mucosa and the oesophagus. Major confounders may be exposure to asbestos, crystalline silica (SCOEL/SUM/94) and life style factors such as smoking and alcohol consumption. Major differences may appear in smoking patterns in different occupational groups. For example, 50% of concrete workers in Sweden were smokers compared to 35% in the general population (Knutsson et al. 2000). Head and neck cancer is strongly associated with smoking and alcohol consumption (Forastiere et al. 2001; Maier and Tisch 1997), but low intake of vegetables, low level of education and different types of occupational exposures were also associated with laryngeal cancer (Maier and Tisch 1977; Maier et al, 2002).This indicates that the control group has to be very similar to the exposed group (Rasmussen et al. 1977) or appropriate corrections have to be applied, which may not always have been the case in the evaluated epidemiological studies.

All together, the main effect of CaO and $Ca(OH)_2$ is the alkali effect, although CaO develops heat by reaction with water and causes desiccation of tissue. Per unit mass, CaO forms slightly more OH^- ions than liberated from $Ca(OH)_2$, but the difference is considered without toxicological importance. In consequence, a common OEL is proposed for the two substances.

3.1. Injuries of the skin

In the U.S. private industry, the median days away from work (DAFW) due to occupational dermatitis was two to four days for most exposures, but CaO and $Ca(OH)_2$ caused a median of nine DAFW, with 27% having more than 20 DAFW in 1993 (Burnett 1998). A review dealing with cement burns from 1960 to 2000 found that 62% of the injuried had to be treated as inpatient. The mean duration of hospital stays was 21 days for the cement burns (Spoo and Elsner 2001). A study of 3194 referrals to an UK hospital centre for burns and plastic surgery in the period from 1998 to 2001 showed that 71 referrals (2%) were related to cement burns. Thirty-seven patients required in-patient hospital treatment. The median length of hospital stays was 3 days (range: 1-22 days), but if an operation was required the median stay was 9 days (Lewis et al. 2004). In the Tasmanian Burn Unit, hospitalization occurred infrequently from skin burn due to lime (~0.2%) and cement (~1%) exposures (Ricketts and Kimble 2003).

Aqueous suspensions of CaO, $Ca(OH)_2$ and cement are highly alkaline (pH~12-13) and can remove lipids from the skin and cause drying, cracking and irritant contact dermatitis (Winder and Carmody 2002). The effect from the high alkalinity can increase to ulcer formation and frank skin burn (Spoo and Elsner 2001; Winder and Carmody 2002). Illustrative examples are shown in Table 2.

3.2. Eye injuries

Eye injuries caused by calcium oxide, including cement, and calcium hydroxide are known world wide from accidents.

In a Norwegian study, 276 patients with burn of the eyes were referred to the department of ophthalmology at a university hospital. Burns due to cement accounted for 8% of the referred patients (Midelfart et al. 2004). In a study of 172 chemical eye burns referred to two university hospitals in Finland, 20 patients (12%) had been exposures to mortar or cement and 5 patients (3%) had been exposed to $Ca(OH)_2$ (Saari et al. 1984). In an Australian study with 121 patients admitted between 1987 and 1998 (Brodovsky et al. 2000), lime and plaster accounted for 36% of the alkali burns of the eyes in patients admitted to a tertiary care ophthalmic hospital. In a study from the Northern India (Saini and Sharma 1993), causes of chemical eye injuries were investigated in 102 consecutive patients treated at the Eye Department at a major referral centre. Calcium hydroxide was implicated in 12% of the eye injuries. Examples of eye injuries are indicated in Table 3.

3.3. Sensitization

No study showing that CaO or $Ca(OH)_2$ cause sensitization or development of allergy has been retrieved. Allergic contact dermatitis has been observed from Cr(VI) in lime,

but the risk is considered lower than the risk from cement (without addition of ferrous sulphate) as lime, in general, has a lower content of Cr(VI) (Weiler and Rüssel 1974)

3.4. Acute effects in humans

CaO and CaOH

During anesthesia, emission of $Ca(OH)_2$ dust from the anesthesia machine caused decrease of lung compliance and wheezing; recovery was uneventful (Lauria 1975).

Individuals (N=315) from 23 plants producing CaO and $Ca(OH)_2$ from limestone were evaluated one day after exposure. Thus, 32% were exposed to CaO, 12% to $Ca(OH)_2$ and 16% to both CaO and $Ca(OH)_2$, and 40% to neither of the compounds. Those exposed to $Ca(OH)_2$ had more eye (Risk Ratio=1.9), nose (4.7), and throat irritation (3.0) as well as acute cough (3.1) than those exposed to neither of the compounds. Those exposed to CaO showed less elevated risk ratios for nose and throat irritation (Wegman et al. 1992). It is noted that it is not possible to evaluate the relative potency of the irritant effect of CaO and $Ca(OH)_2$ from this brief report as the exposure levels were not reported. It is less biologically plausible that CaO is less irritating than $Ca(OH)_2$ as CaO per unit mass forms more hydroxide ions at hydration, being strongly desiccating and its reaction with water is highly exothermal.

Effects of CaO were studied in 12 lightly exercising men breathing through the nose. They were exposures for 20 mins. at 1 to 5 mg/m^3. The parameters studied included nasal resistance, nasal secretion, mucociliary transport time, and chemesthetic magnitude (for example, irritation, pungency, piquancy, cooling and burning), which was calibrated to pungency of CO_2. Each subject served as his own control. The mass median aerodynamic diameter and the SD was 6.53±0.76. Feelings were maximal in the nose, slightly lower in the throat and much lower in the eyes. The blank exposure (0 mg/m^3) corresponded to about 7% CO_2 in the nose and the throat. The CaO exposures caused a steady increase in irritation during the 20 mins. period and no steady state level was reached. In the nose, 1 and 2 mg/m^3 gave rise to an equivalent effect at the end of the exposure, which corresponded to the irritation effect of about 15% CO_2. The 5 mg/m^3 level had an effect equivalent to 20% CO_2. The values were significantly above the background. No significant effect occurred in nasal secretion and mucociliary clearance, determined by the saccharin test. The small effect in nasal airway resistance was ascribed to the exercise. The study interpreted the effects as "very few people used the term irritation to describe the nasal sensation evoked by 10% CO_2. Some would use that term at 15 % CO_2 and the majority would use it at 20 % CO_2" and also the authors conclude "that the psychophysical judgements produced results consistent with the known effect that calcium oxide would evoke irritating chemesthesis at exposures in the range of 2 to 5 $mg/m^{3"}$ (Cain et al. 2004). Two circumstances have to be taken into account. First, the trigeminal nerve chemesthetic threshold is not equivalent to an adverse sensory irritation effect (Nielsen et al. 2007). It is deemed that the effects of CaO, which were not dose dependent in the range from 1 to 2 mg/m^3, were of no adverse health significance. Secondly, the effect had not reached the maximum within the 20 mins. of exposure although the effect was levelling off. Taking these two facts into account, an exposure limit of 1 mg/m^3 is deemed to protect against adverse sensory irritation.

A recent study (Cain et al. 2008) investigated the airway effects of 2.5 mg/m^3 CaO in 6 male and 6 female volunteers, age 18-35 years, who were exposed for 45 min. The mass mean aerodynamic diameter was 6.5 μm and the geometric standard deviation 2.6. The sensory effects were highest in the nose, lower in the throat and lowest in the eyes. The maximum effect was reached about 30 min after the initiation of the exposure that was followed by adaptation. The maximum effect in the nose was equal to that of 17% CO_2. Dilution of CaO with $CaSO_4$ (1:9) showed that the effect of the mixture was driven entirely by CaO. The authors interpreted their results as "people would agree that feel in the niose becomes irritating about 17-18% carbon dioxide". Thus, the 2.5 mg/m^3 level can be considered at the LOAEL. Overall, considering the effect at the 2.5 mg/m^3 level, the limited number of subjects in the study and that sensory irritation increases as a monotonic function, these suggest that an OEL of 1 mg/m^3 can be derived from this study and that is in agreement with the results from the previous study (Cain et al. 2004).

These studies place sensory irritation among the critical effects.

Cement
In a cross-sectional study (Ali et al. 1998), Portland cement workers (N=149) in Saudi Arabia were compared with a control group (N=348) for evaluation of acute effects on lung function during a workday by comparing the changes in pre- and post shift values in the two groups. Indices were forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC%, and forced mid-expiratory flow ($FEF_{25-75\%}$), which were adjusted for age, duration of service, pre-shift value, and smoking. At kilns, clinker milling and cement packing, the mean respirable dust concentrations were 7 (2-22), 11 (7-17), and 15 (4-26) mg/m^3, respectively, with the range in parenthesis. The cement workers developed significantly more bronchoconstriction during the workday. No effect was seen on FVC. At cement production, mean respirable dust levels in the range from 7 to 15 mg/m^3 caused acute airflow obstruction in the exposure range, which also causes an effect on long-term lung function.

Effects of repeated exposures in animals

Two-year daily painting of ears of 12 mice with an aqueous extract of lime, betel vine leaves, betel nut, "gambir" and dried tobacco caused thickened, hardened and partially ulcerated skin with keratin filled cysts and inflammation. Infections of the painted areas were common. Squamous carcinoma of painted ears was seen in two animals. Additionally, one animal had a benign squamous papilloma and one a reticulum type sarcoma (Muir and Kirk 1960). It is noted that the study lasted for up to 32 months, had a low number of animals, had no control group, and the exposure was to an undefined mixture. A similar study with 41 mice was in progress, showing similar skin lesions with epidermal changes, ulcerations and infections. Unequivocal malignancy was not observed. Ten animals had died. Presumably, the study had been in progress for about 13 months. This part of the study was ill reported.

The effects of $Ca(OH)_2$ were studied by administration into the hamster cheek pouches (Dunham et al. 1966). The exposure-effects were compared with the effects in a control group, which was administered a "non-peptizable homogenous mixture of amylase and amylopectin derived from cornstarch, together with 2% magnesium oxide". The treatments were started when the hamsters were about 4 weeks old and they lived out

their life spans, i.e. they were found dead or were killed when moribund. The control group (4 animals) was treated with 250 mg/day 5 days/week, followed by 50 mg/day, 5 days/week. None of the animals had pouch lesions and none of the animals developed tumours. In the $Ca(OH)_2$ group, 250 mg was administered 5 days/week for the first two weeks, followed by 250 mg/day for 3 days/week until about the 40^{th} week and then by 250 mg/day, 5 days/week. All 6 animals had pouch lesions and 2 animals had bowel cancer. In another group, 6 animals received 50 mg/kg $Ca(OH)_2$ in the morning and 50 mg starch mixture 3-5 hours later. Treatment was for 5 days/week. All animals had pouch lesions and 1 animal had granulosa cell tumour of ovary. Additional groups were treated with $Ca(OH)_2$ and gambier or snuff. The hamsters in the $Ca(OH)_2$ groups had chronic inflammation and ulcers in the cheek pouch together with hyperplasia, hyperkeratosis, increased cells in stratum spinosum (acanthosis) and cellular atypia of the epithelium. The forestomach of animals, which received $Ca(OH)_2$, were usually normal though few animals (2/29) showed slight hyperkeratosis and epithelial hyperplasia; the groups were treated with $Ca(OH)_2$ alone or together with gambier, snuff or starch. It is noteworthy for the interpretation of epidemiological findings that few of the $Ca(OH)_2$ treated hamsters had reactions in the forestomach although the doses were considerable; assuming that the body weight of a hamster is 100 g, the exposure would correspond to a $Ca(OH)_2$ dose of 0.5 to 2.5 g/kg/day. The study had a low number of animals in the groups.

In another long-term study (Sirsat and Kandarkar 1968), the palate and buccal mucosa were painted 5 days/week with a commercially sold $Ca(OH)_2$ for betel chew in Wistar rats. The rats were kept on a standard laboratory diet. The treatments lasted up to 12 months. The controls were painted similarly but without $Ca(OH)_2$. The treatment caused marked epithelial cell hyperplasia, cytoplasmic vacuolation, prominent stratum granulosum, hyperkeratosis, and epithelial cord invagination into the corium. The submucosal connective tissue showed proliferation of fibroblasts, oedema, connective tissue hyalinisation, chronic inflammatory exudation and dilated blood vessels. Similar reactions were seen in groups of $Ca(OH)_2$ treated rats on a protein deficient diet, vitamin B deficient diet, and in animals on the standard diet treated locally by deoxycorticosterone acetate on the palate. A total of 139 animals were included in the studies and 115 were treated with $Ca(OH)_2$. No epithelial malignancy was detected. It is noted that the treatment was not life long and the dose was not well defined.

In a life-long study, tobacco, $Ca(OH)_2$ and tobacco, or $Ca(OH)_2$ and vitamin A and tobacco were applied into the cheek pouch of hamsters. The treatments were three times per week and the respective groups contained 30, 41 and 41 animals. In the animals treated with $Ca(OH)_2$, severe epithelial changes were observed, which were similar to those seen in the human buccal mucosa of individuals addicted to the betel chew. Nevertheless, the epithelial changes in the hamsters did not progress to malignant changes (Kandarkar et al. 1981).

These studies indicate that long-term direct skin or mucous membrane contact with $Ca(OH)_2$ cause severe local alterations, which have been confirmed in other studies (e.g. Kandarkar and Sirsat 1978). The severe reactions, which include persistent inflammation, have to be taken into account in evaluations. Thus, chronic inflammation may play a role in the development of cancer, for example, due to cytokine induced suppression of apoptosis, promotion of cell proliferation and angiogenesis (Aggarwal et

al. 2006). Also, inflammation causes production of reactive oxygen species, which may cause DNA damage (Aggarwal et al. 2006).

Effects of repeated studies in humans

Case studies- Cement dust

Four males, 28 to 50 years old and exposed to cement dust for 5 to 17 years, reported cough (3/4), phlegm (3/4), wheeze (2/4), dyspnoea on exertion (1/4), and asthmatic attack (1/4). One had emphysema; he had been exposed for 17 years. Three were light smokers (3 to 5 cigarettes/day) and one was a non-smoker. None had pneumoconiosis and none had tuberculosis. The sputum contained $Ca(OH)_2$ and $CaCO_3$ crystals, and it had a pH of 10 (Eid and el-Sewefy 1969). Thus, it is noted that the similarity between cement dust and dust from CaO and $Ca(OH)_2$ extends beyond the similarity of pH.

Epidemiological studies – CaO and $Ca(OH)_2$

Individuals (about 580) from 31 plants producing CaO and $Ca(OH)_2$ from limestone were studied for chronic effects. Exposures were to CaO, $Ca(OH)_2$ or both, and to neither of the compounds. Those usually exposed to $Ca(OH)_2$ had more chronic cough (Risk Ratio=1.5), phlegme (1.3), bronchitis (1.4), wheeze (2.2), chest tightness (1.7) and dyspnoea (2.2) than those exposed to neither of the compounds. Similar results were not presented for those exposed to CaO. These findings were similar when stratified by smoking habits, although non-smokers had increased relative risks (Wegman et al. 1992). It is noted that it is not possible to evaluate the relative potency of the offending effects of CaO and $Ca(OH)_2$ from this brief report as the exposure levels were not reported. It is less biologically plausible that CaO is less offending than $Ca(OH)_2$ as CaO per unit mass forms more hydroxide ions at hydration, is strongly desiccating and its reaction with water is highly exothermal.

In a Belgian cross-sectional study, the effect of lime production was studied in 75 employees. The study comprised clinical investigations, X-ray pictures of the thorax, ECG and a study of the lung function. The prevalence of chronic bronchitis among the lime exposed was 6/13 (46%) and 3/20 (15%) among individuals, who were neither exposed to lime nor to silica; the mean (±SD) age of the two groups was 46±8 years and 39±11 years, respectively. Silicosis was not observed among the two groups, but two cases of mild silicosis were observed among the other groups. All exposed groups had VC, FEV_1, residual volume and diffusion capacity within the respective normal range; smoking decreased the lung function. The exposures were not well characterized, but the maximum dust level at one position was 620 mg/m^3. All dust samples contained silica (0.03-1%) (Lahaye et al. 1987).

The effects of lime dust were studied in Finnish pulp-mill workers in an intervention study (Torén et al. 1996). In the lime kiln department, 15 workers were compared with 15 matched unexposed referents from the transportation and office departments. The mean total dust level among the kiln workers was 1.2 mg/m^3 (range: 0.4-5.8 mg/m^3) and the temperature was 42˚C. There was no statistically significant difference in self reported symptoms, nasal bleeding, crusts in the nose, nasal blockage and nasal

secretion. Neither did the clinical examination reveal statistically significant more inflammation in the nose and throat among the exposed workers, nor was any statistically significant difference observed in FEV_1, FVC, FEV_1/FVC (%), nasal peak expiratory flow or in eosinophilic cationic protein, myeloperoxidase and hyaluronic acid in the nasal lavage fluid. In contrast, the nasal mucociliary clearance was significantly longer (mean and range: 13.4 min and 6.0-26 min) in the exposed group compared to the controls (10.0 min and 4-20 min), determined by the saccharin test. After rebuilding the kiln, the mean total dust level was reduced to 0.2 mg/m^3 (range: 0.1-0.6 mg/m^3) and the temperature to 28˚C. The mean saccharin transition time normalized in the exposed workers (8.6 min and 1.4-15 min) and it was no longer different from the mean value in the controls (10.2 min and 5.5-20 min). The authors interpreted the normalization to be due to the decrease in the lime dust level, but mentioned that some influence of reduced temperature cannot be excluded. Overall, the NOAEL for all effects, except the nasal mucociliary clearance, is 1.2 mg/m^3 total dust, which is consistent with the NOAEL from the cement exposures, where the upper limit of the range is 3.3 mg/m^3 total dust.

For evaluation of the elongation of the nasal clearance time, the following has to be considered. First, the four time higher CaO level did not influence the mucociliary clearance in the acute study (Cain et al. 2004). Second, a modest increase in transition time is noted in the CaO group, taking into account the normal variation. Thus, in 20 healthy non-smoking volunteers, age from 18 to 41 years and 9/20 were women, the saccharin transport time was more than 30 min in seven subjects and the mean (±SD) was 13.6±6.1 min in the remaining 13 subjects. Additionally, there was a large intraindividual variation in the clearance when measured 4 to 8 weeks apart in 12 of the volunteers that may depend on the properties of the mucus (Lioté et al. 1989). Third, the temperature decreased from 42 to 28˚C, which raises the question about the role of the effect of the temperature. The nasal mucociliary transport depends on two main factors, the ciliary beating and the physiological properties of the mucus (Lioté et al. 1989; Braverman et al. 1998). An increase in temperature in *ex vivo* studied human nasal cilia showed that the beat frequency increased from about 20˚C to about 32˚C (Braverman et al. 1998; Green et al. 1995) and reached a plateau between 32 to 40˚C (Green et al. 1995) or the increase levelled off in that range (Jorissen and Bessems (1995). Above 40˚C the increase in beat frequency further levelled off (Jorissen and Bessems 1995) or began to decline (Green et al. 1995). The normal temperature in the nose is at the level of 30 to 35˚C (c.f. Green et al. 1995) or between 34 to 36˚C (c.f. Braverman et al. 1998). Thus, the direct effect of temperature on the ciliary beat frequency seems unlikely to explain the elongation of the clearance in the CaO group. However, an indirect and unmeasured effect, drying of the nasal mucosa, may well explain the observed effect. Thus, in 11 healthy non-smoking subjects (6 males and 5 females, age 17-38 years), the saccharin nasal transition time (mean ± SD) was 11.9 ± 5.3 min while breathing room air (22-24˚C and 40-43% RH). Breathing dry air (25-29˚C and less than 0.1% RH) through the nose for 30 min increased the transition time to 18.5 ± 8.6 min (Salah et al. 1988). Thus, it is tempting to speculate that the 42˚C hot air has caused an increased evaporation, which may have caused the elongation of the transition time.

Overall, the elongation of the nasal saccharin transition time is considered within the transition time range seen in normal subjects. Also, the effect was reversible and may well have been due to an undetermined confounder effect, drying of the nasal mucosa. The saccharin transition time is not considered useful for setting the OEL for CaO and that is in contrast to the other parameters investigated in this study.

Epidemiological studies – cement dust

Due to the similar alkalinity of CaO, $Ca(OH)_2$, and cement, the cement dust exposures are used to establish concentration-response relationships of CaO and $Ca(OH)_2$. Numerous epidemiological studies have shown that cement dust can affect the respiratory tract and cause lung function impairment as reviewed (Meo 2004; Bazas 1980). However, many of the studies are not applicable for risk assessment as they only contrast exposed individuals with non-exposed. Only studies with measured exposure levels and health effects are used for the construction of exposure-response/effect relationships. Used studies are limited to production and bagging of cement to minimize the influence of confounders; the below mentioned studies are listed in increasing order of exposure levels.

In a cross-sectional study in 16 Portland cement manufacturing plants in the US (Abrons et al. 1988), respiratory symptoms and lung function parameters were compared in 2736 cement workers and 755 controls. In the cement workers, the geometric mean concentration and range for respirable dust was 0.57 (0.01-46) mg/m^3 and the total dust concentration was 2.9 (0.01-79) mg/m^3. The mean respirable concentration in the clinker area and the finishing area was 0.48 and 0.85 mg/m^3, respectively. Only 14.4% of the samples contained a detectable content of quarts and in these samples the mean concentration was 0.079 mg/m^3. There was no exposure to asbestos or cristobalite. The median tenure of the cement workers was 10.9 years (range: 0-45). The prevalence (adjusted for age, sex and smoking) of chronic cough, chronic phlegme, chronic bronchitis with exacerbation, chronic bronchitis with obstruction, wheezing and asthma were not significantly different from the prevalence in the controls. However, reported dyspnoea was more common among the cement workers (5.4% versus 2.7%). Chronic phlegm was positively related with tenure and wheezing was positively related to dust concentration and tenure. There was no difference in the lung function parameters (FVC, FEV_1, peak flow (PF), forced expiratory flow after exhalation of 50% and 75% of the vital capacity (FEF_{50} and FEF_{75})), adjusted for age, sex, race, height and smoking. However, the dust caused an acute decrease in PF with increasing exposure level; the decrease was 1-2% per mg/m^3 of respirable dust.

Men born between 1918 and 1938, and who had worked 1 year or more in a Norwegian Portland cement factory were compared with a similar, but unexposed control group. Number of exposed was 119 and number of controls 50. The mean (±SD) of duration of cement exposure was 21.8±13.8 years. In 1999, the mean concentration (range) for total dust was 7.4 mg/m^3 (0.4-54) and for respirable dust 0.91 mg/m^3 (0.0-2.3). The crystalline quartz level was low (range: < 0.01-0.06 mg/m^3). Of the thirteen respiratory symptoms, which included different types of cough, phlegm, dyspnoea, wheezing, airway infection, and symptoms during work, none of the prevalences was significantly different between the exposed workers and the controls with and without adjustment for age and smoking. The lung function parameters (FVC, FEV_1 and FEV_1/FVC), adjusted for age, height and sex, were not decreased in the cement exposed workers. Spirometric airflow limitation (FEV_1/FVC less than 0.7 and FEV_1 less than 80% of predicted values) was observed in 17.6% of the exposed individuals and 20.0% of the controls. The prevalence of chronic obstructive pulmonary disease (COPD) in the two groups was 14.3% and 14.0%, respectively (Fell et al. 2003).

A Danish cohort was established in 1974, comprising 546 men who had worked one year or more in a Portland cement factory and a group of 544 blue collar workers of the same age and from the same geographic area. In 1974, the median total dust level (25%-75% percentiles) was 3.3 mg/m^3 (2.0-7.8) and the corresponding value for respirable dust 1.5 mg/m^3 (1.0-2.2) in the cement factory. In 1974, the percentage of phlegm was 26% versus 22%, breathlessness 19% versus 18%, and chronic bronchitis 11% versus 10% in the cement exposed workers versus the controls. The cohort was followed-up for hospitalization from 1977 to 1986 for "respiratory disease in general" and COPD. No significant excess of hospitalization was observed among the cement exposed workers. Heavy cigarette smoking was strongly related to hospitalization, whereas this was not the case for long-term cement exposed non-smoking workers (Vestbo and Rasmussen 1990).

In a cross-sectional study in Ethiopia, 53 non-smoking workers in a cement factory were compared with 211 non-smoking workers (controls) from the general population. Mean (±SD) levels were 3.2±3.5 mg/m^3 in the rotary kiln area and 43.1±35.3 mg/m^3 in the packing area; concentrations are probably for total dust. The prevalence in the exposed and in the controls was for chronic cough (30.2 versus 9.0%), for chronic bronchitis (26.4 versus 9.5%) and for bronchial asthma (32.1 versus 8.5%). The lung function parameters were compared among 16 workers in the packing area with a mean duration of exposure of 8.5±3.9 years, and 12 workers in the rotary kiln area with 14.5±11.7 years of exposure. The workers in the packing area had a significantly lower FEV_1(%) (89.8±10.9%) than the workers in the rotary kiln area (98.1±6.5%). No difference was seen in FVC, FEV_1, $FEF_{25-75\%}$, and PF. In the rotary kiln area, the percentages of the predicted values were 101.1±12, 97.8±14.0, 90.6±24.3, and 98.1±11.3, respectively (Mengesha and Bekele 1998). Due to the lack of an effect on the lung function in the kiln workers, this may suggest that the symptoms in the exposed workers may be driven by the high exposure level in the packing area and that dust effects in the kiln area is at or close to the NOAEL, based on the lung function parameters.

A cross-sectional study was conducted among workers exposed for three or more years in a Portland cement factory in Jordan (AbuDhaise et al. 1997). Of the 442 who attended the study, 94 were excluded; 11 had cardiac disease, 5 with either a positive family history of bronchial asthma or known to have had asthma, 20 failed to produce an acceptable spirogram, 24 had additional dust exposures from farming, pigeon breeding, carpentry, construction work or sculpture. Additionally, 29 ex-smokers and 5 pipe-smokers were excluded, leaving 348 for the analyses of symptoms and respiratory function. About half of these workers smoked and half used face mask. Exposures were divided into three groups. The low exposed group had a current exposure level of 0.5±2.1 mg/m^3 respirable dust (geometric mean ± SE). The middle exposed group had an exposure level of 1.6±2.6 mg/m^3; this group included clinker and calcining workers. The highly exposed group was exposed to 3.9±4.0 mg/m^3. This level was, for example, present in the packing and loading area, and in the cement milling area. Bronchitis, dyspnoea and asthma did not increase with tenure, whereas no clear picture appeared for wheeze and cough. Reporting of mild symptoms decreased with increasing exposure level, whereas asthma increased with increasing exposure level. The cement workers had a significantly higher prevalence of symptoms than 189 males engaged in food and diary production (considered dust-free environments); the prevalence for chronic cough

was 16.1 versus 2.0%, for chronic dyspnoea 16.7 versus 9.5% and for asthma 13.4 versus 2.1%. The mean lung function parameters (FVC, FEV_1, $FEF_{25-75\%}$ or FEV_1/FVC), adjusted for height and age, were within normal limits, irrespective of stratifying for tenure and exposure levels. Similarly, in the multiple regression analysis, neither the tenure nor the exposure level showed an independent effect on the lung function. The authors noted that previous exposures had been much higher, that it was difficult to distinguish asthma from cement induced irritation and from chronic bronchitis, and they considered it likely that the healthy worker effects could have influenced the results. It is noted that the study excluded 94 of 442 the attending workers.

Employees from four Portland cement manufacturing plants in Taiwan were divided into 412 male exposed workers (comprising maintenance, skilled/semiskilled craftsmen, machinery operators, crane operators, lorry drivers, and labourers preparing raw materials, grinding clinkers, and involved in blending, packing, and loading) and 179 male controls (comprising accountants, laboratory staff, clerks, timekeepers, storekeepers, canteen staff, and other office workers). Cement exposures were for at least five years. Respirable dust was 3.6 mg/m^3 (range: 1.3-8.1) in the cement dust exposed and 0.4 (0.03-1.6) in the controls. Cough, phlegm, wheezing, and dyspnoea were significantly more prevalent among the cement exposed, but this was not the case with chronic bronchitis. The symptom prevalence was adjusted for age, smoking status, duration of employment and plant. The cement exposed had significantly lower FVC, FEV_1, FEF_{50} and $FEF_{75,}$ but FEV_1/FVC (%) was similar in the two groups. Respiratory parameters were adjusted for age, height, smoking, duration of employment, and plant (Yang et al. 1996).

In a Malaysian Portland cement factory, the lung function and symptoms were studied in 62 workers, including 32 non-smokers, and the results were compared with those from 70 male non-smoking controls, comprising university students and university staff members. The mean PM10 (< total dust) level (±SD) was 5.7±2.3 mg/m^3 in the packing area and the mean level in the kiln area was 0.3 mg/m^3. After stratification for smoking and with and without stratification for age, FEV_1, FEV_1/FVC, and $FEF_{25-75\%}$ was lower in the exposed group compared to the controls. The forced mid-expiratory flow time was longer in the cement exposed workers. There was no significant exposure effect of FVC and FVC% (% of predicted). Cough and phlegm in the morning, and chest tightness was reported significantly more prevalent among cement exposed workers (Noor et al. 2000).

In a plant only packing imported Portland cement, 52 workers (27 in the packaging and 25 in the loading area) were compared with 24 workers in the maintenance group and a control group of 145 healthy Nigerian men. The plant had been operating for six years. The total dust level was 31 mg/m^3 in the cement depot. No type of personal protection was worn. The cement packers, the cement loaders and the maintenance workers had all a lower lung function (FEV_1 and FVC) than the controls. The combined group of packers and loaders had a higher prevalence of symptoms than the (presumably less exposed) maintenance workers: cough and phlegm (88 versus 63%), skin irritation (87 versus 42%), chest tightness (81 versus 38%), conjunctivitis (71 versus 42%), stomach ache (56 versus 25%), skin burns (54 versus 0%), which were mainly in the groins and armpits, dyspnoea (54 versus 0%), and head ache (54 versus 0%). Exposures for 6-36 months caused restrictive lung disease in 57% and in 62% if exposed from 37 to 72

months; restrictive disease was defined as $FEV_1/FVC > 60\%$ and $FVC < 70\%$. The study suggests that the healthy worker effect was present. Less that 8% of the workers were smokers (Oleru 1984).

Overall, the studies suggest exposure-response relationships and that no consistent effect of cement factory dust appeared in the range from 0.57 to 1.5 mg/m^3 respirable dust and from 3.3 mg/m^3 and lower levels of total dust. Decrease in the lung function occurred somewhere in the range from 1.6 to 3.9 mg/m^3 respirable dust and from > 5.7 mg/m^3 total dust. However, it is a limitation for the extrapolation of this range to effects of CaO and $Ca(OH)_2$ that the reported dust concentrations often were mixed levels from production of raw materials (e.g. clay, limestone and quartz) and cement dust. Only one study is available, which allows the comparison of lung function in relation to the specific production processes and their dust levels (Mwaiselage et al. 2004). For example, the levels from the kiln and packing areas and from the controls have been shown in Table 4. Smoking was not common and exposure to crystalline silica was low (Mwaiselage et al. 2004). Looking for consistency within this study, it is surprising that the change in lung function is only modest in the packing area when compared to the kiln and milling area where the exposures were about seven times lower. From the tenure, it is less likely that the small effect can be explained by the healthy worker effect. However, about 38% of the production workers used (P1) face masks regularly. Suggesting that face masks is used at the highest (most irritating) exposure levels, this may have contributed to the relatively low effect in the packing workers. From the effect in the kiln and cement milling workers, it appears that the NOAEL may be about 3 mg/m^3 total dust; it is however noted that the groups are small and an abrupt change in effect from 2.9 to 3.2 mg/m^3 is not biologically plausible taking the modest effect even at much higher concentrations into account. All together, the NOAEL of 3 mg/m^3 total dust from this study is bracketed by the NOAEL of the total dust range, which is up to 3.3 mg/m^3 from the other epidemiological studies.

Overall, an exposure level of 1 mg/m^3 respirable dust is expected to prevent long-term lung effects of cement dust and thus also from CaO and $Ca(OH)_2$. Thus, a change in the lung function due to long-term exposures is a critical effect.

Genotoxicity

Calcium hydroxide has been studied in the Comet assay, which showed that it did not cause DNA damage in the test (Table 5).

In Syrian golden hamsters the cheek pouches were painted daily for 5 days in 5 animals with 50 µl of a 4% lime solution. No increase was observed in micronucleated cells in the cheek pouches when compared to a similar number of controls (Nair et al. 1992).

Carcinogenicity

In Asia, chewing areca nut with $Ca(OH)_2$ folded into betel leaf causes a significant increase in the risk of oral cancer (Kashyap and Kashyap 2002; Bagchi bet al. 2002). However, as neutral extracts of chewing tobaccos (composed of tobacco, areca nut,

lime, and catechu) caused development of oxidative stress and DNA damage (Bagchi et al 2002), no extrapolation can be performed to effects of $Ca(OH)_2$ itself.

The genotoxic studies were negative and animal studies showed no consistent carcinogenic effect of $Ca(OH)_2$. However, the chronic exposures caused local hyperplasia, metaplasia and inflammation. On this basis, there is a potential possibility that CaO, $Ca(OH)_2$ and cement, due to their alkalinity, may cause cancer if chronic irritation is present. Irritant induced effects possess no-observed-effect level; this is well established, for example, from saccharin exposures in rats where bladder tumours developed due to cytotoxicity of the precipitate, erosion and sustained cell proliferation (Dybing 2002).

Due to lack of data on CaO and $Ca(OH)_2$, exposures in the production of cement were used as proxy for CaO and $Ca(OH)_2$ exposures. To limit the influence of confounders, studies dealing with cement production were selected for risk assessment of cancer in the airways and oesophagus; cancer at other sites were neglected. The retrieved cohort studies are listed in (Table 6). Only one study (McDowall 1984) mentioned carcinogenic effect in the oesophagus; the standardized mortality ratio was 1.16 and not significantly different from the reference population. Thus, table 6 is limited to cancer risk at all sites, in the lungs and in the larynx. To facilitate investigation of development of trend over time, studies are listed after year of publication.

In a recent Lithuanian study (Smailyte et al. 2004), cancer at all sites and lung cancer were significantly increased in male cement workers, but there was no significant increase in females. Smoking prevalence in the general male population was 43% in 1994 and 51% in 2000 and blue collar workers smoked more than white collar workers. The authors mention that smoking may have influenced the risks. In a Swedish study (Jakobsson et al. 1993), no carcinogenic effect was apparent from tumours at all sites, and from the local sites, the lungs and the larynx. The study mentions as a strength that it uses the local county rate as control, which is presumably more appropriate than using the rate from the entire population. In a Danish study (Vestbo et al. 1991), no carcinogenic effect was apparent from tumours at all sites and from the lungs; this applied to the standard incidence rate (SIR) based on the national incidence. A similar group of local blue collar workers from the same region, but without exposure to cement showed similar SIR values as observed for the cement exposed workers. The relative risk among cement workers obtained from a comparison with white collar workers from the same area showed no increase in the risk; the comparison took into account age and smoking. Also the study showed that exposures to asbestos increased the overall risk of cancer and the risk of lung cancer, i.e. the study was able to identify the well known risk factors: age, smoking and exposure to asbestos. In a study from the UK (McDowal 1984), no increase was found in the overall cancer risk and the risk of lung and oesophagal cancer.

The elder studies may have had high exposures, which were above 4 mg/m^3 total dust. In the recent study (Smailyte et al. 2004), the total dust concentrations ranged from 5 to 19 mg/m^3. The overall cancer risk and the lung cancer risk were increased in males, but not in females. This study did not adjust for smoking; about 50% of the cement workers may be smokers. In the Danish study (Vestbo et al. 1991), smoking was a risk factor. Overall, there is no consistent indication that cement dust from 4 mg/m^3 and lower concentrations of total dust are associated with cancer in the airways and oesophagus

and, thus, there is no indication of a potential carcinogenic effect of CaO and $Ca(OH)_2$ at that and lower levels due to their similar or lower pH.

RECOMMENDATION

The effects of CaO and $Ca(OH)_2$ are considered to be limited to the external surfaces of the body and no systemic effect is foreseen. At low-level exposures, sensory irritation and a decrease of the lung function parameters at long-term exposures are considered to be the critical effects.
From a well conducted acute study (Cain et al., 2004), sensory irritation is expected to be prevented by 1mg/m^3 respirable dust. A STEL is also set at 4 mg/m^3 respirable dust to prevent sensory irritation as the exposure in the controlled chamber study (Cain et al. 2004) is considered to be to respirable dust and no relation to inhalable dust could be derived.
No relevant respiratory effect was found as an exposure level at 1mg/m^3 (range: 0.4-5.8mg/m^3) of total dust among kiln workers producing (Torén et al. 1996). That
1 mg/m^3 is protective against long-term exposure to CaO and $Ca(OH)_2$ is supportive from cement dust exposures that has a similar alkalinity.

High exposure levels may cause skin and eye burns. Skin absorption is not considered a relevant parameter and, thus, no skin notation is needed.

No measurement difficulties at the levels established are foreseen (see Appendix).

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Table 1. Exposures to CaO, $Ca(OH)_2$ and cement.

Production	Compound	Place and concentration (mg/m^3)	Reference
CaO production at seven beet sugar processing plants in the US	CaO	Lime kiln operator: 12.9±15.9 [a)] Cooler operator: 4.3±3.6 [a)]	Mann 1990
Bleached-kraft pulp mill in British Columbia	CaO	CaO was a processing chemical that was used for recycling of inorganic pulping chemicals; kiln and recaust area: 0.3 (0-1.1) [b)]	Astrakianakis et al. 1998
Pulp-mill in Sweden	CaO	Lime kiln operators. Before rebuilding: 1.2 (0.4-5.8) [b)] After rebuilding: 0.2 (0.1-0.6) [b)]	Torén et al. 1996
Cement factories in the US	Portland cement	Total dust: 2.90 (0.01-79) [c)] Respirable dust: 0.57 (0.01-46) [c)]	Abrons et al. 1988
Cement factory in Norway	Portland cement	Total dust: 7.4 (0.4-54) [d)] Respirable dust: 0.91 (0.0-2.3) [d)]	Fell et al. 2003
Four cement factories in Taiwan	Portland cement	Control group: 0.41 (0.03-1.64) [e)] Exposed workers: 3.6 (1.3-8.1) [e)]	Yang et al. 1996
Cement factory in Malaysia	Portland cement	Rotar kiln: 0.27 [f)] Cement mill: 2.3 [f)] Packing: 5.7±2.3 [f)]	Noor et al. 2000
Cement factory in Saudi Arabia	Portland cement	Rotary kiln: 7.1 (2.1-22.2) [g)] Cement mill: 10.6 (7.1-16.7) [g)] Packing: 14.8 (4.8-25.8) [g)]	Ali et al. 1998
Cement factory in Tanzania	Portland cement	Rotary kiln: 4.1 (1.0-9.9) [h)] Cement mill: 4.2 (1.3-8.3) [h)] Packing: 39.0 (3.2-229) [h)] Maintenance: 2.1 (0.1-10.2) [h)]	Mwaiselage et al. 2005

a) Mean and SD of total dust. Airborne dust contained < 1% silicate. Respiratory protection was seldom worn.
b) Geometric mean and range of total dust.
c) Mean and (range).
d) Mean and (range) in 1999.
e) The control group consisted of accountants, laboratory staff, clerks, timekeepers, storekeepers, canteen staff and office workers. Exposed workers were maintenance, skilled/semiskilled craftsmen, machinery operators, crane operators, lorry drivers, and labourers preparing raw materials, grinding clinkers, and involved in blending, packing and loading. Exposures are geometric mean and range of respirable dust.
f) PM10 (< total dust): mean and SD where indicated.
g) Respirable dust: geometric mean and range.
h) Arithmetic mean and range of total dust. The average ratio of respirable and total dust was 0.40. Workers did not use personal (P1) respiratory protection regularly.

Table 2. Examples of skin effects of CaO, $Ca(OH)_2$ and cement.

Individual(s)	Process	Exposure	Outcome	Reference
Female (42y)	Fertilizing acid soil with lime dust	Dust entered her rubber boots	Burning erythema and brown-black necrotic crust along the upper edge of the boot. Healing with scare formation	Farkas 1981.
Two boys (11 and 16y)	Footbal field marked with CaO	Fallen on the field	Erosive lesions and inflammation. The skin healed rapidly.	Gelmetti and Cecca 1992
Male (47y)	Worked with wet cement	Stood in wet cement in 4 hrs	Full thickness skin burn on lower extremities. Skin grafting was performed and discharge was after 10 days of hospitalization. The skin grafts was well healing 6 months later.	Sherman and Larkin 2005
Male (25y)	Worked with wet cement	Kneeling in wet cement for 3 hrs with a sweat suit on	Ulceronecrotic dermatitis of both shins with superficial to full thickness skin burns. The wound healed with atrophic hyperpigmented scar.	Rados et al. 2005
Two males (43 and 44 y)	Operating a Portland cement kiln	Explosive discharge of hot powder from the kiln	Case 1: full and partial-thickness burns to about 41% of the body surface. Several skin grafting were performed. Case 2: Full and partial thickness burns of about 8% of the body surface.	Morley et al. 1996
Male (51y)	Making a path with flagstone made from cement, which was moulded 12 days before exposure	Carrying the stone resting against his thighs and abdomen.	He developed full-thickness skin burns on upper thighs, lower abdomen, and external genitalia. He was discharged eight days later, but was unfit for work for another six weeks. The pH of the stone was 12.6.	Tindholdt et al. 2005
Two males (both 45y)	Unloading concrete building-stones for 1 hr from a lorry on a rainy day	The stones were carried in contact with the wet shirt covering the stomach	Ulcerative dermatitis, which healed within two weeks, leaving tender scares. The pH=11.2 by elution of the stones with water.	Stoermer and Wolz 1983

Table 3. Examples of eye effects of cement, CaO, $Ca(OH)_2$ and their products.

Individual(s)	Process	Exposure	Outcome	Reference
Male (20y)	?	Cement splash	Corneal opacification, denuded stroma and limbal ischemia. Cornea regained clarity and visual acuity partly normalized after vigorous treatment.	Lim et al. 2006
Male (33y)	Off-loading cement from a tank lorry	Splash of cement into the face	Both corneae were completely opaque. He developed bilateral symblepharon. At discharge he was able to count fingers with each eye	Bodunde and Onadipe 2005
Male (?y)	Liquid cement mixture	Accident	Severe eye burn. During the succeeding 2 ½ -year period, the corneal epithelium had difficulty in healing. Additionally, cornea was infected, and cataract, recurrent erosion and glaucoma developed: Healing occurred after phototherapeutic keratectomy	Kottek et al. 1996.
Males (N=17) and females (N=4); age: 3.8-27 y	Squeezing small pouches with $Ca(OH)_2$	Splash into eyes	Ocular burns were grade 4 in 92% of the eyes. Prognoses were poor, probably due to delayed irrigation.	Agarwal et al. 2006
Males (N=18); Age: 29-66 y	Production of CaO and $Ca(OH)_2$; mainly kiln operators	Particles (~0.5 mm) of CaO and $Ca(OH)_2$ adhere to the cornea	White rings (1 mm or less) of the cornes	Miller 1966
Male (?y)	"Non-explosive" beton cracking product[a)]	Splash of hot mixture	Thermal damage (white opacities) in both corneas. Vigorous treatment (including keratoplasty) resulted in normalization of the cornea.	Newsom et al. 1996

a) The mixture consisted of calcium oxide, silicon oxide, aluminium oxide and magnesium oxide, which when hydrated forms calcium hydroxide in an exothermal reaction. It is mixed with water and poured into drill holes.

Table 4. Dust levels, age of exposed workers, tenure, smoking and lung function parameters in a Portland cement factory in Tanzania (Mwaiselage et al. 2004).

	Kiln [a)] N=26	Cement mill [a)] N=11	Packing [a)] N=30	Maintenance [a)] N=83	Administration [a)] N=19
Total dust [b)]	2.9 (1.0-9.9)	3.2 (1.3-8.3)	21.3 (3.2-229.2)	1.2 (0.1-10.2)	0.3 (0.01-2.4)
Age±SD (y)	30.6±8.8	37.8±5.9	38.0±8.9	39.8±7.8	43.1±9.2
Tenure±SD (y)	7.0±7.1	12.5±6.4	12.9±7.3	14.9±8.1	15.5±8.6
Pack-years±SD	0.9±2.7	3.0±7.0	1.9±5.9	2.4±5.9	3.6±7.5
FVC±SD[c)] (L)	3.6±0.4	3.3±0.4	3.2±0.5	3.5±0.4	3.4±0.6
FEV_1±SD (L/s)	2.9±0.4	2.5±0.4	2.3±0.4	3.0±0.4	2.9±0.6
PEF±SD (L/s)	7.3±0.6	7.2±0.5	6.9±0.6	7.5±0.6	7.6±0.5
FEV_1/FVC ±SD	0.81±0.06	0.75±0.05	0.72±0.10	0.87±0.07	0.86±0.12
Airflow limitation N (%) [d)]	1 (3.8)	2 (18.2)	14 (46.7)	5 (6.0)	1 (5.3)

a) Occupationally exposed group and number of exposed.
b) Geometric mean and range (mg/m^3) of current exposure.
c) Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and peak expiratory flow (PEF).
d) Airflow limitation: $FEV_1/FVC < 0.70$

Table 5. Genotoxic effect of $Ca(OH)_2$ and different types of cement in the comet assay.

Cell line	Substance	Concentration (µg/ml)	DNA breaking [a)]	Reference
Chinese hamster ovary (CHO) cells	$Ca(OH)_2$	100	(-)	Ribeiro et al. 2005b
L5178Y mouse lymphoma cells	$Ca(OH)_2$	20-80	(-)	Ribeiro et al. 2004
Human fibroblasts	$Ca(OH)_2$	20-80	(-)	Ribeiro et al. 2004
Human peripheral lymphocytes	Portland cement White Portland cement	1-1000 1-1000	(-) (-)	Braz et al. 2006
Chinese hamster ovary (CHO) cells	Portland cement White Portland cement	1-1000 1-1000	(-) (-)	Ribeiro et al. 2006
L5178Y mouse lymphoma cells	Portland cement White Portland cement	1-1000 1-1000	(-) (-)	Ribeiro et al. 2005a)

a) DNA damage is detected as DNA breaking. A positive effect is indicated by (+) and no damage by (-)

Table 6. Cohort studies in cement producing plants.

Study [a]	Design	Exposure level (mg/m^3) [b]	Number and gender (M/F)	Risk estimates [c]	All cancer	Lung cancer	Larynx cancer	Confounder control
[1]	Exposure for at least 1 y in 1956-2000. Follow up 1978-2000	Calc. (t.d.): 7-19 Mill. (t.d.): 5-11 Pack. (t.d.): 12-19	1727M 771 F	SMR SIR SMR SIR Reference: Lithuanian population	1.3 (1.0-1.5) 1.2 (1.0-1.4) 0.7 (0.4-1.1) 0.8 (0.6-1.1)	1.4 (1.0-1.9) 1.5 (1.1-2.1) 1.4 (0.3-5.5) 1.7 (0.6-5.4)	- 1.0 (0.4-2.4) - 0 obs.	No control No control No control No control
[2]	Exposure for at least 1 y Mortality: 1952-1986. Morbidity: 1958-1986. Latency from employment for at least 15 y	Calc. (t.d.): 4-20 [x] Mill. (t.d.): 4-12 [x] Pack. (t.d.): 10-17 [x] x) from 20-530 at cleaning	2391M	SMR Reference: National rate SIR Reference: county rate	0.9 (0.7-1.1) 1.1 (0.9-1.3)	0.6 (0.3-1.1) Respira-tory: 0.9 (0.6-1.4) 1.3 (0.7-2.2)	- 1.0 (0.02-5.5)	No control No control
[3]	Exposure for at least 1 y before 1974. Follow up: 1974-1985	Respirable dust > 5 among 9% of the workers	Exposed: 546M Randomly selected controls from the popula-tion: 858M	SIR Reference: National population RR com-paired to white collar workers	1.0 (0.8-1.4)[d] 1.2 (0.9-1.5) [e] -	1.5 (0.9-2.6)[d] 1.6 (1.1-2.4) [e] 1.0 (0.4-2.6) [f]	"No in-crease" [d] - -	No control No control Included age and smoking
[4]	Cement workers in 1939 and alive in 1948. Follow up: 1948-1981.	Not reported	607M	SMR Reference: England and Wales	1.03 (NS) [g]	0.85 (NS)	-	No control

a) [1] : Smailyte et al. (2004) [2]: Jakobsson et al. 1993 [3]: Vestbo et al. 1991 [4]: McDowall (1984).
b) Calcining/kiln operating (Calc.), milling (Mill.), packing/transport (Pack.), total dust (t.d.), respirable dust (r.d.).
c) Standardised mortality ratio (SMR), standardised incidence ration (SIR), relative risk (RR), and in parenthesis (95%CI).
d) Exposure to cement dust (cement workers) for at least 21 years. Respiratory cancer is given as lung cancer.
e) Blue collar workers (controls) from the same region, but with no exposure to cement. Respiratory cancer is given as lung cancer.
f) Cement workers were compared with white collar workers from the same region. Respiratory cancer is given as lung cancer.
g) Not significant (NS).

Table 7. ALPHABETIC LIST OF AUTHORS, METHODS USED FOR DETERMINATION OF THE AIRBORNE DUST, AND CLASSIFICATION OF THE MEASURED TYPE OF DUST.

Author(s)	Method(s) used for the determination of dust	Classification of the type of dust [a)]
Abrons et al. (1988)	Reported to be total dust and respirable dust	Total dust and respirable dust
AbuDhaise et al. (1997)	Respirable dust was collected by a personal sampler ($AFCL_2$3 (Casella-London Ltd.), flow rate of 1L/min)	Respirable dust
Ali et al. (1998)	Reported to be respirable dust	Respirable dust
Astrakianalis et al. (1998)	Collected onto cellulose ester membrane filters. From a picture in the article, the dust collection was with a 37-mm cassette	Total dust
Cain et al. (2004; 2008)	A Sierra multilevel sampling impactor with nine stages served to collect mass for assessment of the size distribution (sampling rate: 7L/min). The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) was 6.53 μm and 2.6, respectively. MMAD x GSD^2=13.29 μm. Gravimetric samples were collcted on 47-mm Pallflex filters at a sampling rate of 2L/min.	Respirable dust
Fell et al. (2003)	Reported to be total dust and respirable dust.	Total dust and respirable dust
Jakobsson et al. (1993)	Reported as total dust	Total dust
Lahaye et al. (1987)	The size of the dust vary from 1-5 μm with a mean of 3 μm	Respirable dust
Mann (1990)	NIOSH P+CAM 173	Total dust
Mengesha and Bekele (1998)	Dust was collected by a 37-mm cassette.	Total dust
Mwaiselage et al. (2005)	The total dust samples were collected by 37-mm cassettes with an airflow rate of 2 L/min	Total dust
Noor et al. (2000)	Area sampling was performed by a two-stage high volume (400 L/min) cascade impactor, which fractionated particles into fine (< 10 μm, PM_{10}) and coarse dust with a larger size.	The PM_{10} fraction is close to the thoracic fraction. Thus, the total dust fraction > PM10. The sum of the fractions is not interpreted.
Oleru (1984)	Dust was collected on a 37 mm filter at a flow rate of 2.5 L/min.	Total dust
Smailyte et al. (2004)	Reported as annual mean of total dust	Total dust
Torén et al. (1996)	Total dust collected by 37-mm cellulose acetate filters at a flow rate of 2 L/min	Total dust
Vestbo et al. (1991)	Reported as respirable dust	Respirable dust
Vestbo and Rasmussen (1990)	Reported to be total dust and respirable dust	Total dust and respirable dust
Yang et al. (1996)	Portable SKC 224 personal air samplers with PVC membrane filters mounted on a cyclone preselector.	Respirable dust

a) The inhalable, thoracic and respirable fractions are the fractions of airborne particles, which enter the head (passes the nares or lips), the lungs (penetrating beyond the larynx) and the alveolar region (the unciliated airways), respectively. The 50% collection efficiency is at the particle aerodynamic diameter (Dae) of ~100, 10 and 4 μm for the inhalable, thoracic and respirable fraction, respectively (e.g. Soderholm 1989; CEN 1993). The thoracic fraction is close to the PM10 fraction (Soderholm 1989). In general, the respirable fraction will not contain particles with a Dae of more than 15 μm and the thoracic fraction of more that 40 μm (CEN 1993). The commonly used "total" dust sampler, the 37-mm closed-face cassette, has lower collection efficiency than the inhalable convention for Dae > 15-20 μm, but the collection efficiency is approximately the same for particles below 10 μm. The thoracic convention has a lower collection efficiency than the total dust sampler for Dae > 10 μm (Soderholm 1993).

APPENDIX: ANALYTICAL INFORMATION ON LIMIT OF DETECTION FOR CALCIUM OXIDE AND CALCIUM HYDROXIDE

The SCOEL proposed in its SCOEL/SUM/137 report an OEL of 1 mg/m^3 of respirable dust and a STEL of 4 mg/m^3 for calcium oxide and calcium hydroxide.

The appendix table below summarises the methods examined and the estimated limit of detection (LOD) of each method.

The analytical techniques used to determine these substances are atomic absorption and ion chromatography (IC).

Limitations and Interferences of the methods:

NIOSH method 7020 is applicable to calcium and compounds as Ca. The use of 1000 µg/mL Cs controls ionization in the flame caused by metals such as Na, K, Li, Mg may interfere.

OSHA method ID-121 is applicable to Metal and metalloid particulates in workplace atmospheres.

DFG and BIA methods are applicable to calcium hydroxide.

ISO 15202 method is applicable to the determination of metals and metalloids in airborne particulate matter.

Conclusion

The revised European Standard EN 482:2005 stipulates the requirements that measurements procedures should fulfil in order to perform a reliable and valid assessment of an exposure to a chemical agent.
According to this European Standard the measuring range of the method should cover at least the concentrations from 0.1 to 2 times the limit value (TWA) and from 0,5 to 2 times for the STEL value, and, in this range, overall uncertainty should be kept under certain values.

On workplaces with calcium oxide and calcium hydroxide no problems exist to measure the long and the short-term exposures with OELs as TWA (8h) = 1 mg/m^3 and STEL (15 min)= 4 mg/m^3 respectively.

APPENDIX TABLE: OVERVIEW OF THE METHODS ON CALCIUM OXIDE AND CALCIUM HYDROXIDE

METHOD	YEAR OF PUBLICATION	ANALYTICAL DATA	LOD	REMARKS	COMPLIANCE WITH OEL
NIOSH 7020 Atomic absorption	1994	Working range: 1-20 mg/m^3 Recommended air volume:85 L Sampling time: Flow rate: 1-3 l/min	0,001 mg per sample	validated	**YES**
OSHA ID-121 Atomic absorption	2002	Working range: Recommended air volume: 480 l Sampling time: 4h Flow rate: 2 l/min	0,0002 mg/m^3	validated	**YES**
BIA 7695 IC analysis with conductivity detection	1998	Working range: 0,4-8 mg/m^3 Recommended air volume: 420 l Flow rate: 3.5 l/min	0,044 mg/m^3	validated	**YES**
DFG Ion Chromatography	2001	Working range: 0,09-9,51 mg/m^3 Recommended air volume: 420 l Sampling time: 2h Flow rate: 3,5 l/min	0,044 mg/m^3	validated	**YES**
ISO 15202 Inductive coupled plasma emission spectrometry	2003	Recommended air volume: 420 l Sampling time: 15 min-8h Flow rate: sampler dependent	No data	N.A.	**N.A.**