Health Council of the Netherlands

Respirable crystalline silica

executive summary

Crystalline silica is a mineral that is abundant in most rocks, sands and soils. The most common forms of crystalline silica are quartz, cristobalite and tridymite. When crystalline silica is cut or crushed, dust containing respirable crystalline silica (RCS) particles, is released into the air. These RCS particles can be inhaled deep into the lungs and cause diseases such as silicosis and lung cancer.

The Dutch Expert Committee on Occupational Safety (DECOS) and the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG) evaluated the health hazards and calculated cancer risk levels for occupational exposure to RCS. They carried out their evaluation at the request of the Dutch ministery of Social Affairs and Employment, and the work environment authorities of Denmark, Finland, Norway and Sweden.

DECOS and NEG both give scientifically based advice in order to protect workers against the potentially harmful effects of substances that they may encounter in the course of their work. The committees assess the toxic properties and health effects of these substances and make recommendations for health-based occupational exposure limits (OELs).

More information on the tasks of the committees can be found on the following websites www.gezondheidsraad.nl and www.nordicexpertgroup.org.

Occupational exposure to RCS in many industries

Because of the extensive natural occurrence and the wide use of crystalline silica, workers in a large variety of industries and occupations are potentially exposed to RCS. In general, any process that involves movement of earth or processing of crystalline silica-containing materials or products may potentially expose workers to RCS. Examples are mining, farming, construction, foundry processes and the production of glass, artificial stone, ceramics or cement.

While occupational exposure levels to RCS have generally decreased over the last sixty years, high exposures may still occur in some work situations. Over the last ten to twenty years the use of artificial stone products has increased, for example in kitchen and bathroom countertops. These artificial stone products can contain high percentages (>93%) of finely crushed crystalline silica, which makes them an emerging source of

exposure for workers who work in manufacturing or who work with artificial stone products.

RCS exposure can cause silicosis and lung cancer

Exposure to RCS has been associated with several diseases. Diseases considered by the committees in the current evaluation include chronic obstructive pulmonary diseases (COPD), renal diseases, cardiovascular diseases, autoimmune diseases and other cancers than lung cancer. The underlying mechanisms by which exposure to RCS may cause these diseases are not fully understood yet and need further research. However, based on epidemiological studies and current knowledge on underlying biological mechanisms, the committees conclude that there is very strong evidence for a causal relationship between exposure to RCS and silicosis and lung cancer.

Silicosis is an irreversible and incurable lung disease and one of the oldest known occupational diseases in the world. It is caused by the inhalation of RCS, which can result in inflammation and scarring (fibrosis) of the lungs. Progression of silicosis can result in death due to respiratory failure. Silicosis may be complicated by severe mycobacterial infections resulting in silico-tuberculosis.

In recent years, numerous cases of silicosis have been reported among workers involved in artificial stone manufacturing or fabrication of products using artificial stone. Artificial stone-associated silicosis has a relatively high occurrence among workers with short exposure periods and with a more rapid progression compared to the more common chronic form of silicosis.

Exposure to RCS is also a known risk factor for lung cancer. Several epidemiological studies including meta- and pooled analyses reported an increased risk of lung cancer in workers exposed to RCS. RCS causes damage to the lung cells, resulting in inflammation and a tumour-promoting environment. In addition, the relationship between silicosis and lung cancer has been investigated as well, because results of some earlier studies did not show a consistent association with lung cancer after excluding subjects with silicosis. Recent studies, however, have shown excess lung cancer risks among workers exposed to RCS even in the absence of silicosis. Although, having silicosis does increase the risk of developing lung cancer.

Lung cancer is used as critical health effect

For the quantitative risk analysis, the committees first decided on a critical adverse health effect. This is the adverse health effect that occurs first at increasing exposure to RCS. As both lung cancer and silicosis can occur at low exposure levels to RCS, both diseases could be used as critical health effect. However, the committees preferred using lung cancer as the critical health effect. They considered the diagnostics and registration of

lung cancer compared to silicosis to be better and found the available data for the exposure-response relationship between RCS and lung cancer to be of higher quality. They assumed that setting OELs based on lung cancer will also protect against other health effects associated with occupational exposure to RCS.

A non-threshold (risk-based) approach is used

The approach taken in the case of a carcinogenic substance such as RCS depends on the mode of action by which the substance causes cancer: the genotoxic mechanism. Based on the available research, the committees conclude that RCS can cause lung cancer mainly by means of an indirect genotoxic mechanism, but possibly also by a direct genotoxic mechanism. RCS can cause damage to lung cells because it causes an inflammatory response, resulting in oxidative stress. This condition can occur when there are too many unstable molecules, called free radicals or oxidants (for example reactive oxygen species (ROS)), in the body and not enough antioxidants to eliminate them. Oxidative stress can lead to cell and tissue damage, ultimately causing DNA damage in lung cells.

However, free radicals such as ROS can also be formed directly at the surface of RCS particles. These free radicals can enter the cell nucleus and directly cause DNA damage. This means that the possibility of a direct genotoxic mechanism of RCS cannot be excluded.

Because a direct genotoxic mechanism is possible, the committees decided to use a non-threshold (risk-based) approach for RCS. With this approach it is assumed that every level of exposure, however low, involves a certain risk of developing cancer. In that case, it is not possible to set an exposure level using a threshold-based approach. The non-threshold-based approach focuses on limiting the cancer risk involved by deriving health-based calculated occupational cancer risk values (HBC-OCRVs).

Calculation of cancer risk levels

The committees used a pooled analysis by Ge et al. (2020) as the key study for the calculation of cancer risk levels. They selected this study because it contained data of almost 40,000 predominantly European participants. In addition, this study obtained information and was able to control for potential confounding by smoking and co-exposures to other lung carcinogens in the workplace. Furthermore, this key study contained more recent exposure measurement data and was more representative of the Dutch and Nordic work populations compared to other available studies.

For the non-threshold (risk-based) approach the Dutch ministry of Social Affairs and Employment has established two cancer risk levels in advance: a target risk level (low level) and a prohibition risk level (high level). The target risk level is the level below which no extra protective

measures have to be taken. The prohibition risk level should not be exceeded. In terms of cancer due to occupational exposure over a 40-year period, these risk levels correspond to four additional cancer deaths which are added to the number of deaths from all causes per 100,000 and per 1,000 workers, respectively.

Advice to the Dutch state secretary and regulatory Nordic authorities

The committees estimate that the HBC-OCRVs for RCS in the breathing zone are as follows:

- 4 additional deaths of lung cancer per 100,000 workers ($4x10^{-5}$), for 40 years of occupational exposure, equal to 0.00038 mg/m^3 (target risk level or low risk level).
- 4 additional deaths of lung cancer per 1,000 workers ($4x10^{-3}$), for 40 years of occupational exposure, equal to 0.0363 mg/m^3 (prohibition risk level or high-risk level).

The recommended exposure levels are 8-hour time-weighted average (TWA) concentrations. This reflects an average working day of 8 hours.

Epidemiological studies showed that quartz, cristobalite and tridymite have generally similar toxicity and carcinogenic potential. Therefore, the committees recommend the same HBC-OCRVs for all three RCS polymorphs.

The committees note that the recommended cancer risk levels are considerably lower than the current legal OELs in the Netherlands, Denmark, Finland, Norway and Sweden. However, the recommended cancer risk levels are in line with recent recommendations from other international work environment organisations such as the Danish *National Research Centre for the Working Environment (NFA)* and the US *Occupational Safety and Health Administration (OSHA)*.

This publication can be downloaded from www.healthcouncil.nl.

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